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## THREE NEW CHROMONE DERIVATIVES FROM *CASSIA PUMILA* AND THEIR ANTI-TOBACCO MOSAIC VIRUS ACTIVITY

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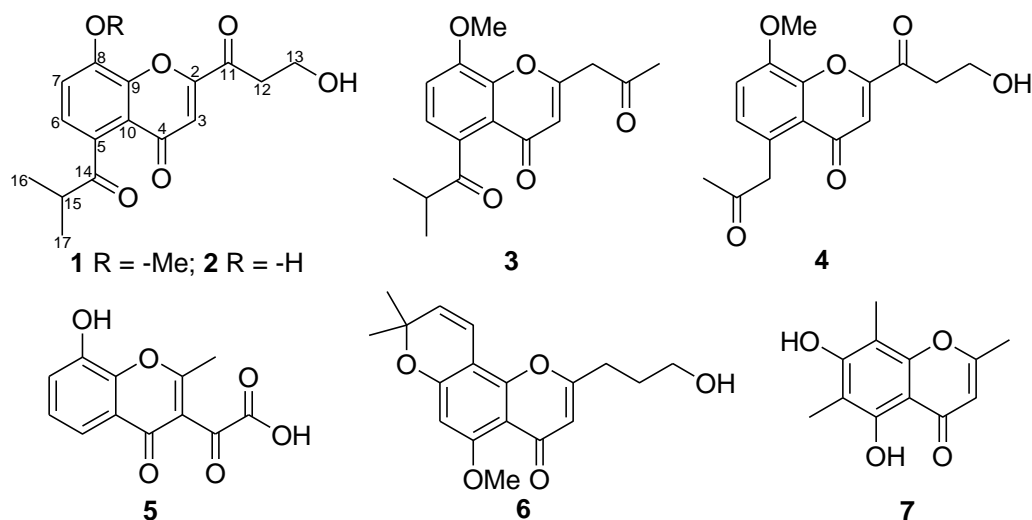
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**Abstract** – Three new (**1-3**), together with four known chromone derivatives (**4-7**), were isolated from *Cassia pumila*. Their structures were elucidated by spectroscopic methods, including extensive 1D and 2D NMR techniques. Compounds **1-3** were evaluated for their anti-tobacco mosaic virus (Anti-TMV) activity. The results showed that compounds **1-3** showed potential anti-TMV activities with inhibition rates of 28.3%, 31.2%, and 34.8%, at the concentration of 20  $\mu$ M, respectively. These rates are close to that of positive control.

*Cassia* is a genus of flowering plants in the legume family, Fabaceae, and the subfamily Caesalpinioideae. Over 1000 species have belonged to this genus over the years.<sup>1</sup> More than 10 species of *Cassia* plants are native in China, and more than 20 species were introduced and cultivated in China now.<sup>2</sup> Most of the plant *Cassia* genus has good medicinal value, and this genus had widely been used as traditional Chinese medicine for treatment of diarrhea, gastritis, ringworm, and fungal skin infections.<sup>2,3</sup> Previous phytochemical studies of genus have shown the presence of anthraquinones,<sup>4,5</sup> steroids,<sup>6,7</sup> chromones,<sup>8-10</sup> terpenes,<sup>11,12</sup> flavonoids,<sup>13-15</sup> alkaloids,<sup>16,17</sup> and the like.

*Cassia pumila* Lam. is an herb plant of the *Cassia* genus, and which is widely distributed in southern China. Its leaves and roots had been used as medicine for dysentery and indigestion, and its seeds have the effect of invigorating stomach, diuresis and eliminating edema.<sup>2</sup> Anthraquinones and flavonoids in this plant had also been reported in the previous literatures.<sup>18,19</sup> In our continuing efforts to identify bioactive natural products from *Cassia* genus, we now investigated the chemical constituents of the whole plant of *C. pumila*. This leads to the isolation of three new (**1-3**), and four known chromone derivatives (**4-7**). The structures of

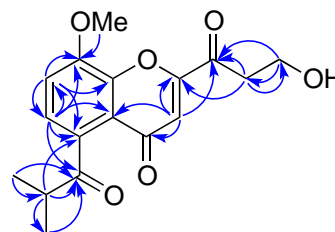
**1-7** were elucidated by spectroscopic methods including extensive 1D and 2D NMR techniques. The isolation, structural elucidation, and bioactivity of these compounds are described in this manuscript.



**Figure 1.** The chromone derivatives from *C. pumila*

The whole plants of *C. pumila* were extracted with 95% methanol (MeOH), followed by repeated column chromatography on silica gel, Sephadex LH-20 and RP-18. Final purification by semi-preparative RP-HPLC afforded seven chromone derivatives (**1-7**). The structures of **1-7** are shown in Figure. 1, and the  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of **1-3** are given in Table 1. The known compounds were identified as 2-(3-hydroxypropanoyl)-8-methoxy-5-(2-oxopropyl)-4*H*-chromen-4-one (**4**),<sup>9</sup> halenichromone A (**5**),<sup>20</sup> siamchromone G (**6**),<sup>21</sup> and 8-methyleugenitol (**7**).<sup>22</sup>

Compound **1** was obtained as a yellow gum. It has the molecular formula  $\text{C}_{17}\text{H}_{18}\text{O}_6$  from HRESIMS ( $m/z$ : 341.1008 [ $\text{M}+\text{Na}$ ] $^+$ , calcd 341.1001), with 9 degrees of unsaturation. The IR absorption bands indicated the presence of hydroxy ( $3392\text{ cm}^{-1}$ ), carbonyl ( $1739$ ,  $1692$ , and  $1655\text{ cm}^{-1}$ ), and



**Figure 2.** Key HMBC (↷) correlations of **1**

aromatic ring ( $1610$ ,  $1563$ , and  $1482\text{ cm}^{-1}$ ) groups, and UV absorptions at 246, 284, and 358 nm suggested a conjugated aromatic ring system. Its  $^1\text{H}$ ,  $^{13}\text{C}$ , and DEPT NMR spectra displayed signals for 17 carbons and 18 hydrogen atoms, corresponding to one chromone ring system<sup>9</sup> (C-2 ~ C-10) with three aromatic protons (H-3, H-6, and H-7), one 3-hydroxypropanoyl moiety<sup>21</sup> (-CO-CH<sub>2</sub>-CH<sub>2</sub>-OH; C-11 ~ C-13; H<sub>2</sub>-12 and H<sub>2</sub>-13), one isobutyryl moiety [(CH<sub>3</sub>)<sub>2</sub>-CH-CO-; C-14 ~ C-17; H<sub>3</sub>-16, H<sub>3</sub>-17 and H-15 ],<sup>21</sup> and a methoxy group ( $\delta_{\text{C}}$  56.0,  $\delta_{\text{H}}$  3.81). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **1** were similar to those of the known compound (**4**).<sup>9</sup> The chemical shift differences resulted from the disappearance of a 2-oxopropyl moiety signals and appearance of an isobutyryl moiety signals. This indicated that the 2-oxopropyl moiety in **1** was converted into an isobutyryl moiety in **2**. The HMBC correlations of H<sub>2</sub>-12

( $\delta_{\text{H}}$  3.40) with C-2 ( $\delta_{\text{C}}$  157.0) and of H-3 ( $\delta_{\text{H}}$  7.10) with C-11 ( $\delta_{\text{C}}$  198.7) indicated that the 3-hydroxypropanoyl moiety was located at C-2. The HMBC correlations of H-15 ( $\delta_{\text{H}}$  4.24) with C-5 ( $\delta_{\text{C}}$  129.3), and of H-6 ( $\delta_{\text{H}}$  7.60) with C-14 ( $\delta_{\text{C}}$  209.0) indicated that the isobutyryl moiety was attached to C-5. The attachment of the methoxy group at C-8 was supported by the HMBC correlations of the methoxy proton ( $\delta_{\text{H}}$  3.81) with C-8 ( $\delta_{\text{C}}$  156.1). Thus, the structure of **1** was established as 5-(isobutyryl)-2-(2-oxopropyl)-8-methoxy-4*H*-chromen-4-one.

**Table 1.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR data for compounds **1-3** ( $\text{CDCl}_3$ , 125 and 500 MHz)

No.	Compound <b>1</b>		Compound <b>2</b>		Compound <b>3</b>	
	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (J in Hz)	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (J in Hz)	$\delta_{\text{C}}$	$\delta_{\text{H}}$ (J in Hz)
2	157.0 s		157.2 s		161.8 s	
3	116.9 d	7.10 s	117.0 d	7.14 s	112.4 d	6.13 s
4	181.0 s		180.1 s		180.3 s	
5	129.3 s		130.8 s		128.8 s	
6	125.4 d	7.60 (d) 8.6	125.2 d	7.49 (d) 8.6	125.8 d	7.59 (d) 8.6
7	121.1 d	6.99 (d) 8.6	122.5 d	6.92 (d) 8.6	120.9 d	6.98 (d) 8.6
8	156.1 s		153.0 s		156.2 s	
9	147.4 s		151.3 s		148.0 s	
10	118.9 s		118.1 s		118.5 s	
11	198.7 s		198.0 s		48.6 t	3.57 s
12	40.3 t	3.40 (t) 6.4	40.0 t	3.37 (t) 6.4	202.3 s	
13	58.8 t	4.41 (t) 6.4	58.2 t	4.38 (t) 6.4	30.2 q	2.15 q
14	209.0 s		208.9 s		208.1 s	
15	38.0 d	4.24 m	39.0 d	4.20 m	38.6 d	4.26 m
16	18.3 q	1.22 (d) 6.8	18.3 q	1.21 (d) 6.8	18.5 q	1.23 (d) 6.7
17	18.3 q	1.22 (d) 6.8	18.3 q	1.21 (d) 6.8	18.5 q	1.23 (d) 6.7
-OMe	56.0 q	3.81 s			56.1 q	3.83 s
Ar-OH				10.14 s		

8-Hydroxy-2-(3-hydroxypropanoyl)-5-(isobutyryl)-4*H*-chromen-4-one (**2**) was obtained as a yellow gum with molecular formula  $\text{C}_{16}\text{H}_{16}\text{O}_6$  as determined by positive HRESI-MS ( $m/z$  327.0852). Its  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were similar to those of **1**. The marked differences between them were due to the inexistence of a methoxy group signal, and appearance of a phenolic hydroxy proton ( $\delta_{\text{H}}$  10.14 s) in compound **2**. This change indicated that the methoxy group in **1** was replaced by a phenolic hydroxy group in compound **2**. The HMBC correlations from phenolic hydroxy ( $\delta_{\text{H}}$  10.14) to C-7 ( $\delta_{\text{C}}$  122.5), C-8 ( $\delta_{\text{C}}$  153.0), and C-9 ( $\delta_{\text{C}}$  151.3) supported phenolic hydroxy group located at C-8. In addition, the other substituents positions also determined by the further analysis of its HMBC correlations. Thus, the structure of **2** was determined as shown.

Compound **3** was isolated as yellow gum and it gave a pseudomolecular ion peak at  $m/z$  325.1047  $[\text{M}+\text{Na}]^+$ , consistent with a molecular formula of  $\text{C}_{17}\text{H}_{18}\text{O}_5$ . Its  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopic data were also similar

to those of **1**, which suggested that compound **3** was structurally related to **1**. The marked differences between them were due to the inexistence of a 3-hydroxypropanoyl moiety, and appearance of a 2-oxopropyl moiety ( $\text{CH}_3\text{-CO-CH}_2\text{-}$ ; C-11~C-13;  $\text{H}_2\text{-11}$  and  $\text{H}_3\text{-13}$ ) in compound **3**. These changes indicated that a 3-hydroxypropanoyl moiety in **1** was replaced by a 2-oxopropyl moiety in compound **3**. This was also supported by the HMBC correlations from  $\text{H}_2\text{-11}$  ( $\delta_{\text{H}}$  3.57) to C-2 ( $\delta_{\text{C}}$  161.8) and C-3 ( $\delta_{\text{C}}$  112.4), from H-3 ( $\delta_{\text{H}}$  6.13) to C-11 ( $\delta_{\text{C}}$  48.6). Moreover, the methoxy group located at C-8 and isobutyryl moiety located at C-5 was supported by the HMBC correlations of the methoxy proton signal ( $\delta_{\text{H}}$  3.83) with C-8 ( $\delta_{\text{C}}$  156.2), of H-15 ( $\delta_{\text{H}}$  4.26) with C-5 ( $\delta_{\text{C}}$  128.8), and of H-6 ( $\delta_{\text{H}}$  7.59) with C-14 ( $\delta_{\text{C}}$  208.1), respectively. Based on the above findings, the structure of **3** was formulated as 5-(isobutyryl)-2-(2-oxopropyl)-8-methoxy-4*H*-chromen-4-one.

Since certain chromones exhibit potential anti-TMV activities,<sup>9,10,21</sup> Compounds **1-3** were tested for their anti-TMV activity. The anti-TMV activity was tested using the half-leaf method. Ningnanmycin (a commercial product for plant disease in China) with inhibition rate of 30.8%, was used as a positive control.<sup>24</sup> The results revealed that compounds **1-3** showed high anti-TMV activity with inhibition rates of 28.3%, 31.2%, and 34.8% at the concentration of 20  $\mu\text{M}$ , respectively. These rates are close to that of positive control.

**General Experimental Procedures.** UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. A Tenor 27 spectrophotometer was used for scanning IR spectra. 1D- and 2D- NMR spectroscopic data were recorded on a DRX-500 NMR spectrometer with TMS as internal standard. Chemical shifts ( $\delta$ ) are expressed in ppm with reference to the TMS signal. HRESIMS was performed on a VG Autospec-3000 spectrometer. Semi-preparative HPLC was performed on a Shimadzu LC-8A preparative liquid chromatograph with Zorbax PrepHT GF (21.2 mm  $\times$  25 cm) or Venusil MP C<sub>18</sub> (20 mm  $\times$  25 cm) columns. Column chromatography was performed using silica gel (200-300 mesh, Qing-dao Marine Chemical, Inc., Qingdao, China), Lichroprep RP-18 gel (40-63  $\mu\text{m}$ , Merck, Darmstadt, Germany), Sephadex LH-20 (Sigma-Aldrich, Inc, USA), or MCI gel (75-150  $\mu\text{m}$ , Mitsubishi Chemical Corporation, Tokyo, Japan). Column fractions were monitored by TLC visualized by spraying with 5%  $\text{H}_2\text{SO}_4$  in ethanol (EtOH) and heating.

**Plant Material.** The whole plants of *Cassia pumila* Lam were collected from Dehong Prefecture, Yunnan province in September 2017. The species was identified by Prof. Chen Y. J. A voucher specimen (YNNI 17-9-86) was deposited in Key Laboratory of Chemistry in Ethnic Medicinal Resources, Yunnan Minzu University.

**Extraction and Isolation.** The samples (4.5 kg) were crushed to 30 mesh, and the powders were extracted with 95% aqueous MeOH (4 $\times$ 8 L) at room temperature and filtered. The filtrate was evaporated under reduced pressure, and the crude extract (385 g) was applied to a silica gel (150-200 mesh) column

eluted with chloroform-methanol (CHCl<sub>3</sub>-MeOH) gradients (20:1, 9:1, 8:2, 7:3, 6:4, 5:5) to afford six fractions (A-F). Further separation of fraction B (9:1, 13.8 g) by silica gel column chromatography, eluted with CHCl<sub>3</sub>-acetone (1:0-1:2), yielded subfractions B1–B7. Subfraction B2 (9:1, 10.5 g) was loaded on to another silica gel column using petroleum ether-ethyl acetate (EtOAc) elution, and then separated semi-preparative HPLC (66% MeOH, flow rate 20 mL/min) to afford **1** (18.6 mg), **3** (15.6 mg), **4** (22.6 mg), and **6** (24.5 mg). Subfraction B3 (8:2, 6.22 g) was separated on a silica gel column eluted by petroleum ether-EtOAc, followed by semi-preparative HPLC (58% MeOH, flow rate 20 mL/min) to give **2** (12.5 mg). Subfraction B4 (7:3, 5.42 g) was separated on a silica gel column eluted by petroleum ether-EtOAc, followed by semi-preparative HPLC (45% MeOH, flow rate 20 mL/min) to give **7** (13.0 mg). Subfraction B5 (6:4, 8.26 g) was separated on a silica gel column eluted by petroleum ether-EtOAc, followed by semi-preparative HPLC (30% MeOH, flow rate 20 mL/min) to give **5** (16.9 mg).

**Anti-TMV Assays.** The anti-TMV activities were tested using the half-leaf method,<sup>24</sup> and Ningnanmycin (2% water solution), a commercial product for plant disease in China, was used as a positive control. The virus was inhibited by mixing with the solution of tested compounds. After 30 min, the mixture was inoculated on the left side of the leaves of *Nicotiana glutinosa*, whereas the right side of the leaves was inoculated with the mixture of DMSO solution and the virus as control. The local lesion numbers were recorded 3-4 days after inoculation. Three repetitions were conducted for each compound. The inhibition rates were calculated according to the formula:

$$\text{inhibition rate (\%)} = [(C-T) / C] \times 100\%$$

where C is the average number of local lesions of the control and T is the average number of local lesions of the treatment. Ningnanmycin, a commercial virucide for plant disease in China, was used as a positive control.

**2-(3-Hydroxypropanoyl)-5-(isobutyryl)-8-methoxy-4H-chromen-4-one (1):** Obtained as yellow gum; UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 210 (4.08), 246 (3.76), 284 (3.81), 358 (3.54) nm; IR (KBr)  $\nu_{\text{max}}$  3392, 3085, 2942, 2867, 1739, 1692, 1655, 1610, 1563, 1482, 1336, 1174, 1049, 873, 786 cm<sup>-1</sup>; <sup>1</sup>H and <sup>13</sup>C NMR data (CDCl<sub>3</sub>, 500 and 125 MHz), see Table 1; positive ESIMS  $m/z$  341 [M+Na]<sup>+</sup>; positive HRESIMS  $m/z$  341.1008 [M+Na]<sup>+</sup> (calcd for C<sub>17</sub>H<sub>18</sub>NaO<sub>6</sub>, 341.1001).

**8-Hydroxy-2-(3-hydroxypropanoyl)-5-(isobutyryl)-4H-chromen-4-one (2):** Obtained as yellow gum; UV (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 210 (4.12), 242 (3.70), 281 (3.75), 356 (3.60) nm; IR (KBr)  $\nu_{\text{max}}$  3412, 3090, 2948, 2855, 1740, 1682, 1658, 1613, 1568, 1479, 1342, 1168, 1053, 906, 817 cm<sup>-1</sup>; <sup>1</sup>H and <sup>13</sup>C NMR data (CDCl<sub>3</sub>, 500 and 125 MHz), see Table 1; positive ESIMS  $m/z$  327 [M+Na]<sup>+</sup>; positive HRESIMS  $m/z$  327.0852 [M+Na]<sup>+</sup> (calcd for C<sub>16</sub>H<sub>16</sub>NaO<sub>6</sub>, 327.0845).

**5-(Isobutyryl)-2-(2-oxopropyl)-8-methoxy-4H-chromen-4-one (3):** Obtained as yellow gum; UV

(MeOH)  $\lambda_{\max}$  (log  $\epsilon$ ) 210 (4.02), 235 (3.68), 274 (3.82), 351 (3.72) nm; IR (KBr)  $\nu_{\max}$  3076, 2935, 2857, 1738, 1680, 1654, 1612, 1547, 1468, 1340, 1143, 1052, 935, 824  $\text{cm}^{-1}$ ;  $^1\text{H}$  and  $^{13}\text{C}$  NMR data ( $\text{CDCl}_3$ , 500 and 125 MHz), see Table 1; positive ESIMS  $m/z$  325  $[\text{M}+\text{Na}]^+$ ; positive HRESIMS  $m/z$  325.1047  $[\text{M}+\text{Na}]^+$  (calcd for  $\text{C}_{17}\text{H}_{18}\text{NaO}_5$ , 325.1052).

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## REFERENCES

1. D. G. Frodin, *Taxon*, 2004, **53**, 753.
2. D. L. Wu, Flora of China, Vol. 39, Beijing, Chinese Science Press, 1988, p 123.
3. A. H. Rahmani, *Pharmacognosy Res.*, 2015, **7**, 217.
4. Y. K. Li, Y. C. Yang, Y. Qin, Y. L. Meng, Y. Q. Ye, H. Y. Yang, X. M. Gao, and Q. F. Hu, *Heterocycles*, 2014, **89**, 481.
5. P. T. N. Trinh, N. Q. Luan, M. D. Tri, V. D. Khanh, N. H. An, P. N. Minh, P. N. An, N. T. L. Thuy, N. K. P. Phung, and L. T. Dung, *Nat. Prod. Res.*, 2017, **31**, 1733.
6. P. Sartorelli, S. P. Andrade, M. S. Melhem, F. O. Prado, and A. G. Tempone, *Phytother. Res.*, 2007, **21**, 644.
7. M. M. Vaishnav, A. K. Tripathi, and K. R. Gupta, *Fitoterapia*, 1993, **64**, 93.
8. Y. K. Li, Y. L. Meng, Y. C. Yang, Y. Qin, C. F. Xia, Y. Q. Ye, X. M. Gao, and Q. F. Hu, *Phytochem. Lett.*, 2014, **10**, 46.
9. Q. F. Hu, L. M. Li, D. L. Zhu, Z. H. Yu, J. B. Zhan, J. Lou, Y. D. Wang, K. Zhou, Y. K. Li, and X. M. Gao, *Heterocycles*, 2015, **91**, 1980.
10. M. Zhou, K. Zhou, X. M. Gao, Z. Y. Jiang, J. J. Lv, Z. H. Liu, G. Y. Yang, M. M. Miao, C. T. Che, and Q. F. Hu, *Org. Lett.*, 2015, **17**, 2638.
11. P. Chandra, R. Pandey, B. Kumar, M. Srivastva, P. Pandey, J. Sarkar, and B. P. Singh, *Ind. Crop. Prod.*, 2015, **76**, 1133.
12. L. C. S. Cunha, S. A. L. de Moraes, C. H. G. Martins, M. M. Martins, R. Chang, F. J. T. de Aquino, A. de Oliveira, T. D. Moraes, F. C. Machado, and C. V. da Silva, *Molecules*, 2013, **18**, 4588.
13. W. Zhao, X. Y. Zeng, T. Zhang, L. Wang, G. Y. Yang, Y. K. Chen, Q. F. Hu, and M. M. Miao, *Phytochem. Lett.*, 2013, **6**, 179.
14. Q. F. Hu, D. Y. Niu, B. Zhou, Y. Q. Ye, G. Du, C. Y. Meng, and X. M. Gao, *Bull. Korean Chem. Soc.*, 2013, **34**, 3013.

15. G. H. Kong, H. H. Xing, Y. P. Wu, Z. Y. Xia, J. Li, L. Ye, W. S. Kong, X. Liu, Y. P. Li, G. X. Rao, Q. F. Hu, G. Y. Yang, Y. K. Li, and X. M. Lie, [Heterocycles, 2017, 94, 2125](#).
16. P. S. Yang, W. Zhang, X. F. Shen, X. L. Wang, C. Li, X. W. Gong, X. D. Zheng, D. L. Zhu, and J. Q. Wang, [Heterocycles, 2016, 92, 1706](#).
17. H. Y. Wu, W. Y. Hu, Q. Liu, Z. H. Yu, J. B. Zhan, K. L. Yan, Y. D. Wang, K. Zhou, W. Dong, Y. K. Li, M. Zhou, and Q. F. Hu, [Phytochem. Lett., 2016, 15, 121](#).
18. K. S. Mukherjee, C. K. Chakraborty, T. P. Chatterjee, and P. Bhattacharya, *J. Indian Chem. Soc.*, 1989, **66**, 66.
19. X. J. Zi, M. Li, H. L. Zhou, G. D. Liu, and X. Hong, *Chin. J. Feed. Res.*, 2012, **5**, 44.
20. Y. W. Sun, G. M. Liu, H. Huang, and P. Z. Yu, [Phytochemistry, 2012, 75, 169](#).
21. Q. F. Hu, B. Zhou, X. M. Gao, L. Y. Yang, L. D. Shu, Y. Q. Shen, G. P. Li, C. T. Che, and G. Y. Yang, [J. Nat. Prod., 2012, 75, 1909](#).
22. L. Y. Ma, S. C. Ma, F. Wei, R. C. Lin, P. P. But, S. H. Lee, and S. F. Lee, [Chem. Pharm. Bull., 2003, 51, 1264](#).
23. Y. P. Wu, G. H. Kong, W. Li, N. J. Xiang, L. X. Liu, G. R. Yang, X. P. Lu, and Q. Liu, *Heterocycles*, 2015, **91**, 1815.
24. M. Zhou, M. M. Miao, G. Du, S. Z. Shang, W. Zhao, Z. H. Liu, G. Y. Yang, C. T. Che, Q. F. Hu, and X.-M. Gao, [Org. Lett., 2014, 16, 5016](#).