



## An Efficient Synthesis of Indolo[1,2-*c*]quinazolines

PEDIREDLA G.V.V. LAKSHMI\* and NITIN T. PATIL

Division of Crop Protection Chemicals, CSIR-Indian Institute of Chemical Technology, Hyderabad-500 007, India

\*Corresponding author: E-mail: [p.g.v.v.lakshmi@gmail.com](mailto:p.g.v.v.lakshmi@gmail.com)

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Gold(I)-catalyzed cascade reaction was developed for the synthesis of new fused indolo[1,2-*c*]quinazolines by using 2-(3-methyl-1*H*-indol-2-yl)aniline and alkynes. This reaction provides a variety of biologically important quinazolines from easily available starting materials.

**Keywords:** Gold(I), Cascade reactions, 2-(3-Methyl-1*H*-indol-2-yl)aniline, Alkynes, Indolo[1,2-*c*]quinazolines.

### INTRODUCTION

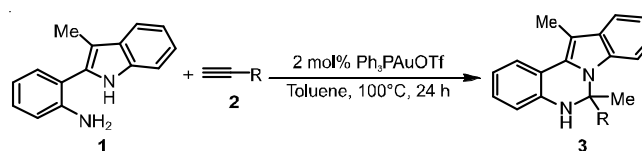
Nitrogen containing polycyclic compounds are identified as attractive templates for drug discovery. Among various nitrogen containing heterocycles<sup>1</sup>, fused quinazolines<sup>2</sup> are important structural motifs found in many natural products and these are pharmaceutically important compounds. General and convenient methods for the construction of these types of compounds would be of great interest to the synthetic organic chemists. The ideal way to access these compounds from easily available starting materials, without isolating any intermediates<sup>3</sup> would be of more interest.

As a part of our interest in the development of metal catalyzed cascade processes<sup>4</sup> that easily produced privileged scaffolds with molecular complexity<sup>5</sup>, we recently reported, Au(I)-catalyzed cascade reaction between aminoaromatics having tethered nucleophiles and alkynes<sup>6</sup>. The hypothesis on which the present work involved the use of 2-(3-methyl-1*H*-indol-2-yl)aniline<sup>7</sup> with different alkynes in the presence of catalyst Ph<sub>3</sub>PAuOTf to produce fused indolo[1,2-*c*]quinazolines.

### EXPERIMENTAL

**General method for the synthesis of fused indoloquinazolines:** To a screw cap vial containing a stir bar, were added 2-(3-methyl-1*H*-indol-2-yl)aniline **1** (0.450 mmol), alkyne **2** (0.540 mmol) and 2 mol % Ph<sub>3</sub>PAuOTf (Ph<sub>3</sub>PAuCl/AgOTf) in toluene (2 mL). The reaction vial was evacuated and filled with nitrogen and heated with stirring at 100 °C for 24 h. The reaction mixture was cooled to ambient temperature, diluted with ethyl acetate and filtered through a plug of silica gel. The filtrate was concentrated and the residue was purified

by silica gel column chromatography with hexane/ethyl acetate as an eluent to afford analytically pure compound **3** (Scheme-I).



Scheme-I

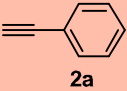
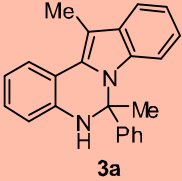
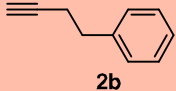
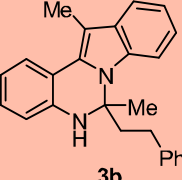
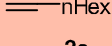

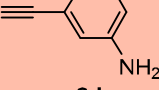
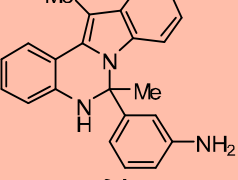
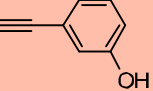
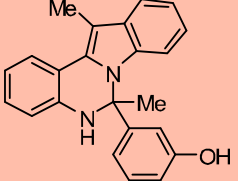
**6,12-Dimethyl-6-phenyl-5,6-dihydroindolo[1,2-*c*]quinazoline (3a):** 80 % yield; liquid; R<sub>f</sub> = 0.42 (hexane/EtOAc = 90/10); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 7.96 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.64-7.63 (m, 1H), 7.57-7.55 (m, 1H), 7.47-7.44 (m, 1H), 7.40-7.39 (m, 1H), 7.12-7.09 (m, 1H), 7.01 (t, *J* = 6.9 Hz, 2H), 6.96-6.92 (m, 1H), 6.80-6.78 (m, 1H), 6.70 (d, *J* = 6.9 Hz, 1H), 6.23 (d, *J* = 7.9 Hz, 1H), 2.60 (s, 3H), 2.03 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz): δ 143.2, 139.9, 133.1, 130.4, 128.9, 128.6, 128.5, 128.2, 127.5, 127.4, 125.1, 121.3, 119.6, 119.0, 118.2, 115.1, 111.5, 107.2, 73.4, 24.8, 11.0; IR (film): ν<sub>max</sub>, cm<sup>-1</sup>, 3393, 3012, 3001, 2999, 2925, 1687, 1649, 1516, 1509, 1320, 1020, 973, 882, 841, 758, 687; HRMS calcd. for C<sub>23</sub>H<sub>21</sub>N<sub>2</sub> (M<sup>+</sup> + H) 325.1705, found 325.1716.

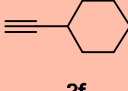
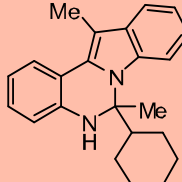
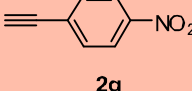
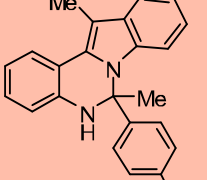

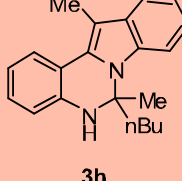
### RESULTS AND DISCUSSION

For the present transformation, the catalyst Ph<sub>3</sub>PAuOTf in toluene was found to be optimal. An equimolar mixture of 2-(3-methyl-1*H*-indol-2-yl)aniline (**1**) and ethynylbenzene (**2a**) in the presence of 2 mol % Ph<sub>3</sub>PAuOTf was heated in

toluene at 100 °C for 24 h. The starting material was completely consumed and giving the required product 6,12-dimethyl-6-phenyl-5,6-dihydroindolo[1,2-*c*]quinazoline (**3a**) in 78 % yield (Entry 1, Table-1). The scope of this transformation was further explored by treating **1** with different terminal alkynes such as but-3-ynylbenzene (**2b**) and oct-1-yne (**2c**), the expected products **3b** and **3c** obtained in 71 and 76 % respectively (Entries 2 and 3, Table-1). Next, the substituents amino and hydroxyl groups present on the aromatic alkynes are also well tolerated under the present reaction conditions. Thus when 3-ethynylaniline (**2d**) and 3-ethynylphenol (**2e**) were treated with **1** gave the corresponding products **3d** and **3e** with 62 and 68 % respectively (Entries 4 and 5, Table-1). Later sterically hindered ethynylcyclohexane (**2f**) on treated with **1** gave **3f** in 76 % yield (Entry 6, Table-1). Unfortunately, the presence of electron withdrawing group present on the aromatic alkyne, *i.e.*, 1-ethynyl-4-nitrobenzene (**2g**) was found to be inert under present reaction conditions (Entry 7, Table-1). Finally when **1** treated with hex-1-yne (**2h**) gave **3h** with 75 % yield (Entry 8, Table-1).

TABLE-1  
SYNTHESIS OF FUSED INDOLO[1,2-*c*]QUINAZOLINES

Entry	Compd. 2	Compd. 3	Yield (%)
1			80
2			71
3			76
4			62
5			68

Entry	Compd. 2	Compd. 3	Yield (%)
6			76
7			100
8			75

## Conclusion

We developed Au(I)-catalyzed cascade reactions for the synthesis of new fused indolo[1,2-*c*]quinazolines from 2-(3-methyl-1*H*-indol-2-yl)aniline and alkynes in the presence of 2 mol % Ph<sub>3</sub>PAuOTf catalyst in toluene at 100 °C for 24 h.

## ACKNOWLEDGEMENTS

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