Synthesis of 5-Methoxy-4-benzyloxazoles from Tyrosine and *m*-Tyrosine under Bischler-Napieralski Conditions*

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Various 2-substituted 5-methoxy-4-benzyloxazoles **6** and **9** were obtained from tyrosine and *m*-tyrosine derived amides **5** and **8** by treatment with phosphoryl chloride. A mechanism is proposed in order to explain the observed steric effects of the substituents in 2-position.

Key words: Amides, Bischler-Napieralski Reaction, 3,4-Dihydroisoquinolines, Oxazoles, Tyrosine

Introduction

Oxazoles are interesting from both a pharmacological and a chemical point of view. For example, they are known to interact with various proteins such as sodium-dependent excitatory amino acid transporters [1] or DNA repair protein OG-alkylguanine DNA-alkyl-transferase [2], and furthermore, they display bacteriostatic [3] and antiinflammatory activity [4]. Additionally, oxazoles provide useful entries into the synthesis of other heterocyclic compounds such as pyridines [5], α -amido oximes [6], and azlactones [7]. Since the seminal finding by Reeve and Paré [8] that acylamidophenylalanine esters **1** can undergo a cyclization to the oxazole **3** instead of the desired dihydroisoquinolines **2** under Bischler-Napieralski conditions [9] (Scheme 1), this reaction was observed by several groups [6, 10]. The electronic influence of substituents at the phenyl moiety has been explored to some extent [10b, 10c], however, substituent effects at the amide function remained unclear. Herein we wish to disclose our studies on this reaction in more detail.

Results and Discussion

As shown in Scheme 2, methyl *L*-O-methyl-tyrosinate (**4**) was first *N*-acylated with 1.1 equivalents of the respective acid chloride in pyridine at 0 °C. The mixture was then kept at r.t. for 16 h and after workup, the amides **5a–h** were obtained in 65–93% yield

Scheme 1. Possible products from acylamidophenylalanine esters **1** under Bischler-Napieralski conditions. EDG = electron donating group.

Scheme 2. Bischler-Napieralski reaction of methyl *L*-O-methyl-tyrosinate (**4**) to oxazoles **6**.

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Table 1. Formation of amides **5** and oxazoles **6**.

Entry	R	Amide	Yield [%]	Time [min]	Oxazole	Yield [%] ^a
1	Et	5a	82	25	6a	49
2	<i>n</i> -C ₅ H ₁₁	5b	86	10	6b	50
3	<i>t</i> -Bu	5c	91	150	6c	28
4	CH ₂ OBn	5d	75	90	6d	40
5	(<i>R</i>)-CHCH ₃ OBn	5e	93	10	6e	— ^b
6	C(CH ₃) ₂ OBn	5f	65	5	6f	— ^b
7	<i>p</i> -ClC ₆ H ₄	5g	74	20	6g	76
8	CO ₂ <i>t</i> -Bu	5h	76	6 h	6h	— ^b

^a Isolated yields are given; ^b only decomposition was observed.

(Table 1). Subsequent treatment of **5** with an excess of phosphoryl chloride at 95 °C following the procedure by Saxena [11] yielded the 5-methoxy-4-benzylloxazoles **6**. The course of reaction was followed by GC, and the reaction mixture was worked up immediately after the starting material could not be detected any more. In the cases of aliphatic acid chlorides, the yields of the oxazoles **6a–c** decreased with steric bulkiness of the alkyl substituent from 50% for 2-ethyl and 2-pentyl-substituted oxazoles **6a, b** (entry 1, 2) to only 28% for 2-*tert*-butyloxazole **6c** (entry 3).

Benzyloxymethyl-substituted oxazole **6d** was also isolated in 40% yield without any problems (entry 4). We were therefore curious whether the cyclization of chiral amide **5e** derived from *O*-benzyl (*R*)-lactate would retain its stereochemistry during oxazole formation. As a further derivative with a quaternary carbon atom the benzyloxymethyl-substituted amide **5f** was tested in the Bischler-Napieralski reaction. However, not even a trace of the desired oxazoles **6e** and **6f** could be detected (entries 5, 6). In contrast, the *p*-chlorophenyl-substituted amide **5g** reacted smoothly to afford the oxazole **6g** (entry 7), while the *tert*-butyl glyoxylate-derived amide **5h** did not give the target oxazole **6h** (entry 8).

Under similar conditions *rac* methyl 3-methoxyphenylalaninate (**7**) was converted with benzoyl chloride to the corresponding benzamide **8** in 92% yield (Scheme 3). Subsequent treatment with an excess of phosphoryl chloride in toluene at 100 °C in analogy to conditions by Chakravorti [12] yielded the oxazole **9** in 63% yield. It should be noted that we did not detect any trace of the corresponding 3,4-dihydroisoquinolinecarboxylate. This finding is in clear contrast to observations by Saxena [11], who found exclusively the 3,4-dihydroisoquinolinecarboxylate under similar reaction conditions.

As shown in Scheme 4, two mechanistic proposals may be drawn for the oxazole formation. According

Scheme 3. Bischler-Napieralski reaction of *m*-tyrosine derivative **7**.

Scheme 4. Mechanistic proposal for the oxazole formation.

to Fodor [13] nitrilium cations such as **10** are intermediates in Bischler-Napieralski reactions. Thus, *via* path A, amide **5** is converted to **10**, which is intramolecularly attacked by the carbonyl group of the ester moiety to give intermediate **11**. The latter is deprotonated to yield oxazole **6**. In path B, initial formation of the chloroiminium ion **12** analogous to the Vilsmeier-Haack reaction [14] is proposed. Intramolecular nucleophilic attack of the ester moiety should lead to the tetrahedral intermediate **13**. Further elimination of HCl and deprotonation should give the oxazole **6**. The sensitivity of the oxazole formation towards steric effects may be taken as evidence for mechanism B rather than A. The linear nitrilium cation **10** should be less prone to steric hindrance by the substituent R as compared to the tetrahedral intermediate **13**.

In conclusion, we found some steric influence of the amide substituent in the phosphoryl chloride-mediated cyclization of tyrosine derivatives **5** and **8** to the oxazoles **6** and **9**. While linear substituents like ethyl, *n*-pentyl or benzyloxymethyl (**5a, b, d**) react without difficulty, a branch at the α -C atom as in amides **5c, e, f** either clearly diminished the yield of the corresponding oxazole **6** or led to decomposition.

Experimental Section

General information

The following compounds were prepared according to literature procedures: benzyloxyacetyl chloride [15], (*R*)-2-D-benzylactic acid chloride [16], 2-benzyloxy-2,2-dimethylacetyl chloride [17, 18], and *tert*-butyl-chloroglyoxylate [19]. Commercial reagents were used without further purification unless otherwise indicated. Phosphoryl chloride was distilled, pyridine and toluene were distilled from CaH₂ prior to use. Reactions were performed in oven-dried glassware under N₂ atmosphere. Flash chromatography was performed on silica gel Fluka 60 (230–400 mesh) or Merck aluminium oxide 90 active neutral or aluminium oxide 90 active basic (0.063–0.200 mm). The following spectroscopic and analytical instruments were used. IR: Bruker Vector 22 FTIR. – NMR: Bruker AC 250 and Avance 500 (¹H: 250.13 MHz, 500.15 MHz, ¹³C: 62.90 MHz, 125.76 MHz). For ¹H spectra, TMS was used as internal standard. Signal assignments are based on DEPT and COSY experiments. – Melting points: Büchi SMP 20, m. p. are uncorrected. – Mass spectrometry: Finnigan MAT 95 and Varian MAT 711. – GC: Hewlett-Packard HP 6890, column HP 5TA (30 m × 0.32 mm), temperature program: 16 °C min^{−1} gradient from 80 °C to 300 °C.

General procedure for the preparation of amides 5, 8, as described for methyl *O*-methyl-*N*-propionyltyrosinate (5a): In a Schlenk flask methyl (*S*)-*O*-methyltyrosinate (**4**) (499 mg, 2.38 mmol) was dissolved in pyridine (7 ml). After cooling with an ice bath, propionyl chloride (0.23 ml, 242 mg, 2.62 mmol) was added *via* syringe. The resulting slurry was allowed to warm to r. t. (16 h) and concentrated to give a colorless, waxy solid. The solid was purified by filtration through 25 g neutral aluminium oxide with ethyl acetate (EtOAc) to give **5a** as colorless crystals (515 mg, 1.94 mmol, 82%). *R*_f = 0.14 (hexanes/EtOAc = 3 : 1). – [α]_D²² = +84.3° (*c* = 1.0, CH₂Cl₂). – M. p. 53 °C. – IR (ATR): ν = 3305 (C-H), 2946, 2189, 1969, 1730 (C=O), 1643 (C=O), 1538 (N-H), 1512, 1434, 1282, 1238 (C-O), 1219, 1174, 1031, 1012, 829 (C-H), 685 cm^{−1}. – ¹H NMR (500.15 MHz, CDCl₃): δ = 1.13 (t, *J* = 7.6 Hz, 3 H, CH₂CH₃), 2.21 (q, *J* = 7.7 Hz, 2 H, CH₂CH₃), 3.04 (dd, ²*J* = 14.0 Hz, ³*J* = 5.6 Hz, 1 H, MeOC₆H₄CH₂), 3.09 (dd, ²*J* = 13.8 Hz, ³*J* = 5.9 Hz, 1 H, MeOC₆H₄CH₂), 3.73 (s, 3 H, OCH₃), 3.78 (s, 3 H, OCH₃), 4.82 (dt, ³*J* = 7.6 Hz, ³*J* = 5.6 Hz, 1 H, MeO₂CCH), 5.92 (br. d, *J* = 7.4 Hz, 1 H, NH), 6.82 (d, *J* = 8.6 Hz, 2 H, *o*-C₆H₄OCH₃), 7.00 (d, *J* = 8.7 Hz, 2 H, *m*-C₆H₄OCH₃). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 9.7 (CH₂CH₃), 29.6 (CH₂CH₃), 37.0 (MeOC₆H₄CH₂), 52.2 (OCH₃), 53.1 (MeO₂CCH), 55.2 (OCH₃), 114.0 (*o*-C₆H₄OCH₃), 127.8 (*p*-C₆H₄OCH₃), 130.3 (*m*-C₆H₄OCH₃), 158.7 (*i*-C₆H₄OCH₃), 172.3, 173.4 (C(O)NH, C(O)OMe). – MS (EI, 70 eV): *m/z* (%) 265 [M⁺] (7), 193 [M⁺ – NHC(O)C₂H₅] (11),

192 [M⁺ – H – NHC(O)C₂H₅] (37), 161 (14), 122 (9), 121 [H₃COC₆H₄CH₂⁺] (100), 91 [C₇H₇⁺] (4), 77 (5), 57 [C(O)C₂H₅⁺] (10), 29 (12). – C₁₄H₁₉NO₄ (265.3): calcd. C 63.38, H 7.22, N 5.28; found C 63.16, H 7.15, N 5.18.

Methyl (*S*)-*N*-hexanoyl-*O*-methyltyrosinate (5b): Yield: 479 mg, 1.56 mmol, 86%, colorless crystals. – M. p. 38 °C. – *R*_f = 0.34 (hexanes/EtOAc = 3 : 1). – [α]_D²² = +72.0° (*c* = 1.0, CH₂Cl₂). – IR (ATR): ν = 3286 (C-H), 2936, 2191, 1970, 1735 (C=O), 1645 (C=O), 1541 (N-H), 1512, 1435, 1244 (C-O), 1175, 1039, 1015, 812 (C-H), 727, 688 cm^{−1}. – ¹H NMR (500.15 MHz, CDCl₃): δ = 0.88 (t, *J* = 7.0 Hz, 3 H, (CH₂)₄CH₃), 1.23–1.33 (m, 4 H, CH₂CH₂CH₂CH₂CH₃), 1.59 (quint, *J* = 7.5 Hz, 2 H, CH₂CH₂CH₂CH₂CH₃), 2.18 (t, *J* = 7.3 Hz, 2 H, CH₂CH₂CH₂CH₂CH₃), 3.03 (dd, ²*J* = 14.0 Hz, ³*J* = 5.7 Hz, 1 H, MeOC₆H₄CH₂), 3.09 (dd, ²*J* = 14.0 Hz, ³*J* = 5.8 Hz, 1 H, MeOC₆H₄CH₂), 3.73 (s, 3 H, OCH₃), 3.78 (s, 3 H, OCH₃), 4.86 (dt, ³*J* = 7.9 Hz, ³*J* = 5.8 Hz, 1 H, MeO₂CCH), 5.89 (br. d, *J* = 7.6 Hz, 1 H, NH), 6.82 (d, *J* = 8.7 Hz, 2 H, *o*-C₆H₄OCH₃), 7.00 (d, *J* = 8.6 Hz, 2 H, *m*-C₆H₄OCH₃). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 13.9 ((CH₂)₄CH₃), 22.4 (CH₂CH₂CH₂CH₂CH₃), 25.3 (CH₂CH₂CH₂CH₂CH₃), 31.4 (CH₂CH₂CH₂CH₂CH₃), 36.5 (CH₂CH₂CH₂CH₂CH₃), 37.1 (MeOC₆H₄CH₂), 52.3 (OCH₃), 53.04 (MeO₂CCH), 55.2 (OCH₃), 114.0 (*o*-C₆H₄OCH₃), 127.8 (*p*-C₆H₄OCH₃), 130.3 (*m*-C₆H₄OCH₃), 158.7 (*i*-C₆H₄OCH₃), 172.3, 172.7 (C(O)NH, C(O)OMe). – MS (EI, 70 eV): *m/z* (%) 307 [M⁺] (5), 193 [M⁺ – C(O)C₅H₁₁] (12), 192 [M⁺ – H – NHC(O)C₅H₁₁] (100), 161 (9), 122 (7), 121 [H₃COC₆H₄CH₂⁺] (64), 91 [C₇H₇⁺] (3), 71 [C₅H₁₁⁺] (3), 43 (11), 28 (16), 18 (17). – C₁₇H₂₅NO₄ (307.4): calcd. C 66.43, H 8.20, N 4.56; found C 66.29, H 8.13, N 4.50.

Methyl (*S*)-*N*-(2,2-dimethylpropanoyl)-*O*-methyltyrosinate (5c): Yield: 446 mg, 1.52 mmol, 91%, colorless crystals. – M. p. 63 °C. – *R*_f = 0.28 (hexanes/EtOAc = 8:1). – [α]_D²² = +66.1° (*c* = 1.0, CH₂Cl₂). – IR (ATR): ν = 3327 (C-H), 2958, 2192, 1968, 1752 (C=O), 1730, 1628 (C=O), 1513 (N-H), 1438, 1245 (C-O), 1200, 1180, 1120, 1034, 1003, 841 (C-H), 785, 633 cm^{−1}. – ¹H NMR (250.13 MHz, CDCl₃): δ = 1.16 (s, 9 H, C(CH₃)₃), 3.04 (dd, ²*J* = 13.9 Hz, ³*J* = 5.6 Hz, 1 H, MeOC₆H₄CH₂), 3.11 (dd, ²*J* = 13.9 Hz, ³*J* = 5.6 Hz, 1 H, MeOC₆H₄CH₂), 3.74 (s, 3 H, OCH₃), 3.78 (s, 3 H, OCH₃), 4.82 (dt, ³*J* = 7.6 Hz, ³*J* = 5.6 Hz, 1 H, MeO₂CCH), 6.05 (br. d, *J* = 7.4 Hz, 1 H, NH), 6.82 (d, *J* = 8.7 Hz, 2 H, *o*-C₆H₄OCH₃), 6.99 (d, *J* = 8.7 Hz, 2 H, *m*-C₆H₄OCH₃). – ¹³C NMR (62.90 MHz, CDCl₃): δ = 27.4 (C(CH₃)₃), 36.9 (MeOC₆H₄CH₂), 38.7 (C(CH₃)₃), 52.3 (OCH₃), 53.0 (MeO₂CCH), 55.2 (OCH₃), 113.9 (*o*-C₆H₄OCH₃), 127.9 (*p*-C₆H₄OCH₃), 130.3 (*m*-C₆H₄OCH₃), 158.7 (*i*-C₆H₄OCH₃), 172.4, 177.8 (C(O)NH, C(O)OMe). – MS (EI, 70 eV): *m/z* (%) 293 [M⁺] (5), 193 [M⁺ – NHC(O)C₄H₉] (8), 192 [M⁺ – H – NHC(O)C₄H₉]

(100), 161 (10), 122 (7), 121 (65), 57 [$C_4H_9^+$] (20), 41 (7), 29 (4). – $C_{16}H_{23}NO_4$ (293.4): calcd. C 65.51, H 7.90, N 4.77; found C 65.34, H 7.90, N 4.69.

Methyl (S)-N-[(benzyloxy)acetyl]-O-methyltyrosinate (5d): Yield: 349 mg, 0.98 mmol, 75%, colorless oil. – $R_f = 0.15$ (hexanes/EtOAc = 2 : 1). – $[\alpha]_D^{22} + 35.3^\circ$ ($c = 1.0$, CH_2Cl_2). – IR (ATR): $\nu = 3401$ (C-H), 2951, 1741 (C=O), 1677 (C=O), 1611, 1510 (N-H), 1439, 1343, 1246 (C-O), 1205, 1176, 1099, 1029, 839 (C-H), 738, 698 cm^{-1} . – ^1H NMR (500.15 MHz, $CDCl_3$): $\delta = 3.08$ (dd, $^3J = 2.8$ Hz, $^2J = 5.9$ Hz, 2 H, $MeOC_6H_4CH_2$), 3.73 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.98 (s, 2 H, $HNC(O)CH_2$), 4.52 (dd, $^3J = 11.7$ Hz, $^2J = 28.5$ Hz, 2 H, $PhCH_2O$), 4.87 (dt, $^3J = 8.4$ Hz, $^3J = 6.0$ Hz, 1 H, MeO_2CCH), 6.79 (d, $J = 8.6$ Hz, 2 H, $o-C_6H_4OCH_3$), 7.02 (d, $J = 8.6$ Hz, 2 H, $m-C_6H_4OCH_3$, NH), 7.25–7.27 (m, 2 H, $o-PhCH_2O$), 7.32–7.38 (m, 3 H, m -, $p-PhCH_2O$). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 37.1$ ($MeOC_6H_4CH_2$), 52.4 (OCH_3), 52.5 (MeO_2CCH), 55.2 (OCH_3), 69.3 ($HNC(O)CH_2$), 73.4 ($PhCH_2O$), 114.0 ($o-C_6H_4OCH_3$), 127.6 ($p-C_6H_4OCH_3$), 127.8 ($o-PhCH_2O$), 128.1 ($p-PhCH_2O$), 128.6 ($m-PhCH_2O$), 130.2 ($m-C_6H_4OCH_3$), 136.8 ($i-PhCH_2O$), 158.7 ($i-C_6H_4OCH_3$), 169.3, 171.8 ($C(O)NH$, $C(O)OMe$). – MS (CI, CH_4): m/z (%) 386 [$M^+ + C_2H_4$] (11), 358 [$M^+ + H$], 326 [$M^+ - OCH_3$] (7), 298 [$M^+ - CO_2CH_3$] (34), 280 (3), 251 (5), 223 (3), 192 [$M^+ - H - NHC(O)CH_2OCH_2Ph$] (100), 161 (5), 121 [$H_3COC_6H_4CH_2^+$] (40), 107 [$PhCH_2O$] (2), 91 [$C_7H_7^+$] (24), 77 (1). – $C_{20}H_{23}NO_5$ (357.4): calcd. C 67.21, H 6.49, N 3.92; found C 67.12, H 6.52, N 3.82.

Methyl (S)-N-[(2S)-2-(benzyloxy)propanoyl]-O-methyltyrosinate (5e): Yield: 816 mg, 2.20 mmol, 93%, colorless oil. – $R_f = 0.32$ (hexanes/EtOAc = 3 : 1). – $[\alpha]_D^{22} + 48.0^\circ$ ($c = 1.0$, CH_2Cl_2). – IR (ATR): $\nu = 3413$ (C-H), 2935, 2191, 1971, 1740 (C=O), 1672 (C=O), 1510 (N-H), 1442, 1337, 1246 (C-O), 1106, 1029, 839 (C-H), 738, 698 cm^{-1} . – ^1H NMR (250.13 MHz, $CDCl_3$): $\delta = 1.40$ (d, $J = 6.8$ Hz, 3 H, OCH_3), 3.03 (dd, $^2J = 14.1$ Hz, $^3J = 6.7$ Hz, 1 H, $MeOC_6H_4CH_2$), 3.11 (dd, $^2J = 14.1$ Hz, $^3J = 5.6$ Hz, 1 H, $MeOC_6H_4CH_2$), 3.73 (s, 6 H, OCH_3), 3.90 (q, $J = 6.8$ Hz, 1 H, $CHCH_3$), 4.41 (s, 2 H, $PhCH_2O$), 4.83 (dt, $^3J = 6.1$ Hz, $^3J = 8.2$ Hz, 1 H, MeO_2CCH), 6.74 (d, $J = 8.7$ Hz, 2 H, $o-C_6H_4OCH_3$), 7.00 (d, $J = 8.7$ Hz, 2 H, $m-C_6H_4OCH_3$), 7.18–7.24 (m, 2 H, o -, m -, $p-PhCH_2O$), 7.27–7.39 (m, 3 H, o -, m -, $p-PhCH_2O$). – ^{13}C NMR (62.90 MHz, $CDCl_3$): $\delta = 18.4$ (CH_3), 36.9 ($MeOC_6H_4CH_2$), 52.3 (OCH_3), 52.6 (MeO_2CCH), 55.2 (OCH_3), 71.7 ($PhCH_2$), 76.0 ($CHCH_3$), 114.1 ($o-C_6H_4OCH_3$), 127.6 (o -, m -, $p-PhCH_2O$), 127.7 ($i-PhCH_2O$), 128.0, 128.5 (o -, m -, $p-PhCH_2O$), 130.2 ($m-C_6H_4OCH_3$), 137.4 ($i-PhCH_2O$), 158.7 ($i-C_6H_4OCH_3$), 171.8, 173.0 ($C(O)NH$, $C(O)OMe$). – MS (EI, 70 eV): m/z (%) 371 [M^+] (3), 265 [$M^+ + H - PhCH_2O$] (5), 193 [$M^+ - NHC(O)CH(CH_3)OCH_2Ph$] (12), 192 [$M^+ - H - NHC(O)CH(CH_3)OCH_2Ph$] (100), 122 (6), 121

[$H_3COC_6H_4CH_2^+$] (55), 91 [$C_7H_7^+$] (36), 43 (6), 28 (7). – $C_{21}H_{25}NO_5$ (371.4): calcd. C 67.91, H 6.78, N 3.77; found C 67.88, H 6.84, N 3.69.

Methyl (S)-N-[2-(benzyloxy)-2-methylpropanoyl]-O-methyltyrosinate (5f): Yield: 769 mg, 2.00 mmol, 65%, colorless oil. – $R_f = 0.50$ (hexanes/EtOAc = 3 : 1). – $[\alpha]_D^{22} + 83.9^\circ$ ($c = 1.0$, CH_2Cl_2). – IR (ATR): $\nu = 3416$ (C-H), 2951, 1741 (C=O), 1675 (C=O), 1612, 1510 (N-H), 1441, 1359, 1246 (C-O), 1175, 1029, 837 (C-H), 736, 697 cm^{-1} . – ^1H NMR (500.15 MHz, $CDCl_3$): $\delta = 1.41$ (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 3.02 (dd, $^2J = 14.1$ Hz, $^3J = 6.5$ Hz, 1 H, $MeOC_6H_4CH_2$), 3.09 (dd, $^2J = 14.1$ Hz, $^3J = 5.6$ Hz, 1 H, $MeOC_6H_4CH_2$), 3.71 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 4.42 (dd, $^2J = 22.3$ Hz, $^3J = 11.0$ Hz, 1 H, $PhCH_2O$), 4.82 (dt, $J = 8.2$ Hz, $J = 6.1$ Hz, 1 H, MeO_2CCH), 6.72 (d, $J = 8.6$ Hz, 2 H, $o-MeOC_6H_4$), 6.97 (d, $J = 6.7$ Hz, 2 H, $m-MeOC_6H_4$), 7.09 (d, $J = 8.2$ Hz, 1 H, NH), 7.23 (d, $J = 7.0$ Hz, 2 H, $o-PhCH_2O$), 7.27–7.36 (m, 3 H, m -, $p-PhCH_2O$). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 23.5$ (CH_3), 24.5 (CH_3), 36.9 ($MeOC_6H_4CH_2$), 52.3 (OCH_3), 52.8 (MeO_2CCH), 55.2 (OCH_3), 65.7 ($(CH_3)_2COCH_2Ph$), 78.8 ($PhCH_2O$), 114.0 ($o-MeOC_6H_4$), 127.4 ($o-PhCH_2O$), 127.6 (m -, $p-PhCH_2O$), 127.7 ($p-MeOC_6H_4$), 128.4 (m -, $p-PhCH_2O$), 130.2 ($m-MeOC_6H_4$), 138.2 ($i-PhCH_2O$), 158.7 ($i-MeOC_6H_4$), 172.0, 175.1 (CO_2Me , $C(O)NH$). – MS (EI, 70 eV): m/z (%) 385 [M^+] (3), 354 [$M^+ - OCH_3$] (1), 326 [$M^+ - CO_2CH_3$] (2), 279 [$M^+ + H - OCH_2Ph$] (25), 262 (1), 236 [$M^+ - C(CH_3)_2OCH_2Ph$] (12), 208 (7), 192 [$M^+ - H - NHC(O)C(CH_3)_2OCH_2Ph$] (100), 176 [$M^+ + H - C(O)C(CH_3)_2OCH_2Ph$] (10), 149 (8), 121 [$H_3COC_6H_4CH_2^+$] (59), 91 [$C_7H_7^+$] (76), 59 [$CO_2CH_3^+$] (2). – $C_{22}H_{27}NO_5$ (385.5): calcd. C 68.55, H 7.06, N 3.63; found C 68.59, H 7.16, N 3.51.

Methyl (S)-N-(4-chlorobenzoyl)-O-methyltyrosinate (5g): Yield: 526 mg, 1.51 mmol, 74%, colorless crystals. – M.p. 111 $^\circ C$. – $R_f = 0.32$ (hexanes/EtOAc = 3 : 1). – $[\alpha]_D^{22} + 14.9^\circ$ ($c = 1.0$, CH_2Cl_2). – IR (ATR): $\nu = 3288$ (C-H), 2949, 1736 (C=O), 1635 (C=O), 1536 (N-H), 1513, 1485, 1436, 1247 (C-O), 1224, 1174, 1089, 1028, 1013, 848 (C-H), 834 (C-H), 765, 658 cm^{-1} . – ^1H NMR (500.15 MHz, $CDCl_3$): $\delta = 3.16$ (dd, $^2J = 14.0$ Hz, $^3J = 5.3$ Hz, 1 H, $MeOC_6H_4CH_2$), 3.23 (dd, $^2J = 14.0$ Hz, $^3J = 5.7$ Hz, 1 H, $MeOC_6H_4CH_2$), 3.78 (s, 6 H, OCH_3), 5.03 (dt, $^3J = 7.6$ Hz, $^3J = 5.5$ Hz, 1 H, MeO_2CCH) 6.56 (d, $J = 7.5$ Hz, 1 H, NH), 6.82 (d, $J = 8.5$ Hz, 2 H, $o-MeOC_6H_4$), 7.03 (d, $J = 8.7$ Hz, 2 H, $m-MeOC_6H_4$), 7.39 (d, $J = 8.4$ Hz, 2 H, $o-ClC_6H_4$), 7.66 (d, $J = 8.6$ Hz, 2 H, $m-ClC_6H_4$). – ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 36.9$ ($MeOC_6H_4CH_2$), 52.5 (OCH_3), 53.7 (MeO_2CCH), 55.2 (OCH_3), 114.0 ($o-MeOC_6H_4$), 127.6 ($p-MeOC_6H_4$), 128.5 ($m-ClC_6H_4$), 128.9 ($o-ClC_6H_4$), 130.3 ($m-MeOC_6H_4$), 132.3 ($i-ClC_6H_4$), 138.1 ($p-ClC_6H_4$), 158.8

(*i*-MeOC₆H₄), 165.7 (C(O)NH), 172.1 (C(O)OMe). – GC-MS (EI, 70 eV): *m/z* (%) 347 [M⁺] (4), 288 (2), 192 [M⁺ – H – NHC(O)C₆H₄Cl] (100), 161 (9), 139 [C(O)C₆H₄Cl⁺] (20), 121 [H₃COC₆H₄CH₂⁺] (73), 111 [C₆H₄Cl⁺] (9), 81 (2), 77 (3), 28 (1). – C₁₈H₁₈ClNO₄ (347.8): calcd. C 62.16, H 5.22, N 4.03 Cl 10.19; found C 62.19, H 5.35, N 3.86, Cl 10.32.

Methyl (S)-O-methyl-N-pyruvoyltyrosinate (5h): Yield: 74 mg, 0.22 mmol, 76%, colorless oil. – *R*_f = 0.44 (hexanes/EtOAc = 2 : 1). – [α]_D²² = +61.8° (*c* = 0.5, CH₂Cl₂). – IR (ATR): ν = 3341 (C–H), 2954, 1744 (C=O), 1698 (C=O), 1612, 1511 (N–H), 1441, 1389, 1298, 1246 (C–O), 1152, 1032, 837 (C–H) cm^{–1}. – ¹H NMR (500.15 MHz, CDCl₃): δ = 1.55 (s, 9 H, C(CH₃)₃), 3.10 (d, *J* = 5.8 Hz, 2 H, MeOC₆H₄CH₂), 3.73 (s, 3 H, OCH₃), 3.79 (s, 3 H, OCH₃), 4.80 (dt, *J* = 5.8 Hz, *J* = 8.2 Hz, 1 H, MeO₂CCH), 6.83 (d, *J* = 8.7 Hz, 2 H, *o*-C₆H₄OCH₃), 7.03 (d, *J* = 8.7 Hz, 2 H, *m*-C₆H₄OCH₃), 7.41 (d, *J* = 7.9 Hz, 1 H, NH). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 27.7 (C(CH₃)₃), 36.9 (MeOC₆H₄CH₂), 52.5 (OCH₃), 53.7 (MeO₂CCH), 55.2 (OCH₃), 84.8 (C(CH₃)₃), 114.2 (*o*-C₆H₄OCH₃), 127.2 (*p*-C₆H₄OCH₃), 130.2 (*m*-C₆H₄OCH₃), 157.0, 158.88, 158.92 (*m*-C₆H₄OCH₃, NHC(O)C(O)Ot-Bu), 171.0 (CO₂Me). – GC-MS (CI, CH₄): *m/z* (%) 338 [M⁺ + H] (45), 322 (2), 310 (9), 296 (3), 282 (100), 250 (7), 236 [M⁺ – CO₂t-Bu] (11), 222 (10), 208 [M⁺ – C(O)CO₂t-Bu] (2), 192 [M⁺ – H – NHC(O)CO₂t-Bu] (72), 176 (4), 161 (3), 121 [H₃COC₆H₄CH₂⁺] (44), 57 [C₄H₉⁺] (12). – C₁₇H₂₃NO₆ (337.4): calcd. C 60.52, H 6.87, N 4.15; found C 60.77, H 6.93, N 4.08.

Methyl N-benzoyl-3-(methoxyphenyl)alaninate (8): Yield: 131 mg, 0.42 mmol, 92%, colorless oil. – *R*_f = 0.24 (hexanes/EtOAc = 3 : 1). – IR (ATR): ν = 3315 (C–H), 2950, 1975, 1739 (C=O), 1639 (C=O), 1601, 1526 (N–H), 1487, 1435, 1256 (C–O), 1213, 1152, 1039, 875 (C–H), 775, 691 cm^{–1}. – ¹H NMR (500.15 MHz, CDCl₃): δ = 3.21 (dd, ²*J* = 13.8 Hz, ³*J* = 5.3 Hz, 1 H, MeOC₆H₄CH₂), 3.28 (dd, ²*J* = 13.8 Hz, ³*J* = 5.8 Hz, 1 H, MeOC₆H₄CH₂), 3.74 (s, 3 H, C₆H₄OCH₃), 3.78 (s, 3 H, CO₂CH₃), 5.09 (dt, *J* = 7.5 Hz, *J* = 5.6 Hz, 1 H, MeO₂CCH), 6.59 (d, *J* = 7.3 Hz, 1 H, NH), 6.66–6.68 (m, 1 H, 5-H), 6.72 (d, *J* = 13.8 Hz, 1 H, 9-H), 6.80 (dd, *J* = 8.1 Hz, *J* = 2.4 Hz, 1 H, 7-H), 7.20 (t, *J* = 7.9 Hz, 1 H, 8-H), 7.42–7.45 (m, 2 H, *m*-C(O)Ph), 7.50–7.53 (m, 1 H, *p*-C(O)Ph), 7.72–7.74 (m, 2 H, *o*-C(O)Ph). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 37.9 (MeOC₆H₄CH₂), 52.5 (CO₂CH₃), 53.5 (MeO₂CCH), 55.1 (C₆H₄OCH₃), 112.8 (C-7), 114.9 (C-5), 121.7 (C-9), 127.0 (*o*-C(O)Ph), 128.6 (*m*-C(O)Ph), 129.6 (C-6), 131.8 (*p*-C(O)Ph), 133.9, 137.3 (C-4, *i*-C(O)Ph), 159.7 (C-6), 166.8 (C(O)Ph), 172.0 (CO₂Me). – GC-MS (EI, 70 eV): *m/z* (%) 314 [M⁺ + H] (2), 313 [M⁺] (12), 282 (1), 254 [M⁺ – CO₂CH₃] (3), 193 [M⁺ – NHC(O)Ph] (12), 192 [M⁺ –

H – NHC(O)Ph] (100), 161 (9), 121 [H₃COC₆H₄CH₂⁺] (3), 105 (51), 91 [C₇H₇⁺] (2), 77 [C₆H₅⁺] (16), 51 (1). – C₁₈H₁₉NO₄ (313.3): calcd. C 68.99, H 6.11, N 4.47; found C 69.15, H 6.21, N 4.24.

General procedure for the preparation of oxazoles 6, as described for 2-ethyl-5-methoxy-4-(4-methoxybenzyl)-1,3-oxazole (6a): In a Schlenk flask **5a** (100 mg, 0.38 mmol) was dissolved in phosphoryl chloride (2.5 ml, 27 mmol). The reaction mixture was heated at 95 °C for 25 min, cooled to r.t. and poured into an ice-cold saturated NaHCO₃ solution (50 ml), and further NaHCO₃ was carefully added to adjust pH 8. After warming to r.t., the mixture was stirred for 15 min and was then extracted with dichloromethane (3 × 30 ml). The combined organic layers were washed with brine (2 × 50 ml), dried (Na₂SO₄), and concentrated. The pale yellow liquid was purified by chromatography on basic aluminium oxide (10 g) with hexanes/EtOAc (4 : 1, *R*_f = 0.58) to give **6a** as a colorless liquid (46 mg, 0.19 mmol, 49%). – IR (ATR): ν = 2942, 1668 (N=C), 1612, 1579, 1511 (C=C), 1461, 1353, 1241 (C–O), 1175, 1141, 1108, 1063, 1034, 974, 795 cm^{–1}. – ¹H NMR (500.15 MHz, CDCl₃): δ = 1.26 (t, *J* = 7.6 Hz, 3 H, CH₂CH₃), 2.64 (q, *J* = 7.6 Hz, 2 H, CH₂CH₃), 3.66 (s, 2 H, MeOC₆H₄CH₂), 3.77 (s, 3 H, C₆H₄OCH₃), 3.83 (s, 3 H, OCH₃), 6.82 (d, *J* = 8.7 Hz, 2 H, *o*-C₆H₄OCH₃), 7.18 (d, *J* = 8.7 Hz, 2 H, *m*-C₆H₄OCH₃). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 11.1 (CH₂CH₃), 22.0 (CH₂CH₃), 30.1 (MeOC₆H₄CH₂), 55.3 (C₆H₄OCH₃), 61.2 (OCH₃), 113.9 (*o*-MeOC₆H₄), 114.9 (C-4), 129.5 (*m*-MeOC₆H₄), 131.7 (*p*-MeOC₆H₄), 154.7, 156.5 (C-2, C-5), 158.05 (*i*-MeOC₆H₄). – MS (EI, 70 eV): *m/z* (%) 247 [M⁺] (67), 219 (6), 218 [M⁺ – C₂H₅] (25), 204 [M⁺ – COCH₃] (11), 190 [M⁺ – C(O)C₂H₅] (9), 188 (20), 186 (9), 161 (5), 147 (8), 133 (26), 121 [H₃COC₆H₄CH₂⁺] (26), 89 (5), 77 (9), 57 (100), 29 [C₂H₅] (19), 28 (14). – HRMS (EI, 70 eV): calcd. for C₁₄H₁₇NO₃ 247.1208, found 247.1210 [M⁺]. – C₁₄H₁₇NO₃ (247.3): calcd. C 68.00, H 6.93, N 5.66; found C 67.62, H 6.88, N 5.62.

5-Methoxy-4-(4-methoxybenzyl)-2-pentyl-1,3-oxazole (6b): Yield: 47 mg, 0.16 mmol, 50%, pale yellow liquid. – *R*_f = 0.37 (hexanes/EtOAc = 20 : 1). – IR (ATR): ν = 2932, 2860, 1668 (N=C), 1611, 1578, 1511 (C=C), 1463, 1354, 1242 (C–O), 1175, 1142, 1084, 1034, 990, 804 cm^{–1}. – ¹H NMR (500.15 MHz, CDCl₃): δ = 0.88–0.90 (m, 3 H, (CH₂)₄CH₃), 1.29–1.35 (m, 4 H, (CH₂)₂CH₂CH₂CH₃), 1.67–1.73 (m, 2 H, CH₂CH₂(CH₂)₂CH₃), 2.59 (t, *J* = 8.7 Hz, 2 H, CH₂(CH₂)₃CH₃), 3.66 (s, 2 H, MeOC₆H₄CH₂), 3.77 (s, 3 H, C₆H₄OCH₃), 3.83 (s, 3 H, OCH₃), 6.82 (d, *J* = 8.7 Hz, 2 H, *o*-MeOC₆H₄), 7.16 (d, *J* = 8.6 Hz, 2 H, *m*-MeOC₆H₄). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 13.9 ((CH₂)₄CH₃), 22.3 ((CH₂)₂CH₂CH₂CH₃), 26.7 (CH₂CH₂(CH₂)₂CH₃), 28.6 (CH₂(CH₂)₃CH₃), 30.1 (MeOC₆H₄CH₂), 31.3 ((CH₂)₂CH₂CH₂CH₃), 55.3 (C₆H₄OCH₃), 61.2 (OCH₃),

113.8 (*o*-MeOC₆H₄), 114.8 (C-4), 129.5 (*m*-MeOC₆H₄), 131.7 (*p*-MeOC₆H₄), 154.7, 155.8 (C-2, C-5), 158.1 (*i*-MeOC₆H₄). – GC-MS (EI, 70 eV): *m/z* (%) 289 [M⁺] (100), 274 (11), 260 (4), 246 [M⁺ – COCH₃] (4), 230 (11), 218 (7), 201 (9), 186 (9), 173 (16), 159 (7), 147 [M⁺ – COCH₃ – C(O)C₅H₁₁] (32), 140 (31), 133 (18), 121 [H₃COC₆H₄CH₂⁺] (61), 103 (10), 91 (15), 83 (33), 71 [C₅H₁₁⁺] (26), 63 (10), 55 (38). – C₁₇H₂₃NO₃ (289.4): calcd. C 70.56, H 8.01, N 4.84; found C 70.47, H 8.07, N 4.87.

2-*tert*-Butyl-5-methoxy-4-(4-methoxybenzyl)-1,3-oxazole (6c): Yield: 26 mg, 0.094 mmol, 28%, colorless liquid. – *R*_f = 0.35 (hexanes/EtOAc = 20 : 1). – IR (ATR): ν = 2971, 1669 (N=C), 1612, 1566, 1511 (C=C), 1461, 1368, 1299, 1241 (C-O), 1174, 1136, 1078, 1035, 987, 819, 782 cm⁻¹. – ¹H NMR (500.15 MHz, CDCl₃): δ = 1.32 (s, 9 H, C(CH₃)₃), 3.69 (s, 2 H, MeOC₆H₄CH₂), 3.79 (s, 3 H, OCH₃), 3.79 (s, 3 H, OCH₃), 6.82 (d, *J* = 8.7 Hz, 2 H, *o*-MeOC₆H₄), 7.16 (d, *J* = 8.6 Hz, 2 H, *m*-MeOC₆H₄). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 28.4 (C(CH₃)₃), 30.2 (C(CH₃)₃), 33.7 (MeOC₆H₄CH₂), 55.3 (C₆H₄OCH₃), 61.0 (OCH₃), 113.7 (*o*-MeOC₆H₄), 114.5 (C-4), 129.5 (*m*-MeOC₆H₄), 131.8 (*p*-MeOC₆H₄), 154.6, 158.0, 161.6 (C-2, C-5, *i*-MeOC₆H₄). – GC-MS (EI, 70 eV): *m/z* (%) 275 [M⁺] (50), 260 (5), 232 [M⁺ – COCH₃] (5), 218 (23), 204 (6), 190 [M⁺ – C(O)C₄H₉⁺] (7), 186 (6), 160 (7), 158 (6), 146 (5), 133 (9), 126 (17), 121 [H₃COC₆H₄CH₂⁺] (21), 108 (5), 91 (7), 89 (7), 77 (13), 63 (7), 57 [C₄H₉⁺] (100). – C₁₆H₂₁NO₃ (275.3): calcd. C 69.79, H 7.69, N 5.09; found C 69.76, H 7.78, N 5.04.

2-[(Benzyloxy)methyl]-5-methoxy-4-(4-methoxybenzyl)-1,3-oxazole (6d): Yield: 16 mg, 0.047 mmol, 40%, pale yellow liquid. – *R*_f = 0.48 (hexanes/EtOAc = 3 : 1). – IR (ATR): ν = 2938, 1964, 1661 (N=C), 1511 (C=C), 1454, 1360, 1244 (C-O), 1176, 1072, 1029, 983, 807 (C-H), 738, 698 cm⁻¹. – ¹H NMR (500.15 MHz, CDCl₃): δ = 3.68 (s, 2 H, MeOC₆H₄CH₂), 3.77 (s, 3 H, C₆H₄OCH₃), 3.85 (s, 3 H, OCH₃), 4.44 (s, 2 H, CH₂OCH₂Ph), 4.58 (s, 2 H, CH₂OCH₂Ph), 6.82 (d, *J* = 8.7 Hz, 2 H, *o*-MeOC₆H₄), 7.17 (d, *J* = 8.5 Hz, 2 H, *m*-MeOC₆H₄), 7.28–7.30 (m, 1 H, *p*-PhCH₂O), 7.33 (d, *J* = 8.1 Hz, 4 H, *o*-, *m*-PhCH₂O). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 30.0 (MeOC₆H₄CH₂), 55.3 (C₆H₄OCH₃), 60.9 (OCH₃), 64.4 (CH₂OCH₂Ph), 72.8 (CH₂OCH₂Ph), 113.9 (*o*-MeOC₆H₄), 115.3 (C-4), 127.9 (*p*-PhCH₂O), 128.0, 128.5 (*o*-PhCH₂O, *m*-PhCH₂O), 129.5 (*o*-MeOC₆H₄), 131.4 (*p*-MeOC₆H₄), 137.3 (*i*-PhCH₂O), 151.2, 155.5 (C-2, C-5), 158.1 (*i*-MeOC₆H₄). – MS (CI, CH₄): *m/z* (%) 679 (5) [2M + H]⁺, 571 (3), 460 (9), 430 (13), 355 [M⁺ + CH₄] (7), 340 [M⁺ + H] (100), 298 (6), 232 [M⁺ – OCH₂Ph] (40), 218 [M⁺ – CH₂OCH₂Ph] (26), 201 (8), 148 (8), 132 (9), 121 [H₃COC₆H₄CH₂⁺] (21), 91 [C₇H₇⁺] (42). – HRMS (DCI): calcd. for C₂₀H₂₁NO₄

339.1471, found 339.1454 [M⁺]. – C₂₀H₂₁NO₄ (339.4): calcd. C 70.78, H 6.24, N 4.13; found C 71.33, H 6.48, N 3.59.

2-(4-Chlorophenyl)-5-methoxy-4-(4-methoxybenzyl)-1,3-oxazole (6g): Yield: 74 mg, 0.22 mmol, 76 %, yellow solid. – M. p. 78–79 °C. – *R*_f = 0.36 (hexanes/EtOAc = 15 : 1). – IR (ATR): ν = 2943, 2832, 1657 (N=C), 1612, 1510 (C=C), 1479, 1449, 1355, 1290, 1241 (C-O), 1178, 1087, 1037, 970, 822 (C-H), 768, 727 (C-Cl), 694, 620, 560 cm⁻¹. – ¹H NMR (500.15 MHz, CDCl₃): δ = 3.76 (s, 2 H, MeOC₆H₄CH₂), 3.79 (s, 3 H, C₆H₄OCH₃), 3.94 (s, 3 H, OCH₃), 6.84 (d, *J* = 8.7 Hz, 2 H, *o*-MeOC₆H₄), 7.23 (d, *J* = 8.6 Hz, 2 H, *m*-MeOC₆H₄), 7.37 (d, *J* = 8.7 Hz, 2 H, *o*-ClC₆H₄), 7.84 (d, *J* = 8.5 Hz, 2 H, *m*-ClC₆H₄). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 30.2 (MeOC₆H₄CH₂), 55.3 (C₆H₄OCH₃), 61.2 (CO₂CH₃), 113.9 (*m*-MeOC₆H₄), 117.1 (C-4), 126.2 (*m*-MeOC₆H₄), 126.7 (*m*-ClC₆H₄), 128.9 (*o*-ClC₆H₄), 129.5 (*m*-MeOC₆H₄), 131.3 (*p*-ClC₆H₄), 135.5 (*i*-ClC₆H₄), 151.3, 155.3 (C-2, C-5), 158.1 (*i*-MeOC₆H₄). – MS (EI, 70 eV): *m/z* (%) 329 [M⁺] (96), 314 (6), 287 (4), 270 [M⁺ – CO₂CH₃] (14), 254 (2), 209 (5), 191 (1), 164 (2), 147 (3), 139 [C(O)C₆H₅Cl⁺] (100), 111 [C₆H₅Cl⁺] (13), 77 (4), 59 [CO₂CH₃⁺] (2), 43 [COCH₃⁺] (1). – C₁₈H₁₆ClNO₃ (329.8): calcd. C 65.56, H 4.89, N 4.25, Cl 10.75; found C 65.39, H 5.01, N 4.14, Cl 10.66.

5-Methoxy-4-(3-methoxybenzyl)-2-phenyl-1,3-oxazole (9): In a Schlenk flask **8** (45 mg, 0.14 mmol) was dissolved in toluene (2.5 ml). Then phosphoryl chloride (0.45 ml, 0.74 g, 4.83 mmol) was added *via* syringe and the reaction mixture was heated at 100 °C for 2.5 h. After cooling to r.t., the mixture was poured into an ice-cold saturated NaHCO₃ solution (35 ml). The reaction mixture was warmed to r.t., stirred for a further 10 min and was then extracted with toluene (1 × 15 ml) and dichloromethane (3 × 30 ml). The combined organic layers were washed with brine (2 × 40 ml), dried (Na₂SO₄), and concentrated. The residual yellow oil was purified by chromatography on silica gel with hexanes/EtOAc (3 : 1, *R*_f = 0.62) to give **9** as a colorless oil (27 mg, 0.091 mmol, 63%). – IR (ATR): ν = 2941, 1654 (N=C), 1599 (C=C), 1487, 1450, 1358, 1260 (C-O), 1147, 1047, 982, 769, 689 cm⁻¹. – ¹H NMR (500.15 MHz, CDCl₃): δ = 3.79 (s, 3 H, C₆H₄OCH₃), 3.81 (s, 2 H, MeOC₆H₄CH₂), 3.95 (s, 3 H, OCH₃), 6.75 (dd, *J* = 8.2 Hz, *J* = 2.5 Hz, 1 H, 3'-H), 6.89–6.91 (m, 2 H, 7'-H, 5'-H), 7.21 (t, *J* = 7.9 Hz, 1 H, 6'-H), 7.37–7.42 (m, 3 H, *m*-, *p*-Ph), 7.84 (d, *J* = 8.5 Hz, 2 H, *o*-Ph), 7.91–7.93 (dd, *J* = 7.9 Hz, *J* = 1.6 Hz, 2 H, *o*-Ph). – ¹³C NMR (125.76 MHz, CDCl₃): δ = 31.0 (MeOC₆H₄CH₂), 55.2 (C₆H₄OCH₃), 61.1 (OCH₃), 111.6 (C-3'), 114.3 (C-7', C-5'), 116.3 (C-4), 120.9 (C-7', C-5'), 125.5 (*o*-Ph), 127.7 (*i*-Ph), 128.6 (*m*-, *p*-Ph), 129.4 (C-6'), 129.6 (*m*-, *p*-Ph), 141.0 (C-2'), 152.2, 155.4, 159.7 (C-2, C-4, C-4'). – MS (EI, 70 eV): *m/z* (%) 295 [M⁺] (100), 294 (24), 252 [M⁺ –

COCH₃] (11), 236 [M⁺ – CO₂CH₃] (32), 234 (8), 209 (9), 192 (3), 179 (5), 147 (5), 133 (5), 121 [H₃COC₆H₄CH₂⁺] (4), 105 [C(O)Ph⁺] (95), 103 (8), 91 [C₇H₇⁺] (3), 77 (10), 51 (2). – HRMS (EI, 70 eV): calcd. for C₁₈H₁₇NO₃ 295.1208, found 295.1207 [M⁺]. – C₁₈H₁₇NO₃ (295.3): calcd. C 73.20, H 5.80, N 4.74; found C 73.00, H 5.96, N 4.60.

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