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Nickel-Catalyzed Enantioselective C(sp)–P Coupling of Secondary Phosphine Oxides with Bromoalkynes

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Abstract

The p-stereogenic alkynylphosphines couple a conformationally well-defined phosphorus center with a linear carbon–carbon triple bond, ready for further functionalization. The synthesis of p-stereogenic alkynylphosphines requires challenging methodology because bromoalkynes can react directly with secondary phosphines, while stereoselective synthesis requires selective formation of a C(sp)–P bond within a chiral metal complex. As we have developed previously, the nickel-catalyzed procedure utilizes bench stable secondary phosphine oxides, in situ reduction using phenylsilane, Ni(COD)2/(S,S)-Et-Duphos catalyst, sodium acetate, mesitylene, and reaction temperature of 0 °C for 72 h. This protocol enables formation of p-stereogenic alkynylphosphines from the tert-butyl phenyl phosphorus component in 72% isolated yield and 86% ee versus 20% product without nickel catalyst. The first group of substituent analysis identifies the role of steric hindrance at phosphorus where the phenyl/ethyl substrate yields 81% yield and 29% ee versus phenyl/tert-butyl substrate, providing slightly reduced yield and enhanced enantiomeric excess. The series of secondary phosphine oxide substrates comprises para-, meta- and ortho-substituted aryl tert-butyl derivatives, giving rise to products such as 3fa–3ka in 63–78% yield and 76–90% ee, 3la in 64% yield and 75% ee, 3ma in 70% yield and 82% ee, and 3na in 68% yield and 90% ee. Bromoalkyne substrates range from variously substituted aryl, heteroaryl, naphthyl, alkyl, bis-alkynyl, to amino acid derived electrophiles. Examples are the product 3na-O in 64% yield and 90% ee, 3nk in 33% yield, 97% ee, and 5:1 diastereomeric ratio, and 3no in 32% yield and 9:1 diastereomeric ratio. Further derivatizations include hydration of 3na-O affording a β-keto phosphine derivative in 73% yield and 84% ee, radical cyclization of 3ba resulting in benzo[b]phosphole oxide in 58% yield, 86% ee, and 3:1 diastereomeric ratio, and formation of phosphhepine from 3wp providing compound with 99% ee upon recrystallization. Reaction works when bond formation by means of the nickel catalyst takes place in the predominant mode, the phosphorus groups show enough difference in their stereochemistry, and the alkyne group remains intact for further applications in carbonyl, heterocyclic, and chiroptical phosphorus chemistry.

Keywords: P-stereogenic phosphorus; alkynylphosphines; nickel catalysis; asymmetric cross-coupling; C(sp)–P bond formation; phosphole oxide; phosphepine; circularly polarized luminescence.

1. Introduction

Stereocontrol of phosphorus-based species is a persistent challenge of modern organophosphorus chemistry because of phosphorus' ability to act both as donor atom, as redox active center, as stereogenic center, and as electronically tunable moiety in functional molecules. Phosphines represent a broad platform for ligands in transition-metal catalysis, phosphine oxides and phosphonates are robust polar units in organic and biochemistry, and phosphorus-containing heteroarenes alter the frontier orbital density distribution in conjugated molecules. In this way, the element links catalysis, small molecule synthesis, drug design, and materials chemistry. Early chiral bisphosphine hydrogenation work established the catalytic value of phosphorus-centered stereocontrol [1]. Knowles-type asymmetric hydrogenation systems further showed that chiral phosphine environments could control product configuration in useful transformations [2]. P-chiral benzophospholane ligands then illustrated how compact phosphorus-based frameworks can be used in asymmetric hydrogenation [3]. Modern ligand reviews confirm that phosphorus substituent design remains central to stereochemical transfer at metal centers [4].

P-stereogenic compounds are different from traditional chiral ligands because the stereocenter is situated in the reactive atom, namely, in the donor phosphorus. In the case when asymmetry is introduced into a backbone of a ligand, asymmetric effect transfer becomes necessary from a scaffold onto a metal-coordination region. In the case of phosphorus stereocenter, the differences between phosphorus substituents in terms of size and electron density play a crucial role in tuning the reactivity of phosphorus and its ligating behavior towards metals. Air-stable P-chiral phosphines have demonstrated how phosphorus-centered stereochemistry can support highly enantioselective metal catalysis [5]. Broader surveys of P-chirogenic phosphorus compounds show their importance as ligands and functional intermediates [6]. P-stereogenic amino-phosphines further illustrate the link between privileged intermediates and asymmetric catalysis [7]. Phosphine-catalyzed asymmetric reactions also show that phosphorus-centered reactivity can be used beyond metal-ligand design [8]. At the same time, phosphorus stereogenic centers represent a particular synthetic challenge due to configurationally labile nature of phosphorus

and special attention which needs to be paid to maintaining phosphorus oxidation state during a reaction and isolating products without loss of configurational integrity.

Conventional routes to phosphorus stereocenters typically included stoichiometric use of chiral auxiliaries or chiral resolving agents or a series of steps based on stereogenic P compounds, followed by substitution reaction. Classical reviews described preparation routes to scalemic P-chiral phosphines and their derivatives [9]. Catalytic enantioselective strategies later broadened the range of accessible P-stereogenic compounds [10]. Desymmetric C–H arylation supplied an important palladium-catalyzed route to P-stereogenic phosphinamides [11]. Enantioselective C–H arylation also provided access to P-stereogenic compounds through direct functionalization [12]. Rhodium-catalyzed enantiotopic C–H activation enabled the synthesis of P-chiral cyclic phosphinamides [13]. Reinvestigation of stereogenic phosphoryl substitution clarified stereochemical and mechanistic issues in phosphorus substitution chemistry [14]. Iridium-catalyzed C–H arylation gave access to P- and axially chiral biaryl phosphine oxides [15]. Dialkynylphosphine oxide desymmetrization demonstrated another route to P-stereogenic motifs with alkynyl functionality [16]. Ethynyl-substituted P-chiral tertiary phosphine oxides were also obtained through Cu-catalyzed azide–alkyne cycloaddition chemistry [17]. Recent updates summarize the rapid development of optically pure P-stereogenic molecule synthesis [18]. Green-synthesis perspectives emphasize the continuing need for efficient construction of P-stereogenic centers [19]. Catalytic asymmetric routes beyond precious metals further show the need for new catalytic designs [20]. Palladium-catalyzed arylation of phosphoramidites additionally confirms the relevance of catalytic stereocontrol in P-chirogenic phosphorus chemistry [21]. The best among these techniques achieve not just C–P bond construction, but generation of a well-defined phosphorus stereocenter with minimal risk for phosphorus oxidation state changes and other side processes.

An extra challenge arises with preparation of P-stereogenic alkynylphosphines with sp-C-P bonds because of high synthetic flexibility and strong interaction with a stereogenic phosphorus center associated with the alkyne fragment. Alkyne substituent is small and weakly steric in character, so it poorly contributes to the differentiation between opposite enantiomers. Transition-metal-catalyzed alkyne couplings show the synthetic value of retaining the carbon–carbon triple bond as a versatile handle [22]. Gold-catalyzed hydroetherification of alkynes with P-stereogenic centers further illustrates how alkyne chemistry can be combined with phosphorus chirality [23]. Circularly polarized luminescence studies show why compact chiral organic frameworks are important in chiroptical materials [24]. P-containing polyaromatic synthesis demonstrates the usefulness of seven-membered phosphorus rings in chiral conjugated systems [25]. On the other hand, the highly energetic and saturated triple bond represents a valuable handle for further modification of alkynylphosphine via hydration, reduction, annulation, and conjugation extension. An enantioenriched alkynylphosphine can thus act as a convenient chiral intermediate which leads to diverse phosphorus-containing π-system.

Development of asymmetric C(sp)-P bond construction via coupling of phosphorus nucleophile with bromoalkyne requires some additional consideration compared to arylation or allylation reactions because of high reactivity of bromoalkynes. Bromoalkynes readily couple with phosphines even in the absence of metal catalysts and thus represent the major obstacle for effective coupling in asymmetric transformation. In this context, the task of a catalytic system is twofold. It should stimulate the bond formation process and do so in a selective way competing with the unwanted and non-selective background reaction. This goal cannot be achieved relying solely on reaction conversion because a high product yield does not necessarily mean high enantiomeric excess due to nonselective formation of enantiomerically diluted material during background reaction.

The choice of nickel-based catalysis for C(sp)-P bond formation is driven by several facts. First, nickel complexes can activate carbon-halogen bonds and promote carbon heteroatom coupling reactions. Cross-dehydrogenative coupling studies show the broader importance of transition-metal methods for constructing heteroatom-containing products [26]. Nickel-catalyzed allylation of secondary phosphine oxides demonstrates that nickel can support asymmetric phosphorus transformations [27]. Nickel-catalyzed enantioselective allylic alkylation of H-phosphinates provides another relevant phosphorus-coupling precedent [28]. Unsymmetric bisphosphine pincer-nickel complexes have also enabled asymmetric synthesis of P-stereogenic secondary phosphine-boranes [29]. Copper-catalyzed dynamic kinetic C–P cross-coupling and cyclization further shows how stereogenic phosphorus heterocycles can be assembled through catalytic C–P bond formation [30]. Nickel-catalysis is therefore usually cheaper and easier than analogous palladium-mediated transformations and remains promising for asymmetric phosphorus transformations. However, a challenge in alkynylphosphine cases comes from the possibility of interaction with phosphorus substituents which might change phosphorus oxidation state and ligating properties and lead to oxidative degradation. Thus, successful strategy should involve the sequence of phosphorus precursor, reaction conditions, and product isolation to preserve phosphorus stereogenicity.

Such an approach has been chosen in our research: secondary phosphine oxide has been employed as the phosphorus precursor, and subsequent reaction with phenylsilane results in formation of phosphorus product which undergoes the coupling reaction in the presence of $Ni(COD)_2$, (S,S)-Et-Duphos, sodium acetate, and mesitylene at 0 °C. Obtained trivalent phosphorus compounds were subsequently converted into oxides, sulfides, or boranes to facilitate their isolation

and evaluation of phosphorus stereogenicity. This procedure allows reducing direct contact of potentially labile trivalent phosphorus compounds with air and performing C(sp)-P bond construction under chiral nickel catalysis at low temperatures.

In our opinion, the most critical aspect of the reaction is overcoming the competition between nickel-controlled C(sp)-P bond formation and direct phosphine-bromoalkyne reaction. The 20% conversion in absence of the catalyst demonstrates that background reaction is chemically viable. The 72% yield and 86% ee for 3ba obtained in presence of the catalyst reveal the advantage of the chiral nickel catalysis. All other observations such as yield, phosphorus substituent shape, alkyne electronics, and product diversification can be considered as the evidences of stereoselectivity of the reaction.

2. Reaction Design and Experimental Conditions

Reaction is based on three consecutive stages: generation of secondary phosphine from secondary phosphine oxide, coupling with a bromoalkyne under nickel catalyst, and isolation of the trivalent phosphorus compound as an oxide, sulfide, or borane derivative. Model experiment was conducted using 0.20 mmol of secondary phosphine oxide, 0.20 mmol of $PhSiH_3$, 0.10 mmol of bromoalkyne, $Ni(COD)_2$ at 5 mol%, (S,S)-Et-Duphos at 6 mol%, 0.25 mmol of sodium acetate, and mesitylene as solvent at 0 °C for 72 h [31]. Reaction conditions allow obtaining product 3ba in 72% yield and 86% ee while reaction in absence of the nickel catalyst yields only 20% of product. This difference reveals the core of the reaction selectivity issue: efficient product formation should preferentially occur in chiral nickel environment.

Table 1: Optimized reaction conditions and model outcome.

Parameter	Reaction condition
Phosphorus precursor	Secondary phosphine oxide, 0.20 mmol
Reductant	$PhSiH_3$, 0.20 mmol
Alkynyl electrophile	Bromoalkyne, 0.10 mmol
Catalyst and ligand	$Ni(COD)_2$, 5 mol%; (S,S)-Et-Duphos, 6 mol%
Additive and solvent	NaOAc, mesitylene, 1 mL
Temperature and time	0 °C, 72 h
Product from model coupling	3ba, 72% isolated yield; 86% ee
Product without nickel catalyst	20% conversion to 3aa

The combination of optimized conditions in Table 1 allows for both stability of the precursor and stereochemical control of the catalysis. The secondary phosphine oxides are more stable and easier to handle than their analogous secondary phosphines and $PhSiH_3$ gives off the partner P-H in situ. The lower temperature used plays a significant role since reaction of secondary phosphine with the bromoalkyne is no longer a strong competitor as it slows down. The use of sodium acetate creates a gentle medium for the reaction while mesitylene ensures that high polarity will not cause excessive reactivity. The catalyst loading and ligand loading are also not incidental: a catalytically competent nickel–Duphos complex must form rapidly enough to capture the phosphorus partner before substantial racemic product accumulates.

Overall, the pattern in Figure 1 shows that the utility of the chemistry depends on the combined value of isolated yield and enantiomeric excess. Model coupling yields both, and downstream hydration, phosphole oxide formation, and phosphepine formation show that stereochemistry retains value even when applied to other compounds.

Enantiomeric excess can be defined through the standard relationship between the major and minor enantiomer populations:

$$ee = \frac{|n_{\text{major}} - n_{\text{minor}}|}{n_{\text{major}} + n_{\text{minor}}} \times 100.$$

In this equation, it becomes clear why both the yield and ee must be understood as a pair. The yield represents the quantity of isolated compound, while ee measures stereochemical deviation from equality. Even if the substrate reacts well, poor ee could be the result of insufficient separation of the enantiomeric pathways or the generation of product away from the chiral metal center. A comparison of the phenyl/ethyl phosphorus partner with phenyl/tert-butyl phosphorus partner makes this difference apparent, as the former gives 81% yield and 29% ee while the latter gives 72% yield and 86% ee. The latter substrate, despite its marginally lower yield, is much more useful for asymmetric synthesis.

The observed yield can be thought of as the sum of the product formed through stereoselective coupling with the nickel complex and that formed through direct, non-selective coupling between the substrates. This definition, although useful as chemical bookkeeping, has nothing to do with kinetics; no rate constants or elementary reaction steps are proposed. Nevertheless, the definition can help understand the substituent effects seen in the results. Less electron-withdrawing bromoalkynes will be less reactive to direct coupling with phosphines, while more bulky phosphorus substituents will enhance the stereocontrol in the nickel-assisted coupling pathway. Numerical comparisons made in later sections will be taken as support for this effect.

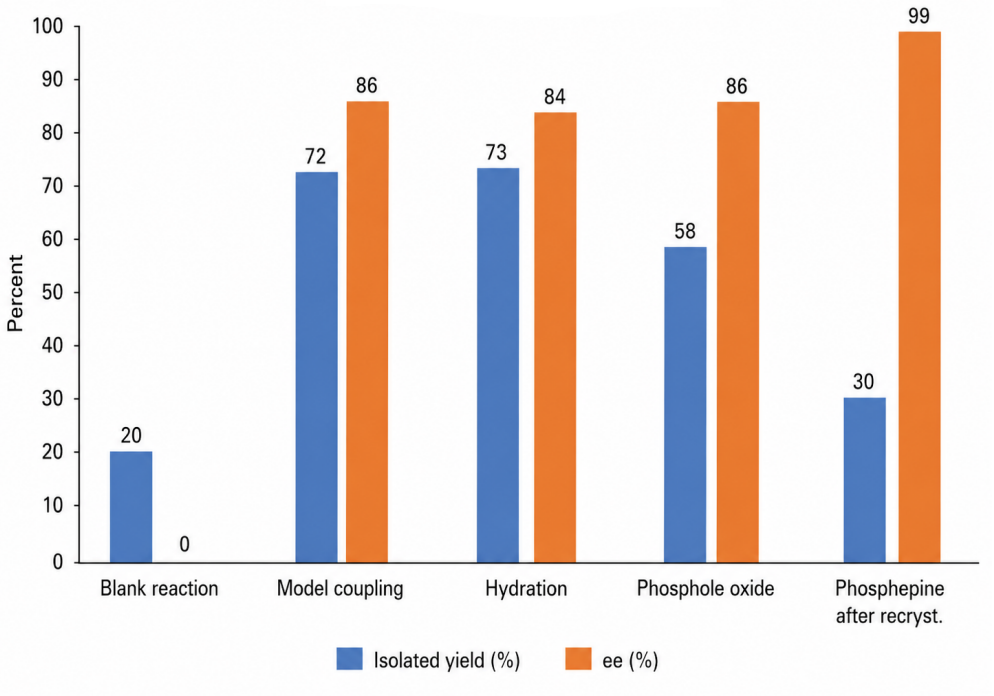
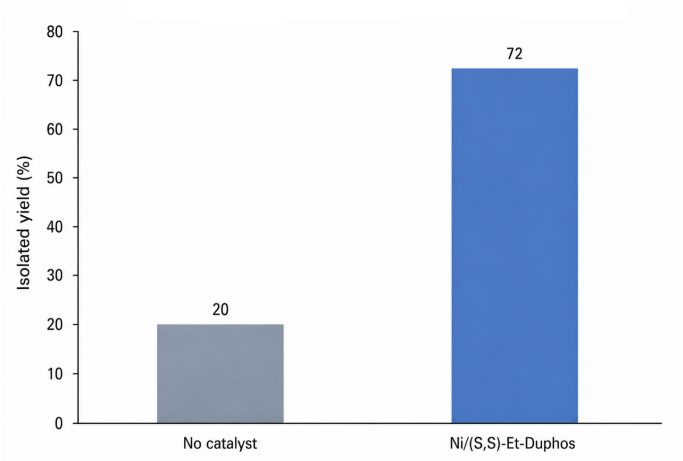


Figure 1: Outcome profile.

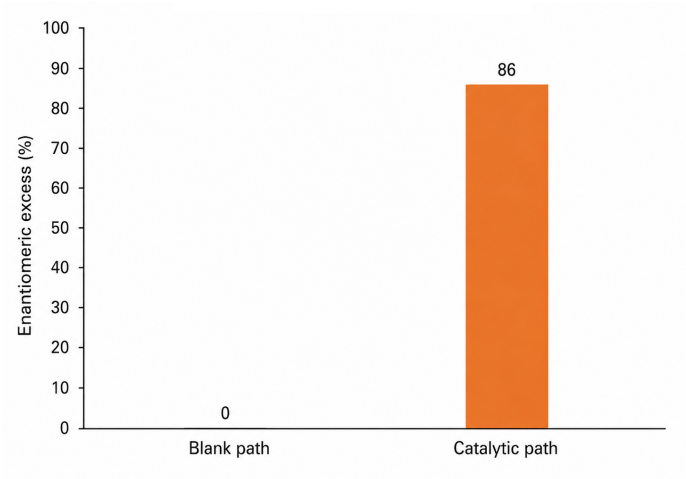
3. Results and Discussion

3.1 Catalysis-controlled coupling with a detectable background reaction

The reaction run without any added nickel is crucial because it shows that the phosphine-based substrate and the bromoalkyne can undergo coupling without the aid of the chiral catalyst. A yield of 20% in an asymmetric reaction is significant. If the catalytic pathway only marginally outperformed the background process or only provided moderate enantioselectivity, the ee value would be greatly reduced. Thus, it becomes clear that the model system of 72% yield and 86% ee reflects the fact that the nickel/(S,S)-Et-Duphos complex controls the reaction pathway to a sufficient extent to determine the observed yield.



(a) Yield without and with catalyst.



(b) Enantiomeric discrimination.

Figure 2: Catalytic control under background reactivity.

The direct comparison provided in Figure 2 clearly demonstrates the key selectivity challenge of the studied transformation. Figure 2a demonstrates that the uncatalyzed background reaction pathway possesses significant chemical meaning, whereas the introduction of the chiral nickel catalyst establishes strong asymmetric control when the catalyst-mediated pathway prevails (Figure 2b).

The background reaction is also responsible for the necessity of evaluating the catalytic process by the measure of enantiomeric excess, not just conversion. Conventional coupling reactions can be optimized through improving both yield and minimizing the side decomposition of the formed product. In the discussed case, an increase of the concentration of the reactive secondary phosphine oxide or a modification of the electrophile bromoalkyne to make it more attractive can

contribute to achieving higher conversion; however, it will result in increasing the contribution of the racemic formation simultaneously. In this way, the 0 °C temperature condition serves as a selectivity parameter and probably inhibits the reaction between phosphine oxide and bromoalkyne, shifting the main product formation toward the chiral catalyst-mediated pathway. Catalytic enantioselective P-stereogenic synthesis highlights why competing pathways must be suppressed rather than merely converted [10]. Recent updates on optically pure P-stereogenic molecules similarly stress the importance of stereochemical control during bond formation [18]. Catalytic asymmetric phosphine synthesis beyond precious metals reinforces the same need for pathway selectivity [20].

The developed catalytic process needs to balance the coordination abilities and reactivity of the nickel center. The secondary phosphines are prone to coordination with the transition metal and even the formed tertiary phosphine oxide products can possess good donor properties. Under such conditions, the nickel complexes can undergo substrate, product, or ligand inhibition. The choice of the chiral bisphosphine ligand plays an important role in the studied catalytic strategy, allowing to create a favorable nickel environment, as well as providing an asymmetric pocket for the formation of the P(sp)-C bond. Sodium acetate and mesitylene provide a moderate solvent mixture avoiding excessively polar and basic conditions, which would promote the undesired reaction of the starting material or side product formation. In terms of practical applicability, it is possible to state that the proposed strategy can convert the stable oxidized precursor into an easily obtainable stereodefined product under a simple operation procedure.

The oxidation-state adjustment of the obtained product is not solely connected with the analytical aspects of the research. The P-stereogenic compounds are often unstable and susceptible to oxidation, coordination, and purification problems. Thus, stabilized derivatives allow obtaining reliable yields of the compound and calculating the e.e. values, as well as provide additional transformation possibilities. Preparation of scalemic P-chiral phosphines and derivatives shows the long-standing importance of isolable phosphorus stereochemical forms [9]. Applications of P-chirogenic phosphorus compounds also show why oxides and protected derivatives remain useful in synthetic design [6]. P-stereogenic amino-phosphines further demonstrate that stabilized intermediates can support later asymmetric catalysis [7]. In the proposed catalytic system, stabilization of the obtained compound can preserve its stereodifferentiation.

The principal conclusion from the optimized record can be summarized in the following statement. The method addresses the selectivity problem associated with competitive pathways of the reaction, rather than just forming a C(sp)-P bond. The key point is that the catalytic pathway generates the predominant fraction of the product, while the direct racemic formation of the desired product still takes place. Such a perspective expands the general importance of the described methodology since numerous asymmetric coupling reactions with reactive nucleophiles and electrophiles encounter the same hidden problem of background pathways. As is seen from the blank experiment results, the problem can be addressed via the appropriate design of substrate in accordance with the catalyst selectivity.

3.2 Phosphorus substituent effects and steric origin of chiral discrimination

The phosphorus substituent effects study represents another efficient reaction record, since it covers four phosphorus oxide derivatives as substrates. Thus, the following substrates were tested within the proposed catalytic strategy: phenyl/isopropyl, phenyl/tert-butyl, phenyl/cyclohexyl, and phenyl/ethyl. The corresponding isolated yields and e.e.'s of the obtained compounds are 80%/78%, 72%/86%, 76%/74%, and 81%/29%, respectively. Such data demonstrate that the phosphorus substituent affects conversion and stereocontrol differently.

Table 2: Phosphorus substituent effect study.

Entry	Phosphorus substituent pattern	Isolated yield	ee
1	phenyl/isopropyl	80%	78%
2	phenyl/tert-butyl	72%	86%
3	phenyl/cyclohexyl	76%	74%
4	phenyl/ethyl	81%	29%

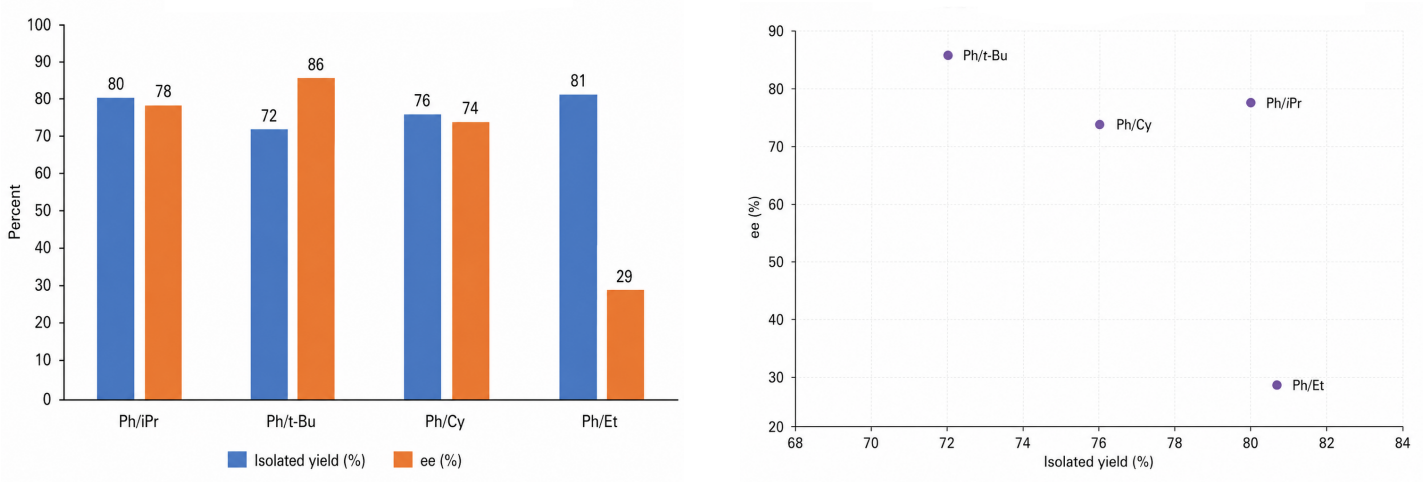
As is evident from the results represented in Table 2, the entry with the highest conversion is not always characterized by the highest stereocontrol. Efficient reactivity was observed when the ethyl-substituted phosphine oxide was used; however, the small substituent cannot produce enough steric differentiation and enable adequate chiral recognition. The replacement of ethyl group with much bulkier tert-butyl substituent resulted in only 9% lower isolated yield but improved the e.e. by 57 percentage points. Thus, steric imbalance of the phosphorus substituents is revealed as the crucial structural requirement. The isopropyl and cyclohexyl substrates lie somewhere in the middle of this trend, which indicates that substituent bulk is not the sole contributor to the ee.

In accordance with the overall design logic for P-stereogenic ligands, a bulky substituent like tert-butyl can act as

a spatial wall, whereas a small or flat substituent will create an unhindered zone around phosphorus. Upon substrate engagement with the chiral nickel catalyst, this structural asymmetry may cause either generation or preferential selection of one phosphorus stereoisomer through reductive elimination or analogous C-P bond formation. This principle has special relevance for the alkynyl substituted ligand due to the small and linear nature of the C(sp) substituent. The alkyne itself offers no significant steric drive toward any particular configuration, and thus the majority of stereoelectronic influence needs to come from the phosphorus substituents. Chiral phosphorus ligand design shows the value of strong steric differentiation around phosphorus [4]. Air-stable P-chiral phosphine ligands provide a related example of substituent-controlled asymmetric induction [5]. Reviews of P-chirogenic compounds further confirm that substituent disparity is central to useful ligand behavior [6].

It is important to note that a lower substrate yield does not imply any weakness of the method. It is common practice in asymmetric synthesis to tolerate a small loss in yield if it is accompanied by a significant increase in enantiomeric excess. The more meaningful finding is that the tert-butyl-substituted substrate strikes an optimal balance between reactivity and stereocontrol. Even a more bulged or crowded phosphorus system would have provided more stereochemical selectivity at the cost of reaction rate, while a less sterically encumbered ligand would favor faster catalysis yet lack the critical steric difference between configurations. The tert-butyl-phenyl combination seems to offer the right level of substitution and thus represents a valuable middle ground between fast and selective reactions.

On the other hand, low ee in the ethyl-substituted case further illustrates the boundaries of stereocontrol in asymmetric catalysis. While a chiral metal complex provides an environment, the stereocenter being constructed resides at phosphorus, and the ratio of the substituents' bulk determines stereochemical potential energies of the competing processes. With only one ethyl substituent, this energy difference becomes too small, leading to less selectivity in substrate transformation. Simultaneously, the absence of substantial steric bias in this system causes the background process to become relatively damaging since the substrate can engage in efficient reactions even without the ordered chiral catalyst. These findings point toward a combined approach in which substrate-encoded steric discrimination and catalyst-induced structural ordering cooperate to generate high ee.



(a) Yield and ee in the initial screen.

(b) Relationship between yield and ee.

Figure 3: Phosphorus substituent effects.

The data summary shown in Figure 3 further emphasizes the differences between conversions and selectivity. While the bars in panel 3a clearly demonstrate the advantage of the tert-butyl moiety, the scatter plot in panel 3b illustrates the point that the most effective substrate does not need to be the most selective.

3.3 Scope of the phosphorus partner and positional effects on aryl substituents

The wider scope of the secondary phosphine oxides shows that the nickel protocol developed here is not limited to the parent aryl tert-butyl system. Indeed, the parent aryl tert-butyl sulfide 3ea is prepared in 76% yield and 86% ee, whereas its borane counterpart 3ea′ is obtained in 62% yield and 84% ee. Para-substituted aryl tert-butyl systems afford 3fa through 3ka in yields from 63 to 78% and enantiomeric excesses of 76 to 90%. Aryl tert-butyl systems substituted in the meta-position result in products 3la and 3ma in 64%/75% and 70%/82%, respectively. Aryl tert-butyl products with ortho-substituents are particularly interesting since they provide additional insight into the influence of a neighboring group on phosphorus since such substituents perturb the geometry around phosphorus. 3Na is prepared in 68% yield and 90% ee, and even at larger scales, the same product is available in 54% yield and 87% ee. Finally, the enantiomeric excess of products 3Sa and 3Ta is

90% and 92% with yields of 63% and 58%, respectively, whereas 3Ua and 3Va are afforded in 68%/88% and 50%/80%.

Table 3: Secondary phosphine oxide scope.

Product	Phosphorus partner feature	Isolated yield	ee
3ea	parent aryl tert-butyl, sulfide	76%	86%
3ea′	parent aryl tert-butyl, borane adduct	62%	84%
3fa	para-OMe aryl tert-butyl	78%	76%
3ga	para-tert-butyl aryl tert-butyl	73%	90%
3ha	para-Me aryl tert-butyl	72%	84%
3ia	para-F aryl tert-butyl	68%	90%
3ja	para-Cl aryl tert-butyl	64%	83%
3ka	para-CF_3 aryl tert-butyl	63%	84%
3la	meta-Me aryl tert-butyl	64%	75%
3ma	meta-F aryl tert-butyl	70%	82%
3na	ortho-Me aryl tert-butyl	68%	90%
3na	ortho-Me aryl tert-butyl, gram scale	54%	87%
3oa	ortho-OMe aryl tert-butyl	73%	76%
3pa	benzo[d][1,3]dioxole aryl tert-butyl	56%	86%
3qa	naphthyl tert-butyl	60%	80%
3ra	thienyl tert-butyl	41%	72%
3sa	ortho-Cl/Me-substituted aryl tert-butyl	63%	90%
3ta	ortho-Me/Me-substituted aryl tert-butyl	58%	92%
3ua	phenyl/isopropyl	68%	88%
3va	mesityl/isopropyl	50%	80%

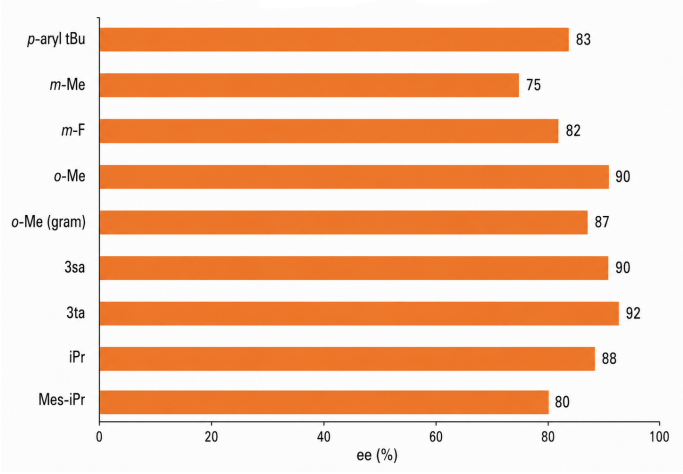
Entries in Table 3 show that aryl substitution can be tolerated in multiple locations, but the positional effect has different chemical interpretations depending on location. Substitution para to the phosphorus center is primarily electronic and remote steric effects. Yield and ee for both para substitutions indicate that the catalyst system can tolerate aryl changes with electron-withdrawing and electron-donating functionality, without sacrificing stereochemical advantage conferred by the tert-butyl moiety. Substitutions meta to the phosphorus center present less symmetric aryl substituents and possibly subtle conformational effects. While the entry with meta-fluorine substitution is out-yielded by its meta-methyl counterpart, the ee of the former is higher; this may imply a beneficial balance of steric and electronic interactions, but a conclusion regarding cause-and-effect cannot be drawn from the available data.

Ortho-substituents have more direct bearing on stereochemistry since a substituent in close proximity to the phosphorus atom may limit rotation or impose a specific spatial orientation of the aryl substituent relative to the phosphorus–hydrogen coupling position. High ee values in substrates with orthogonal control over rotation at the phosphorus center confirm this expectation; in asymmetric C(sp)-P bond formation, a sterically non-demanding alkynyl group allows for a well-defined spatial presentation of the phosphorus site to nickel to enhance chiral discrimination. In other words, an effect of ortho-substituent seems to be reinforcing the same concept discovered in the tert-butyl substituent screen: stereochemically well-defined environment around phosphorus provides an opportunity to exploit chiral discrimination.

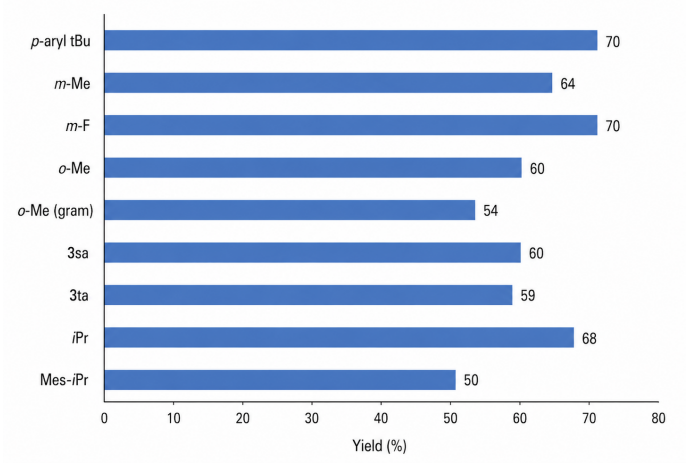
The gram-scale experiment with ortho-methyl substitution deserves special attention since large-scale operation may highlight certain difficulties associated with smaller-scale experiments. First, the yield value is noticeably lower compared to the yield for the tert-butyl derivative, indicating that scaling up may bring problems of conversion and/or separation, yet a fairly high ee value (87%) is observed. These two numbers are significant because asymmetric reactions are normally performed on a small scale, and heat transfer, mixing, and feeding can all be tightly controlled. Maintenance of ee value after scaling up to 5 mmol confirms that the chiral environment remains capable of imparting enantioselective effect, even though the conversion may need adjustment.

The mesityl isopropyl substrate achieves ee of 80%, although its yield is somewhat lower than that of some aryl tert-butyl derivatives. This result is in agreement with a highly crowded phosphorus center that can still produce stereodifferentiation effect but may reduce turnover due to decreased efficiency of reduction, nickel coordination, or C-P bond formation. In other words, the substrate produces a crowded environment, but such steric hindrance enhances enantiospecific discrimination. Thus, it is important to separate the factors that affect the yield from those that control ee value. Low yield should not automatically lead to low ee value, and vice versa. Hence, the discussion of substrate scope in terms of yield is most meaningful when combined with ee.

It is clear from Figure 4 that stability of enantioselectivity surpasses yield of isolated material in the phosphorus-partner set. While panel 4a clearly highlights high enantiomeric excess for all ortho-phosphine oxide and tert-butyl phosphine oxide partners, panel 4b indicates greater variability in preparative yield.



(a) Representative ee values.



(b) Representative isolated yields.

Figure 4: Representative phosphorus-partner outcomes.

3.4 Scope of bromoalkynes, electronics of electrophiles, and class-specific limitations

The second variable that is subject to extensive testing is represented by electrophile type, since bromoalkynes are used both in the context of nickel-mediated coupling and direct nonselective addition. Thus, aryl bromoalkynes provide phosphine oxide products in reasonable yields and enantiomeric excesses. Thus, phosphine oxide 3na-O can be synthesized in 64% yield and 90% ee from parent aryl bromoalkyne. Electrophile featuring electron-releasing para-tert-butyl substituent provides 3nb in 58% yield and 93% ee; similarly, para-substituted aryl bromoalkynes bearing phenyl, fluorine, or bromine groups deliver products 3nc, 3nd, and 3ne in yields of 62%/91%, 62%/86%, and 51%/84%, respectively. Bromoalkynes with meta-substitution of methyl and fluoride groups provide 3nf and 3ng in yields of 65% and 57% along with stereochemical results of 90% and 84% ee. Bromoalkyne containing ortho-substituted methoxy group yields 3nh with 61% yield and 90% ee. Products 3ni and 3nj obtained from naphthyl and thienyl bromoalkynes show yields of 53% and 40% in conjunction with 81% and 78% ee. The double coupling of 1,3-bis(bromoethynyl)benzene gives product 3nk with 33% yield, 97% ee, and 5:1 ratio of diastereomers. Bromoalkynes with alkyl substitution provide phosphine oxides 3nl, 3nm, and 3nn with yields ranging between 38% and 35%, and corresponding ee values are 93%, 90%, and 84%. The electrophile derived from L-phenylalanine affords phosphine oxide 3no with 32% yield and 9:1 ratio of diastereomers.

Table 4: Bromoalkyne scope.

Product	Bromoalkyne feature	Isolated yield	Stereochemical result
3na-O	phenyl	64%	90% ee
3nb	para-tert-butyl phenyl	58%	93% ee
3nc	para-phenyl phenyl	62%	91% ee
3nd	para-fluoro phenyl	62%	86% ee
3ne	para-bromo phenyl	51%	84% ee
3nf	meta-methyl phenyl	65%	90% ee
3ng	meta-fluoro phenyl	57%	84% ee
3nh	ortho-methoxy phenyl	61%	90% ee
3ni	naphthyl	53%	81% ee
3nj	thienyl	40%	78% ee
3nk	1,3-bis(bromoethynyl)benzene	33%	97% ee, 5:1 dr
3nl	linear alkyl	38%	93% ee
3nm	cyclohexyl alkynyl	40%	90% ee
3nn	chloroalkyl	35%	84% ee
3no	L-phenylalanine-derived	32%	9:1 dr

Substrate Scope 3: Aryl Bromoalkyne The substrate class of Table 4, ary bromoalkynes, illustrates that a stereocontrolling environment can be influenced by multiple electrophiles. It is chemically sound to expect that more electron-rich aryl bromoalkynes would give rise to more ee as compared to their electron-poor counterparts due to the background reaction. More electrophilicity means a greater chance for the nonselective mechanism to produce racemic product, while less electrophilicity leaves the nickel-mediated approach as the major source of optical purity. This is a logical trend rather than separate scope cases.

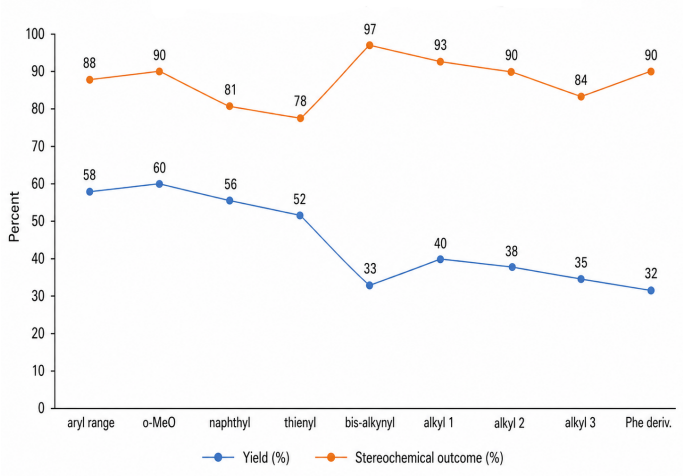
The examples of naphthyl- and thienyl-substituted bromoalkynes in the substrate class show that extended aromaticity or presence of heteroatoms does not preclude high enantioselectivity in this catalysis. However, the low ee observed in these instances suggests that the phosphine-copper system is subjected to steric and coordination influences from the bulky aromatic or heteroaromatic electrophile, thus decreasing the contribution of the selectivity-enhancing environment. A larger aromatic surface and a modified steric field are observed in naphthyl substrates; thienyl compounds can affect the electronic structure and participate in metal complexation differently. While providing sufficient ee, such electrophiles may require additional optimization of the process parameters.

The example with bis(bromoethynyl)benzene is particularly insightful in that the reaction requires coordination of two alkynyl groups simultaneously. The low yield, 33%, might seem inadequate based only on conversion; however, 97% ee and a high dr of 5:1 make this a success case. The simultaneous interaction of several stereocenters with the catalyst is problematic due to the increased potential for catalyst deactivation, substrate inhibition, and loss of stereoselectivity. The high ee value obtained in this substrate system is evidence of strong control exerted by the nickel catalyst even with multiple sites of catalysis. Low yield likely reflects difficulties in achieving complete catalysis with multiple bromoalkyne moieties or partial conversion, or some losses in purification of a compound with more complexity than its predecessors.

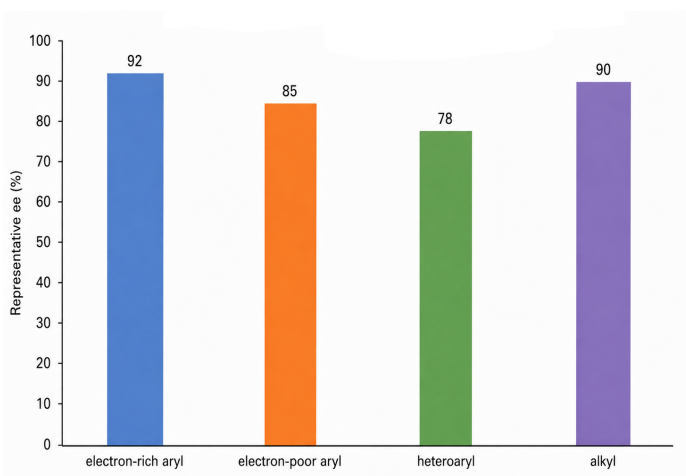
Alkyl bromoalkynes show that aryl groups attached to the alkyne chain do not have to be necessary for high ee production. This is important since the aryl alkyne compounds are electronically stabilized and better known for synthetic purposes. Lower yields indicate that the system is more efficient with particular aryl bromoalkynes. On the other hand, the 84–93% ee value achieved by this example shows that the enantioselectivity control is largely provided by the chiral nickel environment. This is a valuable finding for expanding synthetic applicability since alkyl alkyne substituents allow for obtaining structurally distinct products. Moreover, the stereochemical control in the reaction seems more dependent on the phosphorus moiety and ligand complex surrounding nickel than on the aromatic stabilization of the alkyne.

The bromoalkyne derived from L-phenylalanine is a challenging substrate case in terms of introducing a biological unit into the electrophile, and thus creating another stereocenter to be involved in the interaction. The reduced yield of 32% and dr of 9:1 confirm that this compound works within the proposed catalysis, albeit less efficiently as compared to simpler substrates. An existing stereogenic element in the electrophile makes analysis of the diastereomer ratio complex since the stereospecificity may be compromised by interactions between the catalyst and existing center. Nevertheless, the substrate is included in the scope list due to successful inclusion of a chiral component into the electrophile and thus extending the substrate applicability to complex substrates.

Overall, the data of the scope illustrate that the proposed explanation holds true for the reaction at hand. Substrate classes characterized by reduced yields but preserved ee prove that slow reactions do not preclude high selectivity in this reaction. Aryl bromoalkynes confirm the idea that reducing electrophilicity decreases the background reactions and allows obtaining high ee. Complex bromoalkynes outline the limitations imposed by the reaction while preserving stereochemical information. As a result, the reaction has a promising yet limited electrophile substrate scope. Future development of this methodology should be focused on conditions ensuring control over highly electrophilic or coordinating bromoalkynes.



(a) Representative class outcomes.



(b) Electronic tendency in ee.

Figure 5: Bromoalkyne scope and electronic response.

The two graphs in Figure 5 capture the two facets of the electrophile study. Graph 5a shows that the process maintains its stereoselectivity for aryl, heteroaryl, alkyl, and complex aryl bromoalkynes, whereas graph 5b reveals the reasons behind the success of electronically rich aryl bromoalkynes in achieving enantioselective couplings.

3.5 Mechanistic inference from scope patterns

The mechanism is not wholly inferred from scope studies; however, all findings together contribute to an explanation of the mechanism of the catalytic process. The null test proves that the bromoalkyne/phosphine combination can work without nickel, generating a non-selective pathway of reaction. The catalytic model experiment proved that the catalyst pair $Ni(COD)_2$/ (S,S)-Et-Duphos is sufficient to form a pathway with excellent enantiodiscrimination. The phosphorus substitution experiments prove that bulky and conformational groups attached to phosphorus are effective at increasing ee values. The bromoalkyne electronics trend demonstrates that less electrophilic substrates minimize background couplings. The gram scale ortho methyl substrate example showed that even in realistic loading conditions, stereoselectivity is possible. All these findings together provide strong evidence of a catalytic pathway in which a chiral nickel complex guides the stereogenic C(sp)/P bond formation process.

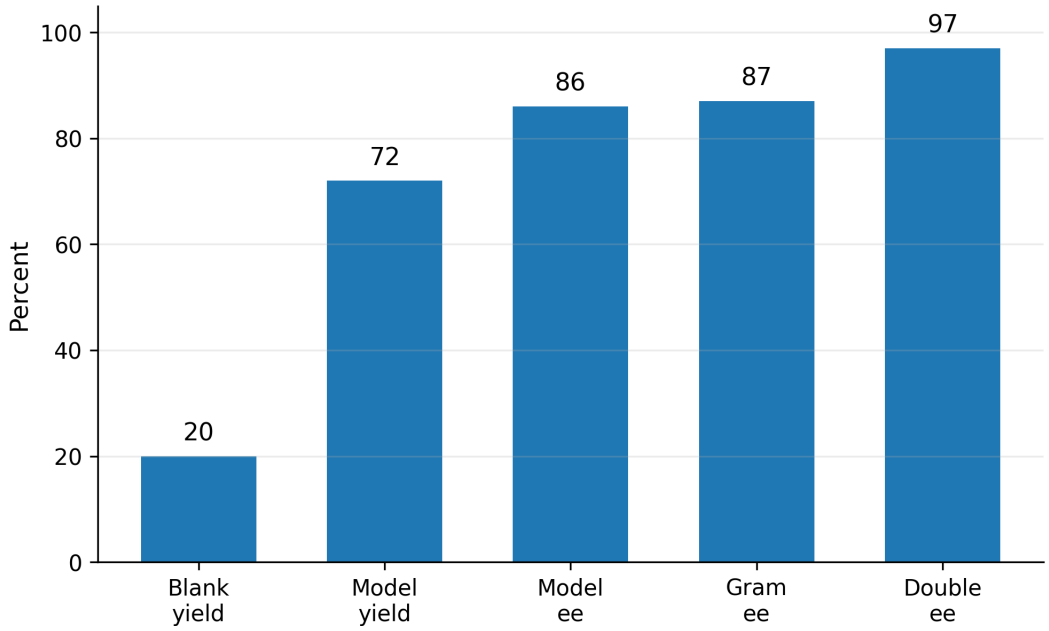


Figure 6: Pathway evidence.

Condensing the key observations into one figure (Figure 6), it appears that blank reaction provides a measure of the strength of the competing pathway, catalysis modeling predicts the optimized catalytic stereocontrol, and the last three observations are evidence that stereocontrol is maintained when conditions become harsher.

One possible route for the transformation starts from the formation of a secondary phosphine from phosphine oxide, interaction with nickel–Duphos complex in which phosphorus and bromoalkyne interact, and the subsequent bond-forming step that results in formation of the C(sp)–P bond. In particular, the nickel center can activate the C–Br bond of bromoalkyne and position phosphorus nucleophile in a manner suitable for a bond-forming process. More specifically, it can include reductive elimination step or something similar. The exact sequence of events and the oxidation states would require further evidence (kinetic, spectroscopic, or computational). Nevertheless, regardless of the specific route, it should be clear that the result supports the hypothesis of stereochemical bias in the stereogenic nickel-bound intermediates and the reduction of that bias under less optimal conditions.

This mechanistic interpretation is crucial for scholarship since one could weaken a manuscript by presenting an elaborate catalytic cycle without providing enough experimental evidence. While such a cycle may be a good illustration, the actual evidence can be much simpler. In our case, the blank reaction is clear evidence of competing nonselective reaction. Substituent-controlled stereochemical discrimination is also a very clear proof. Electron-rich bromoalkynes serve as indirect evidence of reduced competition with the background reaction. Gram-scale ee is evidence of robust stereocontrol under harsh conditions. Bis-alkynyl substrate serves as evidence of preservation of stereocontrol under harsher conditions. It becomes clear from the above observations which results can justify the mechanistic hypothesis and which cannot.

The relative importance of background reaction in determining the stereocontrol is also a convenient way of discussing possible improvements of the reaction. Denoting the amount of catalytically generated product with Y_{cat} and that of the nonselective background product with Y_{bg}, the resulting ee will depend on their ratio: the larger Y_{bg}, the lower the ee. Obviously, this expression is not a kinetic law. However, it is clear that there are several ways of improving ee through either acceleration of catalytic reaction, reduction of background reaction rate, or improved product isolation that favors selective

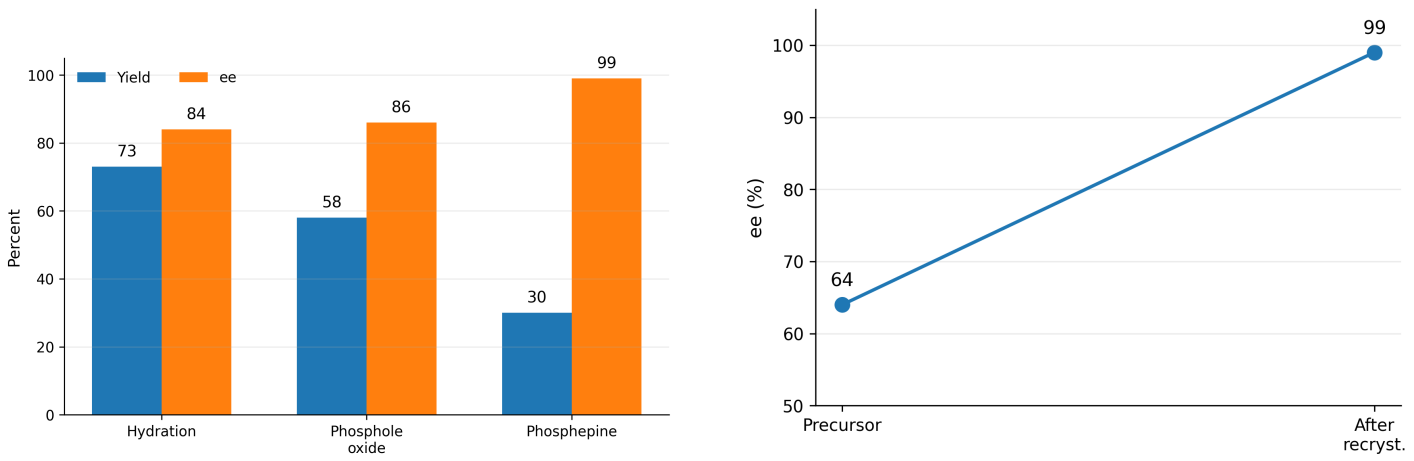
product. The examples include decreased temperature, restricted secondary phosphine liberation, use of less electrophilic alkyne partner, and more substituents at the phosphorus atom.

The proposed mechanism also helps to understand why ee and yield do not always correlate in asymmetric reactions. For example, a faster nonselective reaction increases product yield but decreases ee. On the other hand, a slower but more ordered catalytic reaction leads to increased ee and moderate yield. Strong hindrance of substrate lowers the yield but preserves stereocontrol. Finally, a more reactive electrophile enhances yield but also produces racemic product. In summary, such trade-offs are common in asymmetric methodology but can become evident only in the presence of a measurable background reaction. The reaction should therefore be optimized according to selectivity requirements, not merely yield.

It should be noted that the importance of chiral bisphosphine lies in its capability to arrange nickel complex in a certain spatial configuration. The ligand is rigid due to small size and conformational restriction. Thus, it can create a chiral pocket around nickel, where phosphorus partner and bromoalkyne meet. The phosphorus substrate must exhibit sufficient steric differentiation for the pocket to influence the reaction. Substrate-ligand match can explain the success of the tert-butyl phenyl substrate in giving a balanced ee/yield combination. Neither catalyst nor substrate can achieve stereochemical bias alone; they should cooperate in order to prefer one reaction direction over another.

3.6 Downstream transformations of alkynylphosphine products

Synthetic potential of the product relies on the presence of the alkyne group. Hydration of phosphine oxide 3na-O gives a β-keto phosphine derivative in 73% yield and 84% ee. Addition of a radical followed by intramolecular cyclization of 3ba results in benzo[b]phosphole oxide formation with 58% yield and 86% ee along with diastereoselectivity 3:1. A phosphine oxide can be converted into a phosphepine, the latter being prepared from precursor 3wp with 64% ee and 53% yield in first transformation. Phosphepine can be obtained with 63% isolated yield over two steps, and with further recrystallization yields up to 30% ee 99%. Overall, it is demonstrated that the C(sp)–P coupling product has multiple branching options.



(a) Diversification outcomes.

(b) Enrichment during phosphepine formation.

Figure 7: Downstream transformations of alkynylphosphine products.

The side by side comparison of the results from the figure 7 proves that the alkyne is an effective handle even after the asymmetric coupling reaction. The comparison between the yields and ee values of different transformation reactions downstream are shown in Figure 7a, while the optical purity obtained in phosphine is highlighted in Figure 7b.

Table 5: Post-coupling transformations of P-stereogenic alkynylphosphine products.

Transformation	Product type	Stereochemical outcome	Yield or outcome
Hydration	β-keto phosphine derivative 4	84% ee	73% yield
Radical cyclization	benzo[b]phosphole oxide 5	86% ee, 3:1 dr	58% yield
Phosphepine synthesis	phosphepine 6	64% ee; 99% ee after recrystallization	63% over two steps; 30% after recrystallization

As seen in Table 5, the example of hydration shows that the alkyne group may be transformed into carbonyl-containing derivatives with retained enantioenrichment at the phosphorus center. This transformation can be relevant for further condensation, coordination or derivatization due to the possibility of using β-keto phosphorus-containing compounds as substrates for such processes. The 84% ee value means that the stereochemistry of the phosphorus center is stable enough

despite the reaction conditions used for hydration. This observation supports the conclusion that alkynes are not simple bulky substituents providing steric contrast but functional groups capable of further reactions. Postcoupling reactivity is thus another factor supporting the choice of alkynylphosphines over non-reactive P-stereogenic alkyl or aryl phosphines.

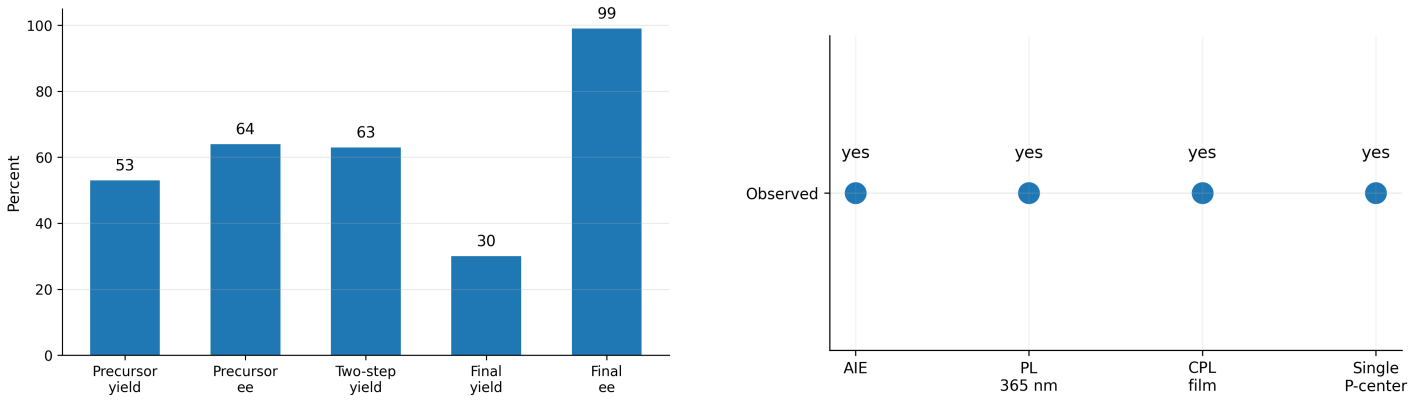
The example of the radical addition and ring formation adds a different product class by forming a new phosphorus-heterocyclic product. The presence of benzo[b]phosphole oxides in materials science is explained by their impact on conjugation properties and emissive behavior. In this case, 58% yield, 86% ee, and 3:1 dr indicate the presence of stereogenic centers after more complicated transformations. Therefore, new stoichiometric relationships are formed by introducing a ring into the molecule, and this process is a valuable test of both configuration stability at phosphorus and possibility of the alkyne participation in the skeleton rearrangement.

The most promising product class obtained in this study is represented by the phosphepin derivative. The precursors 3wp were obtained in 53% yield and 64% ee which are somewhat lower than in the most enantioenriched coupling products, whereas the phosphepin itself reached 99% ee by recrystallization. Though the 30% final yield does not correspond to high purity after enrichment due to material losses, the optical purity of the product is a necessary attribute for chiroptical studies as small amounts of enantiomer in the sample could significantly disturb their results. Thus, this sequence shows that even a moderately enantioenriched coupling product could be converted into the highly enriched materials precursor depending on crystallization.

Product transformations described above make it clear why this reaction may be considered as a much wider approach than the cross-coupling reaction alone. The coupling reaction provides the formation of a stereogenic phosphorus center and installation of a reactive alkyne group. Alkyne hydration forms the carbonyl-containing product with retained stereochemistry. Radical cyclization transforms alkyne to a fused heterocyclic compound, while phosphepin synthesis leads to the formation of a large phosphorus-containing ring. Thus, each of these transformations increases the value of the phosphorus stereocenter, forming a synthetic network in which one reaction may become a source of ligands, heterocycles and materials-oriented molecular structures.

3.7 Relation to chiral phosphorus materials

The importance of the phosphepin derivative for materials science results from combining the phosphorus stereocenter, conjugated structure, aggregated luminescence and circular polarization properties. Various approaches based on helical structures, axial chirality or other expansion methods are used to obtain CPL in chiroptical organic materials. Circularly polarized luminescence studies show that chiral organic architectures can generate useful chiroptical emission [24]. Stereospecific synthesis of P-containing polyaromatics provides a direct phosphorus-heterocycle route toward such materials [25]. Introduction of phosphorus stereogenicity in heterocyclic structure is therefore a compact strategy of CPL generation, which could be useful for small-size emitter synthesis when all these factors should be balanced.



(a) Synthetic profile of the phosphepine route.

(b) Reported materials observations.

Figure 8: Connection between the phosphepine sequence and chiral materials behavior.

The following concise chart in Figure 8 illustrates the link between synthetic methodology and the materials-focused end-product. Yield and ee values for the phosphepine production/enrichment process are shown in Panel 8a, while the observed AIE, PL, CPL, and single P-stereogenic center characteristics that inform the materials chemistry discussion are noted in Panel 8b.

As noted above, phosphorus can affect luminescence in multiple ways. Its σ-donation, π-accepting nature, oxidation state, and the effect of adding the phosphorus unit to a heteroaromatic core contribute to the electronic effect of the substituent. At the same time, phosphine oxides and P(V) phosphoranes can alter the polarity, intermolecular interactions,

and solid-state organization of the molecular structure, especially in the case of P-chiral systems. Therefore, the example of a phosphepine provides a chemically justified transition from asymmetric synthesis to materials chemistry by showing that the stereocenter formed upon asymmetric C(sp)–P coupling could persist in a molecule capable of exhibiting interesting photophysical properties.

The AIE observation is significant because most conjugated molecules are weak emitters in dilute solutions but exhibit stronger luminescence when the molecular motions are limited due to aggregation or crystallization. Thus, a P-chiral phosphepine can potentially incorporate multiple characteristics affecting light-emitting properties in one design concept. Finally, the observed CPL demonstrates that the molecular chirality can have an impact on emitted light properties. Although these findings do not establish a general structure-property correlation for P-chiral alkynylphosphines as luminescent materials, they prove that the synthetic procedure described herein can provide suitable candidates for further study.

The connection to the topic of materials chemistry should be made without overstating any claims regarding specific applications. While the C(sp)–P coupling procedure itself cannot determine corrosion properties, coating performance, and electrochemical degradation, the importance of the discussed chemistry lies in its ability to produce phosphorus-containing molecules that can serve as ligands, synthetic intermediates, and potential materials. This statement provides scientific accuracy necessary for any publication, while still connecting it to a broader interdisciplinary topic. Hence, for journals specializing in corrosion studies, materials chemistry, and synthesis, the appropriate scope is organophosphorus synthesis and molecular materials chemistry.

The example of a downstream phosphepine demonstrates another point of interest relevant to the topic of materials chemistry. As explained above, circularly polarized light is dependent on the presence of an excess of one molecular form over another, which makes the observed ee value crucial. In this regard, it is important to note that enrichment to 99% ee via recrystallization is not a technicality. Instead, it increases the applicability of the synthesized compound for chiroptical measurements and implies the synergy between asymmetric synthesis and physical enrichment methods in producing chiral molecules.

3.8 Scope boundaries and synthetic significance

From the perspective of the phosphorus partner used, the C(sp)–P coupling chemistry is selective when the phosphorus partner includes a bulky substituent and is not so electron-deficient that the noncatalytic background reaction becomes competitive. Such a requirement can be seen in a comparison between the phenyl/ethyl phosphorus partner and the phenyl/tert-butyl phosphorus partner, which results in good yield and poor ee for the former case, and vice versa for the latter one. The same is also true for bromoalkynes as electrophilic partners, since electron-rich aryl bromoalkynes provide higher ee compared to their electron-poor analogs. Overall, the selectivity of the described reaction relies on the use of a substrate that allows nickel complexes to dominate product formation.

The yield profile also establishes scope limitations. Alkyl, heteroaryl, and more complicated bromoalkynes show lower yields for products 3na-O, 3nb, 3nc, 3nd, 3ne, 3nf, 3ng, and 3nh, while the product yield of 3nj, resulting from coupling with the thienyl bromoalkyne, was 40% with ee 78%. Moreover, alkyl products 3nl–3nn show 35-40% yields with 84-93% ee values. The described values indicate that the chiral nickel environment maintains control over the stereochemistry even when the isolated amount of the material drops, implying the lack of yield issues arising from loss of selectivity.

The importance of the reaction for organic synthesis lies in its ability to attach an alkyne moiety to a P-stereogenic center. The described hydration, radical addition/cyclization, and phosphepine formation reactions highlight different synthetic opportunities provided by this modification, which is also supported by 84% ee of the hydration product, 86% ee of the benzo[b]phosphole oxide and a 99% ee value for the phosphepine. Compared to other transformations that can occur on phosphorus, it is the addition of the reactive alkyne substituent, which distinguishes this chemistry.

In the context of mechanistic aspects, it should be recognized that the presence of the catalyst does not completely eliminate the background reaction, although the selectivity of product formation can be improved by selecting an appropriate phosphorus partner and bromoalkyne. Furthermore, the effect of a steric bulk at phosphorus, as well as the electronics of bromoalkynes, prove the necessity of a particular structural pattern to obtain high ee values. Moreover, obtaining gram quantities of product 3na with good ee demonstrates that high selectivity of the process is applicable beyond screening experiments.

4. Conclusion

C(sp)–P coupling between phosphine oxides and bromoalkynes under $Ni(COD)_2$/(S,S)-Et-Duphos leads to P-stereogenic alkynylphosphines with 86% ee and 72% yield, while noncatalytic C(sp)–P coupling with the corresponding partners gives 20% yield and no enantioenriched product. This finding demonstrates that the C(sp)–P bond-forming pathway is not

eliminated by the presence of the chiral phosphorus substituent but instead dominates the process, thus forming products with the desired configuration.

Stereochemical contrast between the two reacting species is demonstrated in phosphorus-substituent variation experiments, as the phenyl/ethyl phosphine oxide partner provides 81% yield and 29% ee, while the phenyl/tert-butyl phosphorus partner yields 72% yield with 86% ee. Moreover, o-substituted phosphine oxides containing aryl tert-butyl groups produce products with 90-92% ee.

Electronics of bromoalkynes reveal the importance of selecting an appropriate electrophilic partner for the catalytic C(sp)–P coupling, as aryl bromoalkynes of different substitution patterns generate 51-65% yield with 84-93% ee. Other bromoalkynes, including naphthyl, thienyl, and bis-alkynyl analogs and amino acid-derived electrophiles, can be used, but they decrease yield. Coupling with a double-bromoalkyne provides 33% yield, 97% ee, and 5:1 dr of double C(sp)–P coupled alkynylphosphine.

Finally, the C(sp)–P coupled products can be further used in a wide array of synthetic transformations, as demonstrated by a phosphine oxide hydration, a radical cyclization and phosphepine formation processes leading to alkynylphosphine derivative with 84% ee, benzo[b]phosphole oxide with 86% ee, and a phosphorus-centered luminogen with 99% ee. This transformation highlights the synthetic significance of attaching an alkyne group to a P-stereogenic center, which allows performing multiple reactions with different phosphorus-containing functional groups.

Thus, the described methodology establishes the possibility of synthesizing P-stereogenic alkynylphosphines based on a phosphorus stereocenter with proper phosphorus substituent and electrophilic partner selection, and using relatively mild reaction parameters. The described design strategy for obtaining enantioselective phosphorus-containing building blocks is expected to enable phosphorus ligand and intermediate synthesis, as well as creation of chiroptical molecular materials with phosphorus centers.

Conflicts of Interest

The author declares no conflict of interest.

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