SYNTHESIS OF SIMPLE (*E*)-3,5-DINITRO-2-(2-NITRO-3-PHENYLALLYLOXY)BENZALDEHYDE DERIVATIVES FROM (*E*)-(3-BROMO-2-NITROPROP-1-ENYL)BENZENE

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Abstract : Synthesis of simple protocol for the bromo derivatives of Baylis-Hillman adducts derived from nitroolefins in good yields. This novel class of bromo derivatives can be utilized as building blocks for wide variety of organic compounds. We also developed a facile method for the transformation of these bromides into an interesting and novel class of functionalized(*E*)-3,5-dinitro-2-(2-nitro-3-phenylallyloxy)benzaldehyde compounds. Hence this novel protocol opens new opportunities for the preparation of libraries of wide variety of new molecules

Keywords- Baylis-Hillman adducts, nitroolefin, Bromo compounds, 2-hydroxy-3,5-dinitrobenzaldehyde with catalyst in K_2CO_3 and acetonitrile

I. INTRODUCTION

The synthesis of heterocycles containing nitrogen and oxygen continues to be an essential and challenging area in the field of organic chemistry.[1] The spiropyrrolidine skeleton is part of many natural products such as horsfiline , elacomine, alstonisine, spirotryprostatin A, etc.[2] In accumulation spiropyrrolidines have been shown to posses anti- cancer, antimicrobial, antibiotic and antineoplastic properties. The cycloaddition reaction is one of the most vital and useful method for the grounding of five membered heterocycles. The reaction of azomethine ylides with alkenes provides the pyrrolidine moiety which is present in various natural products and biologically active molecules.[3,4] Utilizing azomethine ylide based cycloaddition reaction, a variety of phenoxy have been reported in the literature, The Baylis-Hillman adducts and its derivatives are utilized as starting material for various organic reactions which include several named reactions in organic chemistry. For instance, recently the Baylis-Hillman adducts are utilized as dipolarophiles in [3+2] cycloaddition chemistry to produce spiro compounds. On the other hand nitroolefins are very reactive group and have been frequently utilized as Michael acceptor. Interestingly, the nitroolefins are also utilized as dipolarophiles in the [3+2] cycloaddition to prepare a wide variety of pyrrolidines.[5]

Literature survey reveals that spiropyrrolidines and spiropyrrolidizines frameworks constitutes an important structural assembly owing to the presence of these structural units in various molecules of historical importance.[6-9] Hence the development of new, simple and efficient methodologies for the synthesis of novel class of spiro compound frameworks represents an important endeavor in the area of organic chemistry. We envisaged that Baylis-Hillman adduct derived from nitroolefin would be a useful dipolarophile for the construction of spiropyrrolidine and spiropyrrolizidine compounds *via* azomethine ylide based [3+2] cycloaddition reaction. This new methodology is not only useful for the synthesis of 3-spiropyrrolidines and spiropyrrolizidines but also demonstrates the importance of Baylis-Hillman adducts which are derived from nitroolefins. Infact in the Baylis-Hillman chemistry, BH adducts derived from nitroolefins are not explored much. Though various trisubstituted olefins derived from Baylis-Hillman adducts using acrylates, acrylonitrile, MVK have been successfully synthesised and utilized for various

organic transformations, the synthesis of the trisubstituted allyl halides derived from nitroolefins has not been reported so far in the literature and applications of this trisubstituted allyl halides are yet to explore.

2. RESEARCH METHODOLOGY

Triggered by this idea, we have decided to prepare the bromo compound derived from nitroolefins which will open new avenues for several synthetic transformations. In continuation of our ongoing research in our laborotory in the field of Baylis-Hillman chemistry,[6] we envisaged that the (*E*)-2-nitro-3-phenylprop-2-en-1-ol may be a suitable starting material to synthesize the desired bromo compounds easily. Accordingly, the Baylis-Hillman adduct derived from nitroolefin and formaldehyde was treated with aqueous HBr (48%) in DCM solvent which successfully yielded the desired 1-((*E*)-3-bromo-2-nitroprop-1-enyl)benzene.

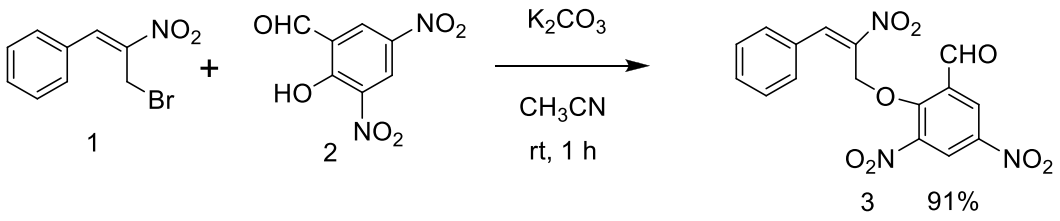
3. RESULTS AND DISCUSSION

Utilizing this [3+2] cycloaddition chemistry variety of tricyclic chromeno pyrrolidine frameworks have also been reported in the literature. Due to the interesting and important biological properties of these tricyclic pyrrolidines, development of simple and convenient routes for the construction of tricyclic chromeno pyrrolidine derivatives with various substituents represents an attractive and interesting endeavor in synthetic organic chemistry and medicinal chemistry. In fact, a number of methodologies/strategies are reported in the literature for the synthesis of these molecules with different functionalities[4]. For example, Bashiardes *et al*[6] developed a new method for the synthesis of tricyclic pyrrolidines and pyrroles *via* the microwave-assisted intramolecular [3+2] cycloaddition reaction of azomethine ylides to the activated and nonactivated alkenes and alkynes.

In the literature survey we found that the tricyclic chromeno [4,3-*b*] pyrrolidine frameworks are known to be non-competitive antagonists of the muscular nicotin receptor.[1] It is well documented in literature that the Baylis-Hillman adducts have been utilized very well for the synthesis of various heterocyclic compounds.[5] We envisaged that the *O*-allylic salicylaldehyde derivatives prepared from the Baylis-Hillman bromides will be a suitable precursor for the synthesis of tricyclic chromeno [4,3-*b*] pyrrolidine frameworks involving substitution followed by a in situ formation of imine, decarboxylation and [3+2] cycloaddition reaction.

After successful synthesis of fused tricyclic chromeno [4,3-b] pyrrolidines having nitro functionality at angular position, we turned our attention towards the synthesis of a phenoxy compounds. To achieve our goal, first we have selected a bromo derivative of the Baylis-Hillman (B.H) adduct obtained *via* reaction of benzaldehyde and methyl acrylate, as the starting material for generation of the reaction. Reaction of bromo compounds and 2-hydroxy-3,5-dinitrobenzaldehyde with catalyst in K_2CO_3 and acetonitrile for 1 h at reflux temperature successfully provided the desired (*E*)-3,5-dinitro-2-(2-nitro-3-phenylallyloxy)benzaldehyde in excellent yield (91%) after work up followed by column chromatography.(Scheme 1).

Schme-1

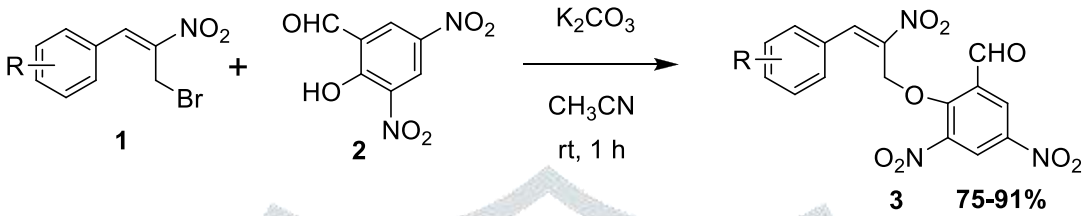


The compound **3** was characterized by IR, ^{1}H, ^{13}C NMR, mass spectral data and elemental analysis

The ^{1}H NMR spectrum of compound **3** showed as singlet at δ 5.38. The olefinic protons appeared as a singlet at δ 8.54 and aldehyde proton appeared as singlet at δ 10.53. The aromatic protons appeared as a multiplet in the region of δ 6.92-7.63.

Encouraged by this result, we prepared a variety of bromo compounds as starting materials. Treatment of compounds **2** with 2-hydroxy-3,5-dinitrobenzaldehyde successfully led to the desired phenoxy compounds **3b-j** in 75-91% yields (Scheme 2). The results are summarized in Table 1

Scheme-2



R = 2-Me, 4-Me, 4-Et, 4-*i*-Pr, 4-OMe, 3,4-di-OMe, 3,4-OCH_2O-, 4-F, 2-Cl, 4-Cl

Table 1. The synthesis of (*E*)-3,5-dinitro-2-(2-nitro-3-phenylallyloxy)benzaldehyde.

S.No	Bromo derivatives	Phenoxy compounds	Yield %
1	1a	3a	91
2	1b	3b	83
3	1c	3c	75
4	1d	3d	88
5	1e	3e	84
6	1f	3f	90
7	1g	3g	87
8	1h	3h	80
9	1i	3i	82
10	1j	3j	76

[a]All reactions were carried out using Bromo derivatives **(1a-j)** with 2-hydroxy-3,5-dinitrobenzaldehyde in CH_3CN at reflux temperature [b]All products gave satisfactory IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. [c]Yields of the pure products (**3a-j**) obtained after column chromatography (silica gel, 5-10% EtOAc in hexanes).

Typical experimental procedure for the synthesis of (*E*)-3,5-dinitro-2-(2-nitro-3-phenylallyloxy)benzaldehyde (**3a**):

To a solution of salicylaldehyde (**2**) (0.22g, 1mmol) in acetonitrile, potassium carbonate (0.15g, 1.5mmol) was added and stirred well for 15 minutes at reflux temperature. To this solution, 1-((*E*)-3-bromo-2-nitroprop-1-enyl)-2-methylbenzene (**1a**) (0.178g, 1.0 mmol) in acetonitrile (20mL) was added dropwise and stirred well for 1 hr. After the completion of the reaction (confirmed by TLC analysis), the reaction mixture was concentrated under reduced pressure and the crude product thus obtained was purified by

column chromatography (EtOAc / hexanes, 5%) to provide **3a** in 91% (0.3.5g) yield, as yellow crystalline solid.

4. CONCLUSION

We have successfully developed a short and simple protocol for the synthesis of bromo derivatives of Baylis-Hillman adducts derived from nitroolefins in good yields. This novel class of bromo derivatives can be utilized as building blocks for wide variety of organic compounds. We also developed a facile method for the transformation of these bromides into an interesting and novel class of functionalized(*E*)-3,5-dinitro-2-(2-nitro-3-phenylallyloxy)benzaldehyde compounds. Hence this novel protocol opens new opportunities for the preparation of libraries of wide variety of new molecules.

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6. REFERENCES

[1] Zeni, G .; Larock, R. C. Synthesis of heterocycles via palladium-catalyzed oxidative addition,*Chem. Rev.* 2006, *106*, 4644.

[2] Bagul, T. D.; Lakshmaiah, G.; Kawabata, T.; Fuji, K. Total synthesis of spirotryprostatin via asymmetric nitroolefination, *Org. Lett*. 2002, *4*, 249.

[3] De, G.P.; Silveira, C.; Coelho, F, Enantioselective synthesis of 2-ethyl-2,3-dihydrobenzofuran carboxylic acid, direct precursor of (+)-efaroxan, from a Baylis–Hillman adduct, *Tetrahedron Letter*. 2005, *46*, 6477-6481.

[4] Pandey, G.; Banerjee, P.; Gadre, S. R. Construction of enantiopure pyrrolidine ring system via asymmetric [3+2]-cycloaddition of azomethine ylides, *Chem. Rev*. **2006**, *106*, 4484.

[5] Coldham, I.; Hufton, R. Intramolecular dipolar cycloaddition reactions of azomethine ylides, *Chem. Rev.* **2005**, *105*, 2765.

[6] Basavaiah, D.; Reddy, B. S.; Badsara, B. S. Recent Contributions from the Baylis-Hillman Reaction to Organic Chemistry *Chemical. Review.*2010, *110*, 5 447–5674.

[7] Krafft, M. E.; Haxell, T. F. N, Organomediated Morita-Baylis-Hillman cyclization reactions. Journal of American Chemical Society 2005, *127*, 10168-10190.

[8] Jellerichs, B. G.; Kong, J. R.; Krische, M. J. Nucleophilic Phosphine Catalysis (non-Morita-Baylis-Hillman), Journal of American Chemical Society. 2003, *125*, 7758.

[9] Gengan Saravanan and Heera, T. R., Ionic Liquids: As a Solvent for Electrodeposition of Metals and Energy Conversions International Journal of Renewable Energy and its Commercialization. (2017) 3(2) 19–38.

[10]. Gengan Saravanan, Kinetics of Nucleation and Growth of Metal Nanoparticles- A Review International journal of Thermodynamics and chemical kinetics, 2017, 3(1).

[11]. Haneefa, M. M. Jayandran M. and Balasubramanian,v, Evaluation of antimicrobial activity of green-synthesized manganese oxide nanoparticles and comparative studies with curcuminaniline functionalized nanoform Asian Journal of Pharmaceutical and Clinical Research, 10 (3), 2017, 347-352.

[12]. A. Margaret Clementpia, A, Nithya P, and. Sivakumar, M. N, Synthesis of 3-(3-Methoxy-2-Nitro-3-Phenylpropyl)-9h-Carbazole from Friedel-Crafts Reaction, Rasayan journal of Chemistry, 11, 2018, 321.