

A triazole hybrid of neolignans as a potential antileishmanial agent by triggering mitochondrial dysfunction

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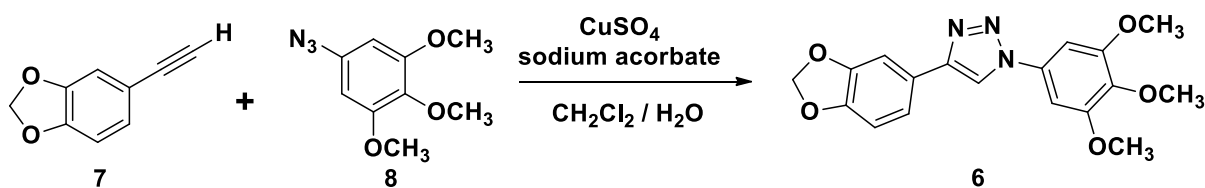
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General Remarks

Anhydrous solvents were dried and distilled before use according to the standard procedure. All chemicals for synthesis were of reagent grade and used without purification unless noted. Reactions were carried out under a nitrogen atmosphere and monitored by TLC using prepared plates (silica gel 60 F254 on aluminum). The chromatograms were examined under both 254 and 360 nm UV light or with the developing agent ethanolic vanillin and heat. Flash column chromatography was performed on silica gel 60 (particle size 200-400 mesh ASTM, purchased from Aldrich, USA). Melting points were determined using Fisatom 430D equipment. The ¹H and ¹³C NMR spectra were recorded in CDCl₃ solutions using a Bruker 75 MHz or 300 MHz spectrometer, as noted. Chemical shifts (δ) are expressed as parts per million (ppm) downfield from tetramethylsilane or deuterated solvent (CDCl₃ ¹H δ 7.27 and ¹³C δ 77.0 ppm; DMSO-D₆ ¹H δ 2.5 and ¹³C δ 39.51 ppm; Acetone ¹H δ 2.05 and ¹³C δ 77.0 ppm) as the internal standard. HR-ESI-MS measurements were carried out on a quadrupole time-of-flight instrument (UltrOTOFT-Q, BrukerDaltonics, Billerica, MA).

1. Preparation of triazole **6** LASQUIM 25

Figure 1. Synthesis of the triazole **6** (LASQUIM 25).



General Method [2]:

It was added CuSO₄·5H₂O pentahydrate (1.0 mmol, 0.249g) and sodium ascorbate (2.0 mmol, 0.396g) to a solution of terminal acetylene **7** (10 mmol, 1.46g) and azide **8** (10 mmol, 2.09g) in dichloromethane (10 mL) and water (10 mL). The reaction mixture was stirred for 24 h. Then was added a saturated solution of NH₄Cl (150 mL) and the product was extracted with dichloromethane (3 x 50 mL). The organic phase was dried over anhydrous MgSO₄, and the solvent was evaporated under reduced pressure. The product was purified by recrystallization from ethyl acetate affording **6** (LASQUIM 25) in 80% yield (1.42g).

2. 4-(benzo[d][1,3]dioxol-5-yl)-1-(3,4,5-trimethoxyphenyl)-1H-1,2,3-triazole **6**

Spectra data in accordance with ref. [2]: ¹H NMR (300 MHz, CDCl₃) δ 3.87 (s, 3H, OCH₃), 3.92 (s, 6H, 2OCH₃), 5.99 (s, 2H, CH₂), 6.86 (d, 1H, *J* 8.0 Hz, Ar-H), 6.96 (s, 2H, Ar-H), 7.36 (m, 2H, Ar-H), 8.02 (s, 1H, *Tr-H); ¹³C NMR (75 MHz, CDCl₃) δ 56.43, 61.03, 98.45, 101.24, 106.43, 108.70, 117.27, 119.57, 124.32, 132.89, 138.32, 147.81, 148.18, 153.91. HRMS (ESI+) *m/z* calcd. for C₁₈H₁₇N₃O₅ [M + H]⁺: 356.1246; found: 356.1253; *Tr: triazole hydrogen.

3. References

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