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Note

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# Zwitterionic ring-opened oxyphosphonium species from the $Ph_3P$-$I_2$ mediated reactions of benzo[*d*]oxazol-2(3*H*)-ones with secondary amines

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## Abstract

Instead of the expected substituted 2-aminobenzo[*d*]oxazoles, relatively stable ring-opened oxyphosphonium betaines were isolated for the first time from the $Ph_3P$-$I_2$ mediated reactions of benzo[*d*]oxazol-2(3*H*)-ones with acyclic secondary amines. The structure of one of these compounds was unambiguously confirmed by single crystal X-ray analysis. Thermolysis of the betaines gave rise to 2-dialkylaminobenzoxazoles with concomitant loss of triphenylphosphine oxide suggesting their possible role as intermediates in an alternative reaction path.

**Keywords** Benzoxazolones; 2-Aminobenzoxazoles; Phosphonium betaines; Triphenylphosphine; Iodine, Aminolysis

Phosphonium-mediated synthesis has been a powerful tool for structure modification of a variety of organic compounds as well as for building up molecularly complex structures.[1] As a consequence, tremendous effort has been devoted to identifying the key phosphonium intermediates in order to better understand the mechanistic aspect of these reactions.

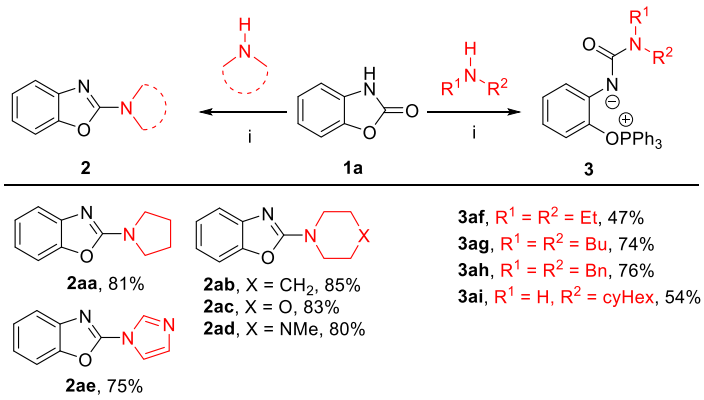
In a number of well-known organophosphorus synthetic methods, including the Mitsunobu,[2] Appel,[3] and Michaelis-Arbuzov[4] reactions, oxyphosphonium species have been proposed as key intermediates. However, these phosphorous species are often difficult to characterize due to their highly reactive nature and moisture sensitivity.[5]

In recent years, we have demonstrated the synthetic utility of the phosphonium coupling strategy with several substrates using a combination of inexpensive and commercially available $Ph_3P$ and $I_2$ as the key reagent.[6] However, despite several attempts we have been unable to isolate and identify any intermediate phosphine-containing species.

Remarkably, in our ongoing work involving $Ph_3P$-$I_2$-mediated deoxygenative amination of benzo[*d*]oxazol-2(3*H*)-ones **1**, instead of the expected substituted 2-aminobenzoxazoles **2**, we have isolated novel aryloxyphosphonium betaines **3** from the reaction using relatively hindered amines as nucleophiles. Herein, we wish to report our preliminary results emphasizing the first isolation and structural characterization of these molecules as well as their possible role as the reaction intermediates toward **2**.

When benzo[*d*]oxazol-2(3*H*)-one (**1a**) was treated with non-hindered cyclic amines under our previously described conditions,[6a] the expected aminobenzoxazoles **2aa**-**2ae** were obtained in high yields within 30 min (Scheme 1). In contrast, the reactions of **1a** with more sterically demanding acyclic amines including diethylamine, dibutylamine, dibenzylamine, and cyclohexylamine were sluggish giving only trace

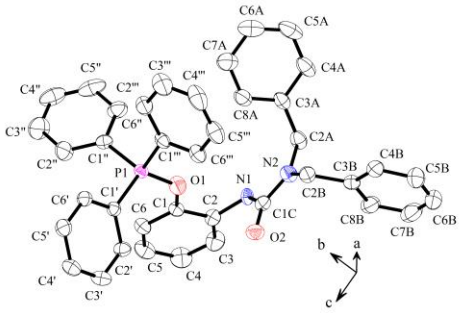
amounts of the corresponding 2-dialkylaminobenzoxazoles **2** along with the betaine products **3af-3ai** in significantly higher yields (Scheme 1).




**Scheme 1.** Reaction conditions: (i) **1a** (0.74 mmol), $PPh_3$ (1.11 mmol), $I_2$ (1.11 mmol), amine (0.89 mmol), $Et_3N$ (2.22 mmol), $CH_2Cl_2$ (5 mL), 0 – 25 $^oC$ , 30 min.

A single-crystal X-ray structural analysis of **3ah** unambiguously confirmed the proposed ring-opened salt free betaine structure. As shown in Figure 1(a), phosphorus arranges in a four-coordinated tetrahedral geometry with C–P–C angles in the range of 104.3(1) – 108.0(2)° and O–P–C angles in the range of 105.6(1)–116.9 (1)°. The O1–P1–C1' angle [116.9(1)°] and O1–P1–C1″ [114.9(1)°] are larger than that of O1–P1–C1''' [105.6(1)°], presumably due to steric repulsion involving the bulky aminophenol fragment. The P1–O1 distance [1.578(3) Å], is virtually similar to previous studies involving quasiphosphonium cations,[5c,5e,8] indicates a single P-O bond rather than a double bond P=O which should be in the range of 1.46(1)–1.484(1) Å.[9]

(a)




(b)

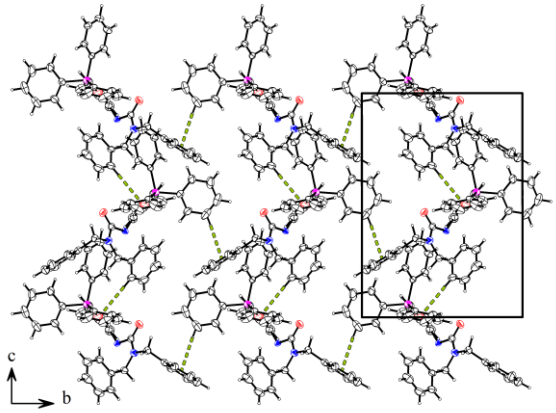



**Figure 1.** (a) Asymmetric unit of **3ah**. Hydrogen atoms were omitted for clarity. (b) Weak C–H…π hydrogen bonds (green dashed line) in crystal structure viewed along *a*-axis of the unit cell.

Since there is no counter anion observed in the X-ray structure, the deprotonation of the urea N–H reasonably occurred to compensate the charge of the quaternary phosphonium cation leading to a stable zwitterionic form.[10] The short C1C–O2 bond distance [1.203(4)Å] and C1C–N1–C2 bond angle [119.0(3)°] also indicates no significant delocalozation of the negative charge over the C=O π system.[8] Interestingly, two independent C–H…π hydrogen bonds important for conformation of the molecule and supramolecular packing were also observed (*see* Figure 1(b)).[11] The C3'–H3'…π hydrogen bond [2.6995(1)Å] presumably forced the benzyl group

(involving C3B–C4B–C5B–C6B–C7B–C8B) to rotate about C2B–C3B bond with torsion angle (N2–C2B–C3B–C4B) of 154.9(4)° to align the phenyl ring as the hydrogen bond acceptor, whereas another benzyl group (involving C3A-C4A–C5A–C6A–C7A–C8A) rotated in the opposite direction with torsion angle (N2–C2A–C3A–C4A) of 134.6(4)° as C4A–H4A…π hydrogen bond donor [2.9066(1) Å] (*see* Figures S2 and S3).

The NMR spectroscopic data of **3af-3ai** were similar and were all consistent with their indicated betaine structures. The $^{31}P\{^{1}H\}$ NMR spectroscopic data of these compounds ($\delta_p$ 3.24-6.34 ppm) indicated that they were tetracoordinate phosphorus species rather than pentacoordinate phosphoranes which should exhibit characteristic phosphorus signals in the negative chemical shift region.[7] Long range phosphorus-carbon couplings observed in compounds **3ag** and **3ah** as well as no $J_{P,C}$ correlation with the *N*-alkyl urea fragment further suggested that the phosphorus atom is directly attached to the former ring oxygen (O-1) of **1a** instead of the urea oxygen (Figure 2). Since the expected $^{31}P$ chemical shifts of aryloxyphosphonium iodide should be at *ca*. 60 ppm,[6h] the significant upfield shift of the $^{31}P$ signals of **3** strongly implied that the phosphorus atom is in close proximity to or under influence of the nearby negatively charged atom which is in consistent with the missing resonance of the NH proton in the $^{1}H$ NMR spectrum. It should be noted that although the interionic [$P1^{+}…N1^{-}$] distance measured from the X-ray structure of a well-ordered crystalline solid **3ah** is rather long (*ca*. 4.297 Å). In solution-state, it could become shorter depending on molecular conformations per free rotations about C1–O1 and/or C1c–N1 single bonds.

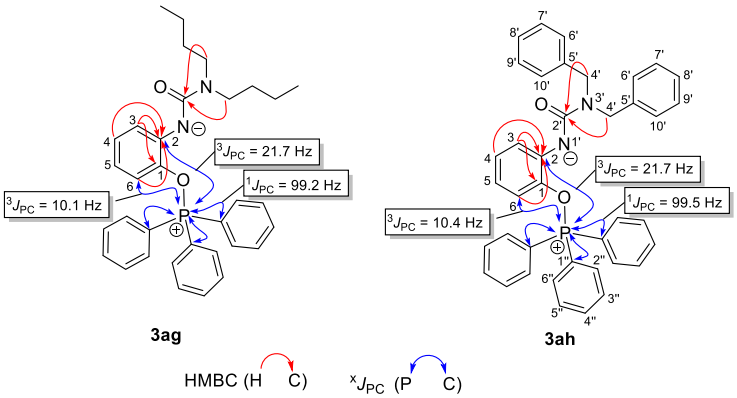
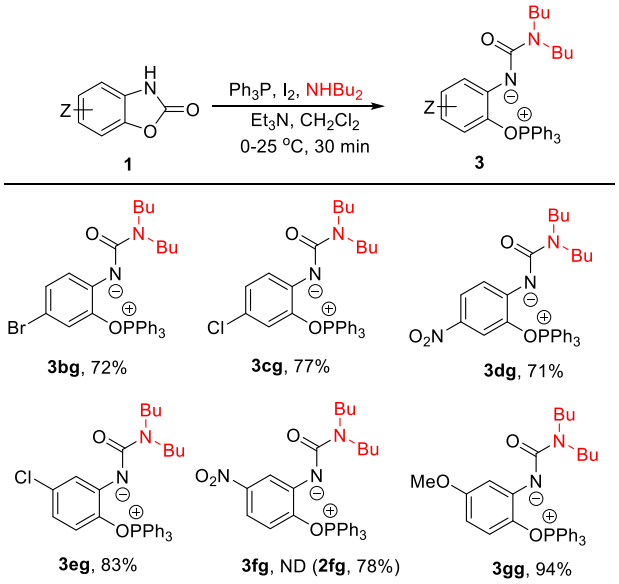


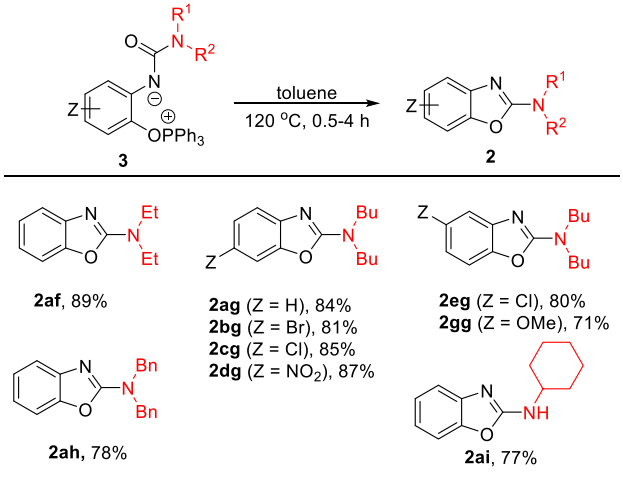

**Figure 2.** Key HMBC correlations and P-C NMR coupling constants ($J_{PC}$) observed in compounds **3ag** and **3ah**.

To examine possible electronic factors governing the formation of the zwitterion **3** in preference to the expected product **2**, the scope of the reaction was further investigated with other substituted benzoxazolone derivatives **1**. According to Scheme 2, the presence of substituent at the C6 position did not significantly affect the yield or stability of **3**. However, when a strong electron-withdrawing nitro group was located on the *para* position of the ring oxygen (at C5), **2fg** was rapidly formed without detectable amount of the expected betaine **3fg**. On contrary, **3gg** derived from the substrate bearing a strong electron-donating -OMe group at C5 position was obtained in high yield. This observation is not surprising since **3fg** would be destabilized preventing its formation and/or leading to rapid conversion to **2fg**.




**Scheme 2.** Formation of oxyphosphonium betaines **3**. Reaction conditions: **1** (0.74 mmol), $PPh_3$ (1.11 mmol), $I_2$ (1.11 mmol), dibutylamine (0.89 mmol), $Et_3N$ (2.22 mmol), $CH_2Cl_2$ (5 mL), 0 °C-RT, 30 min. ND = not detected.

With these results in hand, the possible synthesis of 2-dialkylaminobenzoxazoles **2** from **3** was investigated. According to Scheme 3, upon subject to heating in toluene in a pressure tube, all betaines **3** were converted into the corresponding 2-dialkylaminobenzoxazoles **2** in satisfactory yields although hydrolyzed products **1** could be observed in small amounts.



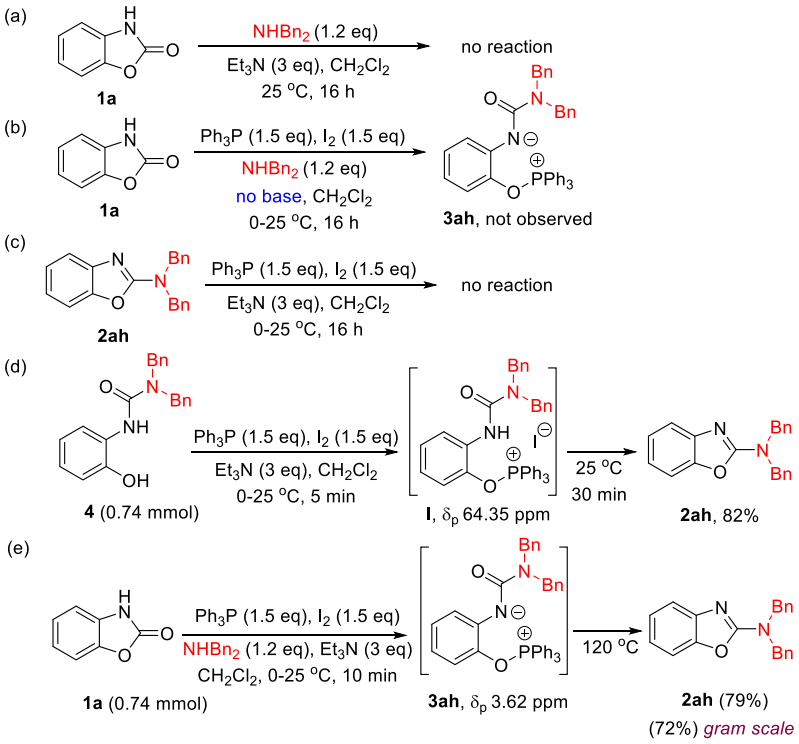
**Scheme 3.** Thermal decomposition of oxyphosphonium betaines **3**. Reaction conditions: **3** (0.50 mmol), toluene (2 mL), 120 $^{o}$C in 10 mL pressure tube.

To gain insight into the mechanism for the formation of **2** and **3**, a series of control experiments were carried out. As shown in Scheme 4(a), no conversion was observed when **1a** was treated with dibenzylamine in the absence of $Ph_3P$-$I_2$ indicating that the ring opening process requires activation by a $Ph_3P$-derived species. This result is consistent with other studies where aminolysis of unactivated cyclic carbamates generally requires more forcing conditions.[12] Additionally, no trace of **3ah** was detected in the absence of $Et_3N$ suggesting the formation of **3** is base-mediated (Scheme 4(b)). Moreover, when **2ah** was subjected to the $Ph_3P$-$I_2$ conditions, no conversion to **3ah** was observed implying that **2ah** is not a precursor toward this betaine (Scheme 4(c)).

Surprisingly, the reaction of 2-hydroxyphenylurea **4** without adding external dibenzylamine did not lead to the expected product **3ah** (Scheme 4(d)). Instead, **2ah** formed in high yield within 30 min at room temperature. Monitoring this reaction by $^{31}P\{^{1}H\}$ NMR revealed a strong phosphorus resonance at 64.35 ppm which could presumably be attributed to the presence of the unisolable intermediate **I** (*see* Figure S4).[5a,6h,13] The fact that this phosphonium species reacts rapidly in contrast to **3ah** indicates that zwitterionic **3ah** is thermodynamically more stable.

To determine the possible role of **3ah** as the reaction intermediate, a direct one-pot synthesis of **2ah** from **1a** was carried out by initial formation of **3ah**, followed by subjected to heating (Scheme 4(e)). Indeed, **2ah** was obtained in satisfactory yield even from gram scale synthesis. $^{31}P\{^{1}H\}$ NMR monitoring of the reaction before heating not only showed a resonance peak at 3.62 ppm corresponding to the betaine **3ah** but also the signal of **I** at *ca*. 64

ppm (*see* Figure S5) suggesting that the formation of **2ah** involves ring opening and ring closing mechanism.




**Scheme 4.** Control experiments

Due to the limited data, it is not conclusive at this point on how the ring opening and ring-closer proceed. Nevertheless, these observations implied that the reaction involved more complicated processes rather than a commonly proposed C=O bond activation-nucleophilic substitution sequence. Especially when the incoming nucleophile with sterically bulky group(s) is sufficiently reactive, the ring-opening toward the intermediates **I** and **3** is highly likely a more favourable pathway due to the release of the ring strain of the initially formed heavily substituted benzofused five-membered ring intermediate. It is also noteworthy that although similar ring-opened intermediates have been proposed in several studies,[14] such species have never been isolated or characterized.

In summary, we have identified stable isolable oxyphosphonium betaines from the phosphonium mediated reaction of benzo[*d*]oxazol-2(3*H*)-ones with certain amines. These compounds could undergo elimination of triphenylphosphine oxide giving rise to substituted 2-aminobenzoxazoles suggesting their roles as the intermediates in an alternative reaction pathway. This discovery not only provided strong evidence for a new mechanism for the deoxygenative amination of cyclic carbamates, but also suggested the possibility of stepwise mechanism in aminolysis of activated esters,[15] a fundamental model for peptide bond formation in biomolecules, in which no intermediate has yet to be determined experimentally. Further expansion of the substrate scope and investigation of the detailed reaction mechanism are ongoing.

## EXPERIMENTAL SECTION

*General information*

All reagents including most of the benzo[*d*]oxazol-2(3*H*)-one precursors **1** (**1a**-**1e**) were purchased from Sigma-Aldrich or TCI and used without further purification. Compound **1f**[16] and **1g**[17] were synthesized according to the reported procedures. All reactions were run in flame- or oven-dried glassware under $N_2$ gas. The reaction was monitored by thin-layer chromatography carried out on silica gel plates ($60F_{254}$, MERCK, Germany) and visualized under UV light (254 nm). Column chromatography was performed over silica gel 60 (70–230 mesh, MERCK, Germany). Melting points were determined using Mettler Toledo DSC equipment at a heating rate of 6 $^{o}$C/min and are uncorrected. NMR spectra were recorded using a Bruker AVANCE$^{TM}$ )400 and 500 MHz for $^{1}$H(. Chemical shifts were reported in parts per million )ppm, δ( downfield from tetramethylsilane (TMS). Splitting patterns are described as singlet )*s*(, doublet )*d*(, triplet )*t*(, quartet )*q*(, quintet (qui), sextet (sex), multiplet )*m*(, broad

)*br*(, doublet of doublets )*dd*), triplet of doublets (td) and doublet of doublet of doublets (ddd). High-resolution mass spectra )HRMS( were recorded using time-of-flight (TOF) via the atmospheric pressure chemical ionization (APCI) or electrospray ionization (ESI).

**General procedure for the reaction of benzo[*d*]oxazol-2(3*H*)-ones 1 with amine.**

To a solution of iodine (281 mg, 1.11 mmol) in freshly distilled dichloromethane (5 mL) was added triphenylphosphine (291 mg, 1.11 mmol) at 0 °C under $N_2$. After that, amine (0.89 mmol) was added, followed by treatment with benzoxazolone **1** (0.74 mmol). Triethylamine (0.31 mL, 2.22 mmol) was added before warming the solution to room temperature. After stirring for 30 min the crude mixture was concentrated under reduced pressure before purification by column chromatography (CC) using ethyl acetate/hexanes as the eluent. It is noted that some compounds such as **3af** and **3ai** are relatively unstable and partially decompose during the NMR study.

**2-(Pyrrolidin-1-yl)benzo[*d*]oxazole** (Scheme 1, **2aa**).[18] White solid; (0.1130 g, 81% yield); mp 135-137 °C (lit.[3] mp 136-137 °C); $R_f$ 0.30 )30% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 6.99 (t, *J* = 8.0 Hz, 1H), 3.65 (s, 4H), 2.03 (s, 4H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) δ 161.0, 148.9, 143.4, 123.9, 120.2, 115.8, 108.7, 47.4, 25.6.

**2-(Piperidin-1-yl)benzo[*d*]oxazole** (Scheme 1, **2ab**).[19] Pale yellow solid; (0.1274 g, 85% yield); mp 70-73 °C (lit.[4] mp 72-75 °C); $R_f$ 0.35 )10% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.98 (td, *J* = 7.5 Hz, 1H), 3.66 (s, 4H), 1.68 (s, 6H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) *δ* 162.5, 148.7, 143.4, 123.8, 120.3, 116.0, 108.6, 46.6, 25.3, 24.1.

**2-Morpholinobenzo[*d*]oxazole** (Scheme 1, **2ac**).[19] White solid; (0.1252 g, 83% yield); mp 90-92 °C (lit.[18] mp 90-94 °C); $R_f$ 0.20 )50% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) *δ*

7.37 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.05 (t, *J* = 8.0 Hz, 1H), 3.82 (t, *J* = 4.5 Hz, 4H), 3.69 (t, *J* = 4.5 Hz, 4H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) $\delta$ 162.1, 148.8, 142.9, 124.1, 121.0, 116.5, 108.9, 66.2, 45.7.

**2-(4-Methylpiperazin-1-yl)benzo[*d*]oxazole** (Scheme 1, **2ad**).[19] White solid; (0.1287 g, 80% yield); mp 36-38 ºC (lit.[18] mp 36-38 ºC); $R_f$ 0.26 (10% MeOH/EtOAc); $^{1}H$ NMR (500 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.16 (td, *J* = 8.0, 1.0 Hz, 1H), 7.02 (td, *J* = 8.0, 1.5 Hz, 1H), 3.74 (t, *J* = 5.0 Hz, 4H), 2.54 (t, *J* = 5.0 Hz, 4H), 2.36 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 162.2, 148.8, 143.1, 124.0, 120.7, 116.3, 108.7, 54.2, 46.2, 45.5.

**2-(1*H*-Imidazol-1-yl)benzo[*d*]oxazole** (Scheme 1, **2ae**).[6a] Yellow solid; (0.1028 g, 75% yield); mp 110-112 °C; $R_f$ 0.26 )30% EtOAc/hexanes); $^{1}H$ NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.73 (t, *J* = 1.5 Hz, 1H), 7.69 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.55 (dd, *J* = 7.5, 2.0 Hz, 2H), 7.39 (td, *J* = 7.5, 2.0 Hz, 1H), 7.36 (td, *J* = 7.5, 2.0 Hz, 1H), 7.25 (d, *J* = 1.5 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 152.0, 149.0, 140.5, 135.9, 131.4, 125.5, 125.1, 119.7, 116.8, 110.5.

**(Diethylcarbamoyl)(2-((triphenylphosphonio)oxy)phenyl)amide** (Scheme 1, **3af**). Brown oil; (0.1636 g, 47% yield); $R_f$ 0.43 )20% EtOAc/hexanes); $^{1}H$ NMR (500 MHz, $CDCl_3$) δ 7.7--7.73 (m, 6H), 7.48 – 7.45 (m, 3H), 7.41 -7.37 (m, 6H), 7.00 (ddd, *J* = 7.8, 2.6, 1.5 Hz, 1H), 6.69 (td, *J* = 7.8, 1.5 Hz, 1H), 6.60 (td, *J* = 7.8, 1.5 Hz, 1H), 6.46 (dt, *J* = 7.8, 1.5 Hz, 1H), 3.52 (q, *J* = 7.0 Hz, 2H), 3.32 (q, *J* = 7.0 Hz, 2H), 1.23 (t, *J* = 7.0 Hz, 3H), 1.08 (t, *J* = 7.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 154.8, 146.5, 146.3 (d, $^{3}Jcp$ = 21.8 Hz), 143.9, 132.8, 132.7 (d, $^{2}Jcp$ = 10.0 Hz), 131.61, 131.59 (d, $^{4}Jcp$ = 2.9 Hz), 130.8 (d, $^{1}Jcp$ = 95.8 Hz), 128.55, 128.45 (d, $^{3}Jcp$ = 11.9 Hz), 125.30 , 122.61, 122.55, 122.46 (d, $^{3}Jcp$ = 10.6 Hz), 117.4, 53.5, 14.3, 13.6; $^{31}P\{^{1}H\}$ NMR (202 MHz, $CDCl_3$) δ 5.14; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{29}H_{30}N_2O_2P$ 469.2039; Found 469.2040.

**(Dibutylcarbamoyl)(2-((triphenylphosphonio)oxy)phenyl)amide** (Scheme 1, **3ag**). Brown oil; (0.2888 g, 74% yield); $R_f$ 0.17 )20% EtOAc/hexanes); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.72 (m, 6H), 7.51 – 7.47 (m, 3H), 7.44 – 7.38 (m, 6H), 6.98 (td, *J* = 8.0, 1.6 Hz 1H), 6.69 (td, *J* = 8.0, 1.6 Hz, 1H), 6.61 (td, *J* = 8.0, 1.6 Hz, 1H), 6.44 (d, *J* = 8.0, 1H), 3.43 (t, *J* = 7.6 Hz, 2H), 3.25 (t, *J* = 7.6 Hz, 2H), 1.65 (qui, *J* = 7.6 Hz, 2H), 1.47 (qui, *J* = 7.2 Hz, 2H), 1.35 – 1.20 (m, 4H), 0.87 (t, *J* = 7.6 Hz, 3H), 0.78 (t, *J* = 7.6 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 155.1, 146.5, 146.3 (d, $^3$*J*cp = 21.7 Hz), 143.8, 132.8, 132.7 (d, $^2$*J*cp = 9.8 Hz), 131.9, 131.48, 131.47 (d, $^4$*J*cp = 2.9 Hz), 130.9 (d, $^1$*J*cp = 99.2 Hz), 128.5, 128.4 (d, $^3$*J*cp = 12.0 Hz), 125.2, 122.7, 122.4, 122.3 (d, $^3$*J*cp = 10.1 Hz), 117.3, 47.5, 31.0, 30.3, 20.17, 20.10, 13.92, 13.85; $^{31}$P{$^1$H} NMR (162 MHz, $CDCl_3$) δ 3.24; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{33}H_{38}N_2O_2P$ 525.2665; Found 525.2659.

**(Dibenzylcarbamoyl)(2-((triphenylphosphonio)oxy)phenyl)amide** (Scheme 1, **3ah**). White solid; (0.3340 g, 76% yield); mp 180 - 181 °C; $R_f$ 0.47 )20% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.73 (m, 6H), 7.47 (t, *J* = 7.5 Hz, 3H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.37 -7.34 (m, 6H), 7.24 (br s, 5H), 7.11 (t, *J* = 7.5 Hz, 1H ), 7.07 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 2H), 6.73 (td, *J* = 8.0, 2.0 Hz, 1H), 6.65 (t, *J* = 8.0 Hz, 1H), 6.46 (d, *J* = 8.0 Hz, 1H), 4.67 (s, 2H), 4.46 (s, 2H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) δ 155.9, 146.2 146.1 (d, $^3$*J*cp = 21.7 Hz), 143.9, 137.6, 132.8, 132.7 (d, $^2$*J*cp = 10.0 Hz), 131.64, 131.61 (d, $^4$*J*cp = 3.0 Hz), 131.4, 131.7 (d, $^1$*J*cp = 99.5 Hz), 128. 7, 128.6, 128.5 (d, $^3$*J*cp = 12.4 Hz), 128.4, 127.3, 127.2, 125.6, 122.8, 122.35, 122.27 (d, $^3$*J*cp = 10.4 Hz), 117.4, 49.4, 49.3; $^{31}$P{$^1$H} NMR (202 MHz, $CDCl_3$) δ 3.39; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{39}H_{34}N_2O_2P$ 593.2352; Found 593.2349.

**(Cyclohexylcarbamoyl)(2-((triphenylphosphonio)oxy)phenyl)amide** (Scheme 1, **3ai**). White solid; (0.1991 g, 54% yield); mp 168 - 170 °C; $R_f$ 0.40 (20% EtOAc/hexanes);$^1$H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.75 (m, 6H), 7.53 – 7.50 (m, 3H), 7.45 – 7.41 (m, 6H), 7.02 (d, *J*

= 7.5 Hz 1H), 6.72 (t, *J* = 7.5 Hz, 1H), 6.63 (t, *J* = 7.5, 1H), 6.45 (d, *J* = 7.5 Hz 1H), 5. 14 (d, *J* = 8.0 Hz, 1H), 3.51 - 3.48 (m, 1H), 1.93 (d, *J* = 9.0 Hz, 2H), 1.69 – 1.56 (m, 3H), 1.36 -1.27 (m, , 2H), 1.19 – 1.09 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 154.8, 146.6, 146.4 (d, $^{3}Jcp$ = 21.8 Hz), 143.9, 132.8, 132.7 (d, $^{2}Jcp$ = 9.9 Hz), 131.78, 131.76 (d, $^{4}Jcp$ = 2.8 Hz), 131.0, 130.2 (d, $^{1}Jcp$ = 99.4 Hz), 128.7, 128.6 (d, $^{3}Jcp$ = 11.9 Hz), 125.5, 122.7, 122.6, 122.5 (d, $^{3}Jcp$ = 11.0 Hz), 117.5, 49.8, 33.4, 25.6, 24.8; $^{31}P\{^{1}H\}$ NMR (202 MHz, $CDCl_3$) δ 3.84; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{31}H_{32}N_2O_2P$ 495.2196; Found 495.2207.

**(4-Bromo-2-((triphenylphosphonio)oxy)phenyl)(dibutylcarbamoyl)amide** (Scheme 2, **3bg**). Brown oil ; (0.3234 g, 72% yield); $R_f$ 0.4 )20% EtOAc/hexanes); $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 6H), 7.53 – 7.49 (m, 3H), 7.45 – 7.40 (m, 6H), 7.12 (t, *J* = 2.4 Hz, 1H), 6.77 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.27 (dd, *J* = 8.4, 1.2 Hz, 1H), 3.41 (t, *J* = 7.6 Hz, 2H), 3.24 (t, *J* = 7.6 Hz, 2H), 1.68 – 1.60 (m, 2H), 1.45 (qui, *J* = 7.6 Hz, 2H), 1.38 – 1.19 (m, 4H), 0.87 (t, *J* = 7.6 Hz, 3H), 0.78 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.6, 146.9, 146.7 (d, $^{3}Jcp$ = 21.6 Hz), 143.4, 132.7, 132.7, 131.6 (d, $^{2}Jcp$ = 9.7 Hz), 131.68, 131.65 (d, $^{4}Jcp$ = 2.8 Hz), 131.4, 130.4 (d, $^{1}Jcp$ = 99.6 Hz), 128.6, 128.5 (d, $^{3}Jcp$ = 12.0 Hz), 128.0, 125.7, 123.0, 122.9 (d, $^{3}Jcp$ = 10.2 Hz), 107.9, 47.5, 31.0, 30.3, 20.2, 20.1, 13.9, 13.8; $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 4.05; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{33}H_{37}{}^{81}BrN_2O_2P$ 605.1751; Found 605.1741, for $C_{33}H_{37}{}^{79}BrN_2O_2P$ 603.1771; Found 603.1776.

**(4-Chloro-2-((triphenylphosphonio)oxy)phenyl)(dibutylcarbamoyl)amide** (Scheme 2, **3cg**). Brown oil; (0.3198 g, 77% yield); $R_f$ 0.4 )20% EtOAc/hexanes); $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 6H), 7.53 – 7.49 (m, 3H), 7.48 – 7.40 (m, 6H), 6.99 (t, *J* = 2.4 Hz, 1H), 6.65 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.31 (dd, *J* = 8.4, 1.2 Hz, 1H), 3.42 (t, *J* = 7.6 Hz, 2H), 3.24 (t, *J* = 7.6 Hz, 2H), 1.64 (qui, *J* = 7.6 Hz, 2H), 1.45 (qui, *J* = 7.6 Hz, 2H), 1.34 – 1.99 (m, 4H), 0.87 (t, *J* = 7.6 Hz, 3H), 0.78 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.6, 146.6, 146.4 (d, $^{3}Jcp$ = 21.6 Hz), 142.9, 132.7, 132.6 (d, $^{2}Jcp$ = 9.7 Hz), 131.7, 131.6 (d, $^{4}Jcp$

= 2.9 Hz), 131.4, 130.4 (d, $^{1}Jcp$ = 99.5 Hz), 128.6, 128.5 (d, $^{3}Jcp$ = 12.0 Hz), 125.1, 123.0, 122.5, 122.4 (d, $^{3}Jcp$ = 10.1 Hz), 121.1, 47.5, 31.0, 30.3, 20.2, 20.1, 13.9, 13.8; $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 3.95; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{33}H_{37}{}^{37}ClN_2O_2P$ 561.2246; Found 561.2255, for $C_{33}H_{37}{}^{35}ClN_2O_2P$ 559.2276, Found 559.2285.

**(Dibutylcarbamoyl)(4-nitro-2-((triphenylphosphonio)oxy)phenyl)amide** (Scheme 2, **3dg).** Yellow oil; (0.2996 g, 71% yield); $R_f$ 0.27 )20% EtOAc/hexanes); $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 7.93 (t, *J* = 2.8 Hz, 1H), 7.77 – 7.72 (m, 6H), 7.64 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.59 – 7.55 (m, 3H), 7.50 – 7.45 (m, 6H), 6.26 (dd, *J* = 9.0, 1.0 Hz, 1H), 3.47 (t, *J* = 7.6 Hz, 2H), 3.26 (t, *J* = 7.6 Hz, 2H), 1.72 – 1.62 (m, 2H), 1.49 – 1.38 (m, 2H), 1.39 – 1.31 (m, 2H), 1.28 – 1.19 (m, 2H), 0.90 (t, *J* = 7.6 Hz, 3H), 0.77 (t, *J* = 7.6 Hz, 3H).; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.3, 153.2, 145.2, 145.0 (d, $^{3}Jcp$ = 23.2 Hz), 137.2, 132.7, 132.6 (d, $^{2}Jcp$ = 9.9 Hz), 132.33, 132.30 (d, $^{4}Jcp$ = 2.9 Hz), 129.7, 128.9, 128.8 (d, $^{3}Jcp$ = 12.2 Hz), 128.7 (d, $^{1}Jcp$ = 100.3 Hz), 122.4, 119.8, 1197 (d, $^{3}Jcp$ = 11.6 Hz), 119.1, 47.6, 31.0, 30.2, 20.2, 20.0, 13.9, 13.8; $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$) δ 8.35; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{33}H_{37}N_3O_4P$ 570.2517; Found 570.2520.

**(5-Chloro-2-((triphenylphosphonio)oxy)phenyl)(dibutylcarbamoyl)amide** (Scheme 2, **3eg).** Brown oil; (0.3444 g, 83% yield); $R_f$ 0.38 )20% EtOAc/hexanes); $^{1}H$ NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.73 (m, 6H), 7.53 – 7.50 (m, 3H), 7.45 – 7.42 (m, 6H), 6.89 (d, *J* = 8.5 Hz, 1H), 6.55 (d, *J* = 8.5 Hz, 1H), 6.35 (s, 1H), 3.43 (t, *J* = 7.5 Hz, 2H), 3.25 (t, *J* = 7.5 Hz, 2H), 1.64 (qui, *J* = 7.5 Hz, 2H), 1.45 (qui, *J* = 7.5 Hz, 2H), 1.29 (hex, *J* = 7.5 Hz, 2H), 1.21 (hex, *J* = 7.5 Hz, 2H), 0.87 (t, *J* = 7.5 Hz, 3H), 0.76 (t, *J* = 7.5 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 154.9, 145.3, 145.2, 145.0 (d, $^{3}Jcp$ = 21.0 Hz), 132.7, 132.6 (d, $^{2}Jcp$ = 9.4 Hz), 131.9, 131.8 (d, $^{4}Jcp$ = 3.0 Hz), 130.9, 130.1 (d, $^{1}Jcp$ = 99.8 Hz), 129.9, 128.7, 128.6 (d, $^{3}Jcp$ = 12.4 Hz), 123.3, 121.7, 121.6 (d, $^{3}Jcp$ = 10.4 Hz), 116.9, 47.5, 31.0, 30.3, 20.2, 20.1, 14.0, 13.9; $^{31}P\{^{1}H\}$ NMR (202 MHz, $CDCl_3$) δ 4.46; HRMS (ESI) m/z: $[M + H]^+$ Calcd for

$C_{33}H_{37}{}^{37}ClN_2O_2P$ 561.2246; Found 561.2254, for $C_{33}H_{37}{}^{35}ClN_2O_2P$ 559.2276; Found 559.2285.

***N,N*-dibutyl-5-nitrobenzo[*d*]isoxazol-3-amine** (Scheme 2, **2fg**).[20] Yellow solid; (0.1690 g, 78% yield); mp 84-87 °C (lit.[5] mp 85-86 °C); $R_f$ 0.41 )10 % EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 3.53 (t, *J* = 7.5 Hz, 4H), 1.68 (qui, *J* = 7.5 Hz, 4H), 1.40 (sex, *J* = 7.5 Hz, 4H), 0.98 (t, *J* = 7.5 Hz, 6H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) δ 164.1, 152.8, 145.0, 144.7, 116.6, 111.2, 108.1, 48.6, 30.0, 20.0, 13.9.

**(Dibutylcarbamoyl)(5-methoxy-2-((triphenylphosphonio)oxy)phenyl)amide** (Scheme 2, **3gg**)**.** Brown oil; (0.3862 g, 94% yield); $R_f$ 0.31 )20% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.78 – 7.74 (m, 6H), 7.50 – 7.47 (m, 3H), 7.43 – 7.40 (m, 6H), 6.87 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.16 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.98 (d, *J* = 2.5 Hz, 1H), 3.43 (t, *J* = 7.5 Hz, 2H), 3.42 (s, 3H), 3.25 (t, *J* = 7.5 Hz, 2H), 1.64 (qui, *J* = 7.5 Hz, 2H), 1.45 (qui, *J* = 7.5 Hz, 2H), 1.31 (hex, *J* = 7.5 Hz, 2H), 1.22 (hex, *J* = 7.5 Hz, 2H), 0.86 (t, *J* = 7.5 Hz, 3H), 0.76 (t, *J* = 7.5 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 156.9, 155.6, 144.6, 140.7, 140.5 (d, $^3$*J*cp = 21.8 Hz), 132.8, 132.7 (d, $^2$*J*cp = 9.4 Hz), 131.7, 131.6, (d, $^4$*J*cp = 2.8 Hz), 131.5, 130.7 (d, $^1$*J*cp = 99.4 Hz), 128.6, 128.5 (d, $^3$*J*cp = 11.9 Hz), 125.2, 122.5, 108.1, 108.0 (d, $^3$*J*cp = 10.9 Hz), 102.0, 55.1, 47.4, 31.0, 30.4, 20.2, 20.1, 14.0, 13.9; $^{31}$P{$^1$H} NMR (202 MHz, $CDCl_3$) δ 3.17; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{34}H_{40}N_2O_3P$ 555.2771; Found 555.2779.

**Thermolysis of Betaines 3.**

In 10 mL pressure tube, betaine **3** (0.50 mmol) was added with dry toluene (4 mL). The tightly capped vessel then subjected to heating in a pre-set oil bath at 120 °C until reaction completion. After cooling down, the mixture was concentrated under reduced pressure before column chromatography using ethyl acetate/hexanes as the eluent to afford the product **2**.

***N,N*-Diethylbenzo[*d*]isoxazol-3-amine** (Scheme 3, **2af**).[19] Yellow oil; (0.0845 g, 89% yield); $R_f$ 0.35 )10% EtOAc/hexanes); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.6 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.16 (td, *J* = 7.6, 1.2 Hz, 1H), 7.00 (td, *J* = 7.6, 1.2 Hz, 1H), 3.61 (q, *J* = 7.2 Hz, 4H), 1.30 (t, *J* = 7.2 Hz, 6H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) *δ* 162.3, 148.9, 143.7, 123.8, 120.0, 115.8, 108.5, 43.0, 13.5.

***N,N*-Dibutylbenzo[*d*]isoxazol-3-amine** (Scheme 3, **2ag**).[19] Yellow oil; (0.1035 g, 84% yield); $R_f$ 0.36 )5% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.25 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.15 (td, *J* = 7.6, 1.2 Hz, 1H), 6.99 (td, *J* = 7.6, 1.2 Hz, 1H), 3.53 (t, *J* = 7.6 Hz, 4H), 1.68 (qui, *J* = 7.6 Hz, 4H), 1.40 (sex, *J* = 7.6 Hz, 4H), 0.98 (t, *J* = 7.6 Hz, 6H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) δ 162.6, 148.7, 143.7, 123.6, 119.8, 115.7, 108.4, 48.3, 30.1, 19.9, 13.8.

**5-Bromo-*N,N*-dibutylbenzo[*d*]isoxazol-3-amine** (Scheme 3, **2bg**). Colorless oil; (0.1318 g, 81% yield); $R_f$ 0.50 )10% EtOAc/hexanes); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 2.0 Hz, 1H), 7.26 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 1H), 3.50 (t, *J* = 7.6 Hz, 4H), 1.66 (qui, *J* = 7.6 Hz, 4H), 1.39 (sex, *J* = 7.6 Hz, 4H), 0.97 (t, *J* = 7.6 Hz, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 162.8, 149.2, 143.1, 126.8, 116.6, 112.0, 111.7, 48.4, 30.1, 20.0, 13.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}{}^{81}BrN_2O$ 327.0895; Found 327.0930, for $C_{15}H_{22}{}^{79}BrN_2O$ 325.0915; Found 325.0915.

***N,N*-Dibutyl-5-chlorobenzo[*d*]isoxazol-3-amine** (Scheme 3, **2cg**). Yellow oil; )0.1192 g, 85% yield); $R_f$ 0.30 )5% EtOAc/hexanes); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 2.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.12 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.50 (t, *J* = 7.6 Hz, 4H), 1.67 (qui, *J* = 7.6 Hz, 4H), 1.40 (sex, *J* = 7.6 Hz, 4H), 0.98 (t, *J* = 7.6 Hz, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) δ 163.0, 148.9, 142.6, 124.8, 124.0, 116.0, 109.3, 48.4, 30.1, 20.0, 13.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}{}^{37}ClN_2O$ 283.1391; Found 283.1408, for $C_{15}H_{22}{}^{35}ClN_2O$ 281.1421; Found 281.1433.

***N,N*-Dibutyl-5-nitrobenzo[*d*]isoxazol-3-amine** (Scheme 3, **2dg**).[20] Yellow oil; (0.1266 g, 87% yield); $R_f$ 0.35 )10% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.17 (dd, *J* = 8.8, 2.4 Hz, 1H), 8.13 (d, *J* = 2.4 Hz, 1H), 7.30 (d, *J* = 8.8 Hz, 1H), 3.56 (t, *J* = 7.2 Hz, 4H), 1.70 (qui, *J* = 7.2 Hz, 4H), 1.41 (sex, *J* = 7.2 Hz, 4H), 0.99 (t, *J* = 7.2 Hz, 6H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) δ 165.4, 150.7, 147.9, 140.9, 121.5, 114.4, 104.8, 48.7, 30.0, 20.0, 13.8.

***N,N*-Dibutyl-5-chlorobenzo[d]oxazol-2-amine** (Scheme 3, **2eg**).[21] Yellow oil; (0.1123 g, 80% yield); $R_f$ 0.45 )10% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.29 (s, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 3.49 (t, *J* = 7.5 Hz, 4H), 1.65 (qui, *J* = 7.5 Hz, 5H), 1.38 (sex, *J* = 7.5 Hz, 5H), 0.96 (t, *J* = 7.5 Hz, 7H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) δ 163.5, 147.4, 145.1, 129.0, 119.6, 115.9, 108.9, 48.4, 30.1, 20.0, 13.9.

***N,N*-Dibutyl-5-methoxybenzo[d]oxazol-2-amine** (Scheme 3, **2gg**). Yellow oil; (0.0981 g, 71% yield); $R_f$ 0.48 )20% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.6 Hz, 1H), 6.93 (s, 1H), 6.54 (d, *J* = 8.6 Hz, 1H), 3.80 (s, 3H), 3.49 (t, *J* = 7.5 Hz, 4H), 1.65 (qui, *J* = 7.5 Hz, 8H), 1.38 (sex, *J* = 7.5 Hz, 5H), 0.96 (t, *J* = 7.5 Hz, 6H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) δ 163.4, 156.88, 156.85, 143.3, 108.3, 106.3, 100.9, 55.9, 48.4, 30.1, 20.1, 14.0. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{25}N_2O_2$ 277.1911; Found 277.1912.

***N,N*-Dibenzylbenzo[*d*]isoxazol-3-amine** (Scheme 3, **2ah**).[19] White solid; (0.1226 g, 78% yield); mp 91-93 °C; $R_f$ 0.44 )5% EtOAc/hexanes); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.6 Hz, 1H), 7.40 – 7.31 (m, 11H), 7.24 (td, *J* = 7.6, 1.2 Hz, 1H), 7.08 (td, *J* = 7.6, 1.2 Hz, 1H), 4.75 (s, 4H); $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$) δ 163.2, 148.9, 143.5, 136.3 , 128.8, 128.0, 127.8, 124.1, 120.6, 116.3, 108.9, 50.4.

***N*-Cyclohexylbenzo[*d*]isoxazol-3-amine** (Scheme 3, **2ai**).[22] Yellow oil; (0.0831 g, 77% yield); $R_f$ 0.22 )10% EtOAc/hexanes); $^1$H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 4.90 (br s, 1H), 3.82

– 3.75 (m, 1H), 2.17 – 2.14 (m, 2H), 1.82 – 1.65 (m, 3H), 1.51 – 1.42 (m, 2H), 1.36 – 1.24 (m, 3H).

**Synthesis of 1,1-dibenzyl-3-(2-hydroxyphenyl)urea 4**

In 10 mL pressure tube, a solution of **1a** (0.74 mmol) in 4 mL toluene was added with dibenzylamine (0.84 mmol) and triethylamine (2.22 mmol). The tightly capped vessel was then heated in a pre-set oil bath at 180 $^{o}$C for 4 h. After cooling down, the mixture was concentrated under reduced pressure before column chromatography using ethyl acetate/hexanes as the eluent to afford the product **4**.

**1,1-dibenzyl-3-(2-hydroxyphenyl)urea** (**4**). Yellow oil; (0.2211 g, 90% yield); $R_f$ 0.40 )20% EtOAc/hexanes); $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.6 Hz, 4H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.6 Hz, 4H), 6.99 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.70 (t, *J* = 8.0 Hz, 1H), 6.56 (s, 1H), 6.52 (d, *J* = 8.0 Hz, 1H), 4.60 (s, 4H); $^{13}$C{$^{1}$H} NMR (125 MHz, $CDCl_3$) δ 157.5, 148.8, 136.4, 129.2, 128.6, 128.4, 128.1, 127.4, 126.6, 126.0, 122.1, 120.3, 119.5, 51.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{21}N_2O_2$ 333.1598; Found 333.1607.

**Direct synthesis of 2ah from 1a.**

To a solution of iodine (281 mg, 1.11 mmol) and triphenylphosphine (291 mg, 1.11 mmol) in freshly distilled dichloromethane (5 mL), dibenzylamine (175 mg, 0.89 mmol), **1a** (0.1000 g, 0.74 mmol), and triethylamine (0.31 mL, 2.22 mmol) were sequentially added at 0 $^{o}$C under $N_2$. After stirring at 25 $^{o}$C for 10 min, the mixture was transferred into a pressure tube before concentrate, followed by adding toluene (4 mL). The tightly capped vessel was heated in a pre-set oil bath at 120 $^{o}$C until reaction completion. After cooling down, the crude mixture was concentrated under reduced pressure before purified by CC to afford the product **2ah** (0.1835 g, 79%) or 1.67 g (72%) from gram scale using **1a** 1.00 g (7.40 mmol).

## ASSOCIATED CONTENT

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### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: Copies of $^{1}H$ NMR, $^{13}C\{^{1}H\}$ NMR spectra of all products, and $^{31}P\{^{1}H\}$ spectra of **3**, X-ray data of **3ah**, and 2D NMR analysis of **3ag** and **3ah**. $^{31}P\{^{1}H\}$ NMR reaction monitoring studies.

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