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Amberlite IR-120H as an efficient and versatile solid phase catalyst for nucleophilic substitution of propargylic alcohols

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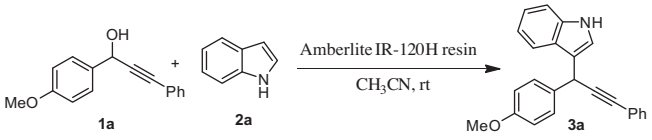
ABSTRACT

A highly efficient Amberlite IR-120H resin mediated nucleophilic substitution of the hydroxyl group of propargylic alcohols with a wide range of nucleophiles is reported. The reactions were achieved under very mild conditions in excellent yields.

A challenging yet important goal in organic synthesis is to maximize synthetic efficiency in transforming starting materials to the target molecules. Readily available starting materials and reagents, high yield, high selectivity, mild reaction conditions, and high atom economy are characteristics of an efficient synthetic method. Propargylic substitution reactions of activated or unactivated propargylic alcohols or propargylic esters with *C*-nucleophiles and heteroatom centered nucleophiles have recently been extensively explored. These reactions are generally achieved through activation of the acetylene moiety by forming cobalt complexes (Nicholas reaction)[1] or through the catalysis of rhenium,[2] ruthenium,[3] or gold[4] metal complexes. However, these reactions suffer from the high cost of reagents and catalysts. Alternative catalysts, including $FeCl_3$,[5] $BiCl_3$,[6] [bmim]PF_6/$Bi(NO_3)_3$,[7] PMA-silica gel,[8] I_2,[9] $InCl_3$,[10a] $InBr_3$,[10b] $Sc(OTf)_3$,[11] $Yb(OTf)_3$,[12] $Al(OTf)_3$,[13] $CeCl_3$,[14] Pd-Sn,[15] and PTSA,[16] have been introduced for these reactions; however, many of them involve either large amount of catalyst or limited to selective nucleophiles. Thus, highly efficient, inexpensive reaction systems with good selectivity for these transformations are still highly desirable.

Heterogeneous catalysis has played a central role in various organic transformations. Among heterogeneous catalysts, ion-exchange resins are widely used owing to their low cost, reusability, wide range of acid/base strength, ease of handling, environmental compatibility, and low toxicity. Moreover, they can be easily recovered from reaction mixtures by filtration and can be reused after activation or even without activation, making the process economically viable. Herein, we report a simple and straightforward method using Amberlite IR-120H ion-exchange resin as a catalyst for the nucleophilic substitution of propargylic alcohols with various nucleophiles in excellent yields under very mild reactions conditions.

Using 1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-ol (**1a**) and indole (**2a**) as model reactants, it was observed that the reaction proceeded smoothly in CH_3CN at room temperature in the presence of Amberlite IR-120H resin (Scheme 1). Amberlite IR-120H



Scheme 1. Substitution of the OH group in propargylic alcohol with indole.

Table 1
Optimization of the reaction conditions[a]

Entry	Amberlite IR-120H (mg/mmol)	Time[b] (min)	Yield[c] (%)
1	50	120	45
2	150	60	70
3	300	30	93

[a] All reactions were carried out with **1a** (1 mmol), and **2a** (1.2 mmol) in CH_3CN at rt.
[b] Reaction time before filtration; both 1 and 2 were incomplete.
[c] Isolated yield.

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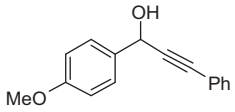
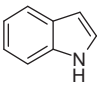
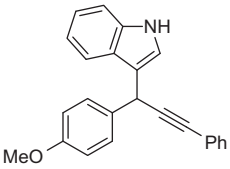
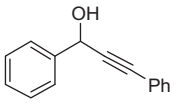
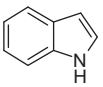
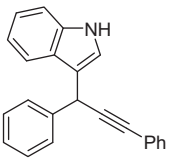
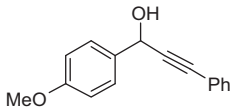
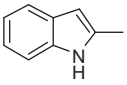
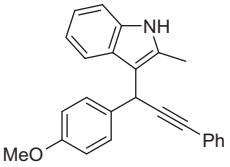
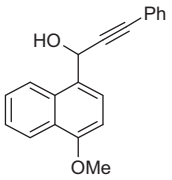
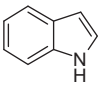
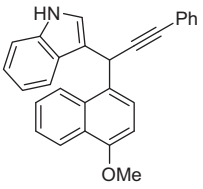
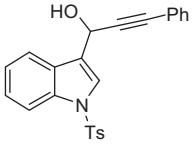
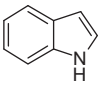
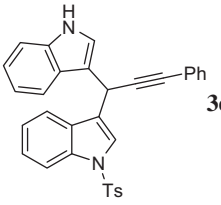
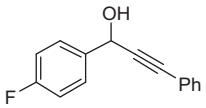
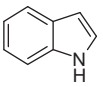
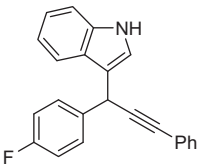
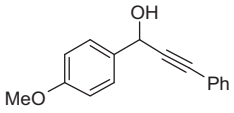
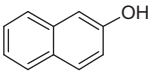
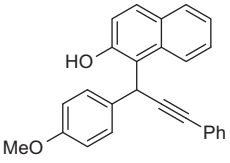
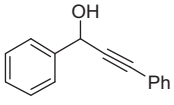
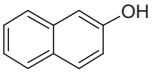
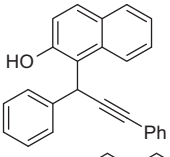
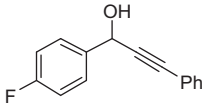
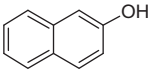
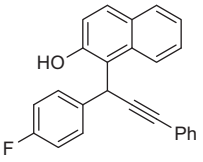
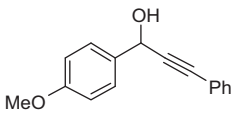
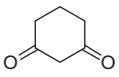
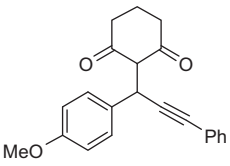
Table 2
Amberlite IR-120H resin promoted substitution of the hydroxyl group in propargylic alcohols with various nucleophiles[a]

Entry	Alcohol	Nucleophile	Product[b]	Time (min)[c]	Temperature (°C)	Yield (%)[d]
a			 **3a**	30	rt	93
b			 **3b**	30	60	87
c			 **3c**	30	rt	90
d			 **3d**	120	rt	87
e			 **3e**	90	rt	87
f			 **3f**	180	60	83
g			 **3g**	60	rt	93
h			 **3h**	90	60	90
i			 **3i**	180	60	90
j			 **3j**	120	rt	90

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