

# Synthesis and Antitumor Activity of Novel 4,5-Disubstituted Triazole Derivatives

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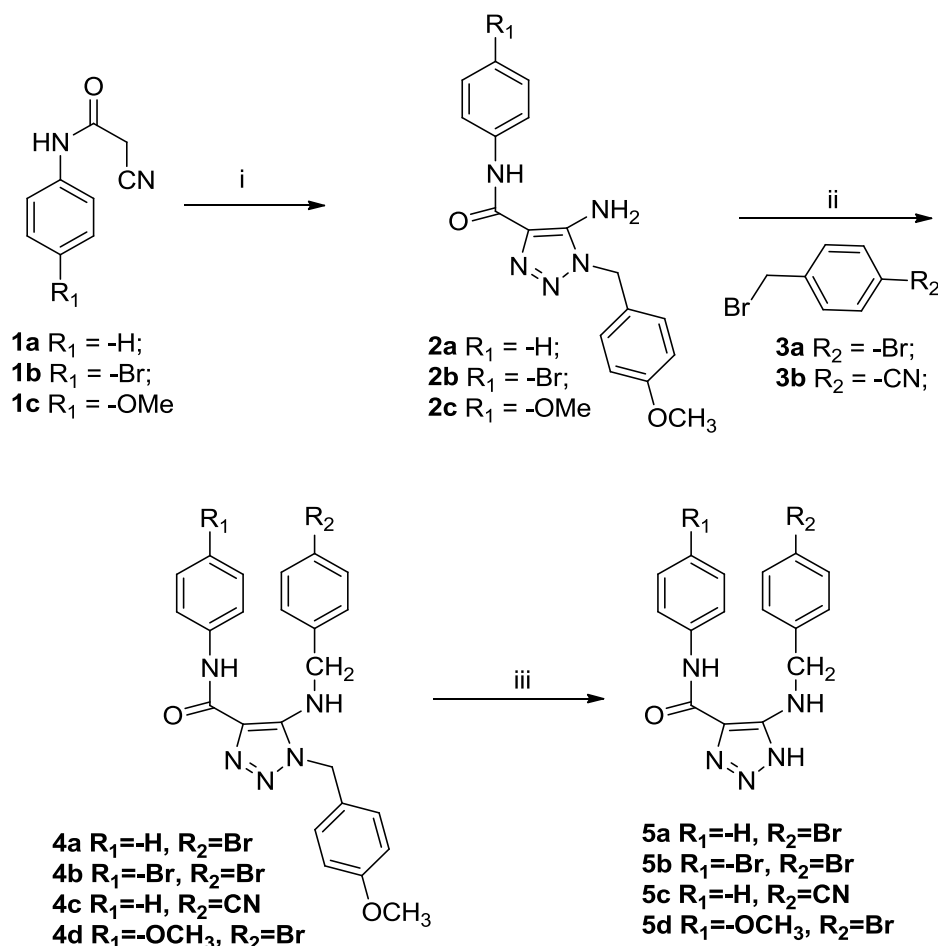
**ABSTRACT:** A series of 4,5-disubstituted triazole derivatives (**5a--5d**) were prepared starting from substituted aniline via aminolysis reaction, cyclisation, alkylation, deprotection. All the synthesized compounds were screened for cytotoxic activity against three human cancer cell lines such as MCF-7, Hela and A549. Compound **5b** was found to be most active with IC<sub>50</sub> values 7.20  $\mu$ M and 7.31  $\mu$ M against MCF-7 and A549, respectively.

**KEYWORD:** triazole; antitumor

## 1 INTRODUCTION

Cancer is the second leading cause of death worldwide[1] and thus discovery and development of suitable agents possessing novel mechanism of

action is highly desirable to treat various types of cancer. Since Sharpless and his coworkers' report on the "click chemistry" [2]---copper (I)-catalyzed azide alkyne cycloaddition (CuAAC), 1,2,3-triazole has emerged as one of the most important heterocycles



Reagents and conditions: i) 4-methoxy-benzyl azide, EtONa, EtOH, reflux; ii) NaH, THF; iii) TFA, anisole.

in current medicinal chemistry[3] and its applications have also been extended to widespread drug discovery.[4] [5] On the other hand, 1,2,3-triazoles present a great stability under acidic, basic, and oxidative conditions.[6] A number 1,2,3-triazole derivatives show good or excellent anticancer activity. [7]

## 2 RESULTS AND DISCUSSION

Treatment of cyanoacetamide **1a-1c** with 4-methoxybenzylazide forms the desired amino triazole ring **2a-2c** in good yields. Alkylation of the amino group in compound **2a-2c** with benzyl bromide was performed to give **4a-4c**. Removal of 4-methoxybenzyl group with trifluoroacetic acid generated the target compounds **5a-5d** in 36 - 47% total yields.

The cytotoxicity of all the above compounds against three human cancer cell lines namely, A549-Lung, MCF-7-Breast, and HeLa-Cervical was screened (Table 1). After exposure of cells to the test compounds for 72 h, all the four compounds show cytotoxicity on the three cell lines. More specifically, compound **5b** exhibits promising activity against all the three cell lines with IC<sub>50</sub> values about 7  $\mu$ M. Compound **5d** shows good activity against MCF-7 cell lines with IC<sub>50</sub> value of about 10.4  $\mu$ M. It also showed moderate activity against HeLa with IC<sub>50</sub> value of about 27  $\mu$ M.

Table 1 Cytotoxicity of triazole Compounds Against Cancer Cell Lines

Compounds	EC <sub>50</sub> ( $\mu$ M) <sup>b</sup>		
	MCF-7	HeLa	A549
5a	59.12	68.33	>100
5b	7.20	75.71	7.31
5c	92.5	>100	>100
5d	10.43	27.52	61.98

## 3 CONCLUSION

In conclusion, a series of novel triazole derivatives were synthesized in 36-47% yield in three steps and their antitumor activity against three human cancer cell lines was evaluated in vitro. Among them, compound **5b** is a most potential anticancer agent. Further structure–activity studies with similar compounds are currently underway in our laboratory.

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