## Simple Synthesis of 3-Acetamido-β-resorcylic Acids as Potential FabF and FabH Inhibitors without Using Protecting Groups

Nenad Maraš,<sup>a</sup> Petra Štefanič Anderluh,<sup>b</sup> Uroš Urleb,<sup>b</sup> Marijan Kočevar<sup>\*a</sup>

<sup>a</sup> Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, 1000 Ljubljana, Slovenia Fax +386(1)2419220; E-mail: marijan.kocevar@fkkt.uni-lj.si

Key words: phenols, acylations, carboxylic acids, drugs, antibiotics

Platensimycin (1a; Figure 1) isolated from Streptomyces platensis was found to be an antibiotic, targeting highly conserved bacterial FabF enzymes involved in fatty acid biosynthesis.<sup>1</sup> Several total and formal syntheses of platensimycin were reported soon after its structural elucidation was published.<sup>2</sup> Recently, the literature on platensimycin synthesis was reviewed.<sup>3</sup> Another very similar compound, platencin (1b; Figure 1), was isolated from a different strain of S. platensis and found to be a dual inhibitor of FabF and FabH.<sup>4</sup> Several of their close analogues, some with high antibacterial potency were also published.<sup>5</sup> The above compounds are essentially amides between complex spirocyclic carboxylic acids and 3-amino-\beta-resorcylic acid (1c; Figure 1). Platensimycin and platencin are prominent lead compounds for developing new, broad-spectrum antibiotics and it would be advantageous from the point of view of medicinal chemistry to identify the parts of platensimycin involved in the FabF binding.6





The synthesis of the protected 1c in the form of methyl 3amino-2,4-bis(methoxymethoxy)benzoate (2; Figure 2) was first described by Nicolaou et al. using a five-step

SYNLETT 2009, No. 3, pp 0437-0440 Advanced online publication: 21.01.2009 DOI: 10.1055/s-0028-1087544; Art ID: G35608ST © Georg Thieme Verlag Stuttgart · New York

synthesis starting from 2-nitroresorcinol (3) and applying organolithium and protecting group chemistry (MOM, Boc and TMS protections).<sup>2a</sup> The original amide synthetic strategy for the preparation of 1a was to couple the appropriate acid with a several-fold excess of 2 using 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) as a coupling reagent, followed by the hydrolysis of ester and MOM protection groups. Recently, a simple preparation of 3-nitro- and 3-amino- $\beta$ resorcylic acid derivatives, starting from  $\beta$ -resorcylic acid was published by Heretsch and Giannis.<sup>7</sup> This strategy was later applied in the preparation of 2-trimethylsilylethyl 3-amino- $\beta$ -resorcylate used in a more recent total synthesis of platensimycin by Nicolaou et al.<sup>8</sup> These approaches certainly seem to be the most rational when starting with precious carboxylic acids.





On the other hand, it would be of interest to form various amides without using protecting groups and to make the synthesis as short as possible. For this reason we decided to prepare a series of 3-acetamido-\beta-resorcylic acids starting from simple, commercially available carboxylic acids or acid chlorides using a new strategy that would allow us to skip the protecting group chemistry.

The obvious way to avoid protecting the carboxy group is to introduce it in the last synthetic step. The MOM protection of the hydroxy groups used in the first published preparation of  $2^{2a}$  is obsolete for the amide bond formation itself, because the N-acylation of aminophenols can be carried out with high chemoselectivity over O-acylation. The MOM protection was only necessary for the lithiation used to introduce the methoxycarbonyl group, a step which becomes superfluous once the carboxy group is introduced last. Moreover, during the preparation of this manuscript, Hayashida and Rawal published their total synthesis of racemic **1b**, where they used unprotected 3amino- $\beta$ -resorcylic acid (1c) in the amide-formation step with DCC as the coupling agent.<sup>9</sup> However, their synthe-

<sup>&</sup>lt;sup>b</sup> Lek Pharmaceuticals d.d., Verovškova 57, 1526 Ljubljana, Slovenia

Received 24 October 2008

Abstract: A simple two-step strategy for the synthesis of 3-acetamido-β-resorcylic acids as potential platensimycin analogues was developed. It avoids the use of protecting group chemistry and starts from 2-aminoresorcinol, which is first N-acylated and then subjected to a modified Kolbe-Schmitt carboxylation to yield the desired 3-acetamido-β-resorcylic acids.



Scheme 1 Reagents and conditions: (a)  $H_2$  (60 psi), Pd/C, EtOAc; (b) RCOCl, pyridine, EtOAc; or RCO<sub>2</sub>H, CDI, THF; or RCO<sub>2</sub>H, DCC, THF, yield from 3 to 5 66–94%; (c) CO<sub>2</sub>, K<sub>2</sub>CO<sub>3</sub>, DMSO, 120 °C, 12 h, 15–52%.

sis of **1c** still required the use of protecting group chemistry.

To avoid the use of protecting groups, we carried out the following reaction sequence: first we hydrogenated 2-nitroresorcinol (3) to 2-aminoresorcinol (4), which was found to readily react with acyl chlorides or carboxylic acids activated with a coupling agent, yielding N-acylated 2-aminoresorcinols 5 (Scheme 1; Table 1).

Methods for the direct introduction of a carboxy group to a phenol are quite limited, and so we considered two reactions. The first is using  $CO_2$  in an electrophilic aromatic substitution via a very old reaction known as the Kolbe-Schmitt carboxylation,<sup>10</sup> which became famous for its use in the synthesis of salicylic acid as well as other industrially important hydroxybenzoic acids. The second one is the copper-catalyzed carboxylation of phenols with CCl<sub>4</sub>, a reaction originally discovered by Reimer and Tiemann.<sup>11</sup> Using N-(2,6-dihydroxyphenyl)-3,3-dimethylbutanamide (5a) as a test substrate, the carboxylation with CCl<sub>4</sub> failed under standard conditions<sup>12</sup> and only gave tarry products. The Kolbe-Schmitt carboxylation using water as a solvent and either  $K_2CO_3$  or  $Na_2CO_3$  as a base also failed, even though we used an autoclave in order to maintain a high CO<sub>2</sub> pressure and temperatures in the range of 100-120 °C. Interestingly, even though there was no conversion on our test compound 5a, we found that the Kolbe-Schmitt carboxylation of 2-aminoresorcinol (4) under the same conditions, at 110 °C for eight hours in water and using  $K_2CO_3$  as a base, gave a 15% conversion to 1c (as shown on the basis of <sup>1</sup>H NMR spectroscopy; the product mixture also contained the unreacted starting material). The lack of reactivity of our test substrate **5a** is, to some extent, surprising, because resorcinol itself reacts easily in the Kolbe-Schmitt reaction in water even at atmospheric pressure and at the temperature of a steam bath to give  $\beta$ -resorcylic acid in a 60% yield.<sup>13</sup> The use of diglyme or isopropanol as co-solvents in water was also checked, but without success. Apparently, the inductive effect of the acylamino group deactivates our substrate enough to be inert under such reaction conditions. It is known that the presence of water inhibits the Kolbe-Schmitt carboxylation; therefore, the less reactive substrates are commonly carboxylated as preformed sodium or potassium phenolates, either in the solid state or in a suspension of high-boiling hydrocarbon solvents.<sup>10</sup> Nevertheless, good results were also reported using phenols with various bases in polar aprotic solvents.<sup>14</sup> We therefore chose DMSO as a solvent in the absence of wa**Table 1**Preparation of Products 6

	1			
Entry	R	Substrate	Product	Yield (%) <sup>a</sup>
1	m f	5a	6a	25
2	€ <u>(</u> /	5b	6b	50
3	₩ (	5c	6c	30
4		5d	6d	25
5		5e	6e	32
6		5f	6f	52
7		5g	6g	20
8		5h	6h	22
9	NH	5i	6i	49
10	€OMe	5j	6j	47
11	OH	5k	6k	15 <sup>b</sup>

<sup>a</sup> Isolated yields are given (not taking into account the recovered starting material).

<sup>b</sup> DCC was used in the anilide formation step. The yield is based on 2-nitroresorcinol, because **5k** could not be properly purified from the N,N'-dicyclohexylurea remains.

ter. We found that by using  $K_2CO_3$  as a base in DMSO at 110–120 °C our substrate **5a** was carboxylated to **6a**, which was isolated in a 25% yield. When reactions were performed with a series of substrates **5b–l** we similarly isolated products **6b–l** in 15–52% yields (Table 1).<sup>15</sup> We

also found that in most cases the majority of the unreacted starting material **5** can be recycled. The reactions were not completely optimized, but they were shown to give reproducible yields of products.

2-Nitroresorcinol (3) was hydrogenated to 2-aminoresorcinol (4) using palladium on carbon in ethyl acetate as a solvent; the catalyst was filtered off, the filtrate split into several aliquots ready for acylations with acid chlorides or acids activated generally with carbonyldiimidazole (CDI). The so-obtained N-(2,6-dihydroxyphenyl)amides 5 were used in the modified Kolbe–Schmitt carboxylation at 120 °C with DMSO as a solvent and in an autoclave charged with dry ice as a source of CO<sub>2</sub>. The isolation generally consisted of an extraction of the reaction mixture diluted with water to separate the unreacted starting material, followed by an acidification to isolate the acidic product 6, which was then further purified by either recrystallization or radial chromatography. The adamantyl derivative **6h** required a modified isolation, because it was found that the product was fully extracted from the basic aqueous mixture with ethyl acetate, presumably still in the form of the potassium salt. Thus, the reaction mixture containing **6h** was first acidified and the product and starting material were extracted into ethyl acetate, from which the product was separated by extraction into aqueous ammonia.

In conclusion, we have developed a simple, short reaction sequence for the preparation of 3-acetamido- $\beta$ -resorcylic acids without applying protecting groups. The method includes a modified Kolbe–Schmitt carboxylation using DMSO as a solvent and K<sub>2</sub>CO<sub>3</sub> as a base. This synthetic strategy allows the preparation of a library of compounds for potential FabF and FabH inhibitors screening.

## Acknowledgment

We thank Lek Pharmaceuticals d.d., the Ministry of Higher Education, Science and Technology of the Republic of Slovenia and the Slovenian Research Agency for financial support (P1-0230-0103). Dr. B. Kralj and Dr. D. Žigon (Center for Mass Spectroscopy, 'Jožef Stefan' Institute, Ljubljana, Slovenia) are gratefully acknowledged for the mass spectrometric measurement.

## **References and Notes**

(a) Wang, J.; Soisson, S. M.; Young, K.; Shoop, W.; Kodali, (1)S.; Galgoci, A.; Painter, R.; Parthasarathy, G.; Tang, Y. S.; Cummings, R.; Ha, S.; Dorso, K.; Motyl, M.; Jayasuriya, H.; Ondeyka, J.; Herath, K.; Zhang, C.; Hernandez, L.; Allocco, J.; Basilio, ; Tormo, J. R.; Genilloud, O.; Vicente, F.; Pelaez, F.; Colwell, L.; Lee, S. H.; Michael, B.; Felcetto, T.; Gill, C.; Silver, L. L.; Hermes, J. D.; Bartizal, K.; Barrett, J.; Schmatz, D.; Becker, J. W.; Cully, D.; Singh, S. B. Nature (London) 2006, 441, 358. (b) Singh, S. B.; Jayasuriya, H.; Ondeyka, J. G.; Herath, K. B.; Zhang, C.; Zink, D. L.; Tsou, N. N.; Ball, R. G.; Basilio, A.; Genilloud, O.; Diez, M. T.; Vicente, F.; Pelaez, F.; Young, K.; Wang, J. J. Am. Chem. Soc. 2006, 128, 11916. (c) Basilio, A.; Genilloud, O.; Hernandez, P.; Singh, S. B.; Tormo, J. R.; Wang, J. Int. Patent, WO2005009391, 2005; Chem. Abstr. 2005, 142, 196607.

- (2) (a) Nicolaou, K. C.; Li, A.; Edmonds, D. J. Angew. Chem. Int. Ed. 2006, 45, 7086. (b) Zou, Y.; Chen, C.-H.; Taylor, C. D.; Foxman, B. M.; Snider, B. B. Org. Lett. 2007, 9, 1825. (c) Nicolaou, K. C.; Tang, Y.; Wang, J. Chem. Commun. 2007, 1922. (d) Nicolaou, K. C.; Edmonds, D. J.; Li, A.; Scott Tria, G. Angew. Chem. Int. Ed. 2007, 46, 3942. (e) Matsuo, J.; Takeuchi, K.; Ishibashi, H. Org. Lett. 2008, 10, 4049. (f) Lalic, G.; Corey, E. J. Org. Lett. 2007, 9, 4921. (g) Tiefenbacher, K.; Mulzer, J. Angew. Chem. Int. Ed. 2007, 46, 8074. (h) Ghosh, A. K.; Xi, K. Org. Lett. 2007, 9, 4013. (i) Li, P.; Payette, J. N.; Yamamoto, H. J. Am. Chem. Soc. 2007, 129, 9534.
- (3) Tiefenbacher, K.; Mulzer, J. Angew. Chem. Int. Ed. 2008, 47, 2548.
- (4) (a) Jayasuriya, H.; Herath, K. B.; Zhang, C.; Zink, D. L.; Basilio, A.; Genilloud, O.; Diez, M. T.; Vicente, F.; Gonzalez, I.; Salazar, O.; Pelaez, F.; Cummings, R.; Ha, S.; Wang, J.; Singh, S. B. *Angew. Chem. Int. Ed.* **2007**, *46*, 4684. (b) Basilio, A.; Genilloud, O.; Jayasuriya, H.; Gonzalez, I.; Singh, S. B.; Salazar, O.; Wang, J. Int. Patent, WO2005115400, **2005**; *Chem. Abstr.* **2005**, *144*, 5523.
- (5) (a) Nicolaou, K. C.; Lister, T.; Denton, R. M.; Montero, A.; Edmonds, D. J. *Angew. Chem. Int. Ed.* 2007, *46*, 4712.
  (b) Nicolaou, K. C.; Tang, Y.; Wang, J.; Stepan, A. F.; Li, A.; Montero, A. *J. Am. Chem. Soc.* 2007, *129*, 14850.
  (c) Singh, S. B.; Herath, K. B.; Wang, J.; Tsou, N.; Ball, R. G. *Tetrahedron Lett.* 2007, *48*, 5429. (d) Yeung, Y.-Y.; Corey, E. J. *Org. Lett.* 2008, *10*, 3877.
- (6) Häbich, D.; von Nussbaum, F. ChemMedChem 2006, 1, 951.
- (7) Heretsch, P.; Giannis, A. Synthesis 2007, 2614.
- (8) Nicolaou, K. C.; Tria, G. S.; Edmonds, D. J. Angew. Chem. Int. Ed. 2008, 47, 1780.
- (9) Hayashida, J.; Rawal, V. H. Angew. Chem. Int. Ed. 2008, 47, 4373.
- (10) Lindsey, A. S.; Jeskey, H. Chem. Rev. 1957, 57, 583.
- (11) Reimer, K.; Tiemann, F. Ber. Dtsch. Chem. Ges. 1876, 9, 1285.
- (12) Sasson, Y.; Razintsky, M. J. Chem. Soc., Chem. Commun. 1985, 1134.
- (13) Nierenstein, M.; Clibbens, D. A. Org. Synth., Coll. Vol. II; Wiley: New York, 1943, 557.
- (14) Meek, W. H.; Fuchsman, C. H. J. Chem. Eng. Data **1969**, *14*, 388.
- (15) General Procedure for the Preparation of N-Acyl-2,6dihydroxyanilines 5a-e Using Acid Chlorides: To a solution of 2-aminoresorcinol (4; 7 mmol) in EtOAc (30 mL) stirred in an ice bath was added pyridine (0.76 mL, 10 mmol) followed a dropwise introduction of a solution of an acid chloride (6 mmol) in EtOAc (30 mL). After 1 h the reaction mixture was washed with H<sub>2</sub>O (30 mL), aq NaHCO<sub>3</sub> (5%, 30 mL), aq HCl (1 M, 30 mL), H<sub>2</sub>O (30 mL), then dried over  $Na_2SO_4$  and evaporated in vacuo yielding 5. General Procedure for the Preparation of N-Acyl-2,6dihydroxyanilines 5f-j Using Acids and CDI: To a solution of a carboxylic acid (1.16 g, 6 mmol) in THF (10 mL) was added carbonyldiimidazole (1.00 g, 6 mmol). After stirring for 1 h at r.t., it was added to a solution of 2aminoresorcinol (4) (7 mmol) in EtOAc (30 mL). The mixture was left stirring for 24 h at r.t., washed with diluted hydrochloric acid (3%; 30 mL), aq NaHCO<sub>3</sub> (3%; 30 mL), H<sub>2</sub>O (30 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated in vacuo to give 5.
  - General Procedure for the Kolbe–Schmitt Carboxylation: To the solution of **5** (4 mmol) in DMSO (35 mL) in an autoclave (300 mL size) was added anhyd  $K_2CO_3$  (1.70 g, 12 mmol) followed by the addition of dry ice (CO<sub>2</sub>; ca. 20 g). The autoclave was immediately closed and heated at 120 °C

Synlett 2009, No. 3, 437-440 © Thieme Stuttgart · New York

for 12 h. After carefully opening the autoclave, in order to release the CO<sub>2</sub> pressure, the reaction mixture was diluted with  $H_2O$  (100 mL) and extracted with EtOAc (4 × 30 mL). The extract was washed with NaHCO<sub>3</sub> (3%, 30 mL),  $H_2O$  (30 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated in vacuo to give the unreacted starting material **5**. The diluted reaction mixture was then acidified with hydrochloric acid (to pH ca. 3), saturated with NaCl and extracted with EtOAc (4 × 30 mL). The extract was washed with brine (30 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated in vacuo to give a crude product **6**, which was further purified.

All the products gave satisfactory analytical and spectroscopic data.

## Selected Characterization Data for the Representative Products:

*N*-(2,6-Dihydroxyphenyl)-3,3-dimethylbutanamide (5a): off-white product (84% yield); mp 164–167 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  = 1.04 (s, 9 H, *t*-Bu), 2.36 (s, 2 H, CH<sub>2</sub>CO), 6.38 (d, *J* = 8.1 Hz, 2 H, ArH), 6.88 (t, *J* = 8.1 Hz, 1 H, ArH), 9.28 (s, 1 H, NH), 9.41 (s, 2 H, 2 × OH). <sup>13</sup>C NMR (DMSO*d*<sub>6</sub>):  $\delta$  = 29.6, 30.7, 48.3, 107.8, 114.5, 126.4, 151.5, 172.1. IR (KBr): 1637, 1591, 1536, 1481, 1371 cm<sup>-1</sup>. MS (EI): *m/z* = 223 (14) [M<sup>+</sup>], 125 (100). HRMS (EI): *m/z* [M]<sup>+</sup> calcd for C<sub>12</sub>H<sub>17</sub>NO<sub>3</sub>: 223.1208; found: 223.1216. Anal. Calcd for C<sub>12</sub>H<sub>17</sub>NO<sub>3</sub>: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.79; H, 7.83; N, 6.09.

*N*-(2,6-Dihydroxyphenyl)-5-oxohexanamide (5g): offwhite crystalline product (77% yield); mp 128–131 °C. <sup>1</sup>H NMR (DMSO- $d_6$ ): δ = 1.77 (m, 2 H, CH<sub>2</sub>), 2.09 (s, 3 H, Me), 2.39 (t, *J* = 7.3 Hz, 2 H, CH<sub>2</sub>), 2.51 (t, *J* = 7.3 Hz, 2 H, CH<sub>2</sub>), 6.34 (d, *J* = 8.1 Hz, 1 H, ArH), 6.87 (t, *J* = 8.1 Hz, 2 H, ArH), 9.22 (s, 1 H, NH), 9.29 (s, 2 H, OH). <sup>13</sup>C NMR (DMSO- $d_6$ ): δ = 19.5, 29.7, 34.3, 41.8, 107.5, 113.9, 126.5, 152.0, 172.7, 208.0. IR (KBr): 1692, 1645, 1605, 1536, 1379 cm<sup>-1</sup>. MS (EI): *m/z* (%) = 237 (7) [M<sup>+</sup>], 125 (100), 113 (10), 85 (20). HRMS (EI): *m/z* calcd for C<sub>12</sub>H<sub>15</sub>NO<sub>4</sub>: 237.1001; found: 237.1006. Anal. Calcd for C<sub>12</sub>H<sub>15</sub>NO<sub>4</sub>: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.85; H, 6.44; N, 5.87.

3-[(3,3-Dimethylbutanoyl)amino]-2,4-dihydroxybenzoic Acid (6a): crystalline solid (25% yield); mp 198-200 °C (dec.). <sup>1</sup>H NMR (DMSO- $d_6$ ):  $\delta = 1.04$  (s, 9 H, t-Bu), 2.21 (s, 2 H, CH<sub>2</sub>), 6.43 (d, J = 8.8 Hz, 1 H, ArH), 7.56 (d, J = 8.8 Hz, 1 H, ArH), 8.91 (s, 1 H, NH), 10.21 (s, 1 H, OH), 11.81 (br s, 1 H, OH), 12.60–14.40 (br s, 1 H, CO<sub>2</sub>H). <sup>13</sup>C NMR  $(DMSO-d_6): \delta = 29.6, 30.6, 48.7, 104.4, 107.9, 113.0, 128.8,$ 158.8, 159.0, 170.7, 172.2. IR (KBr): 1642, 1533, 1437, 1379, 1253 cm<sup>-1</sup>. MS (EI):  $m/z = 267 (24) [M^+]$ , 169 (54), 151 (100), 125 (28). Anal. Calcd for C<sub>13</sub>H<sub>17</sub>NO<sub>5</sub>: C, 58.42; H, 6.41; N, 5.24. Found: C, 58.69; H, 6.69; N, 5.15. 3-[(Adamantan-1-ylacetyl)amino]-2,4-dihydroxybenzoic Acid (6h): mp >180 °C (dec.). <sup>1</sup>H NMR (DMSO- $d_6$ ):  $\delta =$ 1.55–1.72 (m, 12 H, 6 × adamantyl CH<sub>2</sub>), 1.89–1.97 (m, 3 H,  $3 \times$  adamantyl CH), 2.10 (s, 2 H, CH<sub>2</sub>), 6.43 (d, J = 8.8 Hz, 1 H, ArH), 7.56 (d, J = 8.8 Hz, 1 H, ArH), 8.91 (s, 1 H, NH), 10.23 (s, 1 H, OH), 11.84 (br s, 1 H, OH), 13.46 (br s, 1 H, CO<sub>2</sub>H). <sup>13</sup>C NMR (DMSO- $d_6$ ):  $\delta$  = 28.0, 32.4, 36.4, 41.9, 49.7, 104.3, 108.0, 113.1, 128.7, 158.6, 158.8, 170.0, 172.2. IR (KBr): 1709, 1641, 1536, 1449, 1395, 1269 cm<sup>-1</sup>. MS (ESI):  $m/z = 346 \text{ [MH^+]}$ . HRMS (ESI):  $m/z \text{ [M + H]}^+$  calcd for C<sub>19</sub>H<sub>24</sub>NO<sub>5</sub>: 346.1654; found: 346.1662. Anal. Calcd for  $C_{19}H_{23}NO_5$ : C, 66.07; H, 6.71; N, 4.06. Found: C, 66.34; H, 7.02; N, 3.92.

**2,4-Dihydroxy-3-[({[1***R***-(2-***endo***,3-***exo***)]-3-hydroxy-4,7,7-trimethylbicyclo[2.2.1]hept-2-yl}acetyl)amino]benzoic Acid (6k): white powder (15% yield); mp 167–169 °C. <sup>1</sup>H NMR (DMSO-***d***<sub>6</sub>): \delta = 0.78 (s, 3 H, Me), 0.81 (s, 3 H, Me), 1.03 (s, 3 H, Me), 0.91 (m, 2 H), 1.35–1.51 (m, 3 H), 1.64 (br, 1 H), 2.30–2.43 (m, 2 H), 3.07 (br, 1 H, CH<sub>2</sub>, bicycloheptyl), 4.62 (br s, 1 H, OH), 6.43 (d,** *J* **= 8.8 Hz, 1 H, ArH), 7.57 (d,** *J* **= 8.8 Hz, 1 H, ArH), 9.10 (s, 1 H, NH), 10.10 (s, 1 H, OH), 11.84 (br s, 1 H, OH), 13.5 (br s, 1 H, CO<sub>2</sub>H). <sup>13</sup>C NMR (DMSO-***d***<sub>6</sub>): \delta = 11.7, 19.6, 20.0, 20.7, 34.1, 36.9, 46.0, 47.0, 47.8, 49.0, 83.7, 104.4, 107.9, 112.8, 128.8, 158.6, 158.8, 172.1, 172.2. IR (KBr): 1645, 1541, 1383, 1296, 1248 cm<sup>-1</sup>. MS (ESI):** *m***/***z* **= 364 [MH<sup>+</sup>]. HRMS (ESI):** *m***/***z* **[M + H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>26</sub>NO<sub>6</sub>: 364.1760; found: 364.1772.**  Copyright of Synlett is the property of Georg Thieme Verlag Stuttgart and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.