Formyl Fusarochromanone and Diacetyl Fusarochromanone, Two New Metabolites of Fusarium equiseti

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FORMYL FUSAROCHROMANONE AND DIACETYL FUSAROCHROMANONE, TWO NEW METABOLITES OF *FUSARIUM EQUISETI*

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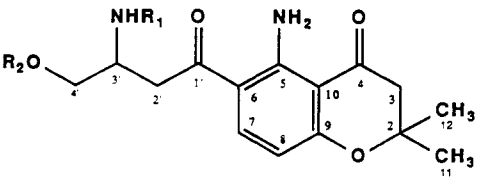
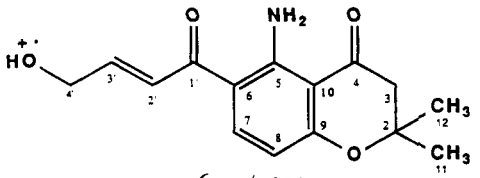
ABSTRACT.—Two new chromone derivatives, 2,2-dimethyl-5-amino-6-(3′-*N*-formyl-4′-*O*-hydroxylbutyryl)-4-chromone [**3**] and 2,2-dimethyl-5-amino-6-(3′-*N*-acetyl-4′-*O*-acetylbutyryl)-4-chromone [**4**], were isolated from the rice culture of *Fusarium equiseti*. Their structures were deduced from chemical and spectral data.

The chromone derivative, fusarochromanone [**1**], has been found in cultures of *Fusarium equiseti* (Corda) Sacc. (previously identified as *Fusarium roseum graminearum*) (1–4) and chicken feed samples (1). This mycotoxin causes tibia dyschondroplasia, a common bone disease in chicks (2,5) and reduced hatchability of fertile chicken eggs (2) under experimental conditions. In a previous report (3), we described the isolation and identification of a monoacetate **2** of fusarochromanone from the rice culture of *F. equiseti*. Further fractionation of the crude extract allowed us to isolate a minor metabolite **3** as a yellow oil from polar fractions and another metabolite **4** as needle-shaped colorless crystals from nonpolar fractions. Both compounds exhibit blue fluorescence under uv.

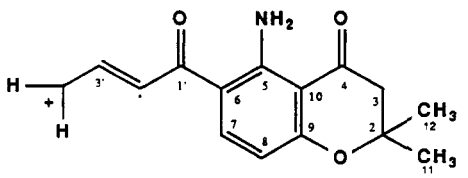
Eims of **3** yielded an $[M]^+$ at *m/z* 320 and $[M-H_2O]^+$ at *m/z* 302 indicating the presence of an -OH group. Acetylation of **3** yielded a monoacetate **5** with an $[M]^+$ at *m/z* 362 in eims, which further supported the presence of an -OH group. Fabms of **3** yielded an $[M+H]^+$ at *m/z* 321 and $[M+Na]^+$ at *m/z* 343; negative cims of **3** yielded $[M]^-$ at *m/z* 320, further supporting the mol wt as 320 amu. Hreims of **3** yielded an $[M]^+$ at *m/z* 320.1355 (calcd 320.1372 for a molecular formula of $C_{16}H_{20}N_2O_5$, which was compatible with 8 double bond equivalents). Eims of **3** was very similar to those of **1** and **2** (3), indicating closely related structures. Mass measurement of fragments at *m/z* 275.1167 (calcd 275.1158 for $C_{15}H_{17}NO_4$) and *m/z* 257.1034 (calcd 257.1051 for $C_{15}H_{15}NO_3$) suggested structures **6** and **7**. A signal at δ 8.14 (1H, d, $J=1.6$) in the ^{1}H-nmr spectrum of **3** indicated the presence of an -NHCHO group. Hydrolysis of **3** in HCl yielded **1**, which was confirmed by tlc and eims. Compound **3** was obtained by reacting **1** with HCO_2H and the structure was confirmed by eims, fabms, ^{1}H-nmr, and tlc. Therefore, the structure of **3** was established as 2,2-dimethyl-5-amino-6-(3′-*N*-formyl-4′-*O*-



1 $R_1=R_2=H$
2 $R_1=Ac$, $R_2=H$
3 $R_1=CHO$, $R_2=H$
4 $R_1=R_2=Ac$
5 $R_1=CHO$, $R_2=Ac$



6 *m/z* 275



7 *m/z* 257

hydroxylbutyryl)-4-chromone or 3′-*N*-formyl fusarochromanone.

The eims of **4** yielded an $[M]^+$ at *m/z* 376. Fabms yielded an $[M+H]^+$ at *m/z* 377 and $[M+Na]^+$ at *m/z* 399, and negative cims yielded an $[M]^-$ at *m/z* 376. The hreims indicated a molecular ion at *m/z* 376.1661 (calcd 376.1634 for $C_{19}H_{24}N_2O_6$). Signals at δ 4.14 (1H, dd, $J=5.3$, 11) and 4.32 (1H, dd, $J=6.1$, 11) in the ^{1}H-nmr spectrum of **4** indicated a downfield shift, compared with 3.70 (2H, m) in the previously reported spectrum of **2** (3). This suggested acetylation of the -OH at C-4′. An absorption band at 1734 cm^{-1} in the ir spectrum also supported the presence of acetyl groups. Hydrolysis of **4** in HCl yielded **1** and **2**, confirmed by tlc and eims. Acetylation of **2** with *N*-acetylimidazole yielded **4**, which was confirmed by tlc and eims. Therefore, the structure of **4** was determined as 2,2-dimethyl-5-amino-6-(3′-*N*-acetyl-4′-*O*-acetylbutyryl)-4-chromone or 3′-*N*-acetyl-4′-*O*-acetyl fusarochromanone.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURE.—Eims were obtained on a VG 7070 EQ operating at 70 eV. Thioglycerol was used as matrix in fabms and CH_4 was used as reactant gas in cims. ^{1}H-nmr spectra were obtained on a Bruker AC-200 at 200 MHz; chemical shifts were given in δ (ppm) with TMS as an internal standard. Ir spectra were recorded on a Nicolet 510P FT-IR. Uv spectra were recorded on Beckman DB-GT in MeOH. Analytical tlc was performed on Machery polygram sil G/UV$_{254}$. Preparative tlc plates were made from Aldrich tlc grade Si gel.

COLLECTION AND ISOLATION PROCEDURE.—*F. equiseti* was isolated from oat kernal collected in Fairbanks, Alaska and deposited in our department as Alaska 2-2. Identification was made by Dr. Paul Nelson (Department of Plant Pathology, The Pennsylvania State University). The isolate was grown on autoclaved rice with 60% H_2O for 4 weeks at room temperature. The dried, powdered rice culture (3 kg) was extracted with 90% aqueous MeOH. The extract was concentrated under reduced pressure, defatted with petroleum ether, and partitioned with CH_2Cl_2. The CH_2Cl_2 layer was concentrated and fractionated on a Florisil column. Elution was with $CHCl_3$-MeOH (19:1) followed by $CHCl_3$-MeOH (9:1). Fractions containing **3** by tlc were combined and further purified by preparative tlc in $CHCl_3$-MeOH (9:1); combined fractions containing **4** were purified by tlc in EtOAc-Me_2CO (9:1). The tlc spots and bands were visualized by long wavelength uv. Compound **3** (3 mg) was obtained as a yellow oil, and **4** (12 mg) wa obtained as needle-shaped colorless crystals in Me_2CO.

2,2-DIMETHYL-5-AMINO-6-(3′-*N*-FORMYL-4′-HYDROXYLBUTYRYL)-4-CHROMONE [**3**].—Ir λ max (film) 3399, 3287, 2932, 2864, 1724, 1682, 1657, 1599, 1568, 1560, 1496, 1466, 1388, 1373, 1277, 1174, 1159, 1109, 893; uv (nm MeOH) 278, 248, 214; ^{1}H nmr ($CDCl_3$, 200 MHz) δ 1.45 (6H, s, H-11 and H-12), 2.70 (2H, s, H-3), 3.12 (1H, dd, $J=5.9$, 16.3 Hz, Ha-2′), 3.34 (1H, dd, $J=6.4$, 16.3 Hz, Hb-2′), 3.79 (2H, d, $J=4.2$ Hz, H-4′), 4.26–4.39 (1H, m, H-3′), 6.08 (1H, d, $J=9.1$ Hz, H-8), 6.57 (2H, d, $J=6.0$ Hz, NH-3′), 7.89 (1H, d, $J=9.1$ Hz, H-7), 8.14 (1H, d, $J=1.6$ Hz, CHO), 9.50 (2H, s, ArNH).

2,2-DIMETHYL-5-AMINO-6-(3′-*N*-ACETYL-4′-*O*-ACETYLBUTYRYL)-4-CHROMONE [**4**].—Ir

λ max (film) 3395, 3285, 2298, 2932, 2856, 1734, 1662, 1653, 1595, 1560, 1498, 1466, 1375, 1319, 1278, 991, 893; uv (nm MeOH) 278, 248, 214; ^{1}H nmr ($CDCl_3$, 200 MHz) δ 1.44 (6H, s, H-11 and H-12), 1.97 (3H, s, NH*Ac*), 2.04 (3H, s, OAc), 2.69 (2H, s, H-3), 3.01 (1H, dd, J = 6.2, 16 Hz, Ha-2′), 3.25 (1H, dd, J = 5.7, 16 Hz, Hb-2′), 4.14 (1H, dd, J = 5.3, 11 Hz, Ha-4′), 4.32 (1H, dd, J = 6.1, 11 Hz, Hb-4′), 4.48 (1H, m, H-3′), 6.02 (1H, d, J = 8.9 Hz, H-8), 6.39 (1H, d, J = 8.3 Hz, N*H*Ac), 7.82 (1H, d, J = 8.9 Hz, H-7), 9.34–9.60 (2H, b, ArNH).

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