Unprecedented Synthesis of 1,2,3-Triazolo-Cinnolinone via Sonogashira Coupling and Intramolecular Cyclization

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General Information:

All reagents were purchased from commercial suppliers and used without further purification. All experiments were carried out under air atmosphere. All the solvents used for the reaction were distilled before use. The product purification by column chromatography was accomplished using silica gel 100-200 mesh. Analytical TLC was performed with Merck silica gel 60 F254 plates, and the products were visualized by UV detection. The 1H NMR and $^{13}$C NMR spectra were recorded on a Bruker-Avance (300 MHz); Inova (400 MHz) and Avance (500 MHz) spectrophotometer using CDCl$_3$ and TMS as the internal standard. Chemical shifts ($\delta =$) are reported in ppm using TMS as an internal standard, and spin -spin coupling constants (J) are given in Hz. Multiplicities in the 1H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, m = multiplet, bs = broad singlet; coupling constants are reported in Hz. Low (MS) and high (HRMS) resolution mass spectra were recorded on a Waters 2695 and Thermo Scientific Exactive spectrometer respectively.
and mass/charge (m/z) ratios are reported as values in atomic mass units. All the melting point is uncorrected.

**General experimental procedure for the synthesis of 2-iodophenyl 4-alkyl/aryl-1H 1,2,3-triazole\(^1\):**

Two necked round bottom flask charged with 2-iodo aniline (3.0 mmol) followed by addition of 4N HCl (10mL) on ice bath under air. Solution was stirred for 5 mins at 0 °C. To this solution NaNO\(_2\) (0.82 gm, 12mmol) was added slowly in portions over a period of 15 mins at same temperature. The reaction mixture was allowed to stir for another 30 mins at same temperature. To the above reaction mixture sodium azide (0.59 gm, 9.0 mmol) was slowly added in portions and the mixture allowed to come to the room temperature and stirred for 4-12 hrs (monitored by TLC using hexane: ethyl acetate (8:2) solvent). The reaction mixture was successively diluted with water. The aqueous layer was extracted with ethyl acetate (3 x 60 mL), and combined organic layers were washed with water, followed by brine, dried over Na\(_2\)SO\(_4\) and concentrated under reduced pressure to obtain crude azide derivatives which was carried forward for the click reaction without any further purification. To a solution of crude azide (0.49 gm, 2.0 mmol) and terminal alkyl/aryl acetylene (2.0 mmol) in DMF (10 mL) was added CuI (10 mol%) and the mixture was heated at 100 °C for 8 hrs. The completion of reaction was monitored by TLC. The aqueous layer was extracted with ethyl acetate (3 x 40 mL), and combined organic layer was washed with water (3 x 50 mL), followed by brine, dried over Na\(_2\)SO\(_4\) and concentrated under reduced pressure to obtain crude triazole derivatives in quantitative yields. The crude product was purified by column chromatography to obtain pure compounds.
$^1\text{H}$ NMR, 376 MHz
3ca, CDCl$_3$
$^1$H NMR, 400 MHz
3jd, CDCl$_3$

$^{13}$C NMR, 125 MHz
3jd, CDCl$_3$
X-Ray Crystallographic Study:

ORTEP structure of 3aa
X-ray data for the compound 3aa was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 Å) and a PHOTON-100 detector. The raw data frames of KA119 were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [1]. The structure was solved using intrinsic phasing method [2] and further refined with the SHELXL [2] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. All C bound H atoms of were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms].

Crystal Data for C20H19N3O (M =317.38 g/mol): orthorhombic, space group Pbca (no. 61), a = 19.497(5) Å, b = 8.597(2) Å, c = 19.553(4) Å, V = 3277.4(13) Å3, Z = 8, T = 294.15 K, μ(MoKα) = 0.081 mm⁻¹, Dcalc = 1.286 g/cm³, 45870 reflections measured (4.66° ≤ 2Θ ≤ 56.59°), 4069 unique (Rint = 0.0296, Rsigma = 0.0158) which were used in all calculations. The final R1 was 0.0440 (I > 2σ(I)) and wR2 was 0.1199 (all data). CCDC 1563687 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].