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ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/gnpl20

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**To cite this article:** Tatsuro Yoneyama, Miki Iguchi, Kento Yoshii, Abdelsamed I. Elshamy, Sayaka Ban, Masaaki Noji & Akemi Umeyama (2021): Xanthone glucoside from an insect pathogenic fungus *Conoideocrella luteorostrata* NBRC106950, Natural Product Research, DOI: 10.1080/14786419.2021.1883607

**To link to this article:** https://doi.org/10.1080/14786419.2021.1883607

NATURAL PRODUCT RESEARCH
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BRIEF REPORT



# Xanthone glucoside from an insect pathogenic fungus *Conoideocrella luteorostrata* NBRC106950

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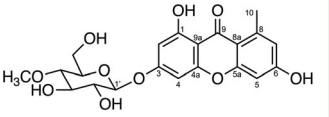
**ABSTRACT**

A new compound, 3-*O*-(4-*O*-methyl-β-D-glucopyranosyl) xanthone (**1**) was isolated from the culture of *Conoideocrella luteorostrata* NBRC106950. The structure of **1** was mainly determined by $^{1}H$, $^{13}C$, 2D-NMR and HREIMS spectral analyses. The absolute configuration of 4-*O*-methylglucopyranosyl moiety was determined by the optical rotation of aqueous layer of hydrolyzed **1** as D-configuration.

*Conoideocrella luteorostrata*



(**1**)

**ARTICLE HISTORY**
Received 26 October 2020
Accepted 27 January 2021

**KEYWORDS**
*Conoideocrella luteorostrata* NBRC106950; Clavicipitaceae; xanthone glucoside; 4-O-methylglucopyranose

## 1. Introduction

Insect pathogenic fungi which belong to the order Hypocreales, such as *Cordyceps* and *Conoideocrella* species produce its fruiting body or perithecium from host insects. *Conoideocrella luteorostrata* (which belongs to the order Hypocreales, the family Clavicipitaceae) primarily parasite on scale insects. Insect pathogenic fungi produce an interesting variety of metabolites, but not many of them have been studied and reported so far, given the existence of about 500 species worldwide. From these reasons, we have focused on the isolation of new compounds and bioactive compounds from Cordyceps. (Grudniewska et al. 2014; Umeyama et al. 2014; Ganaha et al. 2016) In this manuscript, we report the isolation and structural elucidation of a new 1,6-dihydroxy-8-methyl-3-*O*-(4-*O*-methyl-β-D-glucopyranosyl) xanthone (**1**). There are few

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Supplemental data for this article can be accessed at https://doi.org/10.1080/14786419.2021.1883607.

reports of glucose glucoside methylated at the hydroxy group of C-4′ position, limited to examples from some entomopathogenic fungi and other species.

## 2. Result and discussion

*C. luteorostrata* NBRC106950 was cultured with potato sucrose medium for two weeks. Mycelium were collected by filtration and extracted with MeOH twice and $CHCl_3$: MeOH 2:1 once and separated by subsequential liquid-liquid extraction to yield 10.99 g of EtOAc soluble fraction. EtOAc soluble fraction was purified by silica gel column chromatography to isolate 18.3 mg of **1**.

Molecular formula of **1** was determined as $C_{21}H_{22}O_{10}$ by HR-EIMS (calculated as 434.1213). In IR spectrum analysis, presence of hydroxy and carbonyl groups were indicated due to the peaks at 3357 and 1621 $cm^{-1}$, respectively. In $^{1}$H-NMR, four aromatic methine protons ($\delta_H$ 6.90, 6.87, 6.82, and 6.79), five oxygenated methine protons ($\delta_H$ 5.68, 4.36, 4.25, 3.91, and 3.45), a oxygenated methylene proton ($\delta_H$ 4.27 and 4.17), a methoxy proton ($\delta_H$ 3.86) and a methyl proton ($\delta_H$ 2.89) were observed. In $^{13}$C-NMR, 21 signals were observed, including a carbonyl carbon ($\delta_C$ 182.6), eight aromatic quaternary carbons ($\delta_C$ 164.7, 164.4, 164.2, 160.0, 157.2, 143.9, 111.9 and 105.0), four aromatic methine carbons ($\delta_C$ 117.4, 101.39, 99.4 and 94.4), five oxygenated methine carbons ($\delta_C$ 101.36, 80.1, 77.9, 77.7 and 74.8), an oxygenated methylene carbon ($\delta_C$ 61.5), a methoxy carbon ($\delta_C$ 60.6), and a methyl carbon ($\delta_C$ 23.5) (Table S1). HMBC correlations between H-2 ($\delta_H$ 6.82)/C-1 ($\delta_C$ 157.2), C-3 ($\delta_C$ 164.4), C-4 ($\delta_C$ 99.4) and C-9a ($\delta_C$ 105.0) and H-4 ($\delta_H$ 6.79)/C-4a ($\delta_C$ 157.2) and C-9a indicated the phenol moiety (Figure S7). In the same manner, H-10 ($\delta_H$ 2.89)/C-7 ($\delta_C$ 117.4), C-8 ($\delta_C$ 143.9) and C-8a ($\delta_C$ 111.9) and H-5 ($\delta_H$ 6.87)/C-5a ($\delta_C$ 160.0), C-6 ($\delta_C$ 164.7) and C-7 ($\delta_C$ 117.4) revealed the presence of *m*-cresol moiety. In these partial structures, chemical shift values of aromatic quaternary carbons showed down field shift due to the presence of oxygen (C-4a and C-5a) and carbonyl group (C-8a and C-9a). These data confirmed the 1, 6-dihydroxy-8-methyl-xanthone structure.

Glucopyranosyl moiety was successfully determined by the COSY correlations between H-1′ ($\delta_H$ 5.68, d, $J$ = 7.7 Hz)/H-2′ ($\delta_H$ 4.25, dd, $J$ = 7.7, 8.9 Hz), H-2′/H-3′ ($\delta_H$ 4.36, dd, $J$ = 8.9, 8.9 Hz), H-3′/H-4′ ($\delta_H$ 3.91, dd, $J$ = 8.9, 9.7 Hz), H-4′/H-5′ ($\delta_H$ 3.95, ddd, $J$ = 1.8, 4.2, 9.7 Hz), and H-5′/H-6′ ($\delta_H$ 4.27, dd, $J$ = 1.8, 12.3 Hz) and H-6′ ($\delta_H$ 4.17, dd, $J$ = 4.2, 12.3 Hz). HMBC correlation between $\delta_H$ 3.86/C-4′ ($\delta_C$ 80.1) indicated the methoxy group at position C-4′. In addition, H-1′ ($\delta_H$ 5.68)/C-3 ($\delta_C$ 164.4) revealed the substitution at position C-3 by 4-*O*-metylglucopyranose. The β-orientation of 4-*O*-methylglucose was determined by ROE correlation observed between H-1′/H-3′ and H-5′, and H-2′/H-4′, and $J$ value (7.7 Hz) of aromatic proton at $\delta_H$ 5.68. The D-configuration of 4-*O*-methyl-β-glucopyranosyl unit was determined with specific optical rotation of the $H_2O$ soluble layer of hydrolysate of **1**. $^{1}$H-NMR analysis revealed sugar moiety was transferred to aqueous layer, while aglycone, which has planner structure, was dissolved in EtOAc layer (Figure S8 and S9). Aqueous layer of **1** showed positive value, $[\alpha]_D^{21}$ +24.4 (*c* 0.17, MeOH), which correspond to the reported value of 4-*O*-methyl-D-glucopyranose, $[\alpha]_D^{20}$ +80 (*c* 1.3, MeOH). (Smith 1951) The absolute configuration of **1** was determined as 1,6-dihydroxy-8-methyl-3-*O*-(4-*O*-methyl-β-D-glucopyranosyl) xanthone (Figure 1).

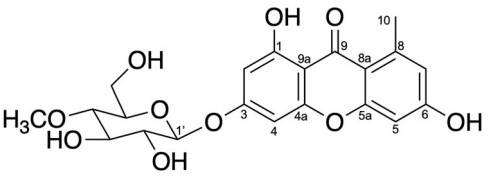


Figure 1. Structure of **1**.

Unfortunately, **1** didn't show significant activity in anti-malarial assay (data not shown).

## 3. Conclusion

In this study, we have isolated a new xanthone derivative, 1, 6-dihydroxy-8-methyl-3-*O*-(4-*O*-methyl-β-D-glucopyranosyl) xanthone from the culture of *C. luteorostrata*. Previously, compounds with 4′-*O*-methylglucose have been isolated from some insect pathogenic fungi, *Akanthomyces novoguineensis*, *Metarrhizium anisopliae*, *Cordyceps javanica*, *Paecilomyces cinnamomeus* and *Orbiocrella* sp., which belong to the orders Hypocreales or Eurotiales. (Bunyapaiboonsri et al. 2007; Isaka et al. 2007, 2014; Kuephadungphan et al. 2017; Helaly et al. 2019; Wang et al. 2020) From the starfish *Anthenea sibogae*, steroids substituted by 3-*O*-methyl-glucopyranose and 4-*O*-methyl-glucopyranose were reported. (Kicha et al. 2018) Hydroxy group at C-6′ position of glucopyranose is more active than others because of its primary alcohol structure, implying this methoxy group at C-4′ position was not substituted artificially while the extraction and purification steps. In addition, glycosyltransferase which is clustered with a methyltransferase isolated from the genome DNA of *Beauveria bassiana* has been demonstrated to contribute on the methylglucosylation of aromatic amino and phenolic moieties. (Xie et al. 2018) These indicate *C. luteorostrata* and other insect pathogenic fungus could have related biosynthetic enzymes for this reaction which could be hardly found in plants and other organisms. Isolation of new compound from Cordyceps will lead the finding of not only new compounds but also new biosynthetic enzymes which have new interesting metabolic functions in further study.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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