Supporting Information for

Base-Promoted Tandem Ring-Opening/Ring-Closing of *N*-Alkynyl-2-oxazolidinones Enables Facile Synthesis of 2-Oxazolines

Xingyuan Ye,[a] Peng Bao,[a] Yan Pan,[b] Han Xiao,[a] Qiuwen Li,[a] and Guangke He*[a]

[a] *Department of Applied Chemistry, School of Chemistry and Molecular Engineering, Nanjing Tech University, Nanjing 211816, P. R. China.*

[b] *Department of Pharmacy School of Pharmaceutical Sciences, Nanjing Tech University, Nanjing 211816, P. R. China.*

*E-mail: hegk@njtech.edu.cn;

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1. General Information

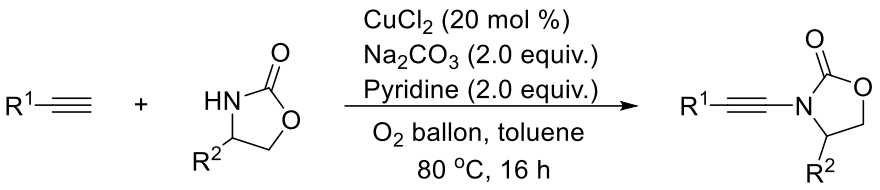
All NMR spectra were recorded on a Bruker ASCEND^{TM} 400 or a JEOL ECZS 400 MHz spectrometer. ^{1}H and ^{13}C NMR spectral data are reported as chemical shifts (δ) in parts per million (ppm) relative to tetramethylsilane. ^{19}F NMR spectra are referenced relative to $CFCl_3$ (as the external standard) in $CDCl_3$. Chemical shifts (δ) are quoted in parts per million (ppm) and coupling constants (J) are measured in hertz (Hz). The following abbreviations are used to describe multiplicities s=singlet, d=doublet, t=triplet, q=quartet, pent=pentet, br=broad, m=multiplet. NMR spectra were processed in Bruker's TopSpin™ or MestReNova software package. High resolution mass spectra (HRMS, m/z) were recorded on a Bruker MicroTOF spectrometer using positive electrospray ionization (ESI) or on a Micromass GCT spectrometer using field ionization (EI/FI) or chemical ionization (CI). IR spectra were recorded on a Thermo Scientific Nicolet iS5 FT-IR spectrometer. Absorptions are measured in wavenumbers and only peaks of interest are reported. Melting points of solids were measured on a Griffin apparatus and are uncorrected. IUPAC names were obtained using the ACD/ILab service. Weighing was perfomed with a 4 decimal place balance. Reactions were monitored by thin-layer chromatography, carried out on 0.25 mm silica gel plates. Visualization was performed with a 254 nm UV lamp or iodine. Characterization data for those compounds not described in the literature are provided.

Phenylacetylene, *p*-methylphenylacetylene, *p*-methoxylphenylacetylene, *p*-bromophenylacetylene, *p*-fluorophenylacetylene, 1-hexyne, 1-heptyne, and 2-(phenylethynyl)thiophene were purchased from commercial sources and used as received.

2. General Procedure for Experiments and Analytical data

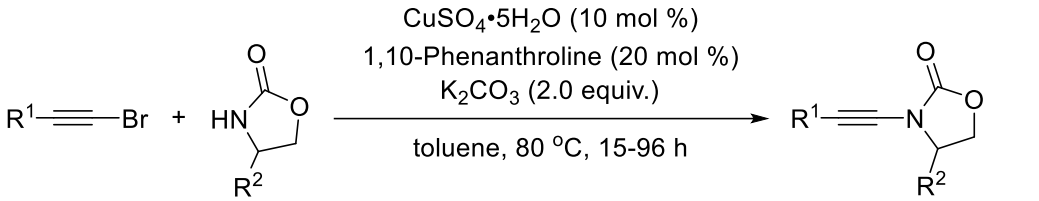
2.1 Synthesis of Ynamides

General procedure I: Copper-Catalyzed Aerobic Oxidative Amidation of Terminl Alkynes



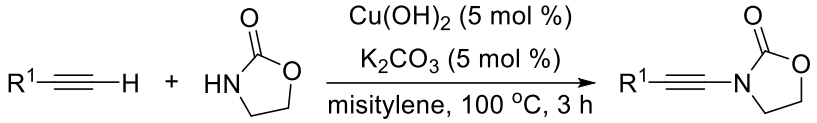
Following Stahl's procedure[1], to a oven-dried 250 mL three-neck round-bottomed flask were added $CuCl_2$ (20 mol%), 2-oxazolidinone (5.0 equiv.) and Na_2CO_3 (2.0 equiv.). The reaction flask was evacuated and backfilled with oxygen. A solution of pyridine (2.0 equiv.) in dry toluene (0.1 M) was added. A balloon filled with oxygen was connected to the flask and the reaction was heated at 70 °C. After 15 minutes, a solution of the alkyne (1.0 equiv.) in dry toluene (0.1 M) was added over 4 hours by using a syringe-pump. After the addition, the green to blue mixture was allowed to stir at 80 °C for additional 16 hours and then was cooled to room temperature. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel.

General procedure II: Copper-Catalyzed Alkynylation of Nitrogen Nucleophiles with Bromoalkynes



Following Hsung's[2] procedure, a 30-mL sealed tube was charged with the nitrogen nucleophile (1.0 equiv.), potassium carbonate (2.0 equiv.), $CuSO_4 \cdot 5H_2O$ (10 mol%), 1,10-phenanthroline (20 mol%) under Ar. The tube was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon three times. Dry and degassed toluene (1 M) and alkynyl bromide (1.1 equiv.) were added, the rubber septum was replaced by a Teflon-coated screw cap and the mixture was stirred at 80 °C for 15-96 hours. The reaction mixture was then cooled to room temperature, filtered over a plug of celite (washed with EtOAc) and concentrated under reduced pressure. The crude residue was purified by flash column chromatography over silica gel.

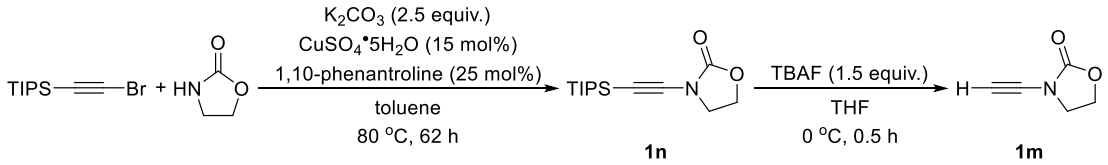
General procedure III: Heterogeneously Catalyzed Selective Aerobic Oxidative Cross-coupling of Terminal Alkynes and Amides with Simple Copper(II) Hydroxide



1.0 equiv. 3.0 equiv. **1d; 1f; 1h**

Following Mizuno's[3] procedure, into a Pyrex-glass screw cap vial (volume: ca. 20 mL) were successively placed $Cu(OH)_2$ (5 mol% with respect to an alkyne), K_2CO_3 (5 mol%), an alkyne (0.1 mmol), an amide (3 equiv. with respect to an alkyne), and mesitylene (1 mL). A Teflon-coated magnetic stir bar was added, and the reaction mixture was vigorously stirred at 100 °C, under 1 atm of air. After the reaction, the crude reaction mixture was directly subjected to column chromatography on silica gel.

General procedure IV: Copper Catalyzed Coupling of Amides and 1-Bromo-2-triisopropyl silylacetylene and Deprotection Step Leading to Terminal Ynamides

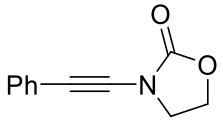


1n **1m**

Synthesis of TIPS-substituted ynamides[2]: Following the slightly modified method by Hsung for coppercatalyzed coupling of amides and 1-bromo-2-triisopropylsilylacetylene1, a oven-dried 30-mL sealed tube was charged with (*R*)-4-phenyloxazolidin-2-one or 2-oxazolidinone (1.0 equiv.), potassium carbonate (2.5 equiv.), $CuSO_4 \cdot 5H_2O$ (0.15 equiv.), 1,10-phenanthroline (0.3 equiv.). The tube was fitted with a rubber septum, evacuated under high vacuum and backfilled with argon three times. Dry and degassed toluene (20 mL) and (bromoethynyl)triisopropylsilane (1.5 equiv.) were added, the rubber septum was replaced by a Teflon-coated screw cap and the mixture was stirred at 80 °C for 62 hours. The reaction mixture was then cooled to room temperature, filtered over a plug of celite (eluted with EtOAc) and concentrated under reduced pressure. The crude product was purified by flash column chromatography over silica gel.

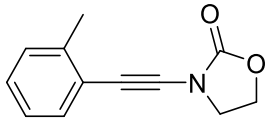
Deprotection of TIPS-substituted Ynamides[4]: To a stirred solution of the appropriate TIPS-substituted ynamide (1.0 equiv., 0.2 M in THF) cooled to 0 °C was added a solution of TBAF (1.5 equiv., 1.0 M in THF). After 0.5 h stirring at 0 °C, the brown reaction mixture was allowed to warm to room temperature and then quenched with sat. aq. NH_4Cl. The aqueous layer was extracted with EtOAc (x3). The combined organics were washed with brine, dried over Na2SO4, filtered and the solvents were evaporated under reduced pressure to afford the crude product. Purification by flash column chromatography over silica gel.

3-(phenylethynyl)oxazolidin-2-one (**1a**).[1]



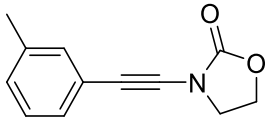
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.40 (m, 2 H), 7.32 - 7.29 (m, 3 H), 3.31 (s, 2 H), 3.13 (s, 2 H).

3-(*o*-tolylethynyl)oxazolidin-2-one (**1b**).[2]



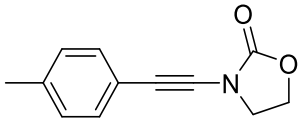
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 - 7.37 (m, 1 H), 7.22 - 7.18 (m, 2 H), 7.16 - 7.10 (m, 1 H), 4.53 - 4.47 (m, 2 H), 4.09 - 3.90 (m, 2 H), 2.44 (s, 3 H).

3-(*m*-tolylethynyl)oxazolidin-2-one (**1c**).[2]



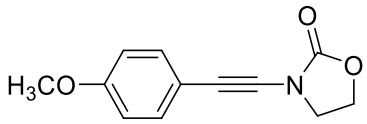
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 - 7.23 (m, 2 H), 7.19 (t, J = 7.5 Hz, 1 H), 7.14 - 7.10 (m, 1 H), 4.51 - 4.46 (m, 2 H), 4.04 - 3.98 (m, 2 H), 2.32 (s, 3 H).

3-(*p*-tolylethynyl)oxazolidin-2-one (**1d**).[3]



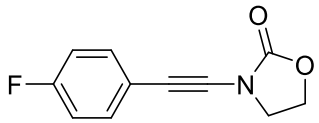
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.1 Hz, 2 H), 7.13 - 7.10 (m, 2 H), 4.51 - 4.46 (m, 2 H), 4.04 - 3.98 (m, 2 H), 2.35 (s, 3 H).

3-((4-methoxyphenyl)ethynyl)oxazolidin-2-one (**1e**).[1]



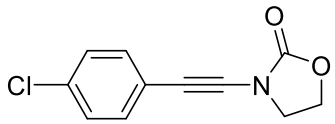
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.8 Hz, 2 H), 6.82 (d, J = 8.8 Hz, 2 H), 4.48 - 4.43 (m, 2 H), 4.00 - 3.94 (m, 2 H), 3.79 (s, 3 H).

3-((4-fluorophenyl)ethynyl)oxazolidin-2-one (**1f**).[3]



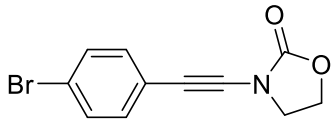
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 - 7.40 (m, 2 H), 7.04 - 6.97 (m, 2 H), 4.52 - 4.47 (m, 2 H), 4.04 - 3.98 (m, 2 H).

3-((4-chlorophenyl)ethynyl)oxazolidin-2-one (**1g**).[2]



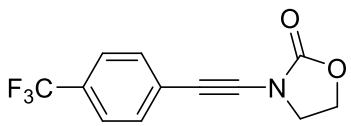
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 - 7.33 (m, 2 H), 7.33 - 7.24 (m, 2 H), 4.58 - 4.43 (m, 2 H), 4.08 - 3.95 (m, 2 H).

3-((4-bromophenyl)ethynyl)oxazolidin-2-one (**1h**).[3]



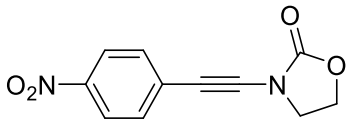
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 10.2 Hz, 2 H), 7.25 (d, J = 9.0 Hz, 2 H), 3.72 (t, J = 7.2 Hz, 2 H), 2.43 (t, J = 8.4 Hz, 2 H), 2.18 - 2.07 (m, 2 H).

3-((4-(trifluoromethyl)phenyl)ethynyl)oxazolidin-2-one (**1i**).[2]



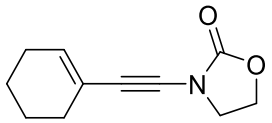
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.5 Hz, 2 H), 7.53 (d, J = 8.5 Hz, 2 H), 4.55 - 4.49 (m, 2 H), 4.07 - 4.01 (m, 2 H).

3-[2-(4-Nitrophenyl)ethynyl]oxazolidin-2-one (**1j**).[1]



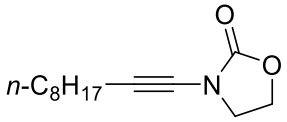
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 - 8.14 (m, 2 H), 7.59 - 7.51 (m, 2 H), 4.55 (t, J = 7.9 Hz, 2 H), 4.07 (t, J = 7.9 Hz, 2 H) ppm.

3-(cyclohex-1-en-1-ylethynyl)oxazolidin-2-one (**1k**).[1]



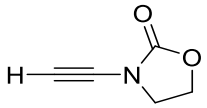
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.11 - 6.08 (m, 1 H), 4.44 - 4.39 (m, 2 H), 3.92 - 3.87 (m, 2 H), 2.14 - 2.05 (m, 4 H), 1.64 - 1.52 (m, 4 H).

3-(dec-1-yn-1-yl)oxazolidin-2-one (**1l**).[1]



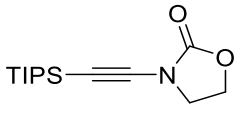
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 - 4.38 (m, 2 H), 3.92 - 3.84 (m, 2 H), 2.30 (t, J = 7.2 Hz, 2 H), 1.58 - 1.47 (m, 2 H), 1.43 - 1.17 (m, 10 H), 0.88 (td, J = 6.9, 2.2 Hz, 5 H).

3-((4-bromophenyl)ethynyl)oxazolidin-2-one (**1m**).[4]



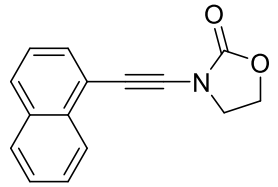
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.48 - 4.43 (m, 2 H), 3.97 - 3.91 (m, 2 H), 2.86 (s, 1 H).

3-((triisopropylsilyl)ethynyl)oxazolidin-2-one (**1n**).[1]



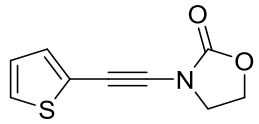
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 (t, J = 7.9 Hz, 2 H), 3.93 (t, J = 7.9 Hz, 2 H), 1.08 (s, 21 H).

3-(naphthalen-1-ylethynyl)oxazolidin-2-one (**1o**).[1]



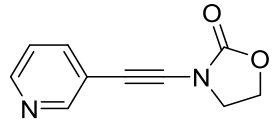
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J_1 = 8.3 Hz, J_2 = 1.1 Hz, 1 H), 7.84 (d, J = 8.0 Hz, 1 H), 7.81 (d, J = 8.3 Hz, 1 H), 7.66 (dd, J_1 = 7.1 Hz, J_2 = 1.2 Hz, 1 H), 7.58 (ddd, J_1 = 8.3 Hz, J_2 = 6.8 Hz, J_3 = 1.4 Hz, 1 H), 7.51 (ddd, J_1 = 8.1 Hz, J_2 = 6.8 Hz, J_3 = 1.4 Hz, 1 H), 7.41 (dd, J_1 = 8.3 Hz, J_2 = 7.1 Hz, 1 H), 4.54 - 4.46 (m, 2 H), 4.11 - 4.02 (m, 2 H).

3-(thiophen-2-ylethynyl)oxazolidin-2-one (**1p**).[1]



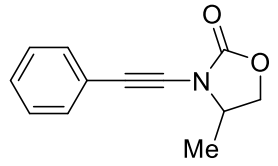
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, J_1 = 5.2 Hz, J_2 = 1.2 Hz, 1 H), 7.23 (dd, J_1 = 3.6 Hz, J_2 = 1.2 Hz, 1 H), 6.97 (dd, J_1 = 5.2 Hz, J_2 = 3.6 Hz, 1 H), 4.50 - 4.45 (m, 2 H), 4.01 - 3.96 (m, 2 H).

3-(pyridin-3-ylethynyl)oxazolidin-2-one (**1q**).[2]



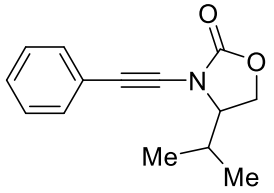
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 0.9 Hz, 1 H), 8.51 (dd, J_1 = 4.9 Hz, J_2 = 1.9 Hz, 1 H), 7.72 (dt, J_1 = 7.9 Hz, J_2 = 1.9 Hz, 1 H), 7.24 (ddd, J_1 = 7.9 Hz, J_2 = 4.9 Hz, J_3 = 0.9 Hz, 1 H), 4.53 - 4.48 (m, 2 H), 4.05 - 4.00 (m, 2 H).

4-methyl-3-(phenylethynyl)oxazolidin-2-one (**1r**).[5]



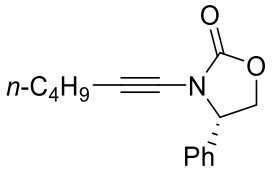
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 - 7.40 (m, 2 H), 7.31 (tt, J_1 = 3.9 Hz, J_2 = 2.5 Hz, 3 H), 4.57 (t, J = 8.4 Hz, 1 H), 4.28 - 4.16 (m, 1 H), 4.02 (dd, J_1 = 8.7 Hz, J_2 = 7.0 Hz, 1 H), 1.50 (d, J = 6.3 Hz, 3 H).

4-isopropyl-3-(phenylethynyl)oxazolidin-2-one (**1s**).[5]



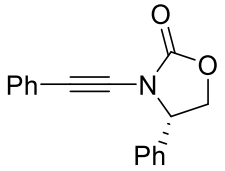
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 - 7.39 (m, 2 H), 7.34 - 7.27 (m, 3 H), 4.43 (t, J = 8.9 Hz, 1 H), 4.20 (dd, J_1 = 9.0 Hz, J_2 = 5.8 Hz, 1 H), 4.05 (ddd, J_1 = 8.7 Hz, J_2 = 5.7 Hz, J_3 = 4.1 Hz, 1 H), 2.29 (pd, J_1 = 6.9 Hz, J_2 = 4.1 Hz, 1 H), 1.03 (dd, J_1 = 6.9 Hz, J_2 = 3.1 Hz, 6 H).

(*S*)-3-(hex-1-yn-1-yl)-4-phenyloxazolidin-2-one (**1t**).[1]



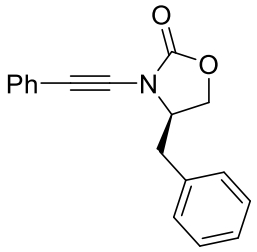
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 - 7.38 (m, 3 H), 7.37 - 7.31 (m, 2 H), 5.00 (dd, J_1 = 8.7 Hz, J_2 = 7.2 Hz, 1 H), 4.71 (t, J = 8.8 Hz, 1 H), 4.23 (dd, J_1 = 8.9 Hz, J_2 = 7.2 Hz, 1 H), 2.16 (t, J = 7.0 Hz, 2 H), 1.65 (s, 1 H), 1.33 (dtd, J_1 = 8.6 Hz, J_2 = 7.0 Hz, J_3 = 5.6 Hz, 2 H), 1.23 - 1.12 (m, 2 H), 0.77 (t, J = 7.3 Hz, 3 H).

(*S*)-4-phenyl-3-(phenylethynyl)oxazolidin-2-one (**1u**).[1]



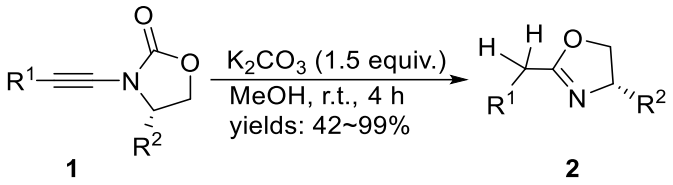
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 - 7.37 (m, 5 H), 7.23 (tdd, J_1 = 10.0 Hz, J_2 = 4.5 Hz, J_3 = 2.1 Hz, 5 H), 5.14 (dd, J_1 = 8.7 Hz, J_2 = 7.1 Hz, 1 H), 4.78 (t, J = 8.8 Hz, 1 H), 4.31 (dd, J_1 = 9.0 Hz, J_2 = 7.1 Hz, 1 H).

(*R*)-4-benzyl-3-(phenylethynyl)oxazolidin-2-one (**1v**).[1]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 - 7.45 (m, 2 H), 7.39 - 7.24 (m, 8 H), 4.39 - 4.35 (m, 2 H), 4.22 - 4.17 (m, 1 H), 3.30 (dd, J_1 = 13.9 Hz, J_2 = 3.8 Hz, 1 H), 3.02 (dd, J_1 = 13.9, J_2 = 7.7 Hz, 1 H)

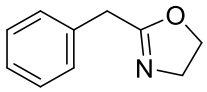
2.2 Synthesis of 2-Oxazolines



1 **2**

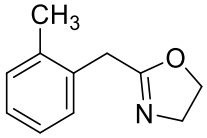
General Procedure for the Synthesis of 2-Oxazolines (**2**). To a 25 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar were added alkynamide **1** (0.4 mmol), K_2CO_3 (0.6 mmol) and MeOH (4 mL). The reaction mixture was stirred for 4 h at room temperature (25 ^{o}C). Alkynamide **1k** and **1l** were conducted at 50 ^{o}C, **1t** was conducted at 80 ^{o}C. Then, upon the completion, the reaction was quenched by the addition of H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the desired products **2**.

2-Benzyl-4,5-dihydrooxazole (**2a**).[6]



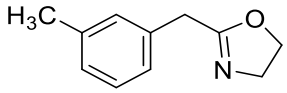
Colorless oil; 32.1 mg; >99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00-7.51 (m, 5 H), 4.23 (t, J = 9.5 Hz, 2 H), 3.84 (t, J = 9.5 Hz, 2 H), 3.62 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 135.1, 128.9, 128.5, 126.9, 67.5, 54.4, 34.6. IR (KBr, cm^{-1}) v 3061, 2973, 2904, 2877, 1646, 1603, 1580, 1496, 1450, 1259, 1062, 942, 778, 691. HRMS (ESI/[M+H]$^+$) Calc. for: $C_{10}H_{12}NO$ 162.0913, found: 162.0917.

2-(2-Methylbenzyl)-4,5-dihydrooxazole (**2b**).



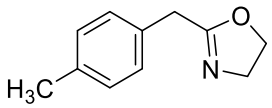
Colorless oil; 62.1 mg; 89% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97-7.39 (m, 4 H), 4.21 (t, J = 9.5 Hz, 2 H), 3.82 (t, J = 9.5 Hz, 2 H), 3.60 (s, 2 H), 2.35 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 136.6, 133.6, 130.2, 129.7, 127.2, 126.0, 67.4, 54.3, 32.3, 19.5. IR (KBr, cm^{-1}) v 3064, 3020, 2973, 2938, 2905, 2882, 1667, 1494, 1462, 1494, 1358, 1239, 1159, 985, 959, 747, 735. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{11}H_{14}NO$ 176.1075, found: 176.1066.

2-(3-Methylbenzyl)-4,5-dihydrooxazole (**2c**).



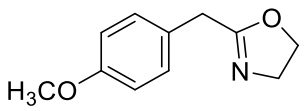
Colorless oil; 63.9 mg; 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17-7.24 (m, 1 H), 6.96-7.15 (m, 3 H), 4.22 (t, J = 9.5 Hz, 2 H), 3.83 (t, J = 9.5 Hz, 2 H), 3.57 (s, 2 H), 2.33 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 138.1, 134.9, 129.6, 128.4, 127.7, 125.9, 67.5, 54.3, 34.5, 21.2. IR (KBr, cm^{-1}) v 3022, 2973, 2907, 2882, 1667, 1608, 1358, 1241, 1160, 985, 961, 756, 691. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{11}H_{14}NO$ 176.1075, found: 176.1067.

2-(4-Methylbenzyl)-4,5-dihydrooxazole (**2d**).



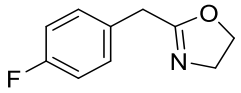
Colorless oil; 32.0 mg; 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, J = 8.0 Hz, 2 H), 7.13 (d, J = 7.6 Hz, 2 H), 4.22 (t, J = 9.5 Hz, 2 H), 3.82 (t, J = 9.5 Hz, 2 H), 3.57 (s, 2 H), 2.32 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 136.5, 132.0, 129.2, 128.8, 67.5, 54.3, 34.2, 21.0. IR (KBr, cm^{-1}) v 2974, 2922, 2882, 1666, 1515, 1361, 1240, 1159, 1022, 1006, 985, 960, 923, 767. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{11}H_{14}NO$ 176.1075, found: 176.1071.

2-(4-Methoxybenzyl)-4,5-dihydrooxazole (**2e**).[7]



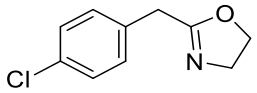
Colorless oil; 38.0 mg; >99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16-7.25 (m, 2 H), 6.79-6.91 (m, 2 H), 4.23 (t, J = 9.5 Hz, 2 H), 3.73-3.93 (m, 5 H), 3.55 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 158.5, 130.0, 127.1, 113.9, 67.5, 55.2, 54.3, 33.8. IR (KBr, cm^{-1}) ν 3063, 2956, 2936, 2906, 2882, 2836, 1667, 1611, 1513, 1360, 1248, 1177, 1158, 1033, 985, 960, 821, 226. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{11}H_{14}NO_2$ 192.1025, found: 192.1018.

2-(4-Fluorobenzyl)-4,5-dihydrooxazole (**2f**).



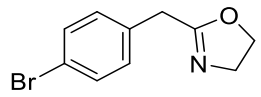
Colorless oil; 33.1 mg; 92.5% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, J_1 = 8.4 Hz, J_2 = 5.1 Hz, 2 H), 7.00 (t, J = 8.5 Hz, 2 H), 4.24 (t, J = 9.5 Hz, 2 H), 3.84 (t, J = 9.5 Hz, 2 H), 3.58 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 162.5 (d, J = 243.6 Hz), 130.8 (d, J = 3.4 Hz), 130.5 (d, J = 8.0 Hz), 130.3 (d, J = 21.4 Hz), 67.6, 54.3, 33.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.9. IR (KBr, cm^{-1}) ν 3046, 2976, 2938, 2909, 2885, 1667, 1605, 1510, 1223, 1158, 985, 838, 826, 781. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{10}H_{11}FNO$ 180.0825, found: 180.0820.

2-(4-Chlorobenzyl)-4,5-dihydrooxazole (**2g**).



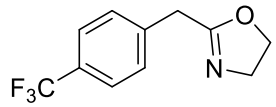
Colorless oil; 76.6 mg; 98% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.32 (m, 2 H), 7.20-7.26 (m, 2 H), 4.23 (t, J = 9.5 Hz, 2 H), 3.83 (t, J = 9.5 Hz, 2 H), 3.57 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 133.5, 132.8, 130.3, 128.6, 67.6, 54.3, 33.9. IR (KBr, cm^{-1}) ν 3047, 2974, 2936, 2906, 2882, 1667, 1492, 1360, 1239, 1163, 1086, 1017, 985, 960, 805, 756. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{10}H_{11}ClNO$ 196.0529, found: 196.0526.

2-(4-Bromobenzyl)-4,5-dihydrooxazole (**2h**).



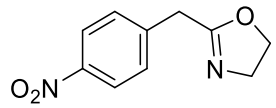
Colorless oil; 44.7 mg; 93% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.50 (m, 2 H), 7.12-7.22 (m, 2 H), 4.23 (t, J = 9.5 Hz, 2 H), 3.83 (t, J = 9.4 Hz, 2 H), 3.55 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 134.1, 131.6, 130.7, 120.9, 67.6, 54.4, 34.0. IR (KBr, cm^{-1}) ν 2973, 2936, 2904, 2881, 1667, 1488, 1360, 1239, 1163, 1071, 1012, 984, 803, 687. HRMS (ESI/[M+H]$^{+}$) Calc. for: $C_{10}H_{11}BrNO$ 240.0024, found 240.0028.

2-(4-(Trifluoromethyl)benzyl)-4,5-dihydrooxazole (**2i**).



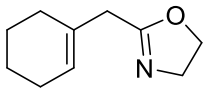
Colorless oil; 85.1 mg; 93% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.1 Hz, 2 H), 7.43 (d, J = 8.0 Hz, 2 H), 4.26 (t, J = 9.5 Hz, 2 H), 3.85 (t, J = 9.5 Hz, 2 H), 3.67 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 139.1, 129.3 (q, J = 32.3 Hz), 129.4, 125.5 (q, J = 3.8 Hz), 124.1 (q, J = 270.4 Hz), 67.7, 54.4, 34.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5. IR (KBr, cm^{-1}) ν 3074, 2917, 2849, 1650, 1326, 1164, 1123, 1067, 1019, 821, 801. HRMS (ESI/[M+H]$^{+}$) Calc. for: $C_{11}H_{11}F_3NO$ 230.0793, found: 230.0797.

2-(4-Nitrobenzyl)-4,5-dihydrooxazole (**2j**).



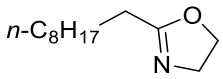
Light yellow solid; 77.9 mg; mp: 85.7-87.2 ºC; 94.5% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.29 (m, 2 H), 7.39-7.60 (m, 2 H), 4.28 (t, J = 9.5 Hz, 2 H), 3.87 (t, J = 9.5 Hz, 2 H), 3.72 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 147.0, 142.6, 129.9, 123.7, 67.7, 54.4, 34.3. IR (KBr, cm^{-1}) ν 3109, 3077, 2923, 2852, 1665, 1518, 1346, 1243, 1164, 1109, 984, 856, 725. HRMS (ESI/[M+H]$^{+}$) Calc. for: $C_{10}H_{11}N_2O_3$ 207.0770, found: 207.0764.

2-(Cyclohex-1-en-1-ylmethyl)-4,5-dihydrooxazole (**2k**).



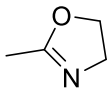
Colorless oil; 49.9 mg; 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.58 (dt, J_1 = 3.6 Hz, J_2 = 2.0 Hz, 1 H), 4.24 (t, J = 9.5 Hz, 2 H), 3.84 (t, J = 9.4 Hz, 2 H), 2.94 (s, 2 H), 1.94-2.08 (m, 4 H), 1.51-1.69 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 131.9, 124.7, 67.2, 54.3, 36.8, 28.0, 25.1, 22.6, 21.9. IR (KBr, cm^{-1}) v 2928, 2857, 2836, 1661, 1239, 1161, 986, 959, 940, 918, 858, 837, 730. HRMS (ESI/[M+H]$^+$) Calc. for: $C_{10}H_{16}NO$ 166.1232, found: 166.1224.

2-Nonyl-4,5-dihydrooxazole (**2l**).[8]



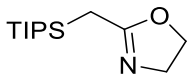
Colorless oil; 66.1 mg; 84% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.22 (t, J = 9.5 Hz, 2 H), 3.82 (t, J = 9.5 Hz, 2 H), 2.21-2.31 (m, 2 H), 1.56-1.68 (m, 2 H), 1.23-1.37 (m, 12 H), 0.87 (t, J = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 67.0, 54.2, 31.8, 29.3, 29.2, 29.1, 27.9, 25.9, 22.6, 14.0. IR (KBr, cm^{-1}) v 2925, 2858, 1683, 1468, 1374, 1233, 1166, 991, 964, 722. HRMS (ESI/[M+H]$^+$) Calc. for: $C_{12}H_{24}NO$ 198.1859, found: 198.1852.

2-Methyl-4,5-dihydrooxazole (**2m**).[7]



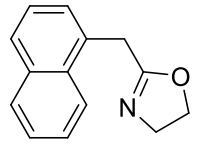
Pale yellow oil; 70.0 mg; 54% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16-4.29 (m, 2 H), 3.74-3.89 (m, 2 H), 1.97 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 67.1, 54.3, 13.5. IR (KBr, cm^{-1}) v 1670. MS (EI, 70 ev) m/z 85, 56, 55, 54, 43.

2-((Triisopropylsilyl)methyl)-4,5-dihydrooxazole (**2n**).



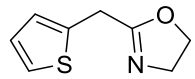
Colorless oil; 70.0 mg; 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (t, J = 9.4 Hz, 2 H), 3.77 (t, J = 9.5 Hz, 2 H), 1.82 (s, 2 H), 1.02-1.89 (m, 21 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 66.9, 54.4, 18.3, 11.1, 10.9. IR (KBr, cm^{-1}) ν 2942, 2892, 2867, 1667, 1578, 1480, 1428, 1363, 1253, 1166, 984, 711. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{13}H_{28}NOSi$ 242.1940, found: 242.1943.

2-(Naphthalen-1-ylmethyl)-4,5-dihydrooxazole (**2o**).



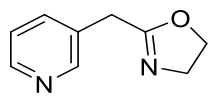
Colorless oil; 87.9 mg; >99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 1 H), 7.85 (d, J = 7.9 Hz, 1 H), 7.78 (dd, J_1 = 6.9 Hz, J_2 = 2.6 Hz, 1 H), 7.40-7.57 (m, 4 H), 4.20 (t, J = 9.5 Hz, 2 H), 4.06 (s, 2 H), 3.83 (t, J = 9.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 133.7, 131.9, 131.4, 128.5, 127.8, 127.5, 126.1, 125.6, 125.4, 123.8, 67.5, 54.3, 32.3. IR (KBr, cm^{-1}) ν 3047, 2971, 2935, 2904, 2881, 1666, 1597, 1510, 1398, 1359, 1244, 1167, 984, 959, 782. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{14}H_{14}NO$ 212.1075, found: 212.1078.

2-(Thiophen-2-ylmethyl)-4,5-dihydrooxazole (**2p**).[9]



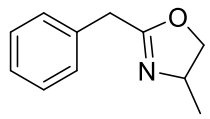
Dark yellow oil; 59.5 mg; 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14-7.23 (m, 1 H), 6.89-6.99 (m, 2 H), 4.27 (t, J = 9.5 Hz, 2 H), 3.80-3.90 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 136.4, 126.7, 126.5, 124.7, 67.7, 54.3, 28.8. IR (KBr, cm^{-1}) ν 3104, 3072, 2972, 2935, 2906, 2882, 1667, 1437, 1422, 1371, 1354, 1231, 1174, 983, 960, 852, 701. HRMS (ESI/$[M+H]^+$) Calc. for: $C_8H_{10}NOS$ 168.0483, found: 168.0473.

2-(Pyridin-3-ylmethyl)-4,5-dihydrooxazole (**2q**).



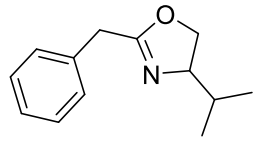
Yellow oil; 26.9 mg; 41.5% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 2.3 Hz, 1 H), 8.51 (dd, J_1 = 4.8 Hz, J_2 = 1.7 Hz, 1 H), 7.66 (dt, J_1 = 7.8 Hz, J_2 = 2.0 Hz, 1 H), 7.26 (ddd, J_1 = 7.8 Hz, J_2 = 4.9 Hz, J_3 = 0.9 Hz, 1 H), 4.26 (t, J = 9.5 Hz, 2 H), 3.85 (t, J = 9.5 Hz, 2 H), 3.62 (s, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 150.1, 148.3, 136.5, 130.8, 123.4, 67.7, 54.4, 31.9. IR (KBr, cm^{-1}) ν 3033, 2977, 2937, 2912, 2884, 1667, 1578, 1480, 1427, 1363, 1166, 1029, 985, 711. HRMS (ESI/$[M+H]^+$) Calc. for: $C_9H_{11}N_2O$ 163.0871, found 163.0862.

2-benzyl-4-methyl-4,5-dihydrooxazole (**2r**).



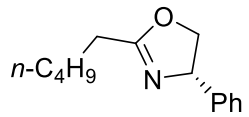
Colorless oil; 70.0 mg; >99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.22 (m, 5 H), 4.31 (dd, J_1 = 9.4 Hz, J_2 = 8.1 Hz, 1 H), 4.24-4.09 (m, 1 H), 3.76 (t, J = 7.8 Hz, 1 H), 3.61 (s, 2 H), 1.25 (d, J = 6.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 135.1, 128.8, 128.5, 126.8, 74.1, 61.3, 34.7, 21.3. IR (KBr, cm^{-1}) ν 3063, 2966, 2924, 2896, 1665, 1496, 1454, 1359, 1242, 1164, 981, 719, 695. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{11}H_{14}NO$ 176.0997, found 175.0990.

2-benzyl-4-isopropyl-4,5-dihydrooxazole (**2s**).



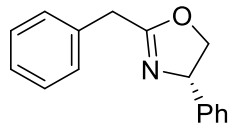
Colorless oil; 80.8 mg; >99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 4.4 Hz, 4 H), 7.27-7.19 (m, 1H), 4.26-4.13 (m, 1 H), 3.99-3.84 (m, 2 H), 3.62 (s, 2 H), 1.74 (p, J = 6.5 Hz, 1 H), 0.96 (s, 3 H), 0.86 (d, J = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 135.2, 128.8, 128.4, 126.8, 71.9, 70.1, 34.7, 32.4, 18.6, 17.9. IR (KBr, cm^{-1}) ν 3030, 2958, 2904, 2873, 1668, 1496, 1455, 1359, 1241, 1162, 984, 716, 695. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{13}H_{18}NO$ 204.1310, found 204.1317.

(*S*)-2-Pentyl-4-phenyl-4,5-dihydrooxazole (**2t**).[10]



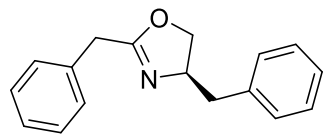
Colorless oil; 31.6 mg; 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15-7.44 (m, 5 H), 5.16 (t, J = 9.1 Hz, 1H), 4.59 (t, J = 9.5 Hz, 1 H), 4.07 (t, J = 8.2 Hz, 1 H), 2.39 (t, J = 7.7 Hz, 2 H), 1.72 (p, J = 7.5 Hz, 2 H), 1.29-1.43 (m, 4 H), 0.91 (t, J = 6.9 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 142.5, 128.6, 127.4, 126.5, 74.5, 69.5, 31.4, 28.0, 25.8, 22.3, 13.9. IR (KBr, cm^{-1}) v 3027, 2955, 2928, 2859, 1665, 1638, 1603, 1496, 1454, 1174, 981, 732, 700. HRMS (ESI/[M+H]$^+$) Calc. for: $C_{14}H_{20}NO$ 218.1539, found: 218.1543.

(*S*)-2-Benzyl-4-phenyl-4,5-dihydrooxazole (**2u**).[10]



Pale yellow oil; 87.6 mg; 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17-7.42 (m, 10 H), 5.19 (dd, J_1 = 10.1 Hz, J_2 = 8.2 Hz, 1 H), 4.60 (dd, J_1 = 10.1 Hz, J_2 = 8.5 Hz, 1 H), 4.08 (t, J = 8.3 Hz, 1 H), 3.77 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 142.2, 135.0, 128.9, 128.6, 128.5, 127.4, 127.0, 126.4, 74.8, 69.5, 34.8. IR (KBr, cm^{-1}) v 3085, 3062, 3028, 2922, 2851, 1666, 1495, 1454, 1359, 1242, 1163, 980, 718, 701. HRMS (ESI/[M+H]$^+$) Calc. for: $C_{16}H_{16}NO$ 238.1232, found: 238.1225.

(*R*)-2,4-Dibenzyl-4,5-dihydrooxazole (**2v**).[10]



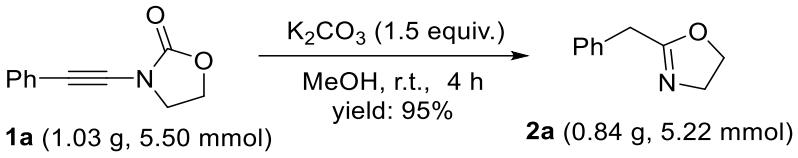
White solid; 50.0 mg; mp: 93.1-94.8 ºC; >99% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 10 H), 4.30-4.46 (m, 1 H), 4.14 (t, J = 8.9 Hz, 1 H), 3.94 (t, J = 7.9 Hz, 1 H), 3.60 (s, 2 H), 3.08 (dd, J_1 = 13.7 Hz, J_2 = 5.1 Hz, 1 H), 2.66 (dd, J_1 = 13.8 Hz, J_2 = 8.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 137.7, 135.0, 129.2, 128.9, 128.5, 128.4, 126.9, 126.4, 71.8, 67.1, 41.5, 34.7. IR (KBr, cm^{-1}) v 3085, 3062, 3029, 3004, 2965,

2917, 2890, 2850, 1664, 1495, 1454, 1359, 1289, 1180, 984, 757, 717, 699. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{17}H_{18}NO$ 252.1388, found 252.1385.

3. Scale-up Experiments and Synthetic Applications

3.1 Scale-up Experiments

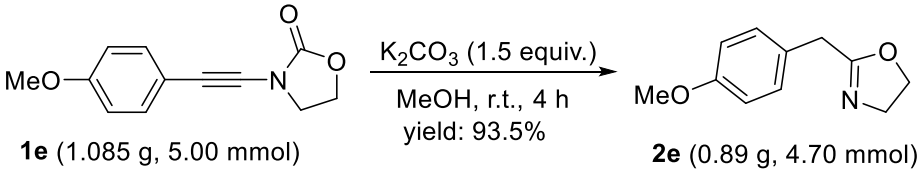
3.1.1 Gram-Scale Synthesis of **2a**



1a (1.03 g, 5.50 mmol) **2a** (0.84 g, 5.22 mmol)

To a 100 mL round-bottomed flask equipped with a Teflon-coated magnetic stir bar were added alkynamide **1a** (5.50 mmol), K_2CO_3 (7.5 mmol) and MeOH (50 mL). The reaction mixture was stirred for 4 h at room temperature (25 °C). Then, upon the completion, the reaction was quenched by the addition of H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the desired product **2a** (0.84 g, 95% yield).

3.1.2 Gram-Scale Synthesis of **2e**

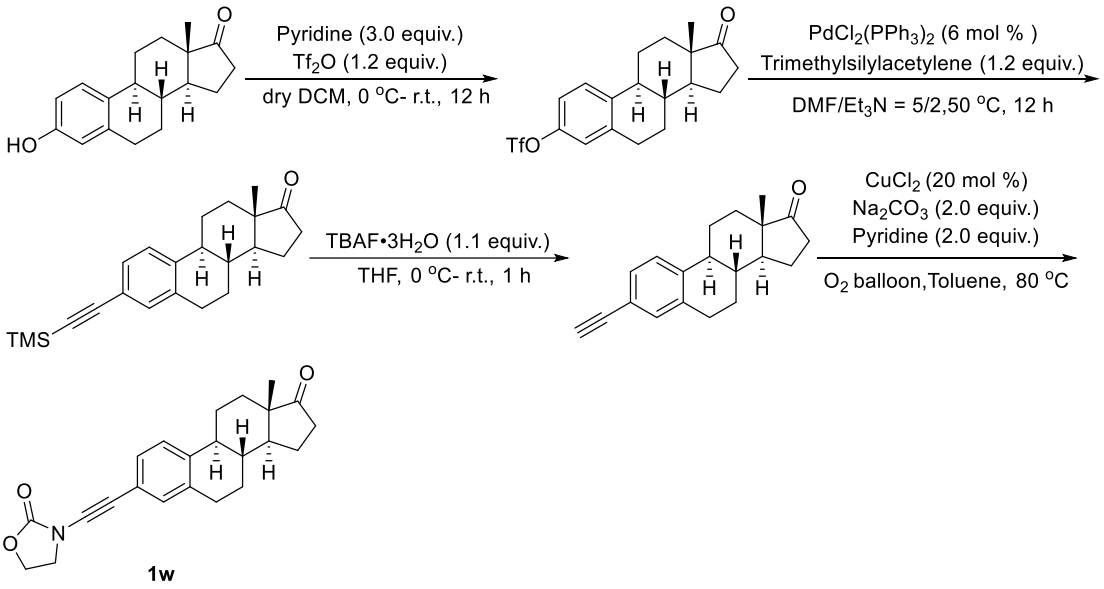


1e (1.085 g, 5.00 mmol) **2e** (0.89 g, 4.70 mmol)

To a 100 mL round-bottomed flask equipped with a Teflon-coated magnetic stir bar were added alkynamide **1e** (5.00 mmol), K_2CO_3 (7.5 mmol) and MeOH (50 mL). The reaction mixture was stirred for 4 h at room temperature (25 °C). Then, upon the completion, the reaction was quenched by the addition of H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the desired product **2e** (0.89 g, 93.5% yield).

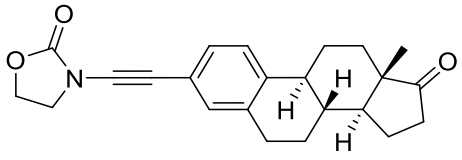
3.2 Synthetic Applications

3.2.1 Synthesis of Compound **1w**



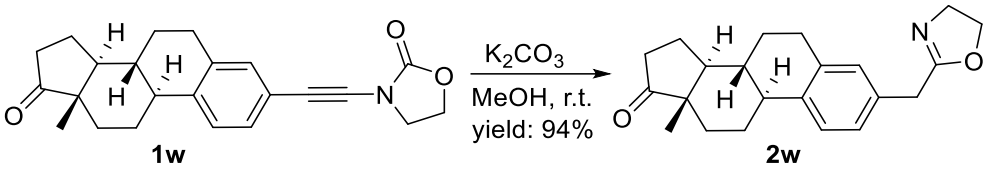
General Procedure for the Synthesis of 1w.[1] Following Stahl's procedure, to an oven-dried 250 mL three-neck round-bottomed flask were added $CuCl_2$ (20 mol%), 2-oxazolidinone (5.0 equiv.) and Na_2CO_3 (2.0 equiv.). The reaction flask was evacuated and backfilled with oxygen. A solution of pyridine (2.0 equiv.) in dry toluene (0.1 M) was added. A balloon filled with oxygen was connected to the flask and the reaction was heated at 80 °C. After 15 minutes, a solution of 3-ethyn-1-ylestra-1,3,5(10)-trien-17-one (1.0 equiv.) in dry toluene (0.1 M) was added over 4 hours by using a syringe-pump.[11] After the addition, the green to blue mixture was allowed to stir at 80 °C for additional 12 hours and then was cooled to room temperature. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel to give the compound **1w** (0.39 g, 28% yield).

3-(((8*R*,9*S*,13*S*,14*S*)-13-Methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)ethynyl)oxazolidin-2-one **(1w).**



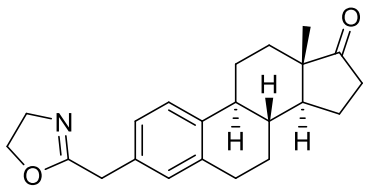
White solid; 0.39 g; m.p.: 218.9-219.8 ºC; 28% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16-7.27 (m, 3 H), 4.37-4.57 (m, 2 H), 3.90-4.08 (m, 2 H), 2.88 (dd, J_1 = 9.1 Hz, J_2 = 4.3 Hz, 2 H), 2.51 (dd, J_1 = 18.8 Hz, J_2 = 8.7 Hz, 1 H), 2.37-2.44 (m, 1 H), 2.25-2.34 (m, 1 H), 2.93-2.20 (m, 4 H), 1.35-1.70 (m, 6 H), 0.91 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 220.6, 155.9, 140.0, 136.5, 131.8, 128.6, 125.2, 119.3, 78.3, 71.0, 63.0, 50.3, 47.8, 46.9, 44.2, 37.7, 35.7, 31.4, 28.9, 26.1, 25.4, 21.4, 13.7. IR (KBr, cm^{-1}) v 2952, 2874, 2864, 2254, 1766, 1735, 1421, 1402, 1208, 1081, 1031, 1009, 969, 903, 824, 749. HRMS (ESI/[M+H]$^+$) Calc. for: $C_{23}H_{26}NO_3$ 364.1913, found: 364.1908.

3.2.2 Synthesis of Compound **2w**



To a 25-mL Schlenk tube equipped with a Teflon-coated magnetic stir bar were added alkynamide **1w** (0.4 mmol), K_2CO_3 (0.6 mmol) and MeOH (4 mL). The reaction mixture was stirred for 4 h at room temperature (25 ºC). Then, upon the completion, the reaction was quenched by the addition of H2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the desired product **2w** (63.3 mg, 94% yield).

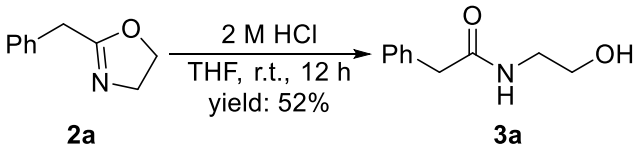
(8*R*,9*S*,13*S*,14*S*)-3-((4,5-Dihydrooxazol-2-yl)methyl)-13-methyl-6,7,8,9,11,12,13, 14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one **(2w).**



Colorless oil; 63.3 mg; 94% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.5 Hz, 1 H), 7.09 (d, J = 8.0 Hz, 1 H), 7.03 (s, 1 H), 4.23 (t, J = 9.5 Hz, 2 H), 3.83 (t, J = 9.5 Hz, 2 H), 3.58 (s, 2 H), 2.90 (dd, J_1 = 8.9 Hz, J_2 = 4.2 Hz, 2 H), 2.50 (dd, J_1 = 18.7

Hz, J_2 = 8.6 Hz, 1 H), 2.38-2.44 (m, 1 H), 2.24-2.32 (m, 1 H), 1.91-2.20 (m, 4 H), 1.36-1.72 (m, 6 H), 0.90 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 220.8, 167.1, 138.3, 136.6, 132.4, 129.5, 126.3, 125.5, 67.5, 54.3, 50.3, 47.8, 44.1, 37.9, 35.7, 34.1, 31.4, 29.2, 26.3, 25.5, 21.4, 13.7. IR (KBr, cm^{-1}) v 2930, 1737, 1666, 1499, 1453, 1372, 1243, 1190, 1160, 1083, 1007, 985, 927, 823, 768. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{22}H_{28}NO_2$ 338.2120, found: 338.2112.

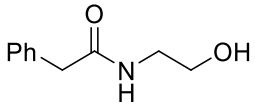
3.2.3 Synthesis of Compound **3a**



2a **3a**

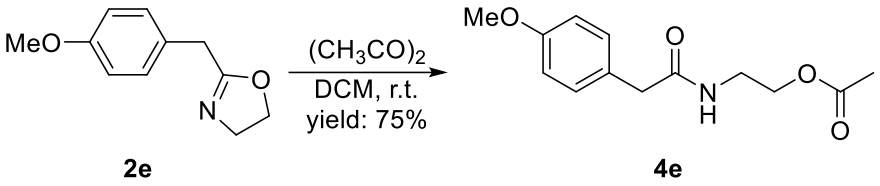
To a solution of **2a** in THF and 2 M HCl was added. The reaction was allowed to stir overnight at room temperature.[12] After completion solvent was removed in vacuo and the resulted mixture was washed with aq. $NaHCO_3$ solution and the organic phase was extracted with ethyl acetate for twice. The organic layers were combined and dried over Na_2SO_4. The solvent was then removed under vacuo. The residue was purified by column chromatography on silica gel to give the corresponding product **3a** in 52% yield.

Methyl-(2-hydroxyethyl)(phenylethynyl)carbamate (**3a**).[6]



Yellow solid; 37.2 mg; m.p.: 52.5-54.3 °C; 52% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.14 (m, 5 H), 6.25 (s, 1 H), 3.67-3.57 (m, 2 H), 3.54 (s, 2 H), 3.45 (s, 1 H), 3.32 (td, J_1 = 5.7 Hz, J_2 = 2.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 134.6, 129.3, 128.9, 127.3, 61.8, 43.4, 42.5. IR (KBr, cm^{-1}) v 3290, 3063, 3029, 2920, 2850, 1645, 1604, 1583, 1495. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{10}H_{14}NO_2$ 180.1019, found: 180.1014.

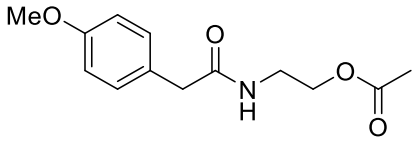
3.2.4 Synthesis of Compound **4e**



2e **4e**

Compound **2e** and acetic anhydride (0.4 mmol) each were allowed to react in 1 mL of dichloromethane at room temperature for 12 h.[13] After completion solvent was removed in vacuo and the resulted mixture was washed with aq. NaCl solution and the organic phase was extracted with dichloromethane for twice. The organic layers were combined and dried over Na_2SO_4. The solvent was then removed under vacuo. The residue was purified by column chromatography on silica gel to give the corresponding product **4e** in 75% yield.

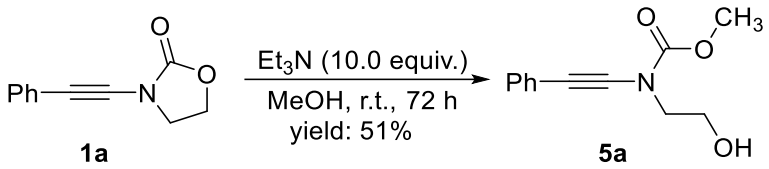
2-(2-(4-Methoxyphenyl)acetamido)ethyl acetate (**4e**).



White solid; 75.7 mg; m.p.: 76.8-77.4 °C; 75% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.16 (m, 2 H), 6.91-6.84 (m, 2 H), 5.63 (s, 1 H), 4.22-4.13 (m, 2 H), 3.80 (s, 3 H), 3.58 (s, 2 H), 3.48 (q, J = 5.5 Hz, 2 H), 1.92 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 170.2, 158.6, 130.1, 125.7, 113.9, 63.3, 55.1, 40.2, 38.5, 22.9. IR (KBr, cm-1) ν 3245, 1725, 1641, 1625, 1569, 1516, 1341, 1301, 1256, 1240, 1156. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{13}H_{18}NO_4$ 252.1236, found: 252.1229.

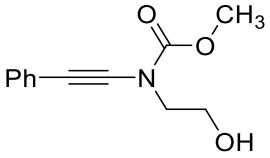
4. Mechanistic Investigation

4.1 Synthesis of 5a



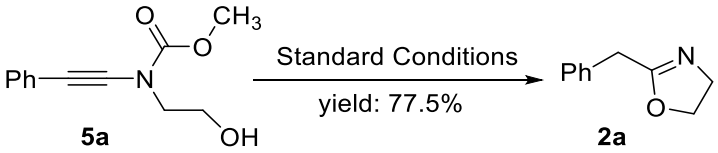
To a 50 mL round-bottomed flask equipped with a Teflon-coated magnetic stir bar were added alkynamide **1a** (3.0 mmol), triethylamine (30.0 mmol) and MeOH (30 mL). The reaction mixture was stirred for 72 h at room temperature (25 ºC). Then, upon the completion, the reaction was quenched by the addition of H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Then, the residue was directly subjected to column chromatography on silica gel giving the pure product **5a**.

Methyl-(2-hydroxyethyl)(phenylethynyl)carbamate **(5a).**



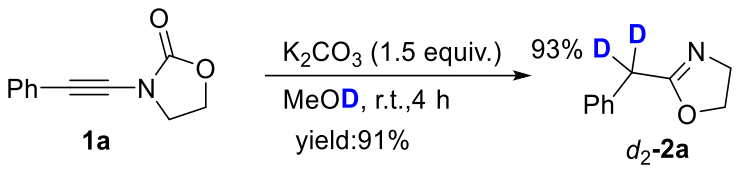
Colorless oil; 0.33 g; 51% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.45 (m, 2 H), 7.24-7.34 (m, 3 H), 3.92 (t, J = 4.2 Hz, 2 H), 3.84 (s, 3 H), 3.75 (t, J = 5.4 Hz, 2 H), 2.48 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 131.2, 128.2, 127.7, 122.8, 82.4, 70.4, 60.1, 54.2, 52.4. IR (KBr, cm^{-1}) v 3440, 2995, 2881, 2252, 1730, 1714, 1444, 1396, 1310, 1224, 1070, 1054, 1026, 981, 755. HRMS (ESI/[M+H]$^+$) Calc. for: $C_{12}H_{14}NO_3$ 220.0974, found: 220.0965.

4.2 Synthesis of 2a *via* the Reaction of Compound 5a at Standard Conditions



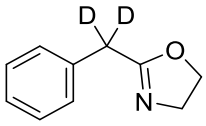
To a 25 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar were added alkynamide **5a** (0.4 mmol), K_2CO_3 (0.6 mmol) and MeOH (4 mL). The reaction mixture was stirred for 4 h at room temperature (25 °C). Then, upon the completion, the reaction was quenched by the addition of H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the desired products **2a** (0.55 g, 77.5% yield).

4.3 General Procedure for the Synthesis of d_2-2a.



To a 25 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar were added alkynamide **1a** (0.3 mmol), K_2CO_3 (0.45 mmol) and MeOD (3 mL). The reaction mixture was stirred for 4 h at room temperature (25 °C). Then, upon the completion, the reaction was quenched by the addition of H_2O and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the desired product d_2-**2a**.

2-(Phenylmethyl-d_2)-4,5-dihydrooxazole **(d_2-2a).**



Colorless oil; 44.5 mg; 91% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07-7.51 (m, 5 H), 4.22 (t, J = 9.5 Hz, 2 H), 3.83 (t, J = 9.5 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 135.0, 128.9, 128.5, 126.9, 67.5, 54.3, 34.5-33.9 (m). IR (KBr, cm^{-1}) v 3061, 3028, 2906, 2882, 1666, 1495, 1449, 1356, 1241, 1206, 1023, 984, 950, 708. HRMS (ESI/$[M+H]^+$) Calc. for: $C_{10}H_{10}D_2NO$ 164.1044, found: 164.1036.

5. X-ray of structure of 2j

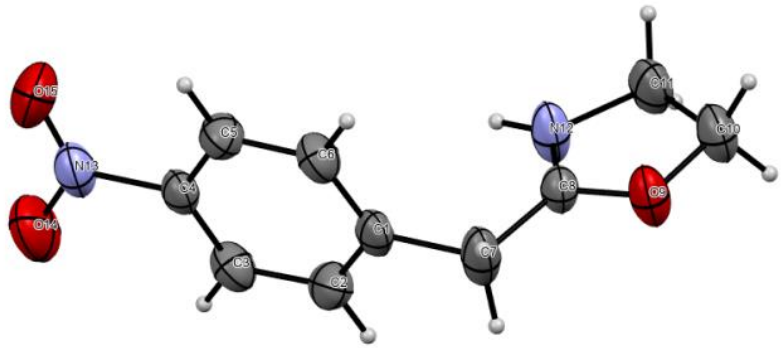


Figure 1. X-ray of structure of **2j**

Crystal data for **2j**: $C_{10}H_{11}N_2O_3$, M = 207.21, monoclinic, space group P 21/n, final R indices [$I > 2\sigma(I)$]: R_1 = 0.0858, wR_2 = 0.1900, R indices (all data): R_1 = 0.0592, wR_2 = 0.1734, a = 10.6496(14), b = 4.9316(6), c = 19.212(2) Å, β = 100.692(12) °, V = 991.5(2) Å 3 , T = 301 K (2), Z = 4, reflections collected/unique: 7026/2282 (R_{int} = 0.0277), number of observations [$I > 2\sigma(I)$]: 1499, parameters: 136. **CCDC 2321759** data for this paper contains the supplementary crystallographic.

6. CheckCIF/PLATON Report

Structure factors have been supplied for datablock(s) 1_auto

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 1_auto

Bond precision: C-C = 0.0031 A Wavelength=0.71073

Cell: a=10.6496(14) b=4.9316(6) c=19.212(2)
alpha=90 beta=100.692(12) gamma=90
Temperature: 301 K

	Calculated	Reported
Volume	991.5(2)	991.5(2)
Space group	P 21/n	P 21/n
Hall group	-P 2yn	-P 2yn
Moiety formula	C10 H11 N2 O3	?
Sum formula	C10 H11 N2 O3	C10 H11 N2 O3
Mr	207.21	207.21
Dx,g cm-3	1.388	1.388
Z	4	4
Mu (mm-1)	0.104	0.104
F000	436.0	436.0
F000'	436.22	
h,k,lmax		14,6,25
Nref		2282
Tmin,Tmax	0.986,0.988	
Tmin'	0.986	

Correction method= Not given

Data completeness= Theta(max)= 29.843

R(reflections)= 0.0592(1499) wR2(reflections)= 0.1900(2282)

S = 1.048 Npar= 136

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

```
PLAT052_ALERT_1_C Info on Absorption Correction Method   Not Given     Please Do !
PLAT241_ALERT_2_C High   'MainMol' Ueq as Compared to Neighbors of         C7 Check
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of        N13 Check
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of         C8 Check
PLAT334_ALERT_2_C Small <C-C> Benzene Dist.   C1       -C6       .       1.37 Ang.
PLAT415_ALERT_2_C Short Inter D-H..H-X       H3       ..H12      .       2.06 Ang.
                                    3/2-x,-1/2+y,3/2-z  =      2_646 Check
PLAT420_ALERT_2_C D-H Bond Without Acceptor  N12      --H12      .     Please Check
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......     12.425 Check
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......      2.408 Check
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600          6 Report
             -10  0  8,  -5  5  9,  -4  5 10,  -4  5 11, -11  0 15,  -9  0 19,
```

Alert level G

```
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..............          1 Report
            H12
PLAT398_ALERT_2_G Deviating  C-O-C   Angle From 120 for O9       .      105.9 Degree
PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary .     Please Do !
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600        540 Note
PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ...........        3.1 Low
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          3 Info
PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by          3 Check
```

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
10 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
7 **ALERT level G** = General information/check it is not something unexpected

2 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
8 ALERT type 2 Indicator that the structure model may be wrong or deficient
4 ALERT type 3 Indicator that the structure quality may be low
1 ALERT type 4 Improvement, methodology, query or suggestion
2 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

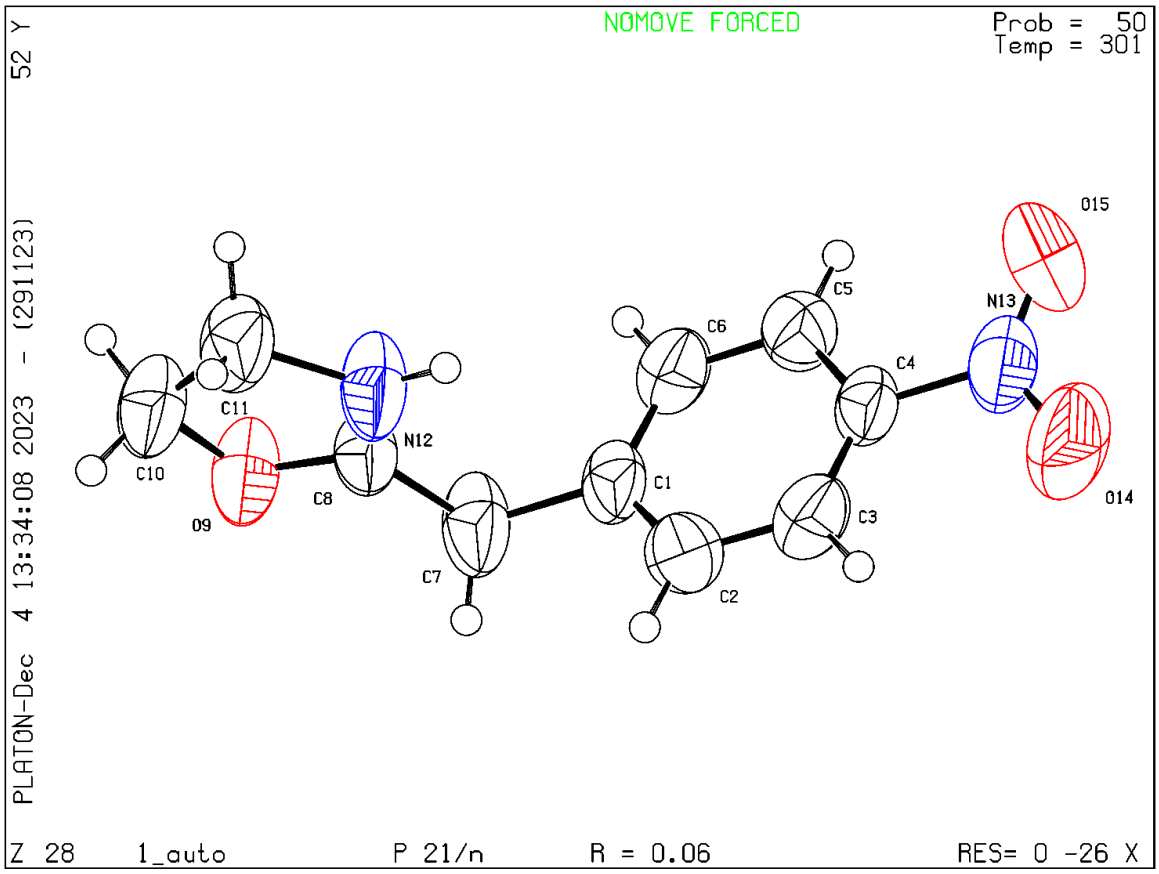
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 29/11/2023; check.def file version of 14/09/2023

Datablock 1_auto - ellipsoid plot



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