



Aluminum promotes easy access to high substituted trihalomethyl triazolyl homoallylic alcohols

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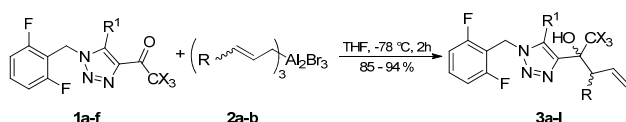
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INTRODUCTION

Homoallylic alcohols are high featured in synthetic procedures to the build of many biologically active molecules, such as macrolides, polyhydroxylated natural products, and polyether antibiotics.¹ To access these versatile synthons, the insertion of allylic organometallics to carbonyl compounds are one of the most remarkable tools found in the literature.² Besides homoallylic alcohols, triazoles also show several applications in many branches of modern chemistry, like pharmacological and agriculture field. Thus, in view of importance of the cited compounds, the aim of this work is to report the results obtained from insertion of allyl aluminum compounds to 5-alkyl(aryl)-1-(2,6-difluorobenzil)-4-trihaloacetyl-1H-1,2,3-triazoles.

RESULTS AND DISCUSSION

The allyl aluminum reagents (**2a-b**) were generated in situ by insertion of aluminum to allyl and (*E*)-crotyl bromide, employing indium as catalyzer. The solutions containing the organometallics reagents were then added to the respective trihaloacetyl triazoles (**1a-f**) at -78 °C, and stirred at this temperature by 2 hours. After the extraction work up with diethyl ether and hydrochloric acid (10% v/v), the crude mixture was purified by chromatography employing silica flash as stationary phase and solution of hexane/ethyl acetate 3:1 (v/v) as eluent (Scheme 1).



X = F, Cl
R = H, Me, Ph
R¹ = H, Me

Scheme 1. Synthesis of the trihalomethyl triazolyl homoallylic alcohols (**3a-l**).

All homoallylic alcohols were obtained in good yields. However, those derived from crotyl bromide (R=Me) furnished a mixture of diastereoisomers in

the proportion of 70:30 (Table 1). We accepted the idea of which these poor selectivities are due the methallotropic rearrangement of the crotyl aluminum reagent. This interpretation is in accordance with the Zimmerman-Traxler transition state model, which establishes that different organometallics lead to different products.³

Table 1. Yields attained from compounds (**3a-l**).

Compound	R	R ¹	X	Yield (%) [*]
3a	H	H	F	90
3b	H	Me	F	94
3c	H	Ph	F	91
3d	H	H	Cl	88
3e	H	Me	Cl	92
3f	H	Ph	Cl	94
3g	Me	H	F	89
3h	Me	Me	F	86
3i	Me	Ph	F	90
3j	Me	H	Cl	85
3k	Me	Me	Cl	90
3l	Me	Ph	Cl	91

^{*} The compounds (**3g-l**) showed a mixture of diastereoisomers at proportion of 70:30 (determined by ¹H NMR).

CONCLUSION

In summary, we have reported an efficient preparation of trihalomethyl triazolyl homoallylic alcohols from the addition of allylic aluminium reagents to trihaloacetyl ketones. This economical protocol, although shows limitations for allyl halides substituted with small groups, was able to furnish the desired compounds in considerable yields under very mild conditions.

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