

Diastereoselective Multicomponent [4+2]/[3+2] Cycloadditions of gamma-(S)-N,N-dibenzylamine Nitroalkenes Derivatives with Ethyl Vinyl Ether (EVE) and Electron-Poor Alkenes Using Li⁺-Containing Catalysts.

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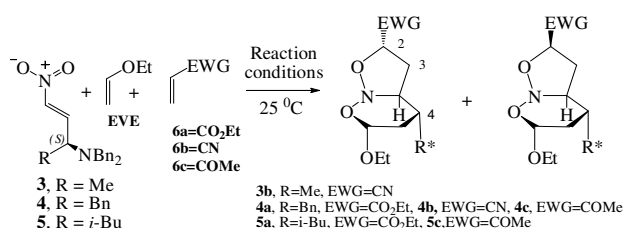
INTRODUCTION

Electrondeficient nitroalkenes exhibit different reactivities in organic synthesis. For example: i) act as dienophiles reacting with dienes to afford nitrocycloadducts derivatives in Diels-Alder reaction; ii) as 1,3-dipolarophiles (DPP) reacting with several 1,3-dipoles in [3+2] cycloadditions and iii) as heterodienes (HD), often in the presence of Lewis acid, to afford cyclic alkyl nitronates in hetero-Diels-Alder reactions.¹

To the best of our knowledge, there are only two examples of the use of chiral nitroalkenes in stereoselective tandem [4+2]/[3+2] cycloadditions. Recently, we synthesized non-racemic nitroalkenes **3-5** from L-alanine, L-phenylalanine and L-leucine, respectively in five steps and 80-90% overall yield. These electrondeficient nitroalkenes have exhibited excellent stereochemical stability, reactivity and diastereoselectivity in a great number of different reactions.² In order to increase the scope of the reactivity of **3-5** herein we investigate the reactivity and diastereoselectivity these new “chirons” in tandem intermolecular [4+2]/[3+2] cycloadditions employing Li⁺ containing catalysts.

RESULTS AND DISCUSSION

The chiral nitroalkenes **3-5**, were reacted, in one pot, with EVE, methyl acrylate (**6a**), acrylonitrile (**6b**) or methyl vinyl ketone (**6c**) in the presence of selected solvents (EtOH/H₂O, THF/H₂O) and Li⁺-containing catalysts. The Scheme/table 1 shows our principal results. According to the outcomes obtained, all nitroalkenes presented a similar reactivity and diastereoselectivity when polar solvents and Lewis acids were investigated. The use of acrylonitrile as dipolarophile led to lowest reaction time (line 1) and acrylate **6a** the higher yield (line 2). The unequivocal assignment of absolute stereochemical will be accomplished by x-ray analysis of **4b**.



Line	HD/ DPP	Catalytic system/time	Diastereoisomer Ratio ^a /yield (%) ^b
1	3/6b	LiClO ₄ (4.7 M) THF:H ₂ O (3:1)/1d	3b , 1:1 (61)
2	4/6a	LiClO ₄ (4.7 M) THF:H ₂ O (3:1)/3d	4a , 2:1 (72)
3	4/6a	LiClO ₄ (4.7 M) EtOH:H ₂ O (3:1)/3d	4a , 1.7:1 (66)
4	4/6a	LiCl (4.7 M) EtOH:H ₂ O/(3:1)/3d	4a , 1.4:1 (60)
5	4/6b	LiClO ₄ (4.7 M) THF:H ₂ O(3:1)/3d	4b , 1.7:1 (30)
6	4/6c	LiClO ₄ (4.7 M) THF:H ₂ O (3:1)/3d	4c , 1.8:1 (53)
7	5/6a	LiClO ₄ (4.7 M) THF:H ₂ O(3:1)/3d	5a , 1.6:1 (54)
8	5/6c	LiClO ₄ (4.7 M) THF:H ₂ O (3:1)/2d	5c , 1.5:1 (34)

a) Measured in C2 by ¹H NMR and ¹³C NMR analysis of the crude reaction mixtures. b) Purified overall yields of the diastereomeric mixtures

CONCLUSIONS

The nitroalkenes **3-5** showed a good reactivity when subjected to tandem cycloaddition protocol in a polar reaction medium. The lithium catalysts present low toxicity and can be recycled several times. Each tandem [4+2]/[3+2] cycloaddition was proceeded in high level of stereofacial selectivity, providing new chiral nitroso acetals.

REFERENCES

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