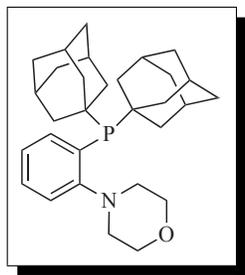


Bis(1-adamantyl)(2-morpholinophenyl)-phosphine (Mor-DalPhos)¹



[1237588-12-3] C₃₀H₄₂NOP (MW: 463.6)
 InChI = 1S/C30H42NOP/c1-2-4-28(27(3-1)31-5-7-32-8-6-31)
 33(29-15-21-9-22(16-29)11-23(10-21)17-29)30-18-24-
 12-25(19-30)14-26(13-24)20-30/h1-4,21-26H,5-20H2
 InChIKey = CCBRRSUORFMQCZ-UHFFFAOYSA-N

(ligand employed in transition metal-catalyzed reactions)

Alternate Name: di(1-adamantyl)-2-morpholinophenylphosphine.

Physical Data: mp 219–224 °C.

Solubility: soluble in most polar organic solvents.

Form Supplied in: White to pale yellow powder or crystals.

Also commercially available as preformed Au-ligand complexes such as (MeCN)(Mor-DalPhos)Au(I) SbF₆ and [Mor-DalPhos]Au(I)Cl.

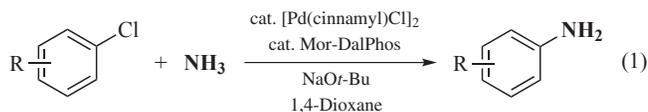
Analysis of Reagent Purity: NMR, Elemental Analysis.

Preparative Method: Pd-catalyzed cross-coupling of *N*-(2-bromophenyl)morpholine and diadamantyl phosphine.²

Handling, Storage, and Precautions: the phosphine is not particularly sensitive to air or moisture although precautions, such as storage under inert atmosphere in a cool place, should be taken during long-term storage.

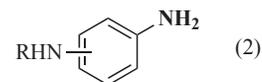
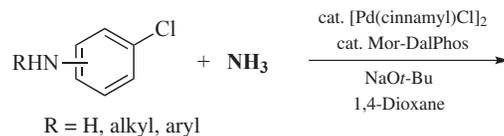
Bis(1-adamantyl)(2-morpholinophenyl)phosphine (Mor-DalPhos) is a phosphine ligand that has been employed in Pd-catalyzed cross-coupling reactions and Au-catalyzed hydroamination and [3+2] annulations. This ligand, when combined with an appropriate Pd-source, is particularly effective for promoting selective monoarylation processes between aryl electrophiles and nucleophiles such as ammonia, hydrazine, and acetone.

Pd-catalyzed Cross-coupling of Aryl Chlorides and Tosylates with Ammonia. Catalytic mixtures of Mor-DalPhos and [Pd(cinnamyl)Cl]₂ enable the selective monoarylation of ammonia, supplied as commercial 0.5 M dioxane stock solutions, employing aryl chlorides or aryl tosylates.² With catalyst loadings of 0.3–5 mol % Pd and 0.6–7.5 mol % ligand, at 50–110 °C, moderate to excellent yields are observed for a range of electronically and sterically diverse aryl and heteroaryl electrophiles (eq 1). Reactions with aryl tosylates proceed at room temperature. High chemoselectivity is observed for the coupling of ammonia in the presence of other amine functionality (eq 2). Reactions can be conducted with aryl chlorides at temperatures as low as 25 °C when using 5 mol % of a preformed (Mor-DalPhos)Pd(aryl)Cl complex.^{2,3}



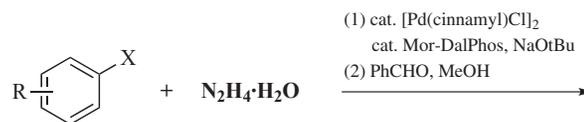
R = alkyl, aryl, olefin, ether, thioether, fluoride, amine

19 examples
55–99% yield



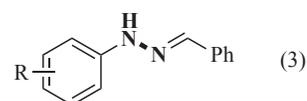
Six examples
61–97% yield

Pd-catalyzed Cross-coupling of Aryl Chlorides and Tosylates with Hydrazine. Mor-DalPhos and [Pd(cinnamyl)Cl]₂ was found to enable the selective cross-coupling of aryl chlorides and tosylates with hydrazine hydrate (eq 3).⁴ Moderate to excellent yields were reported for an array of substituted aryl and heteroaryl electrophiles after trapping of the aryl hydrazine with benzaldehyde to facilitate purification. 3-Chloropyridine and 6-chloroquinoline, substrates not readily amenable to nucleophilic aromatic substitution, can be coupled to hydrazine in good yields (69% and 81%, respectively). Substitution at the 2, 3, or 4 position of the aryl ring is tolerated, as is the presence of other NH-functionality; however, electron-rich aryl chlorides provide lower yields. Related cross-coupling reactions with hydrazine have been conducted using continuous flow technology.⁵



X = Cl or OTs

R = alkyl, aryl, heteroaryl, ether, thioether, fluoride, amine

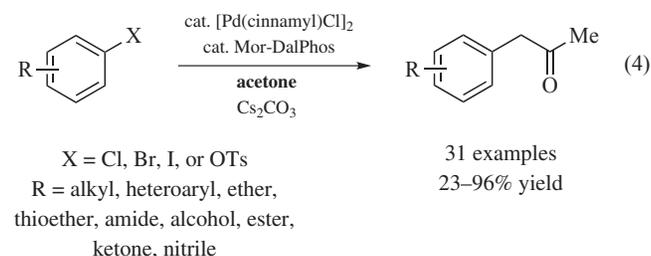


29 examples
27–97% yield

General and Chemoselective Pd-catalyzed Cross-coupling of Amines and Aryl Chlorides. The chemoselective cross-coupling of aminoaryl chlorides with amines as well as the selective monoarylation of polyamines employing Pd/Mor-DalPhos catalyst mixtures has been studied in detail.⁶ The following general reactivity trend was established for amine coupling partners: linear primary alkylamines and imines > unhindered electron-rich primary anilines, primary hydrazones, *N,N*-dialkylhydrazines, and cyclic primary alkylamines > unhindered electron-deficient primary anilines, α -branched acyclic primary alkylamines, hindered

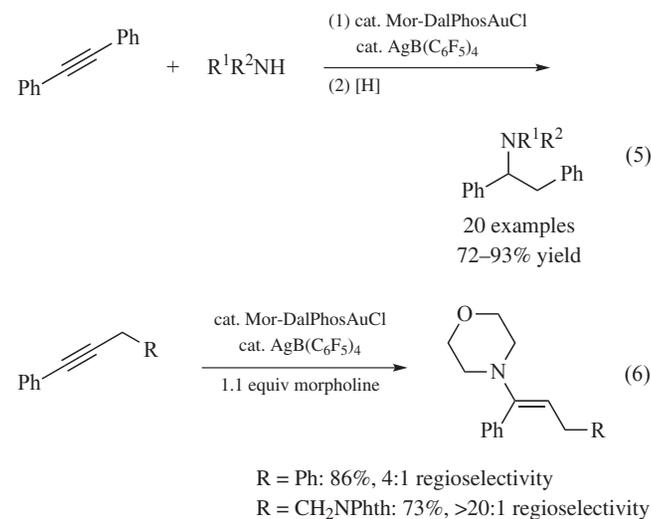
electron-rich primary anilines > cyclic and acyclic secondary dialkylamines, secondary alkyl/aryl and diarylamines, α,α -branched primary alkylamines, and primary amides. Efficient cross-coupling of primary or secondary amines can also be conducted using $[\text{Pd}(\text{cinnamyl})\text{Cl}]_2$ and Mor-DalPhos as the ligand under aqueous or solvent-free conditions.⁷

Pd-catalyzed α -Arylation of Carbonyl Compounds. The first direct, selective arylation of acetone was achieved using Mor-DalPhos in combination with $[\text{Pd}(\text{cinnamyl})\text{Cl}]_2$.⁸ Aryl chlorides, bromides, iodides, and tosylates can all be employed as arylating reagents using Cs_2CO_3 as the base in the presence of excess acetone. The reaction tolerates a wide range of functional groups (ester, ketone, nitrile, amide, sulfide, and alcohol) and heterocycles (eq 4).

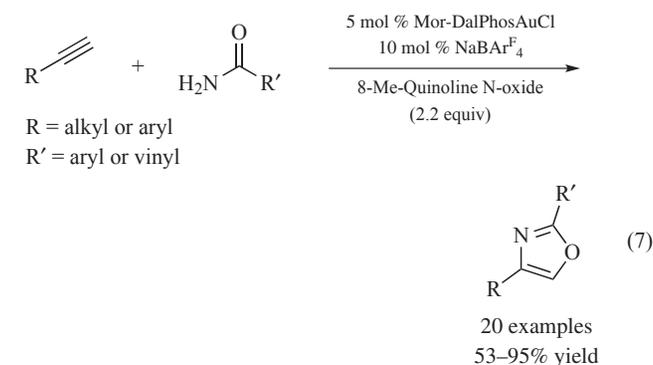


Acetophenones and *tert*-butyl malonates can also be coupled to aryl chlorides and bromides using Pd/Mor-DalPhos.⁹

Au-catalyzed Hydroamination of Alkynes. Mor-DalPhos can be used as a ligand to support cationic Au-catalysts for the hydroamination of internal alkynes with cyclic and acyclic secondary alkyl amines (generally at 2.5–5.0 mol % catalyst).¹⁰ Despite the relatively harsh reaction conditions (110 °C), nitrile, nitro, phenol, amide, ester, and carboxylic acid functional groups are tolerated, with the corresponding amines being isolated after reduction of the product enamine (eq 5). Unsymmetrical aryl alkynes can be hydroaminated with moderate to excellent regioselectivities to deliver the corresponding *E*-enamine (eq 6).¹⁰



Au-catalyzed [3+2] Annulations of Terminal Alkynes and Carboxamides. Zhang and coworkers relied on the unique reactivity afforded by Mor-DalPhos ligated-Au complexes to enable the formal [3+2] annulation of terminal alkynes with aryl carboxamides, generating 2,4-substituted oxazoles using 8-methylquinoline *N*-oxide as the oxidant.¹¹ Notably, nonchelating ligands such as biaryl phosphines or *N*-heterocyclic carbenes provide negligible yields under the optimized conditions. The reaction proceeds in good yield for both aryl and alkyl terminal alkynes as well as vinyl carboxamides (eq 7).



Related Reagents. Tri-*tert*-butylphosphine; dicyclohexyl-(4-(*N,N*-dimethylamino)phenyl)phosphine; 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (X-Phos); [1,3-bis-(2,6-diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)-palladium(II) dichloride (PEPPSI-*i*Pr); 1,2,3,4,5-pentaphenyl-1'-(di-*tert*-butylphosphino)ferrocene (Q-Phos); 5-(di-*tert*-butylphosphino)-1',3',5'-triphenyl-1'*H*-[1,4']bipyrazole (BippyPhos).

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