Synthesis of Tetrazolo[1,5-*c*]quinazolines via Ph_3PAuOTf -Catalyzed Double Hydroamination of Terminal Alkynes

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An efficient tandem process is developed by using Ph_3PAuOTf -catalyzed double hydroamination of alkynes for the synthesis of new fused tetrazolo[1,5-*c*]quinazolines, with 2-(1*H*-tetrazol-5-yl)anilines and alkynes in DCE at 100 °C.

Keywords: Ph_3PAuOTf , 2-(1*H*-Tetrazol-5-yl)anilines, Alkynes, Tetrazolo[1,5-*c*]quinazolines, Double hydroamination.

INTRODUCTION

Metal catalyzed tandem reactions for the addition of nucleophiles to unactivated alkynes is one of the simplest and atom economical¹ synthetic transformation for the synthesis of various poly heterocyclic compounds². Among all transition metals³ shown significant activity for the addition of N-H bonds across unactivated C-C triple bonds⁴.

Metal-catalyzed double addition of nucleophiles to alkynes is playing a prominent role in the synthesis of privileged complex compounds⁵. In this regard we developed double hydroamination of terminal alkynes⁶ by using tetrazole substituted anilines as nucleophiles for the formation of new fused tetrazole quinazolines.

EXPERIMENTAL

General method for the synthesis of fused tetrazoloquinazolines: To a screw cap vial containing a stir bar, were added 2-(1*H*-tetrazol-5-yl)aniline (**1**) (0.621 mmol), alkyne **2** (0.745 mmol) and 2 mol % Ph_3PAuOTf ($\text{Ph}_3\text{PAuCl}/\text{AgOTf}$) in DCE (2 mL). The reaction vial was evacuated and filled with nitrogen and heated at 100 °C for 24 h. The reaction mixture was cooled to room 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 using hexane/ethyl acetate (90/10) as an eluent to afford analytically pure compound **3**.

5-Methyl-5-phenyl-5,6-dihydrotetrazolo[1,5-*c*]quinazoline (3a**):** 85 % yield; light yellow solid; m.p. = 170-172 °C; R_f = 0.31 (hexane/EtOAc = 70/30); ^1H NMR (CDCl_3 , 300 MHz): δ 7.93 (d, J = 6.9 Hz, 1H), 7.40-7.27 (m, 6H), 7.04-

6.95 (m, 2H), 5.40 (bs, 1H), 2.38 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 149, 141.4, 133.3, 128.7, 125.8, 124.9, 120.8, 116.1, 109.1, 76.9, 28.7; IR (KBr, ν_{max} , cm^{-1}): 3369, 3205, 3080, 2861, 1693, 1645, 1612, 1500, 1468, 1453, 992, 910; HRMS Calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_5$ ($\text{M}^{+} + \text{H}$) 264.1249, found 264.1245.

RESULTS AND DISCUSSION

Firstly 2-(1*H*-tetrazol-5-yl)aniline⁷ (**1a**) when treated with ethynylbenzene (**2a**) in the presence of different metal catalysts and with various solvents, finally found that the best condition for the formation of expected product 5-methyl-5-phenyl-5,6-dihydrotetrazolo[1,5-*c*]quinazoline (**3a**) in 85 % yield was in the presence of 2 mol % Ph_3PAuOTf catalyst in DCE at 100 °C for 24 h was optimal. Likewise, treated **1a** with other alkynes oct-1-yne (**2b**) and but-3-ynylbenzene (**2c**) gave the expected products **3b** and **3c** in 78 and 79 % yield, respectively. Next to check the generality methyl substituted **1a** i.e., **1b**⁸ reacted well with the alkynes **2a**, **2b** and **2c** afforded **3d**, **3e** and **3f** in 81, 83 and 72 % yield, respectively. Finally, 4-methoxy-2-(1*H*-tetrazol-5-yl)aniline⁸ (**1c**) was used as the substrate to react with the alkynes **2a**, **2b** and **2c** gave the corresponding products **3g**, **3h** and **3i** in increasing yield, 89, 80 and 82 % respectively (Table-1).

Conclusion

We have developed Ph_3PAuOTf -catalyzed direct double hydroamination of alkynes for the synthesis of new fused tetrazolo[1,5-*c*]quinazolines from 2-(1*H*-tetrazol-5-yl)anilines and alkynes in the presence of 2 mol % Ph_3PAuOTf catalyst in DCE at 100 °C for 24 h.

TABLE-1
 SYNTHESIS OF FUSED TETRAZOLO[1,5-*c*]QUINAZOLINES

Entry	1	2	3	Yield (%)
1	1a	2a	3a	85
2	1a	2b	3b	78
3	1a	2c	3c	79
4	1b	2a	3d	81
5	1b	2b	3e	83
6	1b	2c	3f	72
7	1c	2a	3g	89
8	1c	2b	3h	80
9	1c	2c	3i	82

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