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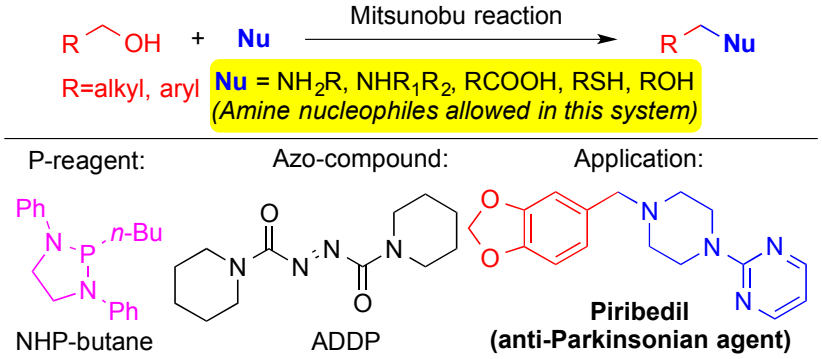
Mitsunobu Reaction Using Basic Amines as Pronucleophiles

Hai Huang, Jun Yong Kang*

Department of Chemistry and Biochemistry, University of Nevada Las Vegas, 4505 S. Maryland Parkway, Las Vegas, Nevada, 89154-4003, United States

E-mail: junyong.kang@unlv.edu



Abstract

A novel protocol for extending the scope of the Mitsunobu reaction to include amine nucleophiles to form C–N bonds through the utilization of *N*-heterocyclic phosphine-butane (NHP–butane) has been developed. Both aliphatic alcohols and benzyl alcohols are suitable substrates for C–N bond construction. Various acidic nucleophiles such as benzoic acids, phenols, thiophenol, and secondary sulfonamide also provide the desired products of esters, ethers, thioether, and tertiary sulfonamide with 43% to 93% yields. Importantly, C–N bond-containing pharmaceuticals, Piribedil and Cinnarizine, have been synthesized in one step from the commercial amines under this Mitsunobu reaction system.

Introduction

Owing to the mild reaction conditions and broad substrate scope, the Mitsunobu reaction has been widely recognized as an essential tool in organic synthesis for the substitution of primary or secondary alcohols with acidic pronucleophiles since its discovery in 1967.[1] This method has been broadly adopted in the synthesis of a majority of functional groups from alcohols and used in a key step of biologically active natural product synthesis to invert the stereochemistry of alcohols

with various nucleophiles.[2] Mitsunobu reaction enables the formation of C–O, C–N, C–S, and C–C bonds in presence of phosphines and azocompounds.[2a, b, 3] Despite these advantages, synthetic applications of Mitsunobu reaction still face two major hurdles: (1. Catalytic Process) the use of stoichiometric amount of phosphines and azocompounds as well as the generation of phosphine oxide and hydrazine by-products, (2. Expansion of Scope) the requirement of acidic pronucleophiles with the pKa below 11 for a successful transformation. Thus, numerous efforts have been continuously devoted to address these hurdles. For the hurdle (1), the use of a catalytic amount of phosphine reagents and azocompounds is a potential solution to reduce the generation of toxic wastes in the Mitsunobu reaction. Toy and co-workers reported the first hydrazine-based redox catalytic protocol of Mitsunobu reaction.[4] However, a limited substrate scope of only acidic pronucleophiles has remained unresolved. As an alternative strategy, Taniguchi group demonstrated azocarboxylate catalytic Mitsunobu reaction based on Fe(Pc) oxidation system in 2013.[5] Recently, the Aldrich group showcased a fully catalytic protocol using a catalytic loading of both phosphine oxides and arylhydrazinecarboxamides, but showed only one working example (with the highly acidic 4-nitrobenzoic acid nucleophile).[6] The scope of these catalytic Mitsunobu reactions continues to be limited to only highly acidic pronucleophiles. These catalytic protocols provide a foundation for potential solutions to overcome the use of stoichiometric amount of P-reagents and azocompounds; however, the expansion of the nucleophile scope to include nonacidic or basic nucleophiles still remains a key, unresolved challenge in Mitsunobu reaction.

Novel P-reagents and azocompounds have been developed to improve the efficiency of Mitsunobu reaction over the past decades. Selected examples[7] include a multipolymer system,[8] ADDP–TBP,[9] CMBP,[10] CMMP[11] and Ishikawa phosphorane.[12] Despite these important advances, the pKa restriction of pronucleophiles using a stable P-reagent has not been realized with non-aromatic nitrogen heterocycles. It is important to note that the stability of P-reagents is key due to the potential application toward a phosphine-catalyzed Mitsunobu reaction.

Compounds containing nitrogen heterocycles such as piperazine, morpholine, and piperidine are significant building blocks because of their both unique biological properties and broad pharmaceutical applications.[13] A large number of medicines containing nitrogen heterocycles such as cinnarizine,[14] flunarizine,[15] piribedil,[16] moclobemide,[17] oxatomide,[18] and fentanyl[19] have been synthesized (Fig 1). Thus, various synthetic methods have been established for C–N bond

formation to construct the nitrogen-containing heterocycles.[20] For example, multiple groups have employed a borrowing hydrogen strategy for the N-alkylation of amines using alcohols to introduce the C–N bond. While this approach has advantages over the traditional halogenated–alkylating reagents,[21] complex transition metal-ligand systems (e.g., Ru,[22] Ir,[23] Ni,[24] Pd,[25] and others[26]) are required. In addition, this approach often requires harsh reaction conditions (high reaction temperatures) and extra purification for the removal of metal impurities in final pharmaceuticals.[27] Thus, a mild, metal-free amination reaction of alcohols is an important, attractive transformation especially for a rapid synthesis of C–N bond containing pharmaceuticals.[28]

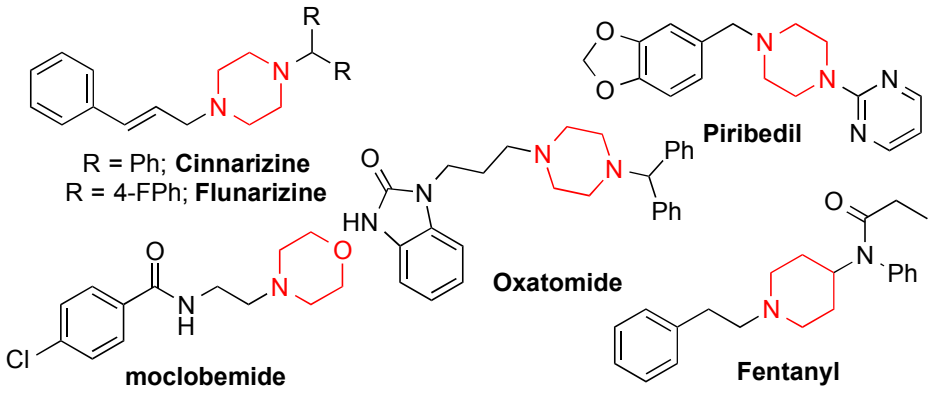
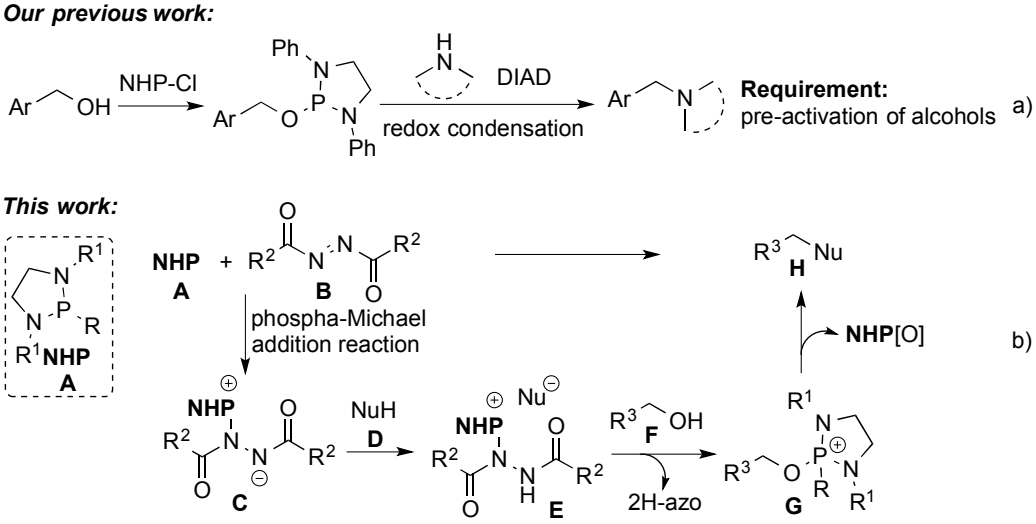


Fig 1. C-N bond containing pharmaceuticals

Our group has actively studied the reactivity of N-heterocyclic phosphine (NHP)-thioureas as bifunctional phosphonylation reagents.[29] With the strong nucleophilicity and versatile application of the NHP units in organic synthesis,[30] we turned our attention to explore their reactivity toward oxidation-reduction condensation reaction. Recently, we successfully demonstrated the utility of strongly nucleophilic diazaphosphites toward the redox condensation for carbon-heteroatom bond construction (Scheme 1, eq a).[31] However, this redox reaction of diazaphosphites needs pre-activation of alcohols and exhibits moderate overall yields from alcohol. Hence, to advance this methodology, we further explored the redox condensation reaction for C–N bond construction directly from alcohols and non-acidic amine pro-nucleophiles. The construction of C-N bonds using weakly acidic amines in the Mitsunobu reaction has remained underdeveloped due to the limitation of currently working pKa below 11. In addition to the pKa restriction of the pronucleophiles, the high nucleophilicity of amines can prohibit a successful C-N bond formation,

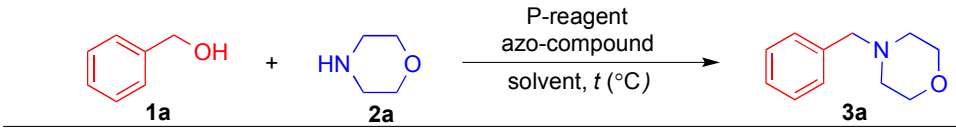
in which the undesired aza-Michael reaction competes with the desired phospha-Michael reaction. Therefore, amines can directly undergo aza-Michael reaction with azo-compound to form a triazine by-product,[32] preventing the desired phospha-Michael addition reaction between phosphines and azo-compounds. Identifying the potential problems with amine nucleophiles in the Mitsunobu reaction, we hypothesized that the highly nucleophilic phosphines would promote the desired phospha-Michael reaction. Hence, this limitation could be addressed by employing a highly nucleophilic NHP **A** to preferentially form the desired betaine intermediate **C**, which deprotonates pronucleophile **D** to generate an azo-phosphonium intermediate **E**. The alcohol **F** attacks the intermediate **E** to produce alkoxyphosphonium **G**, which undergoes nucleophilic substitution reaction with the pronucleophile **D** to afford the target product **H** (Scheme 1, eq b). Alternatively, amine pro-nucleophiles **D** could directly attack the alkoxyphosphonium intermediate **G** to form the C-N bond. Herein, we report that the highly nucleophilic NHPs allow a significant expansion of the scope of the Mitsunobu reaction to include previously restricted nitrogen nucleophiles in C–N bond formation with aliphatic alcohols.

Scheme 1. Exploration of NHPs for the Mitsunobu reaction



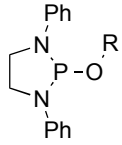
Results and discussion

Table 1. Optimized reaction conditions[a]

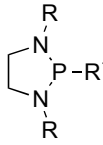


P-reagent

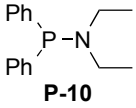
P-1: R, R^1 = Ph
P-2: R, R^1 = *n*-Bu
P-3: R = Ph, R^1 = *n*-Bu
P-4: R, R^1 = 4-MeOPh



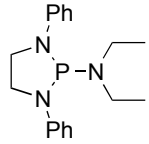
P-5: R = Et
P-6: R = *t*-Bu



P-7: R = *t*-Bu, R^1 = *n*-Bu
P-8: R = Ph, R^1 = *n*-Bu
P-9: R, R^1 = Ph

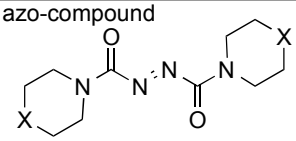


P-10

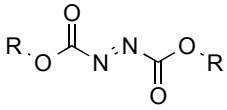


P-11

azo-compound



Azo-1: X = CH_2
Azo-2: X = O



Azo-3: R = Et
Azo-4: R = *i*-Pr
Azo-5: R = *t*-Bu

entry	P-reagent	azo-compound	solvent	*t* (°C)	yield (%)[b]
1	**P-1**	**Azo-1**	THF	80	7
2	**P-2**	**Azo-1**	THF	80	8
3	**P-3**	**Azo-1**	THF	80	7
4	**P-4**	**Azo-1**	THF	80	8
5	**P-5**	**Azo-1**	THF	80	44
6	**P-6**	**Azo-1**	THF	80	trace
7	**P-7**	**Azo-1**	THF	80	9
8	**P-8**	**Azo-1**	THF	80	99
9	**P-9**	**Azo-1**	THF	80	18
10	**P-10**	**Azo-1**	THF	80	<5
11	**P-11**	**Azo-1**	THF	80	21
12	**P-8**	**Azo-2**	THF	80	17
13	**P-8**	**Azo-3**	THF	80	39
14	**P-8**	**Azo-4**	THF	80	50
15	**P-8**	**Azo-5**	THF	80	58
16	**P-8**	**Azo-1**	DCM	40	92
17	**P-8**	**Azo-1**	toluene	80	96
18	**P-8**	**Azo-1**	CH_3CN	80	74
19	**P-8**	**Azo-1**	$CHCl_3$	60	50
20	**P-8**	**Azo-1**	DCE	80	>99 (94)[c]
21	**P-8**	**Azo-1**	DCE	40	>99 (91)[c]
22	**P-8**	**Azo-1**	DCE	rt	90 (85)[c]
23[d]	**P-8**	**Azo-1**	DCE	40	93
24[e]	**P-8**	**Azo-1**	DCE	40	>99 (92)[c]

[a]Reaction condition: benzyl alcohol **1a** (0.1 mmol), morpholine **2a** (1.5 equiv), **p-reagent** (1.5 equiv) and **azo-compound** (1.5 equiv) in solvent (0.5 mL) for 24 h. [b]yield was

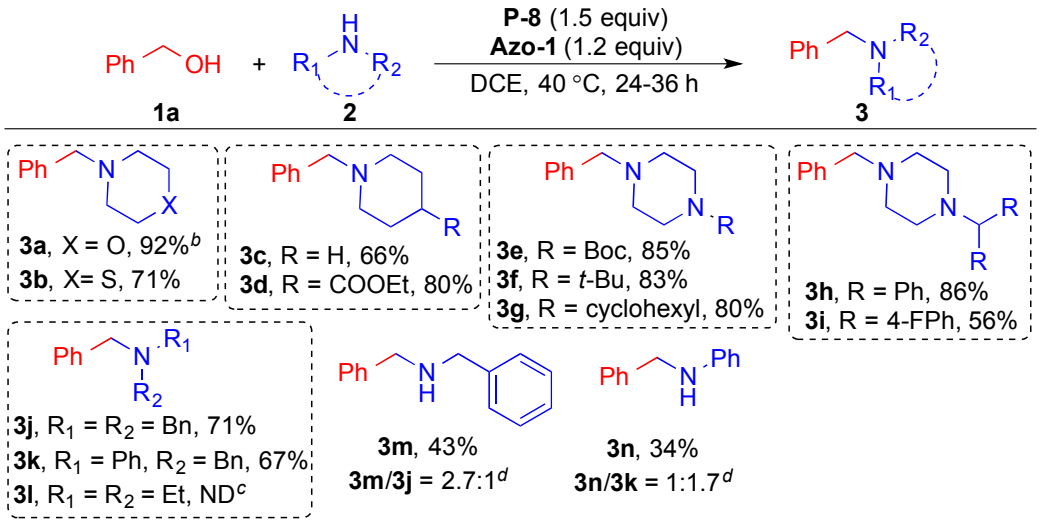
determined by crude ^{1}H NMR using 1,3,5-trimethylbenzene as internal standard. [c]Isolated yield. [d]1.2 equiv of **P-8**. [e]1.2 equiv of **Azo-1**.

To test our hypothesis, benzyl alcohol **1a** and morpholine **2a** were chosen as model substrates to exam the feasibility of C–N bond formation and the results are described in Table 1. **Azo-1** (1,1'-(Azodicarbonyl)dipiperidine) was first employed to screen P-reagents. Although TPP (**P-1**) and TBP (**P-2**) are common P-reagents in Mitsunobu reaction, they generated the corresponding product **3a** in only 7–8% yield by NMR (entries 1 and 2). The modification of **P-1** with stronger electron donating properties did not help to improve the reactivity, providing again 7–8% yield by NMR of **3a** (entries 3 and 4). Utilization of 2-ethoxy-1,3-diphenyl-1,3,2-diazaphospholidine **P-5** (originally developed for a phosphonylation reagent[29a] in our group) produced **3a** in an improved 44% NMR yield. Further modifications of **P-5** to **P-6** to improve the reactivity were unsuccessful due to the decomposition of the NHP–O*t*Bu **P-6** to NHP-oxide *via* the C–O bond cleavage. To prevent the decomposition process while maintaining the strong nucleophilicity of the NHP motif, we synthesized C–P bonded NHPs **P-7**, **P-8** and **P-9**. Among them, the NHP–butane **P-8** provided the desired product **3a** in 99% yield by NMR (entries 7–9). Both aminodiphenylphosphine **P-10** and phosphorus triamide **P-11** were inferior to the NHP-butane **P-8**, affording **3a** in 5% and 21% NMR yields, respectively (entries 10 and 11). With the optimized P-reagent **P-8** in hand, we screened other azocompounds **Azo-2**–**5,** but they were less effective (entries 12–15). Solvent study revealed that DCE is superior to DCM, toluene, CH_3CN, and $CHCl_3$. It is noteworthy that this reaction performs well at room temperature, providing the desired product **3a** with 85% yield (entry 22). Finally, the optimum reaction conditions were achieved with a slight excess of **P-8** (1.5 equiv) and **Azo-1** ADDP (1.2 equiv), furnishing the target product **3a** in 92% yield (entry 24).

With the optimum reaction conditions, we first explored the scope of amine nucleophiles (Scheme 2). Thio-morpoline provided the corresponding substitution product **3b** with 71% yield. Piperidine and an 4-ethyl ester-substituted piperidine afforded the desired products **3c** and **3d** in 66% and 80% yields, respectively. Various 4-substituted piperazines were also successfully employed in this reaction to give the corresponding products **3e**-**3g** in good yields. 1-Methylpiperazine derivatives are important scaffolds of biologically active compounds and they proved to be viable substrates, affording the desired products **3h** and **3i** in 86% and 56% yields, respectively. Moreover, noncyclic secondary amines such as dibenzyl amine **2j** and

N-benzylaniline **2k** were also successful in affording the desired products **3j** and **3k** in 71% and 67% yields, respectively. Interestingly, diethyl amine **2l** was not effective under the standard reaction conditions probably due to its higher basicity and unreacted **1a** was recovered. Finally, we demonstrated that this Mitsunobu reaction protocol is a useful alternative route for a direct synthesis of secondary amines from various primary amines (**2m** and **2n**), providing the corresponding secondary amine products **3m** and **3n** in 43% and 34% yields, respectively (with 2.7:1–1:1.7 ratio of secondary amines and tertiary amines).

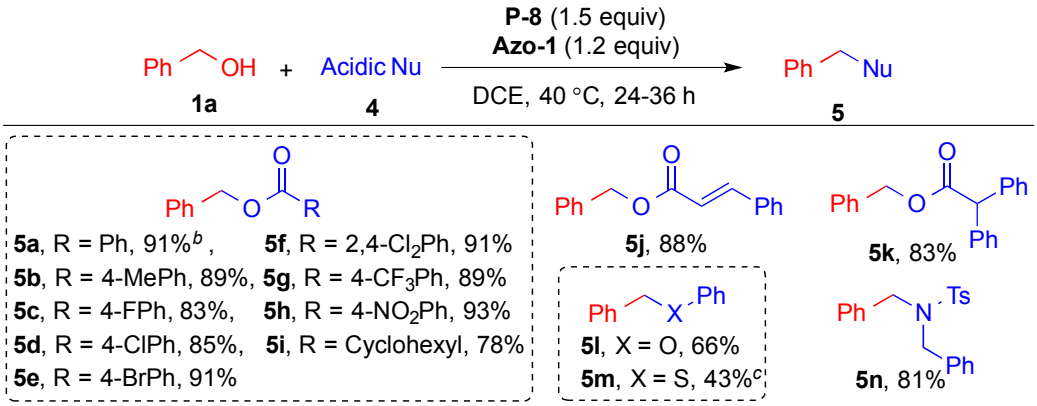
Scheme 2. Scope of amines[a]



[a]Reaction conditions: **1a** (0.1 mmol), **2** (1.5 equiv), **P-8** (1.5 equiv) and **Azo-1** (1.2 equiv) in DCE at 40 °C for 24–36 h. [b]Isolated yield (%). [c]Reaction run for 36 h. [d]Ratio assigned by using ^{1}H NMR of crude reaction mixture. ND = not determined.

Next, acidic nucleophiles were evaluated in this Mitsunobu reaction system (Scheme 3). Benzoic acids with various substituents **4a**–**4h** were proceeded smoothly to provide the desired products in good yields (**5a**–**5h**). Aliphatic acids such as cyclohexanecarboxylic acid **4i** also proved to be a useful substrate to furnish an ester product **5i** under the standard reaction conditions. A conjugated acid **4j** was also successful in producing the desired product **5j** in 88% yield. 2,2-Diphenylacetic acid **4k** provided the corresponding ester **5k** in 83% yield. The reaction of the benzyl alcohol **1a** with phenol **4l** gave the corresponding ether product **5l** in 66% yield. While a disulfide is a major product with thiol nucleophiles in conventional Mitsunobu reaction,[33] a thioether **5m** was obtained as a major product (43% yield) from thiophenol **4m**. A weakly acidic sulfonamide **4n** also furnished the desired product **5n** in 81% yield.

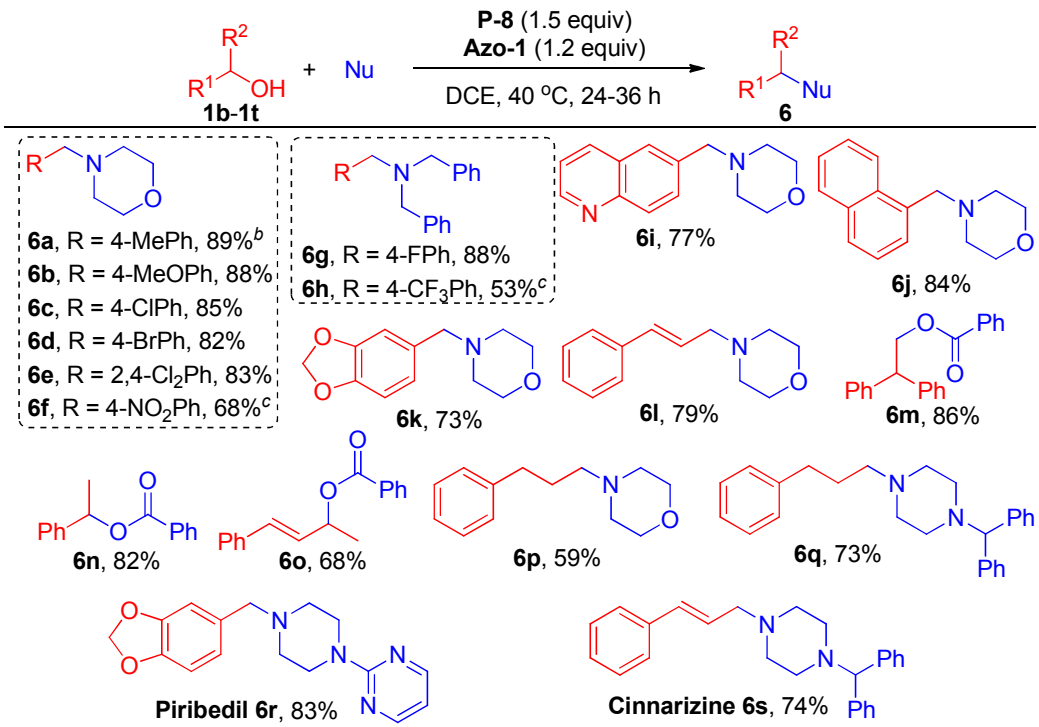
Scheme 3. Scope of acidic nucleophiles[a]



[a]Reaction conditions: **1a** (0.1 mmol), **4** (1.5 equiv), **P-8** (1.5 equiv) and **Azo-1** (1.2 equiv) in DCE at 40 °C for 24–36 h. [b]Isolated yield (%). [c]Reaction run for 36 h.

Finally, the scope of alcohols was investigated and the results are summarized in Scheme 4. Various substituted benzyl alcohols **1b-1i** were well-tolerated and afforded the corresponding products **6a-6h** in moderate to good yields. Benzyl alcohols containing electron-withdrawing groups provided lower yields than more electron rich alcohols. Polycyclic aromatic alcohols such as quinolin-6-yl-methanol **1j** and naphthalen-1-yl-methanol **1k** also turned out to be suitable substrates in this system and furnished the desired products **6i** and **6j** in 77% and 84% yields, respectively. Cinnamyl alcohol **1m** produced the allylamine product **6l** in 79% yield with complete α-regioselectivity.[34] The substitution product of an ester **6m** from 2,2-diphenylethanol **1n** was isolated in 86% yield without any appreciable elimination by-products. Secondary alcohols (**1o**, **1p**) were also suitable substrates for this reaction – providing the desired products **6n** and **6o** in 82% and 68% yields, respectively. Furthermore, aliphatic alcohols such as 3-phenylpropan-1-ol **1p** were also suitable coupling partners in this Mitsunobu reaction system – yielding the corresponding amine products **6p** and **6q** in 59% and 73% yields, respectively. This successful C–N bond formation between aliphatic alcohol and amines may rule out the possibility of formation of a carbocation intermediate, which is a suspected intermediate in Mitsunobu reaction employing allylic or benzylic alcohols.[35] Finally, we applied this Mitsunobu reaction to the synthesis of two C–N bond-containing pharmaceuticals Piribedil **6r** and Cinnarizine **6s**, which were successfully isolated in 83% and 74% yields, respectively.

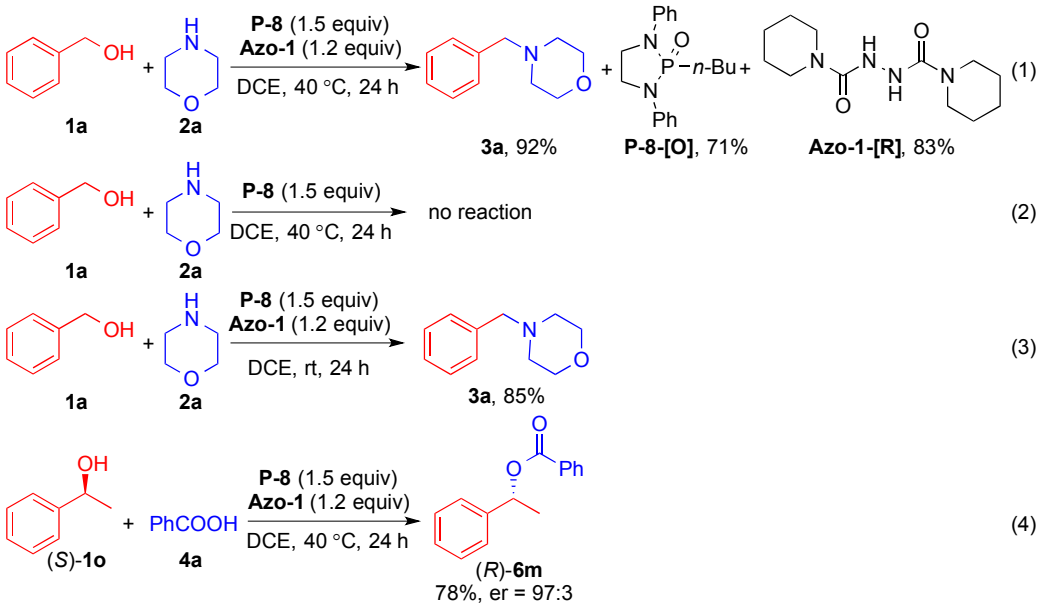
Scheme 4. Scope of alcohols[a]



[a]Reaction conditions: **1** (0.1 mmol), **Nu** (1.5 equiv), **P-8** (1.5 equiv) and **Azo-1** (1.2 equiv) in DCE at 40 °C for 24–36 h. [b]Isolated yield (%). [c]Reaction run for 36 h.

To gain insights into the mechanism for this transformation, an exhaustive isolation-characterization process of all products and by-products from the standard reaction was performed (Scheme 5). Along with the desired substitution product **3a**, we isolated *N*-heterocyclic phosphine oxide **P-8-[O]** and hydrazine **Azo-1-[R]** by-products in 71% and 83% yields, respectively (eq 1). In addition, there was no coupling product generated in the absence of azocompound **Azo-1**, confirming the requirement of azocompound (eq 2) for a successful coupling reaction. Furthermore, we demonstrated that this reaction maintains its high efficiency even at room temperature reaction conditions (eq 3). Finally, we evaluated the stereochemical outcome employing a chiral alcohol (*S*)-**1o** under our Mitsunobu reaction conditions. A complete inversion of configuration at the reaction center was observed when (*S*)-1-phenylethan-1-ol **1o** was treated with benzoic acid **4a** (eq 4). All the outcomes above suggest that this transformation follows the known Mitsunobu reaction mechanism.[36]

Scheme 5. Control experiments for mechanism study.



Conclusion

In summary, a NHP-butane (1,3,2-Diazaphospholidine) **P-8** has been rationally developed for the expansion of the substrate scope to include previously restricted nitrogen nucleophiles in Mitsunobu reaction. With the strong nucleophilicity of the NHP-butane **P-8**, non-acidic amine nucleophiles can undergo substitution reaction with aliphatic alcohols in the presence of ADDP. This transformation also provides an alternative entry to the synthesis of secondary amines. In addition, this reaction takes place under mild conditions and exhibits broad functional group tolerance. A practical application of this Mitsunobu reaction system for the synthesis of the C–N bond-containing pharmaceuticals Cinnarizine and Piribedil (anti–Parkinson agent) was also successfully demonstrated. Further studies on the catalytic Mitsunobu reaction employing the NHPs are underway in our Laboratory and will be reported in due course.

Experimental Section

General Information

All reactions were carried out under atmospheric conditions in oven-dried glassware with magnetic stirring bar. Dry solvents (THF, toluene, and DCM) were obtained by solvent purification system under argon. All commercially available reagents were used as received without further purification. Purification of reaction products was carried out by flash column chromatography using silica gel 60 (230–400 mesh). Analytical thin layer chromatography was

performed on 0.25 mm aluminum-backed silica gel 60-F plates. Visualization was accompanied with UV light and $KMnO_4$ solution. Concentration under reduced pressure refers to the removal of volatiles using a rotary evaporator attached to a dry diaphragm pump (10–15 mm Hg) followed by pumping to a constant weight with an oil pump (<300 mTorr). Infrared (IR) spectra were recorded on an IR spectrometer with KBr wafers or a film on KBr plate. High-resolution mass spectra (HRMS) were recorded on LCMS-IT-TOF mass spectrometer using ESI (electrospray ionization). ^{1}H NMR spectra were recorded in $CDCl_3$ on 400 MHz NMR spectrometer. The ^{1}H chemical shifts are referenced to residual solvent signals at δ 7.26 ($CHCl_3$) or δ 0.00 (TMS). ^{1}H NMR coupling constants (*J*) are reported in Hertz (Hz) and multiplicities are indicated as follows: s (singlet), bs (broad singlet), d (doublet), t (triplet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets). ^{13}C NMR spectra were proton decoupled and recorded in $CDCl_3$ on 100.5 MHz NMR spectrometer. The ^{13}C chemical shifts are referenced to solvent signals at δ 77.16 ($CDCl_3$). ^{31}P NMR spectra were proton decoupled and recorded in $CDCl_3$ on 162 MHz NMR spectrometer. ^{31}P chemical shifts are reported relative to 85% H_3PO_4 (0.00 ppm) as an external standard.

The procedure for the synthesis of P-reagents

Triphenylphosphine (**P-1**): commercial; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 15 H).

Tributylphosphine (**P-2**): commercial; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.46-1.34 (m, 18 H), 0.95-0.88 (m, 9 H).

Butyldiphenylphosphine (**P-3**)[37]: To a solution of diphenylphosphine (177 μL, 1.02 mmol), 1-bromobutane (107 μL, 1.0 mmol) in THF (15 mL) was added *t*-BuOK (301.4 mg, 2.69 mmol) at 0 °C under argon atmosphere. The resulting reaction mixture was refluxed for 22 h. After refluxing for 22 h, the reaction mixture was diluted with Et_2O (15 mL) and then washed with water (15 mL) and brine (15 mL). The organic phase was dried over Na_2SO_4 and Na_2SO_4 was filtered off. The organic solvent was evaporated under reduced pressure to give pure product **P-3** as a colorless oil; 181.6 mg, 75%; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48-7.36 (m, 4H), 7.35-7.28 (m, 6H), 2.07-2.01 (m, 2H), 1.49-1.36 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 139.0 (d, *J* = 12.7 Hz), 132.7 (d, *J* = 17.8 Hz), 128.3 (d, *J* = 9.7 Hz), 128.4, 28.1 (d, *J* = 15.7 Hz), 27.8 (d, *J* = 11.2 Hz), 24.3 (d, *J* = 13.4 Hz), 13.8.

***tris*-(4-Methoxyphenyl)phosphine** (**P-4**): commercial; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 6 H), 6.87 (d, *J* = 8.0 Hz, 6 H), 3.79 (d, *J* = Hz, 9 H).

2-chloro-1,3-diphenyl-1,3,2-diazaphospholidine (NHP-Cl):[29d] To a solution of N,N'-diphenylethylenediamine (2.12 g, 10 mmol) in DCM (40 mL) was added anhydrous triethylamine (2.8 mL, 20 mmol). The resulting solution was cooled to 0 °C and phosphorus trichloride (0.86 mL, 10 mmol) was added dropwise over a period of 10 min giving a brown solution with a small amount of white precipitate. The reaction mixture continued to stir at 0 °C for 30 min and then 2 h at room temperature. After stirring for 2 h at room temperature, the solvent was evaporated under reduced pressure to give orange-brown solid. The orange-brown solid was extracted with THF (3 × 20 mL). The combined organic solutions were evaporated under reduced pressure to give a brown free-flowing solid.

2-Ethoxy-1,3-diphenyl-1,3,2-diazaphospholidine (**P-5**):[29a] To a solution of NHP-Cl (549.2 mg, 2.0 mmol), Et_3N (0.42 mL, 3.0 mmol) in DCM (20 mL) was added ethanol (0.2 mL, 3.0 mmol) at 0 °C under argon atmosphere. The resulting reaction mixture was stirred at 0 °C for 30 min. After stirring for 30 min at 0 °C, it was allowed to warm up to room temperature and stirred for 2 h at room temperature. The reaction mixture was diluted with DCM (20 mL) and the resulting solution was washed with aq. $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and Na_2SO_4 was filtered off. After removal of the solvent under reduced pressure, the residue was purified by flash column chromatography on basic alumina (Hexane/EA = 5:1) to give corresponding product **P-5** as white solid; 181.1 mg, 32 %; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 8.4 Hz, 4H), 7.17-7.15 (m, 4H), 6.92 (t, *J* = 7.3 Hz, 2H), 3.89-3.77 (m, 4H), 3.64 (q, *J* = 7.0 Hz, 2H), 1.05 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 145.2 (d, *J* = 17.2 Hz), 129.3, 119.9 (d, *J* = 1.5 Hz), 115.3 (d, *J* = 14.2 Hz), 59.2, 47.3 (d, *J* = 9.7 Hz), 16.6 (d, *J* = 2.9 Hz).

2-(*tert*-Butoxy)-1,3-diphenyl-1,3,2-diazaphospholidine (**P-6**): To a solution of NHP-Cl (530.8 mg, 1.92 mmol) and Et_3N (0.4 mL, 2.88 mmol) in DCM (20 mL) was added 2-methylpropan-2-ol (0.26 mL, 2.88 mmol) at 0 °C under argon atmosphere. The resulting reaction mixture was stirred at 0 °C for 30 min. After stirring for 30 min at 0 °C, it was allowed to warm up to room temperature and stirred for 2 h at room temperature. The reaction mixture was diluted with DCM (20 mL) and the resulting solution was washed with aq. $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and Na_2SO_4 was filtered off. After removal of the solvent under reduced pressure, the residue was purified by flash column chromatography on basic alumina (Hexane/EA = 5:1) to give corresponding product **P-6** as white solid; 236.7 mg, 39 %; mp 111-112 °C

(decomp.); **IR** ν (KBr, cm^{-1}) 3038, 2954, 2895, 1600, 1502, 1491, 1476, 1302, 1287, 1224, 1133, 1036, 981, 784; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 4H), 7.30-7.24 (m, 4H), 7.08 (ddd, *J* = 8.2, 3.0, 1.2 Hz, 2H), 6.88 (t, *J* = 7.2 Hz, 2H), 3.92-3.82 (m, 2H), 3.68-3.56 (m, 2H), 1.19 (d, *J* = 0.8 Hz, 9H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 145.4 (d, *J* = 17.1 Hz), 129.1, 119.5 (d, *J* = 1.5 Hz), 116.0 (d, *J* = 13.4 Hz), 74.7 (d, *J* = 7.4 Hz), 46.4 (d, *J* = 8.2 Hz), 31.0 (d, *J* = 7.5 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 106.0 ppm. HRMS (ESI-TOF) m/z: found $[M + H]^+$ values corresponding to N^1,N^2-diphenylethane-1,2-diamine; $[M + H]^+$ Calcd for $C_{14}H_{17}N_2$: 213.1386; found: 213.1378.

1,3-di-*tert*-Butyl-2-butyl-1,3,2-diazaphospholidine (**P-7**): To a solution of NHP-Cl (142.2 mg, 0.6 mmol) in Et_2O (4 mL) was added *n*-BuLi (1.24 M in hexane, 0.49 mL) at –78 °C under argon atmosphere. The resulting reaction mixture was allowed to warm up slowly to room temperature. After stirring for 15 h at room temperature, the reaction mixture was diluted with Et_2O (10 mL) and the resulting solution was washed with aq. $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and Na_2SO_4 was filtered off. The organic solvent was evaporated under reduced pressure to give crude product **P-7** as colorless oil; 95.7 mg, 64%; **IR** ν (KBr, cm^{-1}) 2963, 2933, 2873, 1465, 1392, 1378, 1363, 1272, 1248, 1220, 1209, 1059, 978; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.16-3.08 (m, 2H), 3.07-2.99 (m, 2H), 1.40-1.20 (m, 6H), 1.18 (s, 18H), 0.89 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 53.0 (d, *J* = 17.8 Hz), 46.9 (d, *J* = 7.4 Hz), 35.5 (d, *J* = 21.6 Hz), 29.8 (d, *J* = 9.7 Hz), 26.7 (d, *J* = 15.7 Hz), 24.3 (d, *J* = 11.9 Hz), 14.0; **^{31}P NMR** (162 MHz, $CDCl_3$): δ 94.8 ppm; **HRMS** (ESI-TOF): found $[M + H]^+$ values corresponding to 1,3-di-*tert*-butyl-2-butyl-1,3,2-diazaphospholidine 2-oxide; $[M + H]^+$ Calcd for $C_{14}H_{32}N_2OP$: 275.2247; Found: 275.2253.

2-Butyl-1,3-diphenyl-1,3,2-diazaphospholidine (**P-8**): To a solution of NHP-Cl (828 mg, 3.0 mmol) in Et_2O (15 mL) was added *n*-BuLi (1.3 M in hexane, 2.3 mL) at –78 °C under argon atmosphere. The resulting reaction mixture was allowed to warm up slowly to room temperature. After stirring for 5 h at room temperature, the reaction mixture was diluted with Et_2O (20 mL) and the resulting solution was washed with aq. $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and Na_2SO_4 was filtered off. The organic solvent was evaporated under reduced pressure to give crude product **P-8** as white solid; 712.3 mg, 81%; **IR** ν (KBr, cm^{-1}) 3059, 2958, 2870, 1597, 1496, 1298, 1284, 1112, 1091, 991, 925; mp 201-202 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28-7.22 (m, 4H), 7.02-6.97 (m, 4H), 6.81 (tt, *J* = 7.6, 0.8 Hz, 2H), 3.77 (t, *J* = 2.4 Hz, 4H),

1.62-1.56 (m, 2H), 1.42-1.26 (m, 4H), 0.81 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 146.6 (d, J = 17.1 Hz), 129.2 (d, J = 1.5 Hz), 118.4 (d, J = 2.2 Hz), 115.3 (d, J = 14.9 Hz), 46.9 (d, J = 8.9 Hz), 31.6 (d, J = 32.7 Hz), 25.8 (d, J = 14.1 Hz), 24.3 (d, J = 9.7 Hz), 13.8; **^{31}P NMR** (162 MHz, $CDCl_3$): δ 95.6 ppm; **HRMS** (ESI-TOF) m/z: $[M+K]^+$ Calcd for $C_{18}H_{23}N_2PK$: 337.1230; Found: 337.1235.

1,2,3-Triphenyl-1,3,2-diazaphospholidine (**P-9**): To a solution of diamine (424.5 mg, 2.0 mmol) and Et_3N (0.56 mL, 4.0 mmol) in DCM (10 mL) was added dichloro(phenyl)phosphine (0.27 mL, 2.0 mmol) at –78 °C under argon atmosphere. The resulting reaction mixture was allowed to warm up slowly to room temperature and it was stirred for 2 h at room temperature. After stirring for 2 h at room temperature, the reaction mixture was diluted with DCM (20 mL) and the resulting solution was washed with aq. $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4 and Na_2SO_4 was filtered off. After removal of the solvent under reduced pressure, the residue was purified by flash column chromatography on basic alumina (Hexane/EA = 3:1) to give corresponding product **P-9** as white solid; 236 mg, 37%; mp 233-235 °C; **IR** ν (KBr, cm^{-1}) 3066, 3023, 2862, 1596, 1496, 1296, 1288, 1185, 1115, 1088, 937, 740; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 2H), 7.29-7.22 (m, 7H), 7.06-7.01 (m, 4H), 6.84 (tt, J = 7.2, 0.8 Hz, 2H), 3.84-3.74 (m, 2H), 3.68-3.58 (m, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 146.2 (d, J = 17.1 Hz), 140.7 (d, J = 39.5 Hz), 129.6, 129.5 (d, J = 7.5 Hz), 129.3, 128.2 (d, J = 4.5 Hz), 119.1 (d, J = 2.2 Hz), 115.8 (d, J = 14.1 Hz), 46.8 (d, J = 8.2 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 82.8 ppm; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{20}N_2P$: 319.1359; Found: 319.1357.

***N*,*N*-Diethyl-1,1-diphenylphosphinamine** (**P-10**):[38] To a solution of diphenylphosphine (180 µL, 1.0 mmol) and Et_3N (155µL, 1.1 mmol) in Et_2O (2.0 mL) was added diethylamine (115 µL, 1.1 mmol) at 0 °C under argon atmosphere. The resulting reaction mixture was stirred for 10 min at 0 °C. After stirring for 10 min at 0 °C, it was allowed to warm up to room temperature and stirred for 14 h at room temperature. The reaction mixture was diluted with Et_2O (10 mL) and then it was filtered to give crude product **P-10** as white solid; 212.3 mg, 82%; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44-7.38 (m, 4H), 7.36-7.28 (m, 6H), 3.12-3.02 (m, 4H), 0.95 (t, J = 6.8 Hz, 6H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 140.4 (d, J = 14.1 Hz), 131.9 (d, J = 19.4 Hz), 128.1 (d, J = 13.4 Hz), 128.0, 44.3 (d, J = 15.6 Hz), 14.5 (d, J = 3.0 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 61.7 ppm.

***N,N*-Diethyl-1,3-diphenyl-1,3,2-diazaphospholidin-2-amine** (**P-11**): To a solution of NHP-Cl (276.1 mg, 1.0 mmol) and Et_3N (155μL, 1.1 mmol) in DCM (10 mL) was added diethylamine (115 μL, 1.1 mmol) at 0 °C under argon atmosphere. The resulting reaction mixture was stirred for 10 min at 0 °C. After stirring for 10 min at 0 °C, it was allowed to warm up to room temperature and stirred for 20 h at room temperature. After stirring for 20 h at room temperature, the reaction mixture was diluted with Et_2O (10 mL) and then it was filtered. The filtrate was concentrated to give crude product **P-11** as white solid; 103.1 mg, 33%; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29-7.24 (m, 4H), 7.07-7.02 (m, 4H), 6.84 (tt, *J* = 7.2, 1.2 Hz, 2H), 3.96-3.78 (m, 2H), 3.71-3.59 (m, 2H), 3.07-2.98 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 146.1 (d, *J* = 16.4 Hz), 129.0, 118.5 (d, *J* = 1.5 Hz), 115.1 (d, *J* = 14.2 Hz), 46.2 (d, *J* = 9.7 Hz), 39.7 (d, *J* = 19.4 Hz), 14.2 (d, *J* = 2.9 Hz); **^{31}P NMR** (162 MHz, $CDCl_3$): δ 95.6 ppm. **Note**: This compound should be used immediately due to its air sensitivity. **HRMS** (ESI-TOF) m/z: found $[M + H]^+$ values corresponding to 2-(diethylamino)-1,3-diphenyl-1,3,2-diazaphospholidine 2-oxide; $[M + H]^+$ Calcd for $C_{18}H_{25}N_3OP$: 330.1730; found: 330.1740.

The procedure for the Mitsunobu reaction

A mixture of alcohols (0.1 mmol), **Nu** (0.15 mmol), **P-8** (0.15 mmol), Azo-1 (0.12 mmol) and DCE (0.5 mL) in a 2 dram vial with a PTFE cap was stirred for 24-48 h at 40 °C while being monitored with TLC analysis. Upon completion, the reaction mixture was concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel to give corresponding products **3**, **5,** and **6**.

4-Benzylmorpholine (3a):[22c] Pale yellow oil; 16.2 mg, 92%; R_f 0.10 (v_{Hexane}/v_{EA}= 4:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34-7.29 (m, 4H), 7.29-7.23 (m, 1H), 3.71 (t, *J* = 4.8 Hz, 4H), 3.50 (s, 2H), 2.44 (t, *J* = 4.4 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 137.7, 129.2, 128.2, 127.1, 67.0, 63.5, 53.6.

4-Benzylthiomorpholine (3b):[39] Pale yellow oil; 13.7 mg, 71%; R_f 0.40 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (10/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 4H), 7.26-7.24 (m, 1H), 3.51 (s, 2H), 2.72-2.65 (m, 8H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 138.1, 129.0, 128.2, 127.1, 63.7, 54.9, 28.0.

1-Benzylpiperidine (3c):[22c] Pale yellow oil; 11.5 mg, 66%; R_f 0.20 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (5/1, with 2% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33-7.28 (m, 4H), 7.27-7.21 (m,

1H), 3.47 (s, 2H), 2.37 (s, 4H), 1.61-1.53 (m, 4H), 1.46-1.39 (m, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 138.6, 129.2, 128.1, 126.8, 63.9, 54.5, 25.9, 24.4.

Ethyl 1-benzylpiperidine-4-carboxylate (3d):[40] Pale yellow oil; 21.2 mg, 80%; R_f 0.30 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (6/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 4.4 Hz, 4H), 7.28-7.23 (m, 1H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.48 (s, 2H), 2.85 (td, *J* = 12.0, 3.2 Hz, 2H), 2.31-2.23 (m, 1H), 2.02 (dt, *J* = 11.2, 4.0 Hz, 2H), 1.91-1.83 (m, 2H), 1.82-1.70 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 175.2, 138.4, 129.0, 128.2, 126.9, 63.2, 60.2, 52.9, 41.2, 28.3, 14.2.

***tert*-Butyl 4-benzylpiperazine-1-carboxylate (3e)**:[41] Pale yellow oil; 23.5 mg, 85%; R_f 0.20 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (6/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 4.4 Hz, 4H), 7.29-7.23 (m, 1H), 3.51 (s, 2H), 3.42 (t, *J* = 4.8 Hz, 4H), 2.38 (t, *J* = 4.8 Hz, 4H), 1.46 (s, 9H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 154.8, 137.9, 129.1, 128.2, 127.1, 79.5, 63.0, 52.8, 28.4, 28.3.

1-Benzyl-4-(*tert*-butyl)piperazine (3f):[42] Pale yellow oil; 19.2 mg, 83%; R_f 0.10 (v_{EA}/v_{MeOH}= 95:5), v_{EA}/v_{MeOH} (95/5) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 4H), 7.27-7.21 (m, 1H), 3.51 (s, 2H), 2.60 (bs, 4H), 2.50 (bs, 4H), 1.46 (s, 9H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 138.1, 129.3, 128.1, 126.9, 63.1, 53.8, 45.6, 25.9, 21.9.

1-Benzyl-4-cyclohexylpiperazine (3g):[28a] Pale yellow oil; 20.6 mg, 80%; R_f 0.10 (v_{EA}/v_{MeOH}= 98:2), v_{EA}/v_{MeOH} (98/2) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 4.4 Hz, 4H), 7.28-7.22 (m, 1H), 3.51 (s, 2H), 2.63 (bs, 4H), 2.53 (bs, 4H), 2.27 (br, 1H), 1.94-1.76 (m, 4H), 1.65-1.58 (m, 1H), 1.30-1.05 (m, 5H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 138.0, 129.3, 128.2, 127.0, 63.6, 63.1, 53.3, 48.8, 28.8, 26.2, 25.8.

1-Benzhydryl-4-benzylpiperazine (3h):[43] White solid; 29.4 mg, 86%; R_f 0.40 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (9/1 to 4/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43-7.37 (m, 4H), 7.30-7.20 (m, 9H), 7.15 (tt, *J* = 7.2, 2.0 Hz, 2H), 4.22 (s, 1H), 3.51 (s, 2H), 2.47 (bs, 4H), 2.42 (bs, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 142.8, 138.1, 129.2, 128.4, 128.1, 128.0, 126.9, 126.8, 76.2, 63.1, 53.3, 51.9.

1-Benzyl-4-(bis(4-fluorophenyl)methyl)piperazine (3i):[44] White solid; 21.0 mg, 56%; R_f 0.20 ($v_{Hexane}/v_{EA}/v_{DCM}$= 8:1:4), $v_{Hexane}/v_{EA}/v_{DCM}$ (8/1/4) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.26 (m, 8H), 7.26-7.20 (m, 1H), 6.95 (tt, *J* = 8.4, 2.0 Hz, 4H), 4.21 (s, 1H), 3.51 (s, 2H),

2.46 (bs, 4H), 2.38 (bs, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 161.8 (d, J = 244.1 Hz), 138.3 (d, J = 2.9 Hz), 140.0, 129.3, 129.2, 128.1, 127.0, 115.3 (d, J = 21.6 Hz), 74.5, 63.0, 53.4, 51.7.

Tribenzylamine (3j):[22c] Pale yellow oil; 20.3 mg, 71%; R_f 0.50 (v_{Hexane}/v_{EA}= 8:1), v_{Hexane}/v_{EA} (10/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44-7.36 (m, 6H), 7.36-7.28 (m, 6H), 7.22 (tt, J = 7.2, 1.2 Hz, 3H), 3.55 (s, 6H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 139.6, 128.7, 128.2, 126.8, 57.9.

***N*,*N*-Dibenzylaniline (3k)**:[28a] Pale yellow oil; 18.3 mg, 67%; R_f 0.05 (v_{Hexane}/v_{EA}= 100:1), v_{Hexane}/v_{DCM} (20/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35-7.29 (m, 4H), 7.27-7.22 (m, 6H), 7.19-7.17 (m, 2H), 6.74 (d, J = 8.0 Hz, 2H), 6.70 (t, J = 7.2 Hz, 1 H), 4.65 (s, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 149.2, 138.6, 129.2, 128.6, 126.8, 126.6, 116.7, 112.4, 54.2.

Dibenzylamine (3m):[28a] Pale yellow oil; 8.5 mg, 43%; R_f 0.20 (v_{Hexane}/v_{EA}= 4:1), v_{Hexane}/v_{EA} (5/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 8H), 7.27-7.23 (m, 2H), 3.81 (s, 4H), 1.61 (s, 1H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 140.4, 128.4, 128.1, 126.9, 53.2.

***N*-Benzylaniline (3n)**:[28a] Pale yellow oil; 6.3 mg, 34%; R_f 0.40 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.31 (m, 4H), 7.30-7.29 (m, 1H), 7.20-7.19 (m, 2H), 6.71 (tt, J = 7.2, 1.2 Hz, 1H), 6.66-6.61 (m, 2H), 4.33 (s, 2H), 4.01 (s, 1H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 148.1, 139.4, 129.3, 128.6, 127.5, 127.2, 117.5, 112.8, 48.3.

Benzyl benzoate (5a):[45] Pale yellow oil; 19.3 mg, 91%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10-8.06 (m, 2H), 7.58-7.53 (m, 1H), 7.47-7.31 (m, 7H), 5.37 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 166.4, 136.0, 133.0, 129.7, 128.6, 128.4, 128.2, 128.1, 66.7.

Benzyl 4-methylbenzoate (5b):[45] Pale yellow oil; 20.1 mg, 89%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 7.2 Hz, 2H), 7.41-7.30 (m, 3H), 7.23 (d, J = 8.0 Hz, 2H), 5.35 (s, 2H), 2.40 (s, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 166.5, 143.7, 136.2, 129.7, 129.1, 128.6, 128.2, 128.1, 127.4, 66.5, 21.6.

Benzyl 4-fluorobenzoate (5c):[46] Pale yellow oil; 19.1 mg, 83%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12-8.06 (m, 2H), 7.46-7.32 (m, 5H), 7.14-7.07 (m, 2H), 5.35 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 165.8 (d, J = 253.0 Hz), 165.4, 135.9, 132.2 (d, J = 9.7 Hz), 128.6, 128.3, 128.2, 126.4 (d, J = 3.0 Hz), 115.5 (d, J = 22.3 Hz), 66.8.

Benzyl 4-chlorobenzoate (5d):[45] Pale yellow oil; 20.9 mg, 85%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.46-7.32 (m, 7H), 5.35 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 165.6, 139.5, 135.8, 131.1, 128.7, 128.6, 128.5, 128.4, 128.2, 66.9.

Benzyl 4-bromobenzoate (5e):[45] Pale yellow oil; 26.4 mg, 91%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.93 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.57 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.45-7.32 (m, 5H), 5.35 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 165.7, 135.8, 131.7, 131.2, 129.0, 128.6, 128.4, 128.2, 128.1, 66.9.

Benzyl 2,4-dichlorobenzoate (5f):[46] Pale yellow oil; 25.5 mg, 91%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.4 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.46-7.42 (m, 2H), 7.41-7.32 (m, 3H), 7.28 (dd, *J* = 8.8, 2.0 Hz, 1H), 5.36 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 164.5, 138.4, 135.3, 135.1, 132.6, 131.0, 128.6, 128.5, 128.4, 128.1, 127.0, 67.4.

Benzyl 4-(trifluoromethyl)benzoate (5g):[45] Pale yellow oil; 24.9 mg, 89%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20-8.16 (m, 2H), 7.72-7.68 (m, 2H), 7.47-7.33 (m, 5H), 5.39 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 165.2, 135.5, 134.5 (d, *J* = 32.7 Hz), 133.3 (d, *J* = 1.5 Hz), 130.1, 128.7, 128.5, 128.3 (d, *J* = 1.5 Hz), 125.4 (q, *J* = 3.7 Hz), 123.6 (d, *J* = 271.6 Hz), 67.2.

Benzyl 4-nitrobenzoate (5h):[45] White solid; 24.0 mg, 93%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30-8.22 (m, 4H), 7.48-7.34 (m, 5H), 5.41 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 164.5, 135.5, 135.2, 130.8, 128.7, 128.6, 128.4, 123.53, 123.52, 67.6.

Benzyl cyclohexanecarboxylate (5i):[46] Pale yellow oil; 16.9 mg, 78%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H), 5.11 (s, 2H), 2.40-2.30 (m, 1H), 1.97-1.89 (m, 2H), 1.79-1.71 (m, 2H), 1.67-1.60 (m, 1H), 1.52-1.41 (m, 2H), 1.34-1.16 (m, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 175.9, 136.3, 128.5, 128.0, 127.9, 65.9, 43.2, 29.0, 25.7, 25.4.

Benzyl cinnamate (5j):[46] Pale yellow oil; 20.9 mg, 88%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 16.0 Hz, 1H), 7.53-7.49 (m, 2H),

7.44-7.31 (m, 8H), 6.49 (d, J = 16.0 Hz, 1H), 5.25 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 166.8, 145.2, 136.1, 134.4, 130.3, 128.9, 128.6, 128.3, 128.2, 128.1, 117.9, 66.4.

Benzyl 2,2-diphenylacetate (5k):[47] White solid; 25.0 mg, 83%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34-7.23 (m, 15H), 5.18 (s, 2H), 5.07 (s, 1H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 172.3, 138.6, 135.7, 128.6, 128.5, 128.4, 128.2, 128.1, 127.3, 66.9, 57.0.

(Benzyloxy)benzene (5l):[39] Pale yellow oil; 12.2 mg, 66%; R_f 0.10 (v_{Hexane}/v_{EA}= 100:0), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.2 Hz, 2H), 7.41-7.36 (m, 2H), 7.34-7.26 (m, 3H), 7.00-6.94 (m, 3H), 5.07 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 158.8, 137.1, 129.5, 128.6, 127.9, 127.5, 120.9, 114.8, 69.9.

Benzyl(phenyl)sulfane (5m):[48] Pale yellow oil; 8.6 mg, 43%; R_f 0.10 (v_{Hexane}/v_{EA}= 100:0), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32-7.20 (m, 9H), 7.17 (tt, J = 7.6, 1.2 Hz, 1H), 4.12 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 137.4, 136.3, 129.8, 128.8, 128.7, 128.5, 127.1, 126.3, 39.0.

***N*,*N*-dibenzylaniline (5n)**:[49] White solid; 28.4 mg, 81%; R_f 0.20 (v_{Hexane}/v_{EA}= 10:1), v_{Hexane}/v_{EA} (15/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (dt, J = 8.0, 1.6 Hz, 2H), 7.29 (d, J = 7.6 Hz, 2H), 7.23-7.18 (m, 6H), 7.08-7.03 (m, 4H), 4.31 (s, 4H), 2.44 (s, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 143.2, 137.7, 135.7, 129.7, 128.6, 128.4, 127.6, 127.2, 50.5, 21.5.

4-(4-Methylbenzyl)morpholine (6a):[50] Pale yellow oil; 17.0 mg, 89%; R_f 0.10 (v_{Hexane}/v_{EA}= 4:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 3.70 (t, J = 4.8 Hz, 4H), 3.46 (s, 2H), 2.43 (t, J = 4.8 Hz, 4H), 2.33 (s, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 136.7, 134.6, 129.2, 128.9, 67.0, 63.2, 53.6, 21.1.

4-(4-methoxybenzyl)morpholine (6b):[50] White solid; 19.2 mg, 88%; R_f 0.10 (v_{Hexane}/v_{EA}= 4:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (dt, J = 8.8, 2.4 Hz, 2H), 6.85 (dt, J = 8.4, 2.0 Hz, 2H), 3.80 (s, 3H), 3.70 (t, J = 4.8 Hz, 4H), 3.44 (s, 2H), 2.42 (t, J = 4.8 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 158.8, 130.3, 129.7, 113.6, 67.0, 62.8, 55.2, 53.5.

4-(4-Chlorobenzyl)morpholine (6c):[50] Pale yellow oil; 17.7 mg, 85%; R_f 0.10 (v_{Hexane}/v_{EA}= 4:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33-7.24 (m, 4H),

3.70 (t, J = 4.4 Hz, 4H), 3.45 (s, 2H), 2.42 (t, J = 4.8 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 136.4, 132.8, 130.4, 128.4, 67.0, 62.6, 53.5.

4-(4-Bromobenzyl)morpholine (6d):[39] Pale yellow oil; 21.0 mg, 82%; R_f 0.10 (v_{Hexane}/v_{EA}= 4:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (dt, J = 8.4, 2.0 Hz, 2H), 7.23-7.19 (m, 2H), 3.70 (t, J = 4.8 Hz, 4H), 3.44 (s, 2H), 2.42 (t, J = 4.8 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 136.9, 131.3, 130.8, 120.9, 66.9, 62.7, 53.5.

4-(2,4-Dichlorobenzyl)morpholine (6e):[51] Pale yellow oil; 20.4 mg, 83%; R_f 0.10 (v_{Hexane}/v_{EA}= 4:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (d, J = 8.4 Hz, 1H), 7.37 (d, J = 2.0 Hz, 1H), 7.22 (dd, J = 8.4, 2.4 Hz, 1H), 3.72 (t, J = 4.4 Hz, 4H), 3.57 (s, 2H), 2.50 (t, J = 4.4 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 134.9, 134.3, 133.2, 131.5, 129.2, 126.9, 67.0, 59.1, 53.6.

4-(4-Nitrobenzyl)morpholine (6f):[39] Pale yellow oil; 14.9 mg, 68%; R_f 0.10 (v_{Hexane}/v_{EA}= 4:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.19 (dd, J = 8.8, 1.2 Hz, 2H), 7.53 (dd, J = 8.0, 0.8 Hz, 2H), 3.73 (t, J = 6.0 Hz, 4H), 3.60 (s, 2H), 2.47 (t, J = 4.4 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 174.2, 145.9, 129.5, 123.5, 66.9, 62.5, 53.6.

***N*,*N*-Dibenzyl-1-(4-fluorophenyl)methanamine (6g)**:[28a] Pale yellow oil; 26.8 mg, 88%; R_f 0.50 (v_{Hexane}/v_{EA}= 8:1), v_{Hexane}/v_{EA} (10/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40-7.28 (m, 10H), 7.22 (tt, J = 7.2, 2.4 Hz, 2H), 6.99 (t, J = 8.8 Hz, 2H), 3.53 (s, 4H), 3.50 (s, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 161.9 (d, J = 243.3 Hz), 139.5, 135.3 (d, J = 3.0 Hz), 130.1 (d, J = 7.4 Hz), 128.7, 128.2, 126.9, 115.0 (d, J = 20.9 Hz), 57.9, 57.1.

***N*,*N*-Dibenzyl-1-(4-(trifluoromethyl)phenyl)methanamine (6h)**:[52] Pale yellow oil; 18.8 mg, 53%; R_f 0.50 (v_{Hexane}/v_{EA}= 8:1), v_{Hexane}/v_{EA} (10/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (dd, J = 19.2, 8.4 Hz, 4H), 7.39 (d, J = 6.8 Hz, 4H), 7.32 (t, J = 7.2 Hz, 4H), 7.26-7.21 (m, 2H), 3.59 (s, 2H), 3.56 (s, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 144.0, 139.1, 129.2 (d, J = 32.0 Hz), 128.8, 128.7, 128.3, 127.0, 125.1 (q, J = 3.7 Hz), 124.3 (d, J = 270.2 Hz), 58.1, 57.4.

4-(Quinolin-6-ylmethyl)morpholine (6i):[53] Pale yellow oil; 17.6 mg, 77%; R_f 0.20 (v_{Hexane}/v_{EA}= 1:2), v_{Hexane}/v_{EA} (1/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.90 (dd, J = 4.0, 1.6 Hz, 1H), 8.14 (dq, J = 8.0, 0.8 Hz, 1H), 8.09-8.05 (m, 1H), 7.75 (dd, J = 6.4, 2.0 Hz, 2H), 7.40 (dd, J = 8.0, 4.0 Hz, 1H), 3.74 (t, J = 4.8 Hz, 4H), 3.70 (s, 2H), 2.51 (t, J = 4.8 Hz, 4H); **^{13}C NMR**

(100.5 MHz, $CDCl_3$) δ 150.2, 147.8, 136.2, 135.8, 130.9, 129.4, 128.0, 127.4, 121.2, 66.9, 63.1, 53.6.

4-(Naphthalen-1-ylmethyl)morpholine (6j):[54] Pale yellow oil; 19.1 mg, 84%; R_f 0.40 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (8/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.82 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.78 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.54-7.46 (m, 2H), 7.44-7.36 (m, 2H), 3.90 (s, 2H), 3.69 (t, *J* = 4.8 Hz, 4H), 2.50 (t, *J* = 4.8 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 133.8, 133.6, 132.5, 128.4, 128.0, 127.5, 125.7, 125.6, 125.0, 124.8, 67.1, 61.6, 53.8.

4-(Benzo[*d*][1,3]dioxol-5-ylmethyl)morpholine (6k):[22c] Pale yellow oil; 16.1 mg, 73%; R_f 0.30 (v_{Hexane}/v_{EA}= 1:1), v_{Hexane}/v_{EA} (3/1, with 0.5% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.86 (s, 1H), 6.74 (d, *J* = 0.8 Hz, 2H), 5.94 (s, 2H), 3.70 (t, *J* = 4.8 Hz, 4H), 3.40 (s, 2H), 2.42 (t, *J* = 4.4 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 147.6, 146.6, 131.7, 122.2, 109.4, 107.8, 100.9, 67.0, 63.1, 53.5.

4-Cinnamylmorpholine (6l):[55] Pale yellow oil; 16.0 mg, 79%; R_f 0.15 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40-7.36 (m, 2H), 7.34-7.28 (m, 2H), 7.23 (tt, *J* = 6.8, 1.6 Hz, 1H), 6.54 (d, *J* = 16.0 Hz, 1H), 6.26 (dt, *J* = 15.6, 7.2 Hz, 1H), 3.74 (t, *J* = 4.4 Hz, 4H), 3.16 (dd, *J* = 6.8, 1.2 Hz, 2H), 2.51 (t, *J* = 4.4 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 136.8, 133.4, 128.6, 127.6, 126.3, 126.0, 67.0, 61.5, 53.7.

2,2-Diphenylethyl benzoate (6m):[56] Pale yellow oil; 26.2 mg, 86%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.52 (tt, *J* = 7.6, 1.2 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.35-7.28 (m, 8H), 7.26-7.21 (m, 2H), 4.86 (d, *J* = 7.6 Hz, 2H), 4.52 (t, *J* = 7.6 Hz, 1H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 166.4, 141.2, 132.9, 130.1, 129.5, 128.6, 128.3, 128.2, 126.8, 67.2, 49.9.

1-Phenylethyl benzoate (6n):[57] Pale yellow oil; 20.0 mg, 82%; R_f 0.30 (v_{Hexane}/v_{EA}= 16:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10-8.08 (m, 2H), 7.58-7.52 (m, 1H), 7.47-7.40 (m, 4H), 7.39-7.33 (m, 2H), 7.32-7.24 (m, 1H), 6.14 (q, *J* = 6.4 Hz, 1H), 1.67 (dd, *J* = 6.8, 1.6 Hz, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 165.8, 141.8, 132.9, 130.5, 129.6, 128.5, 128.3, 127.9, 126.0, 72.9, 22.4.

(*E*)-4-phenylbut-3-en-2-yl benzoate (6o):[58] Colourless oil; 17.1 mg, 68%; R_f 0.30 (v_{Hexane}/v_{EA}= 50:1), v_{Hexane}/v_{EA} (100/1) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10-8.06 (m, 2H), 7.58-7.52

(m, 1H), 7.46-7.37 (m, 4H), 7.31 (t, J = 7.6 Hz, 2H), 7.26-7.21 (m, 1H), 6.70 (d, J = 16.0 Hz, 1H), 6.31 (dd, J = 16.0, 6.4 Hz, 1H), 5.83-5.75 (m, 1H), 1.55 (d, J = 6.4 Hz, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 165.8, 136.4, 132.8, 131.7, 130.7, 129.6, 128.9, 128.6, 128.3, 127.9, 126.6, 71.6, 20.5.

4-(3-Phenylpropyl)morpholine (6p):[59] a threefold scale-up reaction, pale yellow oil; 36.2 mg, 59%; R_f 0.28 (v_{EA}/v_{MeOH} = 98:2), v_{EA}/v_{MeOH} (98/2, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 2H), 7.21-7.14 (m, 3H), 3.74-3.67 (m, 4H), 2.67-2.60 (m, 2H), 2.46-2.30 (m, 6H), 1.87-1.76 (m, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 142.0, 128.4, 128.3, 125.8, 67.0, 58.3, 53.7, 33.6, 28.2.

1-Benzhydryl-4-(3-phenylpropyl)piperazine (6q):[60] Pale yellow oil; 27.0 mg, 73%; R_f 0.34 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (3/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43-7.37 (m, 4H), 7.29-7.21 (m, 6H), 7.19-7.13 (m, 5H), 4.21 (d, J = 3.2 Hz, 1H), 2.64-2.57 (m, 2H), 2.53-2.30 (m, 10H), 1.83-1.75 (m, 2H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 142.8, 142.2, 128.4, 128.3, 127.9, 126.9, 125.7, 58.1, 53.5, 51.9, 33.8, 28.6.

2-(4-(Benzo[*d*][1,3]dioxol-5-ylmethyl)piperazin-1-yl)pyrimidine (6r):[22c] White solid; 24.7 mg, 83%; R_f 0.15 (v_{Hexane}/v_{EA}= 2:1), v_{Hexane}/v_{EA} (5/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (d, J = 4.4 Hz, 2H), 6.89 (s, 1H), 6.76 (d, J = 0.4 Hz, 2H), 6.46 (t, J = 4.8 Hz, 1H), 5.95 (s, 2H), 3.82 (t, J = 4.8 Hz, 4H), 3.45 (s, 2H), 2.48 (t, J = 5.2 Hz, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 161.6, 157.7, 157.6, 147.6, 146.6, 131.9, 122.2, 109.7, 109.5, 107.9, 100.9, 62.8, 52.8, 43.7.

1-Benzhydryl-4-cinnamylpiperazine (6s):[43] White solid; 27.2 mg, 74%; R_f 0.25 (v_{Hexane}/v_{EA}= 3:1), v_{Hexane}/v_{EA} (6/1, with 1% Et_3N) for column; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43-7.38 (m, 4H), 7.37-7.33 (m, 2H), 7.31-7.17 (m, 7H), 7.16 (tt, J = 7.6, 1.2 Hz, 2H), 6.50 (d, J = 15.6 Hz, 1H), 6.26 (dt, J = 15.6, 6.8 Hz, 1H), 4.23 (s, 1H), 3.16 (dd, J = 6.8, 1.2 Hz, 2H), 2.54 (bs, 4H), 2.45 (bs, 4H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 142.7, 136.9, 133.1, 128.5, 128.4, 127.9, 127.4, 126.9, 126.3, 76.1, 61.0, 53.4, 51.8, 45.8.

Control experiments

Isolation of by-products and characterization

A mixture of benzyl alcohol **1a** (10.5 μL, 0.1 mmol), morpholine **2a** (13.0 μL, 0.15 mmol), **P-8** (44.8 mg, 0.15 mmol), **Azo-1** (30.0 mg, 0.12 mmol) and DCE (0.5 mL) in a 2 dram vial with a

PTFE cap was stirred for 24 h at 40 °C. After stirring for 24 h at 40 °C, the reaction mixture was concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel to give corresponding products **3a** (16.3 mg, 92%), **P-8-[O]** (21.1 mg, 71%), and **Azo-1-[R]** (21.0 mg, 83%).

2-Butyl-1,3-diphenyl-1,3,2-diazaphospholidine-2-oxide (**P-8-[O]**): mp 197-198 °C; **IR** ν (KBr, cm^{-1}) 2957, 2928, 2864, 1600, 1500, 1489, 1280, 1232, 1188, 1122, 958, 754; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37-7.32 (m, 4H), 7.31-7.26 (m, 4H), 7.03 (tt, J = 7.2, 1.2 Hz, 2H), 3.88-3.77 (m, 4H), 2.30-2.20 (m, 2H), 1.28-1.12 (m, 4H), 0.70 (t, J = 6.8 Hz, 3H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 141.8 (d, J = 7.5 Hz), 129.5, 121.8, 116.5 (d, J = 4.5 Hz), 43.7 (d, J = 8.2 Hz), 27.7 (d, J = 111.6 Hz), 24.7 (d, J = 4.4 Hz), 23.2 (d, J = 18.6 Hz), 13.8; **^{31}P NMR** (162 MHz, $CDCl_3$): δ 33.9 ppm; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}N_2OP$: 315.1621; Found: 315.1620.

***N*'-(Piperidine-1-carbonyl)piperidine-1-carbohydrazide** (**Azo-1-[R]**):[61] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.09 (s, 2H), 3.40 (t, J = 5.6 Hz, 8H), 1.65-1.52 (m, 12H); **^{13}C NMR** (100.5 MHz, $CDCl_3$) δ 158.4, 44.9, 25.5, 24.4.

***Asymmetric synthesis of* (*R*)-1-phenylethyl benzoate, (*R*)-6m**

A mixture of (*S*)-1-phenylethanol (0.1 mmol) (*S*)-**1o**, benzoic acid (0.15 mmol) **4a**, **P-8** (0.15 mmol), **Azo-1** (0.12 mmol) and DCE (0.5 mL) in a 2 dram vial with a PTFE cap was stirred for 24 h at 40 °C. After stirring for 24 h at 40 °C, the reaction mixture was concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel to give corresponding (*R*)-1-phenylethyl benzoate (*R*)-**6m** in 78% yield. HPLC: Chiral Luxcellulose-1 column, 100% hexane, 1.0 mL/min, 254 nm: t_R (major) = 4.476 min; t_R (minor) = 4.958, 94% ee.

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Supporting Information

Spectral data of all new products. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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