

Domino Reaction for the Synthesis of Nitroolefin Heterocyclic Compound *Via* Thiazole Formation Followed by Claisen Rearrangement

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Abstract

The Baylis-Hillman adducts derived from nitroolefins have been conveniently transformed into Claisen rearrangement. These substances, which include benzothiazole moiety, are very biologically reactive substances. This novel nitro derivative of 2-((E)-2-nitro-3-phenylallyloxy)-3-ethoxybenzaldehyde was simply treated with mole percentage of 2-(2-(2-aminophenyl) disulfanyl) benzenamine in melt reactive condition. Hence this novel 2-(benzo[d]thiazol-2-yl)-6-ethoxy-4-((E)-2-nitro-3-phenylallyl)phenol core unit compounds was very intriguing and new opportunities for the preparation of closely related to the different [3,3] sigmatropic rearrangements related to the Claisen rearrangement molecule. In situ production of a monomer succeeded from an intramolecular [4 + 2] cycloaddition reaction have been shown to be a solid-state melt reaction (SSMR) for the manufacturing of tetracyclic chromenopyran pyrimidinedione frameworks employing Baylis-Hillman derivatives. High stereoselectivity and stereospecificity were used to create the tetracyclic frameworks without the need of a catalyst or solvent. The isolated yield is very good, and the pure product can be obtained without using column chromatography for purification.

Keywords: Nitroolefins, baylis-hillman adducts, claisen rearrangement, ethoxybenzaldehyde, disulfanylbzenamine, phenylallyl) phenol

INTRODUCTION

Cyclic compounds very interesting biological active and natural products compounds. Amongst the various heterocyclic systems, chromanone / chromenone ring is one of the most widely investigated [1]. During the past decade, domino reactions have emerged as a powerful and efficient method for the construction of heterocyclic compounds. Among such reactions, the Claisen rearrangement has proven to be a useful tool for the synthesis of polyheterocyclic compounds [2]. The Claisen rearrangement reaction has also been extensively employed for the synthesis of polycyclic compounds; however the synthesis of chromanone/chromenone ring system was not explored much in the literature.

There has been a flurry of activity in the synthesis of coumarin derivatives due to their proven biological activity and medicinal utility. For example, they possess anticoagulant, antifungal, [3] antioxidative [4] activities. In fact, these coumarin derivatives are wide spread in nature and an integral part of many natural products such as prethulia

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coumarin (I), isoferprenin (II), pterophyllin (III), isoethuliacoumarin A (IV), isoethuliacoumarin B (IV), isoethuliacoumarin C (V), ethuliacoumarin A (VI), and ethuliacoumarin B (VII) etc.

Synthetic tools for the rapid construction of building blocks and intermediates for target-oriented synthesis are most important part in synthetic organic chemistry. In this regard, Pericyclic reactions, including [3, 3] sigmatropic rearrangements, appreciate impact value for the synthesis of many natural and bio active organic compounds [4]. Particularly, the Claisen rearrangement reaction is very important and useful strategy for the synthesis of many natural and bio active organic compounds, over the past century [5]. Therefore, the Claisen rearrangement continues to be the focus of considerable synthetic chemistry research effort. Subsequently, the supremacy of the Claisen rearrangement has been recognized as indicated by its widespread application.

So many natural products whose syntheses include some step closely related to any of the different [3, 3] sigmatropic rearrangements related to the Claisen rearrangement such as acorone (I), homogynolide B (II), aplysin (III), saudin (IV) and pancratistatin (V) are shown in Figure 1.

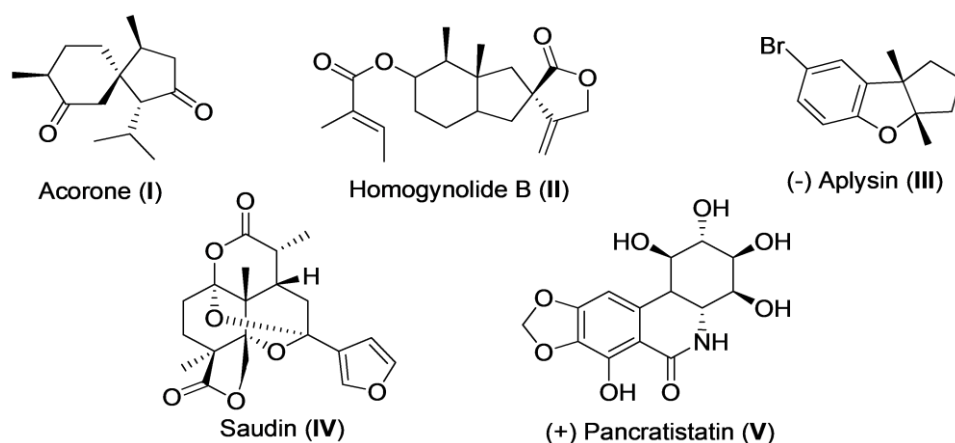


Figure 1. Some of the representative examples for synthesis of natural products *via* claisen rearrangement.

RESULTS AND DISCUSSION

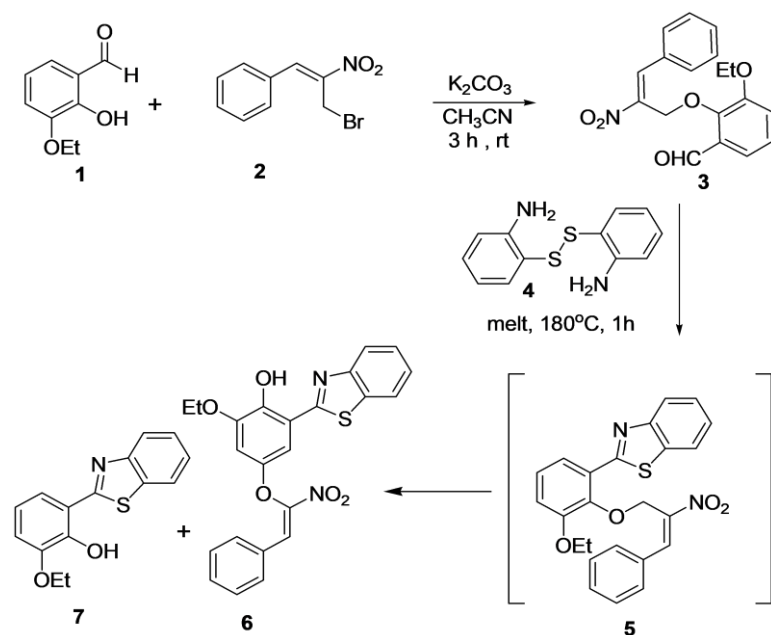
Attracted by this fascinating Claisen rearrangement, we have initiated programme for the synthesis of novel nitro 2-nitro-3-phenylallyl)phenol scaffolds through Claisen rearrangement. we describe the solvent and catalyst free Claisen rearrangement on Baylis-Hillman derivatives for the nitro compounds. We envisaged that the B.H derivatives synthesized from Baylis-Hillman bromides and salicylaldehyde will undergo Claisen rearrangement under thermal condition to provide the rearranged product. To execute our idea, we have melted the *O*-allylated salicylaldehyde at 180°C for 1 h to give intermediated compounds [6–10].

After the successful synthesis of *ortho*-migrated Claisen rearranged products from Baylis-Hillman derivatives, we envisaged that the *para* migrated Claisen product *i.e.* 2-(benzo[d]thiazol-2-yl)-6-ethoxy-4-((*E*)-2-nitro-3-phenylallyl)phenol can be achieved from the *ortho* substituted Baylis-Hillman derivatives *via* Claisen rearrangement through *para* migration [11]. Triggered by this idea, we treated *ortho* substituted Baylis-Hillman derivative (2a) with 2-(2-(2-aminophenyl)disulfanyl)benzenamine at 180°C for 1h which successfully afforded the desired *para* migrated Claisen rearranged product *i.e.* 2-(benzo[d]thiazol-2-yl)-6-ethoxy-4-((*E*)-2-nitro-3-phenylallyl)phenol (5a) containing benzothiazole moiety in 65% yield along with minor product (benzothiazole) in 10% yield. Encouraged by this result, we have treated *ortho* substituted cinnamyl salicylaldehyde derivatives 3a with 2-(2-(2-aminophenyl)disulfanyl)benzenamine at 180°C for 1 h, which successfully afforded the desired *para* migrated Claisen products 5a in 65-73% yields along with minor product 6a (benzothiazole) in 10–16% yields as shown in Scheme1 [12–13].

Scheme 1 caption-*para* migrated Claisen products

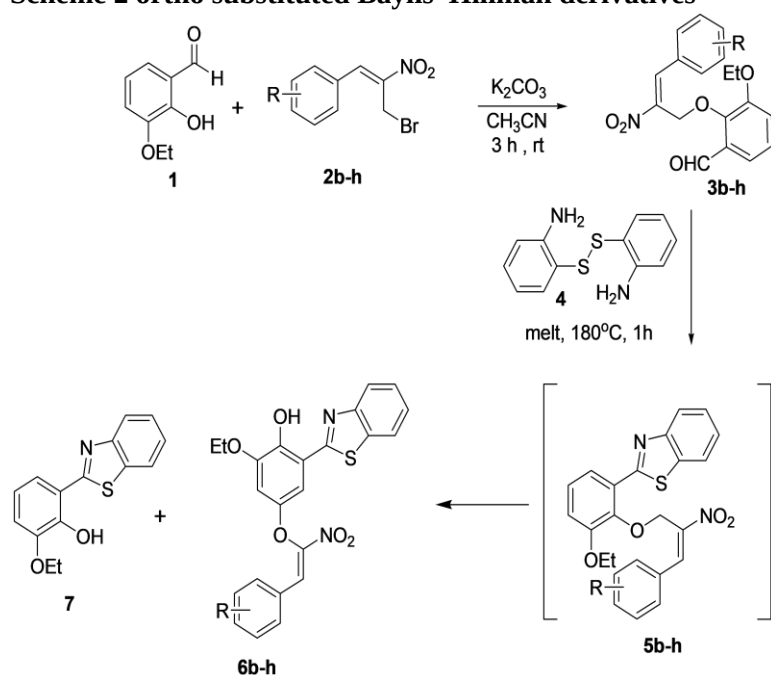
Howed $O\text{-}C_2H_5$ protons as a triplet at δ 1.35 and as a quartet at δ 4.31, the benzylic CH_2 protons appeared as one singlet at δ 4.31. The phenolic OH proton appeared as a singlet at δ 11.42. The remaining aromatic protons appeared as multiplets in the region of δ 6.74–7.95 [14–15].

The 1H NMR spectrum of compound 5 s



To further expand the generality of the *para* migration in Claisen rearrangement, we decided to engage the *ortho* substituted Baylis-Hillman derivatives synthesized from B.H. bromide) and salicylaldehyde. Accordingly, we treated the *ortho* substituted Baylis–Hillman derivatives with 2-(2-(2-aminophenyl)disulfany)benzene -amine at 180°C for 1 h which successfully led to the desired *para* migrated Claisen rearrangement Scheme 2.

Scheme 2 *ortho* substituted Baylis–Hillman derivatives



CONCLUSION

Effectively developed a capable and new protocol for the construction of heterocyclic compounds. *via* benzothiazole formation followed by Claisen rearrangement and lactamization reaction sequence through a domino process using Baylis-Hillman derivatives. The multifunctional Baylis-Hillman derivatives for the domino process for para migration of Claisen rearrangement having highly biologically active molecules.

Typical Experimental Procedure for the Synthesis of Benzothiazoles

A mixture of (*E*)-methyl 2-((3-ethoxy-2-formylphenoxy)methyl)-3-phenylacrylate (119r, 1mmol), and 2-(2-(2-minophenyl)disulfany)benzenamine (0.5 mmol) was placed in a round bottom flask and melted at 180°C for 1 h. After completion of the reaction as indicated by TLC, The crude reaction mass was purified by column chromatography on silica gel (Acme 60–120 mesh), using ethylacetate : hexanes (0.5 : 9.5) to afford as a colourless solid in 73% (0.19 g) yield.

The ¹H NMR spectrum of compound **5** showed O-C₂H₅ protons as a triplet at δ 1.35 and as a quartet at δ 4.31, the benzylic CH₂ protons appeared as one singlet at δ 4.31. The phenolic OH proton appeared as a singlet at δ 5.74. The remaining aromatic protons appeared as multiplets in the region of δ 6.74–7.95.

2-(Benzo[d]thiazol-2-yl)-6-Ethoxy-4-(2-Nitro-3-Phenylallyl)phenol compound

Nature of the compound	: Colorless solid
Yield	: 73%
M. P	: 152-155°C
IR (KBr)	: 1635, 1727, 3423 cm ⁻¹
¹ H NMR (300 MHz, CDCl ₃)	: δ 1.35 (t, <i>J</i> = 6.3 Hz, 3H), 4.60 (s, 2H), 4.31 (s, 2H), 5.74 (br s, 1H), 6.83 – 7.95 (m, 12H)
¹³ CNMR (75 MHz, CDCl ₃)	: δ 14.67, 32.72, 64.52, 115.83, 116.67, 119.92, 123.45, 122.11, 125.43, 125.64, 127.71, 128.81, 129.16, 130.17, 132.70, 135.37, 141.17, 146.97, 149.23, 154.82, 163.57
MS (m/z)	: 432 (M+1)
Elemental Analysis for C ₂₄ H ₂₀ N ₂ O ₄ S	
Calculated	: C, 66.65; H, 4.66; N, 6.48.
Found	: C, 66.67; H, 4.65; N, 6.46.

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