Tetrahedron Letters 58 (2017) 3545–3548

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis of highly functionalized indeno[1,2-*b*]furans

Leema Dutta, Pulak J. Bhuyan *

Applied Organic Chemistry Group, CSIR-North East Institute of Science & Technology, Jorhat 785006, Assam, India

ARTICLE INFO

Article history:
Received 29 June 2017
Revised 26 July 2017
Accepted 28 July 2017
Available online 29 July 2017

Keywords:
Indandione
Indeno[1,2-*b*]furan
4-Hydroxycoumarin
Aldehyde
Iodine
Dimethyl sulfoxide

ABSTRACT

Some novel functionalized indeno[1,2-*b*]furans were synthesized from the reaction of indandione/indanone and aldehydes at room temperature followed by the reaction of the Knoevenagel condendensed intermediate with 4-hydroxycoumarins in the presence of iodine as catalyst in dimethyl sulfoxide (DMSO) under thermal conditions. The reaction involved in a condensation and Michael addition followed by lactone ring opening and intramolecular cyclization process to afford the product in high yield in easy work-up procedure.

Indenofurans which exist both as indeno[1,2-*b*]furans and indeno[1,2-*c*]furans constitute the structural motifs of a large number of biologically relevant compounds of natural as well as synthetic origin. Indeno[1,2-*b*]furan moiety is the basic structure of strigolactones **1** (Fig. 1), the family of plant hormones responsible for diverse biological activity such as growth regulation, nodule formation, root architecture and inhibition of shoot branching etc.[1,2] Again, solanacol **2**, which is also a natural strigolactones isolated from the root exudates of tobacco and tomato possess the indeno[1,2-*b*]furan-2-one skeleton.[3] A synthetic analog of this compound GR24 **3** is used as the reference compound in seed germination bioassay of parasitic weeds.[4] In spite of the importance of the indeno[1,2-*b*]furans, only a few methods have been developed for the synthesis of these compound. The existing methods include ring-closing metathesis/ atom-transfer ring closure strategy,[5] lactonization of 2-substituted indanone,[6] [2+2] cycloaddition-oxidation sequence,[7] cobalt-catalyzed domino reaction between 2-bromoaryl aldehyde and dimethyl itaconate,[8] acid catalyzed double cyclization,[9] intramolecular carboxypalladation of alkynoic acids followed by intramolecular olefin insertion[10] etc. Recently, Gong et al. reported few compounds containing indeno[1,2-*b*]furan moiety along with other furochromenes by using addition-cycloisomerization process.[11] Similarly, Majumder et al. synthesized some dihydroindeno[1,2-*b*]furans utilizing microwave reaction strategy.[12]

Dimethyl sulfoxide (DMSO) is not only a nontoxic solvent but also a mild oxidizing agent which is used in various organic transformation reactions *e.g.* Pfitzner-Moffat oxidation, Swern oxidation etc.[13] DMSO in combination with iodine is an efficient system of reagent which is successfully utilized in many important organic reactions.[14]

In continuation of our work on the preparation of varied heterocyclic compounds of biological significance,[15] recently we synthesized some furo[3,2-*c*]coumarins from the reaction of 4-hydroxycoumarins and aldehydes.[16] Taking the advantage from the mechanism of that reaction, we have developed an efficient method for the synthesis of some novel and highly functionalized indeno[1,2-*b*]furans **4/6** from the reaction of indandione/indanone **1/5**, aldehydes **2** and 4-hydroxycoumarins **3** in the presence of iodine as catalyst and using DMSO as solvent as well as oxidizing agent, which is reported in this paper (Scheme 1). The products were isolated through a very simple work-up procedure and filtration process.

At the beginning of the study, we utilized three components *viz* 1,3-indandione **1**, benzaldehyde **2** ($R^1 = C_6H_5$) and 4-hydroxycoumarin **3** ($R^2 = H$) in one-pot reaction protocol in the presence of iodine as catalyst and DMSO as solvent at different temperature (Scheme 1). It was observed that, a new product was formed without the involvement of 4-hydroxycoumarin **3** ($R^2 = H$) when the reaction was performed at room temperature, and the compound

* Corresponding author.
E-mail address: pulak_jyoti@yahoo.com (P.J. Bhuyan).

http://dx.doi.org/10.1016/j.tetlet.2017.07.097
0040-4039/

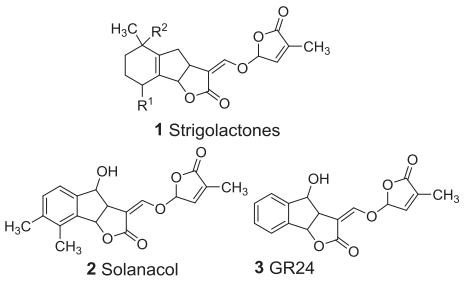
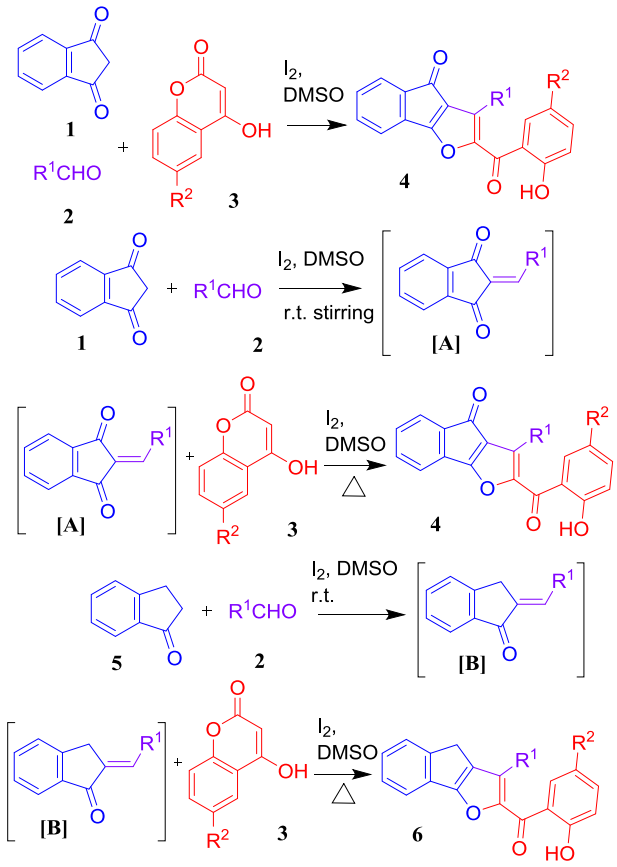


Fig. 1. Natural and synthetic indeno[1,2-*b*]furan-2-ones.

Synthesis of indeno[1,2-*b*]furans 4 and 6



Scheme 1.

was confirmed as the Knoevenagel condensation product [**A**] of 1,3-indandione **1** and benzaldehyde **2** ($R^1 = C_6H_5$). Then the temperature of the reaction was slowly raised, and within 60–90 °C a few other compounds formed in addition to the desired product **4** ($R^1 = C_6H_5$, $R^2 = H$). Interestingly, when the three-component reaction was carried out initially at room temperature and then at 90 °C, it produced the desired product **4** ($R^1 = C_6H_5$, $R^2 = H$) in good yield. It could be justified from the study that benzaldehyde **2** ($R^1 = C_6H_5$) reacts with 1,3-indandione **1** at room temperature to give their Knoevenagel condensed products, and in contrary 4-hydroxycoumarin **3** ($R^2 = H$) needs high temperature for the identical condensation process. Therefore, at high temperature, benzaldehyde **2** ($R^1 = C_6H_5$) produced two distinct Knoevenagel condensed products by reacting with 1,3-indandione **1** as well as 4-hydroxycoumarin **3** ($R^2 = H$) respectively. The two compounds so formed reacted further with 4-hydroxycoumarin **3** ($R^2 = H$) leading to the formation of a number of compounds in addition to the desired product **4**. On the other hand, when the reaction was performed initially at room temperature, only the Knoevenagel condensed compound of 1,3-indandione **1** and benzaldehyde **2** ($R^1 = C_6H_5$) was formed which reacted with 4-hydroxycoumarin **3** ($R^2 = H$) at 90 °C leading to the formation of the desired indeno [1,2-*b*]furans **4** in good yield. However, the best result was obtained when 1,3-indandione **1** was reacted with benzaldehyde **2** ($R^1 = C_6H_5$) in DMSO in the presence of iodine first to produce the knovenagel condensed product **[A]**, and then added the 4-hydroxycoumarin **3** ($R^2 = H$) to the same pot without isolating the compound [**A**] and refluxed the reaction mixture. It was further confirmed by performing the reaction in two steps. Then, we optimized the load of the catalyst and observed that 10 mol% of iodine is sufficient to afford maximum yield of the product, and further increase or decrease in the load of the catalyst did not improve the yield of the product.

After optimizing the reaction conditions, the standard reaction was carried out[17] by taking equimolar amounts of 1,3-indandione **1** and benzaldehyde **2** ($R^1 = C_6H_5$) using iodine (10 mol%) as catalyst and DMSO as solvent at room temperature under stirring conditions. A solid compound appeared in the reaction mixture. After completion of the reaction (monitored by TLC) equimolar amount of 4-hydroxycoumarin **3** ($R^2 = H$) was added to the same pot and heated at 90 °C till the completion of the reaction (monitored by TLC). The mixture was cooled to room temperature and poured into a beaker containing water. The iodine was neutralized with sodium thiosulphate solution. The solid product appeared was isolated by filtration and purified by recrystallization from ethanol which afforded the pure indeno[1,2-*b*]furan derivative **4a** ($R^1 = C_6H_5$, $R^2 = H$) in 82% yield. The structure of the compound was ascertained from the spectroscopic data. The ^{1}H NMR spectra of the compound showed the presence of the typical hydroxyl proton at δ 5.06 ppm as singlet and the presence of other thirteen aromatic protons at the range of δ 6.89–8.16 ppm. The mass spectrum showed sharp distinguishable peak of compound **4a** at 367.1 $(M+H)^+$. Generality of the reaction was established by synthesizing a series of indeno[1,2-*b*]furan derivatives **4b-q** by utilizing 1,3-indandione **1** with various substituted aryl aldehydes **2** and 4-hydroxycoumarins **3**, and characterizing them (Table 1). The reaction was also studied by utilizing aliphatic aldehyde in the reaction process, but no satisfactory results were obtained under our reaction conditions.

Again, when ketones, *viz* acetophenone was utilized in the reaction process, no reaction occured at room temperature, and at elevated temperature a number of compounds were formed from which we could not isolate any desired product. It is because arylglyoxal formed from acetophenone at high temperature under the reaction conditions[18] might have reacted with 1,3-indandione **1** as well as 4-hydroxycoumarins **3** and prevented the formation of the desired indeno[1,2-*b*]furans. As a result, we restricted our studies to aldehydes only.

The reaction was also studied by utilizing indan-1-one **5** with aldehydes **2** and 4-hydroxycoumarins **3** in the reaction process (Scheme 1) and found to be comparatively less reactive and took more time to provide lower yield of the product indeno [1,2-*b*]furans **6** (Table 1).

The effect of substituent on the substrates was also studied carefully, and observed that aldehydes and coumarins with electron withdrawing substituent in the aromatic ring were more reactive than the electron donating substituent and provided better yield of the products.

A plausible mechanism of the reaction is outlined in the Scheme 2 taking the formation of product **4a** as example. First,