# A Short and Efficient Methodology for the Synthesis of Novel 3-Aryloxazolidin-2-one Derivatives

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**Abstract:** An efficient synthesis of novel oxazolidinone derivatives is disclosed. Novel oxazolidinone derivatives were synthesized by a copper-catalyzed *N*-arylation reaction with control of the substituents on both the sides of the phenyl ring.

**Keywords:** amination; copper; diiodobenzene; ethylenediamine; *N*-arylation; oxazolidinone

## Introduction

Recently there has been an upsurge of interest in the synthesis and development of antimicrobial agents against multi-drug resistant pathogens.[1] This is evident from the array of reports on the synthesis of novel compounds effective against Gram-positive bacterial pathogens.[2] Among them, Linezolid, an oxazolidinone derivative, represents a novel and important class of antimicrobial agent that possesses excellent activity against antibiotic-sensitive and MIC90 Gram-positive bacteria.[3] As a part of a program to synthesize novel antimicrobial agents of the oxazolidinone class, we have carried out the synthesis of the key oxazolidinone pharmacophore present in Linezolid, Eperezolid etc. by a copper-catalyzed *N*-arylation reaction.

The palladium- and copper-catalyzed C–N bond formation using aryl iodides has been an area of intense research in the last few years. The pioneering work by Buchwald,[4] Hartwig[5] and others[6] on the palladium-catalyzed *N*-arylation of different nitrogen-containing compounds is an excellent alternative to the classical Ullmann coupling. Recently, a report by Buchwald et al. on the operationally simple C–N bond forming protocol using copper has generated lot of interest in heterocyclic chemistry.[7] Except for the scant information available,[8] there is no report on the copper-catalyzed *N*-arylation of oxazolidinones and its application to the synthesis of Linezolid-type antibacterial agents. The results of our investigation on the controlled coupling of diiodobenzene with oxazolidinone leading to mono and bis-coupled products are presented here.

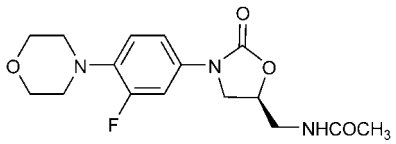


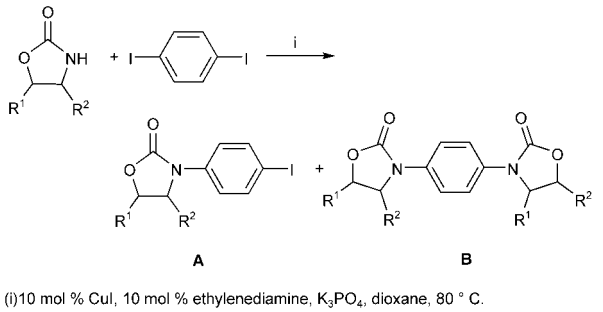

**Figure 1.** Linezolid.

## Results and Discussion

Our studies commenced with the reaction of 4-methyl-5-phenyl-2-oxazolidinone with diiodobenzene in the presence of CuI/ethylenediamine at 80 °C in dioxane. The reaction afforded both the mono- and bis-coupled products in 72% yield (Scheme 1).

The ratios (mono:bis) of the coupled products were found to be 59:13 and 26:40 at 80 °C for reaction times of 5 h and 24 h, respectively. It is clear that the higher yields of mono-coupled product were obtained by controlling the reaction time and the results are given in Table 1.

In most cases both mono- and bis-coupled products were formed. This controlled coupling was found to be general with all other oxazolidinones tried. The products of the coupling were characterized on the basis of




**Scheme 1.**

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**Table 1.** CuI-mediated *N*-arylation of oxazolidinones with diiodobenzene.[a]

| Entry | Substrate | Reaction time | Ratio A:B | Yield [%][b] |
|---|---|---|---|---|
| 1 | $R^1$ = Ph, $R^2$ = $CH_3$ | 3 h | 43:9 | 52 |
| | | 5 h | 59:13 | 72 |
| | | 24 h | 26:40 | 66 |
| 2 | $R^1$ = H, $R^2$ = $CH_2Ph$ | 5 h | 61:17 | 78 |
| 3 | $R^1$ = H, $R^2$ = $CH(CH_3)_2$ | 5 h | 45:0 | 45 |
| 4 | $R^1$ = H, $R^2$ = $CH_2CH(CH_3)_2$ | 5 h | 54:24 | 78 |

[a] Reaction conditions: 1 equiv. of oxazolidinone, 1 equiv. of diiodobenzene, 10 mol % CuI, 10 mol % ethylenediamine, 3 mL dioxane, 80 °C.
[b] Yield of isolated product.

spectral data. The high-resolution mass spectra of both the mono- and bis-coupled products further confirmed the proposed structures.

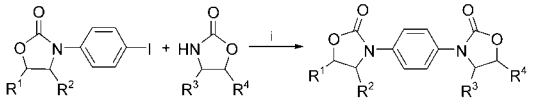
The mono-coupled products **A** (entries 1–4) can effectively couple with a suitable substrate to yield a novel class of oxazolidinone derivatives. An important compound of this class is Linezolid. The special architecture of Linezolid with two C–N bonds at the *para*-positions of the phenyl ring can be synthesized using the copper-catalyzed coupling reaction with control of substituents and the synthetic route is given in Scheme 2.

In order to confirm the validity of this methodology, we have carried out the CuI/ethylenediamine-mediated coupling of the mono-coupled product with different oxazolidinones and the results are summarized in Table 2.

A one-pot synthesis of bis-coupled product with same substituent was achieved by conducting the reaction with 2 equivalents of oxazolidinone as depicted in Scheme 3.

It is clear from the above results that both the substituents on the phenyl ring were controllable and can be used for the synthesis of novel oxazolidinone derivatives including the Linezolid- and Eperezolid-type compounds in an efficient way. In most of the reported procedures for the synthesis of Linezolid, the oxazolidinone

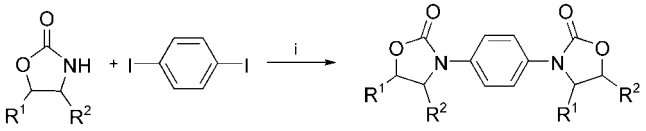
**Table 2.** CuI-mediated *N*-arylation of mono-coupled products.[a]




(i) 10 mol % CuI, 10 mol % ethylenediamine, $K_3PO_4$, dioxane, 80 ° C.

| Entry | Substituents | Yield [%][b] |
|---|---|---|
| 1 | $R^1$ = Ph, $R^2$ = $CH_3$, $R^3$ = Ph, $R^4$ = $CH_3$ | 65 |
| 2 | $R^1$ = Ph, $R^2$ = $CH_3$, $R^3$ = $CH_2Ph$, $R^4$ = H | 66 |
| 3 | $R^1$ = Ph, $R^2$ = $CH_3$, $R^3$ = $CH(CH_3)_2$, $R^4$ = H | 79 |
| 4 | $R^1$ = Ph, $R^2$ = $CH_3$, $R^3$ = $(CH_2)_2SCH_3$, $R^4$ = H | 93 |
| 5 | $R^1$ = H, $R^2$ = $CH_2Ph$, $R^3$ = $CH_2Ph$, $R^4$ = H | 76 |
| 6 | $R^1$= H, $R^2$ = $CH_2Ph$, $R^3$ = $CH(CH_3)_2$, $R^4$ = H | 67 |
| 7 | $R^1$ = H, $R^2$ = $CH_2Ph$, $R^3$ = $CH_2CH(CH_3)_2$, $R^4$ = H | 67 |
| 8 | $R^1$ = H, $R^2$ = $CH_2CH(CH_3)_2$, $R^3$ = $CH(CH_3)_2$, $R^4$ = H | 90 |
| 9 | $R^1$ = H, $R^2$ = $CH_2Ph$  | 58[c] |

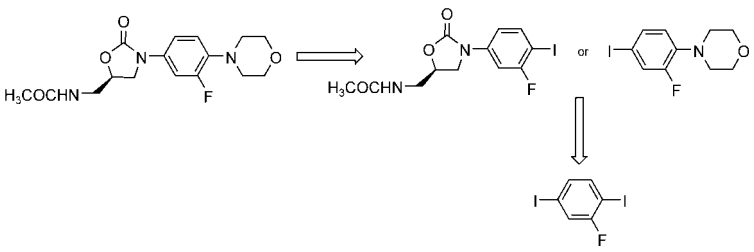
[a] Reaction conditions: 1 equiv. of oxazolidinone, 1 equiv. of diiodobenzene, 10 mol % CuI, 10 mol % ethylenediamine, $K_3PO_4$, 3 mL dioxane, 80 °C, 24 h.
[b] Yield of isolated product.
[c] Coupling of mono-coupled product with morpholine.




(i)10 mol % CuI, 10 mol % ethylenediamine, $K_3PO_4$, dioxane, 80 ° C.
$R^1$ = Ph, $R^2$ = $CH_3$, 65%, $R^1$ = H, $R^2$ = $CH_2Ph$, 70%

**Scheme 3.**

core was introduced either by a series of reactions or in a few cases by the palladium-catalyzed *N*-arylation of oxazolidinones with properly substituted aryl halides. In




**Scheme 2.**

both these methods, one of the substituents on one side of the phenyl ring is fixed. But the above-mentioned methodology offers the freedom to select the substituents on both sides of the benzene ring.

## Conclusions

In summary, we have reported here the first efficient mono- and bis-coupling reactions of diiodobenzene with oxazolidinones in the presence CuI/ethylenediamine catalyst system. The route is flexible and one can control the mono-coupling reaction by means of the reaction time. This procedure gives an easy and efficient methodology for the synthesis of novel oxazolidinone derivatives, which are important cores of antimicrobial agents like Linezolids, Eperezolid, etc.

## Experimental Section

### General Considerations

All reactions were performed under an atmosphere of argon in oven-dried glass ware. Solvents used for the experiments were distilled or dried as specified. Copper(I) iodide was used without recrystallization. $^1$H- and $^{13}$C-NMR spectra were recorded on a Bruker 300 MHz NMR spectrometer. NMR spectra were obtained using $CDCl_3$ as solvent. Chemical shifts are given as δ (ppm) with tetramethylsilane as internal standard. Mass spectra were recorded on a JEOL-JMX-600 H mass spectrometer.

### General Procedure for the Coupling of Oxazolidinones with Diiodobenzene

CuI (10 mol %) and $K_3PO_4$ (2 mmol) were added to a Schlenk tube with a Teflon cap. The tube was evacuated and back-filled with argon three times. The respective oxazolidinone (1 mmol), diiodobenzene (1 mmol), ethylenediamine (10 mol %) and 3 mL dry dioxane were added. The tube was sealed and heated at 80 °C. The reaction mixture was cooled to room temperature after heating for the specified time. The reaction mixture was filtered and the filtrate was concentrated under vacuum. The crude product was purified by column chromatography using EtOAc and hexane (1:2) as eluants to afford the coupled products.

### 3-(4′-Iodophenyl)-4-methyl-5-phenyl-2-oxazolidinone A and the Bis-Coupled Product B (Table 1, entry 1)

Following the general procedure, the oxazolidinone (177 mg, 1 mmol), diiodobenzene (330 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 5 h gave the mono- (yield: 223 mg, 59%) and bis-coupled (yield: 55.6 mg, 13%) products. Total yield: 72%.

**Mono-coupled product A:** $^1$H NMR: δ = 7.69–7.66 (m, 2H, Ar), 7.41–7.25 (m, 7H, Ar), 5.77 (d, $J$ = 7.64 Hz, 1H, O-CH), 4.69 (d, $J$ = 7.64 Hz, 1H, N-CH), 0.84 (d, $J$ = 6.45 Hz, 3H, $CH_3$);$^{13}$C-NMR: δ = 154.4 (C=O), 138.1, 137.4, 136.8, 134.3, 130.1, 128.6, 125.9, 122.8, 78.0, 56.5, 14.3; HR-MS: calcd. for $M^+$: 379.0070; found: 379.0071.

**Bis-coupled product B:** mp 224–226 °C; $^1$H NMR: δ = 7.59–7.55 (m, Ar, 4H), 7.41–7.25 (m, Ar, 10H), 5.79 (d, $J$ = 7.7, 2H), 4.73–4.64 (m, 2H, N-CH), 0.84–0.83 (m, 6H, $2CH_3$); $^{13}$C NMR: δ = 154.87, 134.5, 133.9, 128.6, 128.0, 122.24, 78.2, 56.8, 14.61; HR-MS: calcd. for $M^+$: 428.1736; found: 428.1743.

### 3-(4′-Iodophenyl)-4-methylphenyl-2-oxazolidinone A and Bis-Coupled Product B (Table 1, entry 2)

Following the general procedure, the oxazolidinone (177 mg, 1 mmol), diiodobenzene (330 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 5 h. gave mono- (yield: 231 mg, 61%) and bis-coupled (yield: 72.7 mg, 17%) products. Total yield: 78%.

**Mono-coupled product A:** $^1$H NMR: δ = 7.73–7.70 (d, $J$ = 8.6 Hz, 2H, Ar,), 7.3–7.2 (5H, Ar), 7.1–7.08 (m, 2H, Ar), 4.63–4.57 (m, 1H, CH-N), 4.36 (t, $J$ = 8.8 Hz, 1H, O-$CH_3$), 4.21–4.17(dd, J = 4.5, 8.8 Hz,1H, O-$CH_2$), 3.14–3.08 (dd, $J$ = 3.2, 13.7 Hz, 1H, Ph-$CH_2$), 2.79–2.72 (dd, $J$ = 9.7, 13.7 Hz, 1H, Ph-$CH_2$); $^{13}$C NMR: δ = 154.8 (CO), 138.3, 129.1, 129.0, 127.4, 122.9, 65.8, 56.9, 37.6; HR-MS: calcd. for $M^+$: 379.0069; found: 379.0073.

**Bis-coupled product B:** mp 160–162 °C; $^1$H NMR: δ = 7.63–7.60 (m, Ar, 3H), 7.30–7.24 (m, Ar, 7H), 7.16–7.11 (m, Ar, 4H), 4.66–4.61 (m, 2H, N-CH), 4.44–4.32 (m, 2H, O-$CH_2$), 4.2–4.03 (m, 2H, O-$CH_2$), 3.17–3.12 (dd, $J$ = 3.24, 13.7 Hz, 2H, $CH_2$), 2.85–2.73 (m, 2H, $CH_2$); $^{13}$C NMR: δ = 155.3 (CO), 135.06, 133.70, 129.12, 128.97, 127.71, 127.34, 127.24, 122.20, 121.71, 66.03, 53.76, 37.89; HR-MS: calcd. for $M^+$: 428.1736; found: 428.1741.

### 3-(4′-Iodophenyl)-4-isopropyl-2-oxazolidinone (Table 1, entry 3)

Following the general procedure, the oxazolidinone (129 mg, 1 mmol), diiodobenzene (330 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 5 h. gave only the mono-coupled product; yield: 149 mg (45%); mp 70–72 °C; $^1$H NMR: δ = 7.6–7.58 (m, $J$ = 8.79 Hz, 2H, Ar), 7.27 (m, Ar, 2H), 4.35–4.27 (m, 2H, O-$CH_2$), 4.19–4.11 (m, 1H, N-CH), 2.08–1.96 (m, 1H, CH), 0.85–0.83 (m, 3H, $CH_3$), 0.77–0.75 (m, 3H, $CH_3$); $^{13}$C NMR: δ = 155.9 (C=O), 138.1, 136.7, 123.5, 62.3, 60.1, 27.5, 17.7, 14.2; HR-MS: calcd. for $M^+$: 331.0069; found: 331.0075.

### 3-(4′-Iodophenyl)-4-(2-methylpropyl)-2-oxazolidinone A and Bis-Coupled Product B (Table 1, entry 4)

Following the general procedure, the oxazolidinone (143 mg, 1 mmol), diiodobenzene (330 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 5 h.

gave the mono- (yield: 196.6 mg, 54%) and bis-coupled (yield: 86.4 mg, 24%) products. Total yield: 78%.

**Mono-coupled product A:** $^1$H NMR: δ = 7.60–7.58 (d, *J* = 8.79 Hz, 2H, Ar), 7.12–7.09 (d, *J* = 8.8 Hz, 2H, Ar), 4.47–4.25 (t, *J* = 8.2 Hz, 1H, -N-CH), 4.34–4.26 (m, 1H, O-$CH_2$), 4.04–4.00 (dd, *J* = 5.0, 8.32 Hz, 1H, O-$CH_2$), 1.59–1.54 (m, 2H, $CH_2$), 1.40–1.34 (m, 1H, CH), 0.88–0.84 (m, 6H, 2$CH_3$); $^{13}$C NMR: δ = 155.03, 138.0, 136.6, 123.0, 67.39, 54.5, 40.8, 29.6, 24.6, 23.5; HR-MS: calcd. for $M^+$: 345.0226; found: 345.0227.

**Bis coupled product B:** $^1$H NMR ($CDCl_3$): δ = 7.36 (m, 4H, Ar), 4.50–4.41 (t, *J* = 8 Hz, 2H), 4.35–4.33 (m, 2H), 4.07–4.02 (dd, *J* = 5.3, 8.08 Hz, 2H), 1.64–1.53 (m, 4H), 1.36–1.0 (m, 2H), 0.89–0.85 (12H, 4$CH_3$); $^{13}$C NMR: δ = 155.5, 133.7, 122.2, 67.5, 54.9, 41.1, 24.7, 23.5, 21.6; HR-MS: calcd. for $M^+$: 360.2049; found: 360.2045.

## Bis-Coupled Product (Table 2, entry 1)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-5-phenyl-2-oxazolidinone (379 mg, 1 mmol), the respective oxazolidinone (177 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 24 h gave the bis-coupled product; yield: 278 mg (65%); data same as for Table 1, entry 1B above.

## Bis-Coupled Product (Table 2, entry 2)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-5-phenyl 2-oxazolidinone (379 mg, 1 mmol), the oxazolidinone (177 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 24 h gave the bis-coupled product; yield: 282.4 mg (66%); mp 188–190 °C; $^1$H NMR ($CDCl_3$): δ = 7.51–7.41 (m, 3H, Ar), 7.3–7.29 (m, 6H, Ar), 7.2–7.1 (m, 3H, Ar), 7.06–7.03 (m, 2H, Ar), 5.75 (d, *J* = 7.7 Hz, CH-Ph), 4.71–4.60 (m, 2H, O-$CH_2$), 4.31 (t, *J* = 8.5 Hz, N-CH), 4.14 (dd, *J* =4.7, 8.7 Hz, 1H, N-CH), 3.0 (dd, *J* = 3.24, 13.7 Hz, 1H, Ph-$CH_2$), 2.75 (dd, *J* = 9.1, 13.7 Hz, 1H, Ph-$CH_2$), 0.79 (t, *J* = 6.4 Hz, 3H, $CH_3$); $^{13}$C NMR: δ = 155.0, 154.6, 134.7, 134.3, 133.7, 133.3, 128.9, 128.4, 127.0, 125.7, 122.1, 122.0, 77.9, 66.7, 65.7, 56.9, 37.5, 14.3; HR-MS: calcd. for $M^+$: 428.1736; found: 428.1739.

## Bis-Coupled Product (Table 2, entry 3)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-5-phenyl 2-oxazolidinone (379 mg, 1 mmol), the oxazolidinone (129 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 5 h gave the bis-coupled product; yield: 300 mg (79%); $^1$H NMR ($CDCl_3$): δ = 7.5–7.1 (m, 9H, Ar), 5.72 (d, *J* = 7.7 Hz, 1H, O-CH-Ph), 4.6–4.58 (m, 1H, $CH_3$-CH-N), 4.37–4.30 (m, 2H, O-$CH_2$-), 4.19–4.12 (m, 1H, N-CH), 2.09–2.06 (m, 1H, CH), 0.85 (d, *J* = 7.10 Hz, 3H, $CH_3$), 0.78–0.75 (m, 6H, 2$CH_3$); $^{13}$C NMR: δ = 155.83, 154.92, 134.59, 133.93, 133.67, 128.66, 126.03, 122.83, 122.38, 122.29, 121.68, 78.18, 62.40, 60.51, 56.96, 27.52, 17.7, 14.5, 14.2; HR-MS: calcd. for $M^+$: 380.1736; found: 380.1743.

## Bis-Coupled Product (Table 2, entry 4)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-5-phenyl-2-oxazolidinone (379 mg, 1 mmol), the oxazolidinone (161 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 24 h gave the bis-coupled product; yield: 383 mg (93%); mp 140–142 °C; $^1$H NMR ($CDCl_3$): δ = 7.51–7.20 (m, 9H, Ar), 5.7 (d, *J* = 7.7 Hz, O-CH-Ph), 4.68–4.59 (m, 1H, N-CH-$CH_3$), 4.51–4.46 (m, 2H, O-$CH_2$), 4.13–4.09 (m, 1H, N-CH-), 2.52–2.39 (m, 2H, $CH_2$-S-), 1.97 (s, 3H, -S-$CH_3$), 1.81–1.75 (m, 2H, -S-$CH_2$-$CH_2$-), 0.76 (d, *J* = 6.4 Hz, $CH_3$); $^{13}$C NMR: δ = 155.3, 154.8, 134.4, 133.9, 133.3, 128.5, 125.9, 122.28, 122.25, 78.1, 69.8, 56.7, 55.2, 34.1, 29.2, 15.6, 14.4.

## Bis-Coupled Product (Table 2, entry 5)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-phenyl-2-oxazolidinone (379 mg, 1 mmol), the oxazolidinone (177 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 24 h gave the bis-coupled product; yield: 325 mg (76%); data same as for Table 1, entry 2B above.

## Bis-Coupled Product (Table 2, entry 6)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-phenyl-2-oxazolidinone (379 mg, 1 mmol), oxazolidinone (129 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 24 h gave the bis-coupled product; yield: 254 mg (67%); mp 268–270 °C; $^1$H NMR ($CDCl_3$): δ = 7.52–7.43 (m, 3H, Ar), 7.26–7.22 (m, 2H,Ar), 7.18 (m, 2H, Ar), 7.11–7.04 (m, 2H, Ar), 4.56–4.52 (dd, *J* = 4.2, 8.7 Hz, 1H, -CH-$CH_2$-Ph), 4.39–4.35 (m, 2H, O-$CH_2$-), 4.31–4.25 (m, 1H, -CH-N-), 4.19–4.11 (m,2H, O-$CH_2$-), 3.12 (dd, *J* = 3.5, 13.7 Hz, 1H, Ph-$CH_2$- ), 2.7 (dd, *J* = 9.4, 13.7 Hz, 1H, $C_6H_5$-CH-), 2.11 (m, -CH-), 0.88–0.80 (m, 6H, 2$CH_3$); $^{13}$C NMR: δ = 155.8 (C=O), 154.7 (C=O), 134.5, 133.8, 133.2, 128.8, 126.2, 123.5, 122.7, 78.4, 57.1, 56.2, 27.6, 14.7, 14.3; HR-MS: calcd. for $M^+$: 380.1736; found: 380.1740.

## Bis-Coupled Product (Table 2, entry 7)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-phenyl-2-oxazolidinone (379 mg, 1 mmol), the oxazolidinone (143 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 24 h gave the bis-coupled product; yield: 263 mg (67%); $^1$H NMR ($CDCl_3$): δ = 7.59–7.46 (m, 4H, Ar), 7.29–7.25 (m, 3H, Ar), 7.13–7.11 (m, 2H, Ar), 4.63–4.34 (m, 4H, $OCH_2$), 4.23–4.16 (m, 2H, -N-CH), 3.19 (dd, *J* = 3.3 Hz, 13.6 Hz, 1H, Ph-$CH_2$), 2.8 (dd, *J* = 13.7, 9.5 Hz, 1H, Ph-$CH_2$), 1.6–1.2 (m, 3H, Ph-$CH_2$-CH-), 0.98–0.86 (m, 6H, 2$CH_3$); $^{13}$C NMR: δ = 155.46 (C=O), 155.3 (C=O), 135.2, 134.0, 133.8, 129.1, 129.0, 127.3, 122.5, 122.2, 121.8, 77.4, 70.6, 51.6, 44.6, 41.3, 38.0, 25.1, 22.9, 22.2; HR-MS: calcd. for $M^+$: 394.1893; found: 394.1890.

### Bis-Coupled Product (Table 2, entry 8)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-isopropyl-2-oxazolidinone (345 mg, 1 mmol), the oxazolidinone (143 mg, 1 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80 °C for 24 h gave the bis-coupled product; yield: 311 mg (90%); $^1$H NMR ($CDCl_3$): δ = 7.49–7.40 (m, 4H, Ar), 4.57 (m, 2H, $OCH_2$), 4.53–4.39 (m, 2H, $OCH_2$), 4.14–4.05 (m, 2H), 1.7–1.6 (m, 3H), 1.47 (m, 1H), 0.97–0.85 (m, 12H, $4CH_3$); $^{13}$C NMR: δ = 155.7 (C=O), 155.4 (C=O), 133.8, 133.7, 122.6, 122.3, 68.4, 62.3, 58.3, 41.1, 27.8, 23.5, 22.6, 21.6, 17.7, 14.5; HR-MS: calcd. for $M^+$: 346.1893; found: 346.1894.

### Bis-Coupled Product (Table 2, entry 9)

Following the general procedure, 3-(4′-iodophenyl)-4-methyl-phenyl-2-oxazolidinone (379 mg, 1 mmol), morpholine (130 mg, 1.5 mmol), CuI (19 mg, 10 mol %), ethylenediamine (6 mg, 10 mol %), $K_3PO_4$ (424 mg, 2 mmol) and 3 mL of dry dioxane at 80° C for 24 h gave the bis-coupled product; yield: 196 mg, (58%); $^1$H NMR ($CDCl_3$): δ = 7.71–7.6 (m, 2H, Ar), 7.35–7.25 (m, 5H, Ar), 7.20–7.16 (m, 2H, Ar), 4.31–4.22 (m, 2H, $OCH_2$), 4.15–4.00 (m, 1H), 3.79–3.6 (m, 4H, morph), 3.10–3.07 (m, 5H, morph. and $CH_2Ph$), 2.80–2.71 (m, 1H, $CH_2Ph$); $^{13}$C NMR: δ = 155.1 (C=O), 135.1, 133.7, 129.4, 126.4, 121.6, 120.3, 67.4, 65.1, 54.3, 49.6, 36.1.

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