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Supporting Information

Photocatalyzed Alkylative Cyclization of 2-Isocyanobiphenyls with Unactivated Alkyl Iodides

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Synthesis of 2-isocyano biaryls:



2-isocyanobiaryls **2a-I** were prepared according to known literature procedure.^[1]

Synthesis of iodo alkanes



Iodo alkanes **2a**, **2b**, **2e**, **2g**, **2h**, **2i**, **2r**, **2t**, **2u**, **2v**, **2w** were purchased from commercial suppliers. Iodo alkanes **2c**, ³ **2d**, ³ **2f**², **2j**, ³ **2k**, ⁴ **2l**, ⁴ **2m**, ⁴ **2n**, ² **2o**², **2p**, ² **2q**, ³ **2s**⁵ were prepared according to known literature procedure.

Optimization details:

General procedure for the optimization:



An oven-dried 10 mL glass vial was charged with **1a** (17.9 mg, 0.1 mmol), **2a** (31.5 mg, 0.15 mmol), amine (0.3 mmol), photocatalyst (3 mol%) and a PTFE coated magnetic bar. The glass vial was sealed with a PTFE septum. Under the positive pressure of argon, degassed EtOAc (1.5 mL) was added to the reaction vial. The reaction vials were placed in a pre-programmed temperature-controlled blue LED reactor (as shown in Figure 1) and the reaction mixture was irradiated with 455 nm blue LED light sources. After 12 h, the product was confirmed by TLC and a sample of this solution was analyzed by ¹HNMR using benzyl alcohol as the internal standard to determine the yield of the reaction.





Figure 1: Blue LED reactor with magnetic stirring

Screening of amines:



Entry	Variation in amines	Yield
1	Tributylamine	90
2	DIPEA	51
3	Et ₃ N	45
4	Bn ₃ N	00
5	Bn ₂ NCy	76
6	DABCO	00
7	Bn ₂ NC ₅ H ₁₁	32
8	TMP	20
9	PMP	18

Optimization of the Reaction Conditions. **1a** (0.1 mmol), **2a** (0.15 mmol). NMR yields using benzyl alcohol as internal standard.

Screening of solvents:

NC 1a	+	NBu ₃ (3 eq) Solvent (0.15 M) 4CzIPN (3 mol%) Blue LEDs, 30 °C, 12 h 2a		N 3a
	Entry	Variation in solvents	Yield	
	1	EtOAc	90	
	2	CH ₃ CN	64	
	3	DMF	70	
	4	Toluene	79	
	5	THF	85	
	6	Ethanol	63	
	7	DCM	80	
	8	Dioxane	85	

Optimization of the Reaction Conditions. **1a** (0.1 mmol), **2a** (0.15 mmol). NMR yields using benzyl alcohol as internal standard.

Screening of photocatalysts





Screening of different light sources and variation in reaction condition



Optimization of the Reaction Conditions. **1a** (0.1 mmol), **2a** (0.15 mmol). NMR yields using benzyl alcohol as internal standard.

Mechanistic Studies

ON/OFF experiments:

A 10 mL glass vial was charged with 2-isocyano-1,1'-biphenyl (**1a**, 0.2 mmol), iodocyclohexane (**2a**, 0.3 mmol), tributylamine (0.6 mmol), 4CZiPN (3mol%), benzyl benzoate (0.1 mmol, internal standard) and a PTFE-coated stirring bar. The glass vial was sealed with a PTFE septum and dry degassed EtOAc solvent (3 mL) was added to the reaction vial. The reactions were placed in a pre-programmed temperature (30 °C) controlled blue LED reactor (as shown in Figure 1) and the reaction mixture was irradiated with a 455 nm blue LED. After the selected time has expired, a small aliquot was removed and subjected to workup with brine solution and EtOAc. The combined organic layer was concentrated under reduced pressure and analyzed by ¹H NMR to determine the yield.



The reaction profile of the on/off experiment showing light is important throughout the reaction.

Radical clock experiment



Following the general procedure two reactions of **1a** (0.1 mmol, 18 mg) and cyclopropyl methyl iodide **2w** (0.15 mmol, 27.2 mg), afforded ring opening product **3ai** in 54% yield (25.1 mg). ¹H NMR (400 MHz, CDCl₃) δ 8.65 (d, J=8.24 Hz, 1H), 8.56-8.54 (m, 1H), 8.27-8.25 (m, 1H), 8.14-8.12 (m, 1H), 7.86-7.82 (m, 1H), 7.74-7.68 (m, 2H), 7.65-7.61 (m, 1H), 6.10-6.00 (m, 1H), 5.20-5.14 (m, 1H), 5.06-5.03 (m, 1H), 3.49-3.45 (m, 2H), 2.75-2.69 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 161.41, 143.84, 138.17, 133.05, 130.45, 129.73, 128.73, 127.42, 126.50, 126.28, 125.35, 123.79, 122.64, 122.05, 115.20, 35.56, 33.30. HRMS (ESI): m/z calculated for C₁₇H₁₆N⁺(M+H)⁺: 234.1277, found: 234.1279. The analytical data are consistent with published ones.¹

Radical trapping experiments:



An oven-dried 10 mL glass vial was charged with 2-isocyano-1,1'-biphenyl (18 mg, 0.1 mmol), Iodo cyclohexane (0.15 mmol, 31.5 mg), 4CzIPN (2.3 mg, 3 mol%), Bu_3N (55.5 mg, 0.3 mmol), ethene-1,1-diyldibenzene (54.0 mg, 0.3 mmol), and a PTFE-coated stirring bar and the glass vial was sealed with a PTFE septum. Under the positive pressure of argon, degassed EtOAc (1.5 mL) was added to the reaction vial. The reactions were placed in a temperature-controlled blue LED reactor (as shown in Figure 1) and the reaction mixture was irradiated with a 455 nm blue LED. After 12 h, a sample of this solution was analyzed by HRMS observed (2-cyclohexylethene-1,1-diyl) dibenzene (5). **HRMS** (APCI): m/z calculated for $C_{20}H_{22}(M)$: 262.1722, found: 262.1716.

The crude NMR of this reaction also indicates the formation of radical trapping product 5 in 20% yield using benzyl alcohol as internal standard.



Crude 1 H NMR (500 MHz) spectra of the reaction mixture in CDCl₃ at 298K



S12



An oven-dried 10 mL glass vial was charged with 2-isocyano-1,1'-biphenyl (18 mg, 0.1 mmol), Iodo cyclohexane (0.15 mmol, 31.5 mg), 4CzIPN (2.3 mg, 3 mol%), Bu₃N (55.5 mg, 3.0 eq), Tempo (31.2 mg, 0.2 mmol) and a PTFE-coated stirring bar and the glass vial was sealed with a PTFE septum. Under the positive pressure of argon, degassed EtOAc (1.5 mL) was added to the reaction vial. The reactions were placed in a temperature-controlled blue LED reactor (as shown in Figure 1) and the reaction mixture was irradiated with a 455 nm blue LED. After 12 h, a sample of this solution was analyzed by HRMS observed 1-(cyclohexyloxy)-2,2,6,6-tetramethyl piperidine (4).

HRMS (ESI): m/z calculated for C₁₅H₃₀NO⁺(M+H)⁺: 240.2322, found: 240.2320.



Luminescence quenching experiments:

Fluorescence spectra were collected on Fluorolog Horiba Jobin Yvon spectrofluorimeter. Samples for the quenching experiments were prepared in a 4 mL glass cuvette with a septum screw cap. 4CzIPN was irradiated at 470 nm and the emission intensity at 570 nm was observed. In a typical experiment, the emission spectrum of a 0.00025 M solution of 4CzIPN in EtOAc was collected.

Sample preparation of 2-isocyano-1,1'-biphenyl (1a):

The sample solution is prepared by mixing 3µl of **1a** to the 4ml of stock solution of 4CzIPN to get concentrations (approximately) in a range of 4 mM, 8 mM, 12 mM, 16 mM, 20 mM.

Sample preparation of iodocyclohexane (2a):

The sample solution is prepared by mixing 2µl of crude **2a** to the 4ml of stock solution of 4CZiPN to get concentrations (approximately) in a range of 4mM, 8mM, 12mM, 16mM, 20mM.

Sample preparation of Tributylamine:

The sample solution is prepared by mixing 4µl of tributylamine to the 4ml of stock solution of 4CzIPN to get concentrations (approximately) in a range of 4mM, 8mM, 12mM, 16mM, 20mM.

As shown below, a significant decrease of 4CzIPN luminescence was observed in presence of Amine, suggesting that the mechanism might operate via a canonical photoredox cycle consisting of a reductive quenching with an amine.



Storn-

As shown below there is negligible change in the luminescence graph by increasing the amount of 2-isocyano-1,1'-biphenyl (1a) to the cuvette containing a stock solution of 4CzIPN (4ml), indicating that there is no quenching of 4CzIPN with 1a.



Storn-

As shown below there is negligible change in the luminescence graph by increasing the amount of iodocyclohexane (**2a**) to the cuvette containing a stock solution of 4CzIPN (4ml), indicating that there is no quenching of 4CzIPN with **2a**.



Storn-

Quantum yield determination:

The determination of the quantum yield of the reaction was carried out using light sources of a photoreactor. All manipulations and preparation of samples were carried out in a dark condition using aluminum foil. The measurement of the photon flux of light sources was determined by standard ferrioxalate actinometry following already reported procedures.

Blue LED strip photoreactor (Irradiation at 450 nm) (QY of ferrioxalate at 450 nm estimated to be 0.99). Photon flux (average of 3 measurements) = 3.10×10^{-9} einstein s⁻¹

Quantum yield determination using Blue LED (450nm) light source

An oven-dried 10 mL glass vial was charged with 2-isocyano-1,1'-biphenyl **1a** (0.1 mmol, 18 mg), Iodoalkane **2a** (0.15 mmol, 31.5 mg), tributylamine (55.5 mg, 0.3 mmol), 4CzIPN (2.3 mg, 3 mol%) and a PTFE coated magnetic bar. The reaction vial was sealed with a PTFE septum. Under the positive pressure of argon, degassed EtOAc (1.5 mL) was added to the reaction vial. The reaction vials were placed in a pre-programmed temperature-controlled blue LED reactor (as shown in Figure 1) and the reaction mixture was irradiated with a 455 nm blue LED light source. After 1800 seconds of irradiation the aliquot amount is taken from the vial for measuring the fraction of light absorbed. Followed by a sample of this solution was analyzed by ¹HNMR using trimethoxy benzene (0.1 mmol) as the internal standard to determine the yield of the reaction.

The fraction of light absorbed (f) = $1-10^{-A} = 1-10^{-1.87} = 0.986$

(Where A is the average of 3 absorption value)

The yield of the reaction is found to be 15%.

$$\Phi = \frac{mol \ of \ 3a}{flux \cdot t \cdot f}$$

$$\Phi = \frac{1.5 \ X \ 10 - 5 \ mol}{3.10 \ X \ 10 - 9 \ einstein \ s - 1 \cdot 1800 sec \ \cdot \ 0.986} \setminus$$

$$\Phi = 2.72$$

Crystal data of compound 3j



 Table 1. Crystal data and structure refinement for 3j.

Identification code	shelx	
Empirical formula	C21 H21 N O2	
Formula weight	319.39	
Temperature	296(2) K	
Wavelength	0.71073 A	
Crystal system, space group	Monoclinic, P 21/c	
Unit cell dimensions	a = 12.3306(9) Å	α = 90 °.
	b = 15.8437(12) Å	$\beta = 94.257(3)$ °
	c = 8.6085(7) Å	γ = 90 °.

Volume	1677.1(2) A^3
Z	4
Calculated density	1.265 Mg/m ³
Absorption coefficient	0.081 mm ⁻¹
F(000)	680
Crystal size	0.085 x 0.048 x 0.038 mm
Theta range for data collection	1.656 to 28.392 deg.
Limiting indices	-15<=h<=16, -21<=k<=21, -11<=l<=11
Reflections collected / unique	25392 / 4194 [R(int) = 0.0618]
Completeness to theta = 25.242	100.0 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4194 / 0 / 225
Goodness-of-fit on F ²	0.993
Final R indices [I>2sigma(I)]	R1 = 0.0543, wR2 = 0.1204
R indices (all data)	R1 = 0.1318, wR2 = 0.1542
Extinction coefficient	n/a
Largest diff. peak and hole	0.209 and -0.226 e.A^-3

NMR Spectra



Figure S1. ¹H NMR (500 MHz) spectra of **3a** in CDCl₃ at 298K.



Figure S2. $^{13}C{^{1}H}$ NMR (125 MHz) spectra of **3a** in CDCl₃ at 298K.



Figure S3. 1 H NMR (500 MHz) spectra of **3b** in CDCl₃ at 298K.



Figure S4. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz) spectra of 3b in CDCl3 at 298K.



Figure S5. ¹H NMR (500 MHz) spectra of **3c** in CDCl₃ at 298K.



Figure S6. $^{13}C\{^{1}H\}$ NMR (125 MHz) spectra of 3c in CDCl3 at 298K



Figure S7. ¹H NMR (500 MHz) spectra of **3d** in CDCl₃ at 298K

* * *



Figure S8. $^{13}C{^{1}H}$ NMR (125 MHz) spectra of 3d in CDCl₃ at 298K



Figure S9. ¹H NMR (500 MHz) spectra of **3e** in CDCl₃ at 298K



Figure S10. $^{13}\text{C}\{^1\text{H}\}\,\text{NMR}$ (100 MHz) spectra of 3e in CDCl3 at 298K



Figure S11. ¹H NMR (500 MHz) spectra of **3f** in CDCl₃ at 298K

*



Figure S12. $^{13}C{^{1}H}$ NMR (125 MHz) spectra of 3f in CDCl₃ at 298K



Figure S13. ¹H NMR (500 MHz) spectra of **3g** in CDCl₃ at 298K



Figure S14. $^{13}C{^{1}H} NMR$ (125 MHz) spectra of 3g in CDCl₃ at 298K



Figure S15. ¹H NMR (500 MHz) spectra of **3h** in CDCl₃ at 298K


Figure S16. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz) spectra of 3h in CDCl3 at 298K



Figure S17. ¹H NMR (400 MHz) spectra of **3i** in CDCl₃ at 298K



Figure S18. $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz) spectra of 3i in CDCl3 at 298K



Figure S19. ¹H NMR (500 MHz) spectra of 3j in CDCl₃ at 298K



Figure S20. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz) spectra of 3j in CDCl3 at 298K



Figure S21. ¹H NMR (500 MHz) spectra of **3k** in CDCl₃ at 298K



Figure S22. ${}^{13}C{}^{1}H{} NMR$ (125 MHz) spectra of **3k** in CDCl₃ at 298K



Figure S23. ¹H NMR (500 MHz) spectra of 3I in CDCl₃ at 298K



Figure S24. ¹³C{¹H} NMR (125 MHz) spectra of 3I in CDCl₃ at 298K



Figure S25. 1 H (500 MHz), 13 C (125 MHz) HMQC NMR spectrum of **3I** in CDCl₃, 298 K.



Figure S26. Part of ¹H (500 MHz), ¹³C (150 MHz) HMQC NMR spectrum of 3I (region of the aliphatic proton, carbon is shown) in CDCl₃, 298 K

The compound **3I** has N-benzoyl piperidine functionality. The four methylene protons near to the nitrogen are chemically different at room temperature probably because of restricted rotation about the C-N bond due to the partial double bond character. This is the reason why in ¹H NMR the broad peak was observed for protons. Also, due to this restricted rotation, the two methylene carbons have different chemical shift values in ¹³C NMR.⁶⁻⁷



Figure S27. ¹H NMR (500 MHz) spectra of **3m** in CDCl₃ at 298K



Figure S28. $^{13}C{^1H}$ NMR (125 MHz) spectra of **3m** in CDCl₃ at 298K



Figure S29. ¹H NMR (500 MHz) spectra of **3n** in CDCl₃ at 298K



Figure S30. $^{13}\text{C}\{^1\text{H}\}\,\text{NMR}$ (125 MHz) spectra of 3n in CDCl3 at 298K



Figure S31. ¹H NMR (500 MHz) spectra of **30** in CDCl₃ at 298K



Figure S32. $^{13}C{^{1}H} NMR{^{1}H} (125 MHz)$ spectra of **30** in CDCl₃ at 298K



Figure S33. ¹H NMR (500 MHz) spectra of **3p** in CDCl₃ at 298K



Figure S34. $^{13}C{^{1}H}$ NMR (125 MHz) spectra of **3p** in CDCl₃ at 298K



Figure S35. ¹H NMR (500 MHz) spectra of **3q** in CDCl₃ at 298K



Figure S36. $^{13}C\{^{1}H\}$ NMR $\{^{1}H\}$ (125 MHz) spectra of 3q in CDCl3 at 298K



Figure S37. ¹H NMR (500 MHz) spectra of **3r** in CDCl₃ at 298K



Figure S38. $^{13}C{^{1}H} NMR{^{1}H}$ (125 MHz) spectra of **3r** in CDCl₃ at 298K



Figure S39. 1 H NMR (700 MHz) spectra of 3s in CDCl₃ at 298K



Figure S40. $^{13}C\{^{1}H\}$ NMR $\{^{1}H\}$ (125 MHz) spectra of 3s in CDCl3 at 298K



Figure S41. ¹H NMR (500 MHz) spectra of 3t in CDCl₃ at 298K



Figure S42. ${}^{13}C{}^{1}H$ NMR ${}^{1}H$ (125 MHz) spectra of **3t** in CDCl₃ at 298K



Figure S43. ¹H NMR (500 MHz) spectra of **3u** in CDCl₃ at 298K



Figure S44. $^{13}C\{^{1}H\}$ NMR $\{^{1}H\}$ (100 MHz) spectra of 3u in CDCl3 at 298K



Figure S45. ¹H NMR (500 MHz) spectra of **3v** in CDCl₃ at 298K



Figure S46. $^{13}\text{C}\{^{1}\text{H}\}\,\text{NMR}$ (125 MHz) spectra of 3ν in CDCl3 at 298K



Figure S47. ^1H NMR (500 MHz) spectra of 3w in CDCl3 at 298K



Figure S48. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz) spectra of 3w in CDCl3 at 298K



Figure S49. ¹H NMR (500 MHz) spectra of 3x in CDCl₃ at 298K



Figure S50. $^{13}C{^{1}H}$ NMR (125 MHz) spectra of **3x** in CDCl₃ at 298K


Figure S51. ¹H NMR (400 MHz) spectra of 3y in CDCl₃ at 298K



Figure S52. $^{13}C{^{1}H} NMR$ (100 MHz) spectra of **3y** in CDCl₃ at 298K



Figure S53. ^1H NMR (500 MHz) spectra of 3z in CDCl3 at 298K



Figure S54. $^{13}C{^{1}H}$ NMR (125 MHz) spectra of 3z in CDCl₃ at 298K



Figure S55. ¹H NMR (500 MHz) spectra of **3aa** in CDCl₃ at 298K



Figure S56. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz) spectra of **3aa** in CDCl₃ at 298K



Figure S57. ¹H NMR (500 MHz) spectra of **3ab** in CDCl₃ at 298K



Figure S58. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz) spectra of **3ab** in CDCl₃ at 298K



Figure S59. ¹⁹F NMR (471 MHz) spectra of **3ab** in CDCl₃ at 298K



Figure S60. ¹H NMR (500 MHz) spectra of **3ac** in CDCl₃ at 298K



Figure S61. ${}^{13}C{}^{1}H$ NMR (125 MHz) spectra of **3ac** in CDCl₃ at 298K



Figure S62. $^{19}\mathsf{F}$ NMR (471 MHz) spectra of 3ac in CDCl3 at 298K



Figure S63. ¹H NMR (500 MHz) spectra of **3ad** in CDCl₃ at 298K



Figure S64. $^{13}C{^{1}H}$ NMR (125 MHz) spectra of **3ad** in CDCl₃ at 298K



Figure S65. ¹H NMR (500 MHz) spectra of **3ae** in CDCl₃ at 298K



Figure S66. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz) spectra of **3ae** in CDCl_3 at 298K



Figure S67. ¹H NMR (500 MHz) spectra of **3af** in CDCl₃ at 298K



Figure S68. $^{13}C{^{1}H}$ NMR (125 MHz) spectra of **3af** in CDCl₃ at 298K



Figure S69. ¹H NMR (500 MHz) spectra of **3ag** in CDCl₃ at 298K



Figure S70. $^{13}C{^1H}$ NMR (125 MHz) spectra of **3ag** in CDCl₃ at 298K



Figure S71. ¹H NMR (500 MHz) spectra of **3ah** in CDCl₃ at 298K



Figure S72. $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz) spectra of **3ah** in CDCl₃ at 298K



Figure S73. 1 H NMR (400 MHz) spectra of **3ai** in CDCl₃ at 298K



Figure S74. $^{13}\text{C}\{^{1}\text{H}\}$ NMR (100 MHz) spectra of 3ai in CDCl3 at 298K

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