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3-ARYL-3,4-DIHYDROISOCOUMARINS WITH AMINO-ACID FRAGMENTS

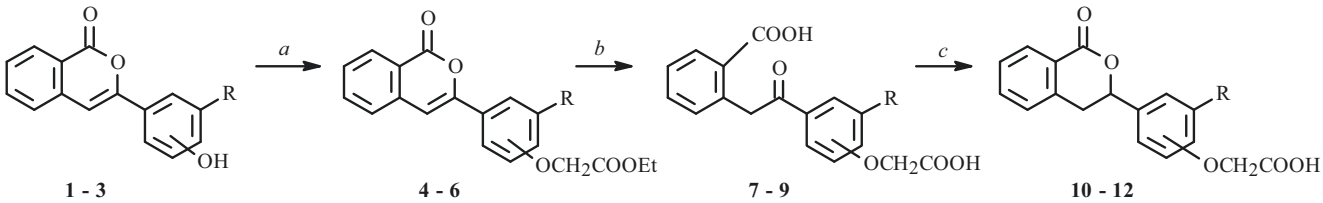
S. V. Shilin, O. V. Shablykina,* V. V. Ishchenko, Yu. N. Zabolotnaya, and V. P. Khilya

New amino-acid derivatives of 3-aryl-3,4-dihydroisocoumarins were prepared via acylation of the amine of natural amino acids by phenoxyacetic acids containing 3,4-dihydroisocoumarin substituents on the benzene ring.

Keywords: isocoumarins, dihydroisocoumarins, 3-aryl-3,4-dihydroisocoumarins, activated esters method, *N*-hydroxysuccinimide, amino-acid derivatives.

In continuation of research on new syntheses of isocoumarins modified by natural amino-acid fragments [1], we focused on 3,4-dihydroisocoumarin derivatives mainly because natural compounds with the 1-oxoisochromane core are dominated by saturated species [2]. Dihydroisocoumarins in living subjects can be associated with their unsaturated analogs, e.g., glycosides of dihydrohomalicine and homalicine [3], the aglycons of which are 3-(3-hydroxyphenyl)-3,4-dihydroisocoumarin and 3-(3-hydroxyphenyl)isocoumarin, respectively. According to recent reports [4, 5], dihydroisocoumarins are often encountered among compounds produced by fungal microorganisms. Furthermore, ochratoxin A [6] and amicoumacin B [7], two of few known natural isocoumarins with amino-acid fragments, also contain a 3,4-dihydroisocoumarin ring and are characterized by high biological activity.

Starting 3-phenyl-3,4-dihydroisocoumarins **10–12** with a hydroxyacetic-acid fragment as a linker for attaching amino acids were synthesized by known methods [8] using an equivalent amount of ethyl chloroacetate instead of methyl bromoacetate as indicated in the article (Scheme 1).



1: 4-OH, R = H; **2:** 4-OH, R = CH_3; **3:** 2-OH, R = CH_3; **4:** 4-OCH_2COOEt, R = H; **5:** 4-OCH_2COOEt, R = CH_3
6: 2-OCH_2COOEt, R = CH_3; **7, 10:** 4-OCH_2COOH, R = H; **8, 11:** 4-OCH_2COOH, R = CH_3; **9, 12:** 2-OCH_2COOH, R = CH_3

a. $ClCH_2COOEt$, K_2CO_3, Me_2CO; *b*. 1. OH^-, 2. H^+; *c*. 1. $NaBH_4$, 2. H^+

Scheme 1

Activated esters [9, 10] were used as before [1] to attach amino acids to the carboxylic group of **10**–**12** through an amide bond. Thus, the acid group to be modified was converted to the *N*-hydroxysuccinimide (SuOH) ester (Scheme 2).

The resulting esters **13**–**15** reacted with an optically pure natural L-amino acid to give *N*-acyl amino-acid derivatives **16**–**18** (Table 1).

Taras Shevchenko Kiev National University, 64/13 Vladimirskaya St., Kiev, 01601, Ukraine, e-mail: shablykina@ukr.net. Translated from *Khimiya Prirodnykh Soedinenii*, No. 4, July–August, 2016, pp. 516–521, original article submitted September 30, 2015.

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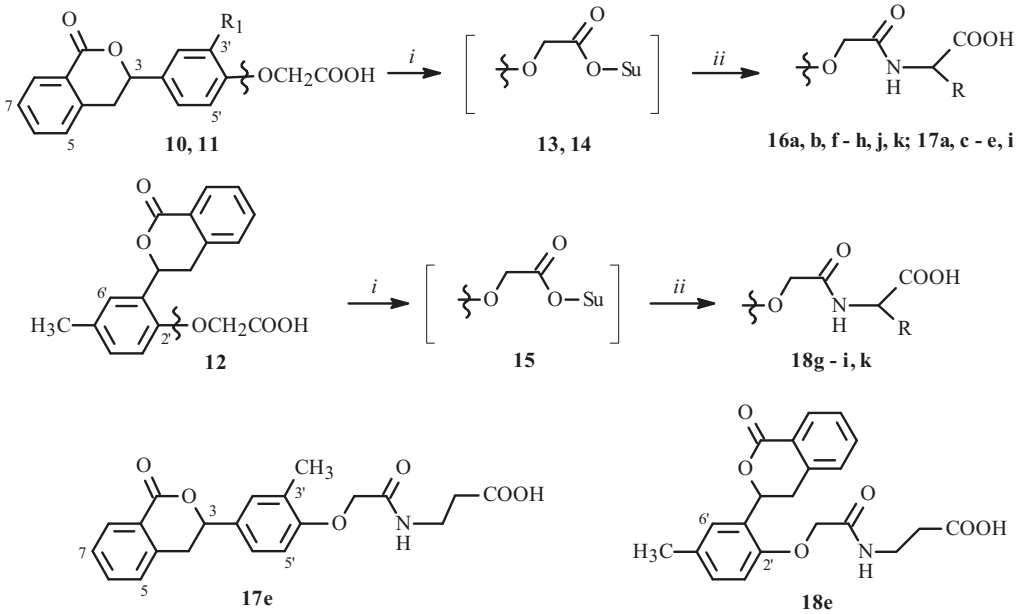
TABLE 1. Yields and Melting Points of **16**–**18**

Amino acid	Compound	mp,°C	Yield, %	Compound	mp,°C	Yield, %	Compound	mp,°C	Yield, %
Glycine	**16a**	206–207	78	**17a**	237–238	44			
Alanine	**16b**	176–177	57						
Leucine				**17c**	196–197	65			
Norleucine				**17d**	177–178	69			
β-Alanine				**17e**	92–93	74	**18e**	144–145	70
Phenylalanine	**16f**	169–170	69						
Tyrosine	**16g**	123–124	40				**18g**	147–148	53
Tryptophan	**16h**	178–179	78				**18h**	205–206	69
Methionine				**17i**	186–187	69	**18i**	88–89	66
Asparagine	**16j**	169–170	73						
Citrulline	**16k**	159–160	27				**18k**	157–158	57



16a, 17a: R = H; **16b:** R = CH_3; **17c:** R = $CH_2CH(CH_3)_2$; **17d:** R = $(CH_2)_3CH_3$; **16f:** R = CH_2Ph; **16g, 18g:** R = $CH_2(4\text{-}HOC_6H_4)$
16h, 18h: R = CH_2(indol-3-yl); **17i, 18i:** R = $CH_2CH_2SCH_3$; **16j:** R = CH_2CONH_2; **16k, 18k:** R = $(CH_2)_3NHCONH_2$
10, 13, 16: R_1 = H; **11, 14, 17:** R_1 = CH_3

i. 1. DCC, anhydr. dioxane, RT, 2. SuOH; *ii*. 1. amino acid, $NaHCO_3$, dioxane – H_2O (1:1), RT, 2. HCl

Scheme 2

An advantage of the modified activated-ester method used by us was the ability to carry out the two-step synthesis of the amino-acid derivatives without isolating intermediate succinimide esters **13**–**15**. The completion of their formation was monitored using TLC. TLC also indicated that the conversion was high and side products did not form during the transformation of **13**–**15** into **16**–**18**.

Yields of the derivatives were low in several instances. This was related primarily to specifics of the isolation of these products. Thus, the dicyclohexylurea formed from dicyclohexylcarbodiimide (DCC) was filtered off before amino-acid derivatives **16**–**18** were precipitated according to the procedure in the Experimental section. This led to partial loss of the target compound for slightly soluble compounds (e.g., tyrosine derivatives) and those precipitating from the reaction mixture simultaneously with the urea.

Conversely, the main losses of products that were highly soluble in aqueous solutions (in particular, citrulline derivatives) occurred during their isolation in the last step, i.e., crystallization from weakly acidic aqueous solutions. Of course, the target compounds could be isolated by extraction from aqueous solutions. However, separation of them from other organic components was problematical (chromatography of amino-acid derivatives with a free carboxylic acid is extremely difficult). Thus, the simplicity of the procedure used by us compensated fully in several instances for the slight quantitative losses.

Structural changes on going from the (isocoumarinyl)phenoxyacetic acids described by us [1] to the (3,4-dihydroisocoumarinyl)phenoxyacetic acids presented herein could affect considerably the activity of the carboxylic acid, which could not lie in the same plane with the phenoxyl fragment because the isochromone 3- and 4-positions were saturated. The reactivity and, as a result, the time required to form the activated ester of **10**, in which the carboxylic acid was distant from the isochromanone substituent, were practically the same as those for the unsaturated analog. We found that **10**, like the corresponding isocoumarin derivative [1], reacted completely with *N*-hydroxysuccinimide in 2–3 h and produced activated ester **13**.

A different picture was observed for compounds with an isochromone substituent in the position *ortho* to the hydroxyacetic acid on the phenyl ring. [4-Methyl-2-(3,4-dihydroisocoumarin-3-yl)phenoxy]acetic acid (**12**) was significantly more active than [4-methyl-2-(isocoumarin-3-yl)phenoxy]acetic acid. The activated ester of dihydroisocoumarin **12** required 3–4 h to form (Experimental section) whereas at least 96 h were required for the conversion into the ester of the corresponding acid with an isocoumarin fragment [1].

Racemates of dihydroisocoumarins **10**–**12** were formed from the reactions of **7**–**9** with $NaBH_4$. Therefore, subsequent addition of the optically pure amino acid should produce a mixture of diastereomers. However, as a rule, PMR spectra of **16**–**18** had only one set of resonances because the chemical shifts (CSs) of the isomers were obviously the same. Instances where resonances of certain protons were more complicated were explained completely by steric hindrance to rotation around single bonds because they were observed in spectra of compounds with rather bulky *ortho* substituents. For example, methylene resonances of hydroxyacetic acids in PMR spectra of **17c**, **18g**, **i**, and **k** were rather broad multiplets (Experimental section) although this group appeared in spectra of most compounds as a narrow 2H singlet. ^{13}C NMR spectra of all amino-acid dihydroisocoumarin derivatives **16**–**18** also showed one set of resonances. Resonances of C-3 and C-4 of the 3,4-dihydroisocoumarin ring (67 and 34 ppm, respectively) were characteristic of these heterocyclic systems. Resonances of carboxylic acids fell in the range 165–174 ppm. The hydroxyacetic-acid methylene CS depended on its position on the phenyl ring and was 78–79 ppm for **16** and **17** with the *para*-position and 74–75 ppm for *ortho* derivatives **18**. IR spectra given in the Experimental section were also typical of this class of compounds and confirmed their structures. In particular, a strong broad carboxylic-acid absorption band (1730–1700 cm^{-1} with a maximum at 1720 as a rule) and strong absorption bands of single C–O bonds (~1240 and 1120 cm^{-1}) were consistently observed.

EXPERIMENTAL

The course of reactions and purity of products were monitored by TLC on Merck 60 F_{254} plates using $CHCl_3$–MeOH (9:1). Melting points were measured on a Kofler apparatus. NMR spectra were recorded on a Varian Mercury-400 spectrometer vs. TMS (internal standard) (Scheme 2 shows the proton numbering). IR spectra were taken on a PerkinElmer BX II spectrometer. Elemental analyses were obtained using a Vario Micro Cube instrument and agreed with those calculated.

The method for synthesizing **10**–**12** was published [8] and also gives the yields, melting points, elemental analyses, mass spectra, and PMR spectra of **10** and **12** and their synthetic intermediates **7** and **9**.

Ethyl 2-[4-(1-Oxo-1*H*-isochromen-3-yl)phenoxy]acetate (4). Yield 86%, mp 100–101°C. IR spectrum (KBr, ν, cm^{-1}): 3433 (br), 3052, 2981, 1747, 1726, 1634, 1604, 1514, 1314, 1299, 1238, 1207, 1184, 1072, 1027, 1013, 845, 825, 753, 689. ^1H NMR spectrum (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 1.31 (3H, t, J = 7.2, $CH_2C\underline{H}_3$), 4.22 (2H, q, J = 7.2, $C\underline{H}_2CH_3$), 4.75 (2H, s, 4′-OCH_2), 7.02 (2H, d, J = 8.4, H-3′, 5′), 7.16 (1H, s, H-4), 7.49 (1H, t, J = 7.6, H-7), 7.59 (1H, d, J = 7.6, H-5), 7.75 (1H, t, J = 7.6, H-6), 7.85 (2H, d, J = 8.4, H-2′, 6′), 8.16 (1H, d, J = 7.6, H-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 14.7, 33.5, 61.4, 65.4, 101.3, 115.7, 120.1, 125.4, 126.9, 127.2, 128.7, 129.4, 135.9, 138.2, 153.1, 159.7, 162.0, 169.1.

Ethyl 2-[2-Methyl-4-(1-oxo-1*H*-isochromen-3-yl)phenoxy]acetate (5). Yield 92%, mp 198–199°C. IR spectrum (KBr, ν, cm^{-1}): 3432 (br), 3080, 3063, 2976, 2924, 2910, 1758, 1730, 1633, 1606, 1564, 1507, 1481, 1430, 1334, 1295, 1267, 1243, 1209, 1145, 1081, 1026, 957, 887, 820, 799, 756, 689. ^1H NMR spectrum (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 1.30 (3H, t, J = 8.0, $CH_2C\underline{H}_3$), 2.33 (3H, s, CH_3-3′), 4.22 (2H, q, J = 8.0, $C\underline{H}_2CH_3$), 4.81 (2H, s, 4′-OCH_2), 6.92 (1H, d, J = 7.6, H-5′), 7.22 (1H, s, H-4), 7.52 (1H, t, J = 7.6, H-7), 7.62 (1H, d, J = 7.6, H-5), 7.68–7.72 (2H, m, H-2′, 6′), 7.80 (1H, t, J = 7.6, H-6), 8.15 (1H, d, J = 7.6, H-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 14.7, 16.7, 61.4, 65.6, 101.1, 112.4, 120.0, 124.7, 124.9, 126.9, 127.4, 127.9, 128.7, 129.5, 136.0, 138.3, 153.3, 157.9, 162.1, 169.2.

Ethyl 2-[4-Methyl-2-(1-oxo-1*H*-isochromen-3-yl)phenoxy]acetate (6). Yield 78%, mp 134–135°C. IR spectrum (KBr, ν, cm^{-1}): 3422 (br), 3112, 1034, 2986, 2925, 1757, 1720 (br), 1621, 1603, 1563, 1504, 1478, 1448, 1408, 1384, 1339, 1323, 1286, 1262, 1244, 1211 (br), 1150, 1083, 1034, 1017, 949, 884, 858, 797, 785, 767, 693. ^{1}H NMR spectrum (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 1.25 (3H, t, J = 7.0, $CH_2C\underline{H}_3$), 2.28 (3H, s, CH_3-5′), 4.23 (2H, q, J = 7.0, $C\underline{H}_2CH_3$), 4.83 (2H, s, 2′-OCH_2), 6.94 (1H, d, J = 8.0, H-3′), 7.15 (1H, br.d, J = 8.0, H-4′), 7.52–7.59 (3H, m, H-5, 7, 6′), 7.75 (1H, s, H-4), 7.80 (1H, t, J = 7.8, H-6), 8.13 (1H, d, J = 7.8, H-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 14.7, 20.7, 61.5, 66.0, 107.8, 113.6, 120.5, 127.2, 128.6, 129.0, 129.3, 130.8, 131.8, 135.7, 138.3, 150.0, 153.8, 162.0, 169.0.

2-[2-(4-Carboxymethoxy-3-methylphenyl)-2-oxoethyl]benzoic Acid (8). Yield 83%, mp 162–163°C. IR spectrum (KBr, ν, cm^{-1}): 3449 (br), 2915, 2563 (br), 1727, 1688, 1602, 1500, 1433, 1379, 1330, 1242, 1217, 1137, 1082, 928, 803, 786, 730, 650. ^{1}H NMR spectrum (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 2.31 (3H, s, CH_3-3′), 4.67 (2H, s, CH_2), 4.75 (2H, s, CH_2), 6.89 (1H, d, J = 8.0, H-5′), 7.25 (1H, d, J = 7.6, H-3), 7.36 (1H, t, J = 7.6, H-5), 7.49 (1H, t, J = 7.6, H-4), 7.82 (1H, br.s, H-2′), 7.86 (1H, br.d, J = 8.0, H-6′), 7.96 (1H, d, J = 7.6, H-6), 12.58 (2H, br.s, 2 COOH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 16.7, 44.8, 65.5, 111.5, 126.8, 127.5, 128.6, 130.6, 131.1, 131.2, 131.4, 132.5, 133.4, 138.0, 160.4, 169.0, 170.6.

2-[2-Methyl-4-(1-oxo-1*H*-isochroman-3-yl)phenoxy]acetic Acid (11). Yield 87%, mp 153–154°C. IR spectrum (KBr, ν, cm^{-1}): 3449 (br), 3120, 3075 (br), 2946, 2907, 1734 (br), 1690 (br), 1607, 1510, 1460, 1423, 1365, 1341, 1275 (br), 1231 (br), 1128, 1082, 987, 914, 896, 831, 806, 751, 736, 696, 656, 644. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 2.23 (3H, s, CH_3-3′), 3.16 (1H, dd, J = 16.4, 2.1, H-4α), 3.40 (1H, dd, J = 16.4, 12.0, H-4β), 4.74 (2H, s, CH_2O-4′), 5.60 (1H, dd, J = 12.0, 2.1, H-3), 6.90 (1H, d, J = 7.8, H-5′), 7.28 (1H, br.d, J = 7.8, H-6′), 7.34 (1H, br.s, H-2′), 7.43 (1H, d, J = 7.6, H-5), 7.47 (1H, t, J = 7.6, H-7), 7.65 (1H, t, J = 7.6, H-6), 7.98 (1H, d, J = 7.6, H-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 16.8, 34.6, 65.5, 79.9, 111.8, 125.4, 126.0, 126.8, 128.2, 128.5, 129.7, 130.0, 131.7, 134.6, 140.4, 156.7, 165.4, 170.9.

General Synthesis of Amino-acid Derivatives 16–18. A solution of the acid (**10**–**12**, 2 mmol) and SuOH (0.26 g, 2.2 mmol) in anhydrous dioxane (20 mL) at room temperature was stirred vigorously, treated with DCC (0.46 g, 2.2 mmol), and stirred at room temperature for 2–3 h (**16** and **17**) or 3–4 h (**18**) (course of reactions monitored by TLC). The resulting activated ester was added to a solution of the appropriate amino acid (2.2 mmol) and $NaHCO_3$ (0.28 g) in H_2O (20 mL). The mixture was stirred at room temperature for 2 h with TLC monitoring of the reaction. The precipitate of dicyclohexylurea was filtered off. The filtrate was poured into H_2O (100 mL). The resulting solution was acidified with dilute HCl until weakly acidic. The resulting precipitate was filtered off and recrystallized from *i*-PrOH.

***N*-{2-[4-(1-Oxoisochroman-3-yl)phenoxy]acetyl}glycine (16a).** IR spectrum (KBr, ν, cm^{-1}): 3393 (br), 3319, 3059 (br), 2937, 2861, 1764, 1708, 1648, 1613, 1557, 1515, 1460, 1450, 1412, 1291, 1249, 1193, 1124, 1077, 1032, 1006, 834, 750, 692. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 3.16 (1H, dd, J = 16.4, 2.6, H-4α), 3.39 (1H, dd, J = 16.4, 12.0, H-4β), 3.83 (2H, d, J = 4.0, $C\underline{H}_2$COOH), 4.56 (2H, s, CH_2O-4′), 5.56 (1H, dd, J = 12.0, 2.6, H-3), 7.03 (2H, d, J = 8.4, H-3′, 5′), 7.39–7.51 (4H, m, H-5, 7, 2′, 6′), 7.64 (1H, t, J = 7.6, H-6), 7.97 (1H, d, J = 7.6, H-8), 8.41 (1H, br.t, J = 4.0, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 34.6, 41.1, 67.5, 79.8, 115.4, 125.4, 128.3, 128.5, 128.7, 130.1, 132.4, 134.6, 140.4, 158.4, 165.4, 168.7, 171.7.

***N*-{2-[4-(1-Oxoisochroman-3-yl)phenoxy]acetyl}alanine (16b).** IR spectrum (KBr, ν, cm^{-1}): 3389 (br), 3042, 2993, 2928, 2611, 2540, 1728, 1711, 1627, 1546, 1517, 1461, 1438, 1370, 1348, 1278, 1249, 1221, 1183, 1122, 1087, 1011, 998, 913, 857, 825, 800, 742, 692. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 1.37 (1H, d, J = 7.2, CH[C$\underline{H}_3$]COOH), 3.17 (1H, br.d, J = 16.4, H-4α), 3.34 (1H, dd, J = 16.4, 12.0, H-4β), 4.33 (1H, m, C$\underline{H}$[CH_3]COOH), 4.49 (2H, s, CH_2O-4′), 5.56 (1H, br.d, J = 16.4, H-3), 7.00 (2H, d, J = 8.0, H-3′, 5′), 7.37 (1H, d, J = 7.6, H-5), 7.40–7.45 (3H, m, H-7, 2′, 6′), 7.59 (1H, t, J = 7.6, H-6), 7.98 (1H, d, J = 7.6, H-8), 8.10 (1H, br.d, J = 7.6, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 16.97, 33.8, 47.13, 66.6, 78.9, 124.6, 127.7, 114.6, 127.4, 127.9, 129.2, 131.4, 133.8, 139.6, 157.7, 164.6, 167.2, 173.64.

***N*-{2-[4-(1-Oxoisochroman-3-yl)phenoxy]acetyl}phenylalanine (16f).** IR spectrum (KBr, ν, cm^{-1}): 3420 (br), 3382, 3028, 3068, 2928, 2866, 2531 (br), 1721, 1711, 1630, 1459, 1429, 1348, 1248, 1226, 1184, 1122, 1086, 1070, 1031, 1012, 914, 826, 740, 703. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 3.02 (1H, dd, J = 13.6, 8.8, CH[C$\underline{H}_\alpha$Ph]COOH), 3.11–3.20 (2H, m, CH[C$\underline{H}_\beta$Ph]COOH, H-4α), 3.34 (1H, dd, J = 16.0, 12.0, H-4β), 4.45 (2H, s, CH_2O-4′), 4.56 (2H, m, C$\underline{H}$[Bn]COOH), 5.56 (1H, dd, J = 12.0, 2.4, H-3), 6.91 (2H, d, J = 8.4, H-3′, 5′), 7.18–7.26 (5H, m,

*The amino-acid COOH proton resonance was not observed in PMR spectra because of exchange.

CH[CH_2Ph]COOH), 7.37–7.46 (5H, m, H-7, 5, 2′, 6′), 7.60 (1H, t, J = 8.0, H-6), 7.98–8.03 (2H, m, NH, H-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 33.8, 36.4, 52.9, 66.6, 78.9, 114.5, 124.7, 126.3, 127.4, 127.8, 128.0, 128.9, 129.2, 131.5, 133.7, 137.3, 139.5, 157.7, 164.5, 167.4, 172.5.

***N*-{2-[4-(1-Oxoisochroman-3-yl)phenoxy]acetyl}tyrosine (16g).** IR spectrum (KBr, ν, cm^{-1}): 3430, 3070, 3033, 2934, 2862, 2743, 1719, 1690, 1666, 1613, 1531, 1517, 1461, 1444, 1349, 1298, 1279, 1221, 1179, 1126, 1072, 990, 836, 742. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.86 (1H, dd, J = 13.2, 9.2, CH[C$\underline{H}_\alpha$(4-HOC_6H_4)]COOH), 3.00 (1H, dd, J = 13.2, 4.4, CH[C$\underline{H}_\beta$(4-HOC_6H_4)]COOH), 3.18 (1H, br.d, J = 16.8, H-4*α*), 3.35 (1H, dd, J = 16.8, 10.8, H-4*β*), 4.41–4.47 (1H, m, CH[C$\underline{H}_2$(4-HOC_6H_4)]COOH), 4.50 (2H, s, CH_2O-4′), 5.63 (1H, br.d, J = 10.8, H-3), 6.65 (2H, d, J = 8.0, H-3″, 5″ (4-HOC_6H_4)), 6.91 (2H, d, J = 7.2, H-3′, 5′), 7.00 (2H, d, J = 8.0, H-2″, 6″ (4-HOC_6H_4)), 7.24–7.50 (4H, m, H-5, 7, 2′, 6′), 7.67 (1H, t, J = 7.2, H-6), 7.98 (1H, d, J = 7.2, H-8), 8.21 (1H, br.d, J = 6.0, NH), 9.25 (1H, br.s, 4-$\underline{H}$OC_6H_4). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 34.6, 36.4, 54.0, 67.2, 79.8, 115.3, 115.7, 125.4, 128.1, 128.3, 128.6, 128.7, 130.1, 130.8, 132.2, 134.6, 140.5, 156.6, 158.5, 165.4, 168.1, 173.5.

***N*-{2-[4-(1-Oxoisochroman-3-yl)phenoxy]acetyl}tryptophan (16h).** IR spectrum (KBr, ν, cm^{-1}): 3464, 3411 (br), 3382, 3062, 2938, 2910, 2866, 2533 (br), 1719, 1711, 1629, 1612, 1546, 1516, 1460, 1426, 1365, 1355, 1338, 1294, 1278, 1249, 1222, 1184, 1122, 1087, 1069, 1011, 824, 755, 745. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 3.12–3.19 (2H, m, H-4*α*, CH[C$\underline{H}_\alpha$(indol-3-yl)]COOH), 3.25 (1H, dd, J = 14.0, 4.8, CH[C$\underline{H}_\beta$(indol-3-yl)]COOH), 3.42 (1H, dd, J = 16.4, 12.0, H-4*β*), 4.51 (2H, s, CH_2O-4′), 4.55–4.58 (1H, m, C$\underline{H}$[CH_2(indol-3-yl)]COOH), 5.63 (1H, dd, J = 12.0, 2.0, H-3), 6.91 (2H, d, J = 8.4, H-3′, 5′), 6.98 (1H, t, J = 7.2, H-5″ (indol-3-yl)), 7.07 (1H, t, J = 7.2, H-6″ (indol-3-yl)), 7.14 (1H, br.s, H-2″), 7.35 (1H, d, J = 7.6, H-4″), 7.40–7.50 (4H, m, 5, 7, 2′, 6′), 7.56 (1H, d, J = 7.6, H-7″), 7.67 (1H, t, J = 7.6, H-6), 7.99 (1H, d, J = 7.6, H-8), 8.20 (1H, br.d, J = 6.8, NH), 10.89 (1H, s, NH (indol-3-yl)). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 26.7, 33.8, 52.6, 66.5, 78.9, 109.5, 111.3, 114.5, 118.0, 118.3, 120.8, 123.6, 124.6, 127.1, 127.4, 127.7, 127.8, 129.2, 131.4, 133.8, 136.0, 139.6, 157.6, 164.6, 167.3, 172.9.

***N*-{2-[4-(1-Oxoisochroman-3-yl)phenoxy]acetyl}asparagine (16j).** IR spectrum (KBr, ν, cm^{-1}): 3406 (br), 3076, 2928, 2857, 1720 (br), 1676 (br), 1608, 1534, 1502, 1460, 1438 (br), 1276 (br), 1229 (br), 1117, 1086, 1070, 1032, 996, 807, 749, 693. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 2.56–2.61 (1H, m, CH[C$\underline{H}_\alpha$$CONH_2$]COOH), 2.67–2.72 (1H, m, CH[C$\underline{H}_\beta$$CONH_2$]COOH), 3.18 (1H, br.d, J = 16.8, H-4*α*), 3.34 (1H, dd, J = 16.8, 12.0, H-4*β*), 4.51 (2H, m, CH_2O-4′), 4.58 (1H, m, C$\underline{H}$[CH_2CONH_2]COOH), 5.56 (1H, br.d, J = 12.0, H-3), 5.95 (1H, br.s, CH[CH_2CON$\underline{H}_\alpha$]COOH), 7.01 (2H, br.d, J = 7.2, H-3′, 5′), 7.38–7.45 (5H, m, H-5, 7, 2′, 6′, CH[CH_2CON$\underline{H}_\beta$]COOH), 7.59 (1H, t, J = 7.2, H-6), 7.98 (1H, d, J = 7.2, H-8), 8.19 (1H, br.d, J = 6.8, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 34.6, 37.0, 49.2, 67.6, 79.7, 115.5, 125.4, 128.3, 128.5, 128.7, 130.1, 132.4, 134.6, 140.4, 158.4, 165.4, 168.1, 172.3, 173.1.

***N*-{2-[4-(1-Oxoisochroman-3-yl)phenoxy]acetyl}citrulline (16k).** IR spectrum (KBr, ν, cm^{-1}): 3465, 3388, 3333 (br), 3069, 2928, 2878, 2594, 2548, 1721, 1642 (br), 1589, 1552, 1515, 1460, 1432, 1370, 1349, 1278, 1249, 1184, 1122, 1087, 1071, 1006, 913, 894, 822, 740, 691. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 1.42 (2H, m, CH[CH_2C$\underline{H}_2$$CH_2$NHCO$NH_2$]COOH), 1.68 (1H, m, CH[C$\underline{H}_\alpha$$(CH_2)_2$NHCO$NH_2$]COOH), 1.80 (1H, m, CH[C$\underline{H}_\beta$$(CH_2)_2$NHCO$NH_2$]COOH), 2.99 (2H, m, CH[$(CH_2)_2C\underline{H}_2$NHCO$NH_2$]COOH), 3.19 (1H, br.d, J = 16.4, H-4*α*), 3.35 (1H, dd, J = 16.4, 10.8, H-4*β*), 4.31 (2H, br.s, NHCON$\underline{H}_2$), 4.54 (2H, m, CH_2O-4′), 5.57 (1H, br.d, J = 10.8, H-3), 5.95 (1H, br.s, N$\underline{H}$CONH_2), 7.01 (2H, d, J = 7.6, H-3′, 5′), 7.38–7.45 (4H, m, H-5, 7, 2′, 6′), 7.61 (1H, t, J = 7.2, H-6), 7.98 (1H, d, J = 7.2, H-8), 8.10 (1H, br.d, J = 6.8, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 27.4, 29.1, 34.0, 34.6, 52.3, 67.4, 79.8, 115.4, 125.4, 128.3, 128.5, 128.7, 130.1, 132.23, 134.6, 140.5, 158.5, 159.5, 165.4, 168.3, 174.1.

***N*-{2-[2-Methyl-4-(1-oxoisochroman-3-yl)phenoxy]acetyl}glycine (17a).** IR spectrum (KBr, ν, cm^{-1}): 3397 (br), 2926 (br), 2737, 2624, 2539, 1723 (br), 1630 (br), 1547, 1512, 1460, 1422, 1347, 1267 (br), 1227 (br), 1145, 1120, 1069, 1011, 990, 912, 889, 813, 770, 736, 692. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 2.27 (3H, s, CH_3-3′), 3.16 (1H, br.d, J = 16.8, H-4*α*), 3.39 (1H, m, H-4*β*), 3.84 (2H, br.d, J = 4.2, C$\underline{H}_2$COOH), 4.58 (2H, s, CH_2O-4′), 5.60 (1H, br.d, J = 9.6, H-3), 6.92 (1H, d, J = 7.8, H-5′), 7.29 (1H, br.d, J = 7.8, H-6′), 7.35 (1H, br.s, H-2′), 7.42–7.49 (2H, m, H-5, 7), 7.65 (1H, t, J = 7.2, H-6), 7.97 (1H, d, J = 7.2, H-8), 8.23 (1H, br.t, J = 4.2, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 16.9, 34.6, 41.2, 67.8, 79.8, 112.2, 125.4, 126.0, 127.0, 128.3, 128.5, 129.7, 130.1, 132.0, 134.6, 140.4, 156.5, 165.4, 168.9, 171.7.

***N*-{2-[2-Methyl-4-(1-oxoisochroman-3-yl)phenoxy]acetyl}leucine (17c).** IR spectrum (KBr, ν, cm^{-1}): 3382 (br), 3070, 2959, 2871, 2733, 2531 (br), 1719 (br), 1624 (br), 1543, 1508, 1460, 1431, 1368, 1346, 1273, 1230, 1138, 1121, 1072, 1032, 994, 913, 812, 737, 692. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 0.84 (6H, d, J = 6.0, CH[CH_2CH(C$\underline{H}_3$)$_\alpha$]COOH), 0.88 (6H, d, J = 6.0, CH[CH_2CH(C$\underline{H}_3$)$_\beta$]COOH), 1.52–1.63 (3H, m, CH[C$\underline{H}_2$C$\underline{H}$$(CH_3)_2$]COOH),

2.25 (3H, s, CH_3-3′), 3.16 (1H, dd, J = 16.4, J = 2.8, H-4α), 3.32 (1H, dd, J = 16.4, 11.6, H-4β), 4.28 (1H, m, C<u>H</u>[*i*-Bu]COOH), 4.53–4.64 (2H, m, CH_2O-4′), 5.51 (1H, dd, J = 11.6, 2.8, H-3), 6.87 (1H, d, J = 7.6, H-5′), 7.26 (1H, br.d, J = 7.6, H-6′), 7.34 (1H, br.s, H-2′), 7.42–7.49 (2H, m, H-5, 7), 7.65 (1H, t, J = 7.2, H-6), 7.97 (1H, d, J = 7.2, H-8), 8.19 (1H, br.d, J = 7.2, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 16.9, 22.1, 23.6, 25.1, 34.7, 50.9, 67.7, 79.8, 112.1, 125.4, 125.9, 126.8, 128.3, 128.5, 129.6, 130.0, 131.9, 134.6, 140.4, 156.7, 165.4, 168.2, 174.7.

***N*-{2-[2-Methyl-4-(1-oxoisochroman-3-yl)phenoxy]acetyl}norleucine (17d).** IR spectrum (KBr, ν, cm^{-1}): 3420 (br), 3385, 2958, 2933, 2864, 2539 (br), 1720, 1630, 1542, 1460, 1440, 1370, 1349, 1277, 1230, 1137, 1122, 1087, 812, 740, 690. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 0.90 (3H, m, CH[$(CH_2)_3C\underline{H}_3$]COOH), 1.30 (4H, m, CH[$CH_2(C\underline{H}_2)_2CH_3$]COOH), 1.68 (1H, m, CH[$C\underline{H}_\alpha(CH_2)_2CH_3$]COOH), 1.79 (1H, m, CH[$C\underline{H}_\beta(CH_2)_2CH_3$]COOH), 2.31 (3H, s, CH_3-3′), 3.16 (1H, m, H-4α), 3.32 (1H, dd, J = 15.6, 12.0, H-4β), 4.29 (1H, m, C<u>H</u>[*n*-Bu]COOH), 4.53 (2H, s, CH_2O-4′), 5.51 (1H, dd, J = 12.0, J = 1.8, H-3), 6.86 (1H, d, J = 8.0, H-5′), 7.24 (1H, br.d, J = 8.0, H-6′), 7.29 (1H, br.s, H-2′), 7.37 (1H, d, J = 7.6, H-5), 7.43 (1H, t, J = 7.6, H-7), 7.60 (1H, t, J = 7.6, H-6), 7.89 (1H, br.d, J = 6.8, NH), 7.97 (1H, d, J = 7.6, H-8). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 13.6, 16.0, 21.5, 27.2, 30.5, 33.8, 51.4, 66.8, 79.0, 111.3, 124.6, 125.1, 126.0, 127.4, 127.7, 128.8, 129.2, 131.1, 133.7, 139.6, 155.8, 164.6, 167.5, 173.2.

***N*-{2-[2-Methyl-4-(1-oxoisochroman-3-yl)phenoxy]acetyl}-β-alanine (17e).** IR spectrum (KBr, ν, cm^{-1}): 3481 (br), 3416 (br), 3077, 2924, 2949, 2612 (br), 1728, 1648, 1610, 1546, 1508, 1461, 1439, 1367, 1358, 1271, 1226, 1194, 1135, 1122, 1080, 1032, 1000, 955, 910, 887, 821, 780, 736, 692. ^{1}H NMR spectrum (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 2.29 (3H, s, CH_3-3′), 2.42 (2H, m, NHC<u>H</u>$_2$$CH_2$COOH), 3.15 (1H, m, H-4$\alpha$), 3.29–3.41 (3H, m, H-4$\beta$, $NHCH_2C\underline{H}_2$COOH), 4.45 (2H, s, CH_2O-4′), 5.51 (1H, dd, J = 12.0, 2.4, H-3), 6.83 (1H, d, J = 8.0, H-5′), 7.25 (1H, br.d, J = 8.0, H-6′), 7.29 (1H, br.s, H-2′), 7.37 (1H, d, J = 7.2, H-5), 7.43 (1H, t, J = 7.2, H-7), 7.60 (1H, t, J = 7.2, H-6), 7.85 (1H, br.t, J = 3.6, NH), 7.97 (1H, d, J = 7.2, H-8), 12.45 (1H, br.s, COOH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 16.0, 33.6, 33.8, 34.4, 67.1, 79.0, 111.3, 125.2, 126.13, 127.4, 127.7, 128.8, 129.2, 129.2, 131.2, 133.7, 139.5, 155.7, 164.6, 167.5, 172.9.

***N*-{2-[2-Methyl-4-(1-oxoisochroman-3-yl)phenoxy]acetyl}methionine (17i).** IR spectrum (KBr, ν, cm^{-1}): 3425 (br), 3383, 2921, 2529 (br), 1719, 1711, 1630, 1543, 1508, 1461, 1439, 1370, 1348, 1277, 1259, 1229, 1138, 1122, 1088, 1064, 1032, 952, 814, 746, 691. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 1.90–2.01 (2H, m, $CH[CH_2C\underline{H}_2SCH_3]$COOH), 2.05 (3H, m, CH[$(CH_2)_2SC\underline{H}_3$]COOH), 2.31 (3H, s, CH_3-3′), 2.45 (2H, m, CH[$C\underline{H}_2CH_2SCH_3$]COOH), 3.15 (1H, br.d, J = 16.4, H-4α), 3.33 (1H, dd, J = 16.4, 12.0, H-4β), 4.43 (1H, m, C<u>H</u>[$(CH_2)_2SCH_3$]COOH), 4.54 (2H, s, CH_2O-4′), 5.52 (1H, br.d, J = 12.0, H-3), 6.86 (1H, d, J = 8.8, H-5′), 7.25 (1H, br.d, J = 8.8, H-6′), 7.29 (1H, br.s, H-2′), 7.37 (1H, d, J = 7.6, H-5), 7.43 (1H, t, J = 7.6, H-7), 7.60 (1H, t, J = 7.6, H-6), 7.98 (1H, d, J = 7.6, H-8), 8.03 (1H, br.d, J = 6.0, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 14.4, 16.0, 29.5, 30.3, 33.8, 50.5, 66.9, 79.0, 111.3, 124.6, 125.1, 126.0, 127.4, 127.7, 128.8, 129.2, 131.1, 133.8, 139.6, 155.9, 164.6, 167.8, 172.8.

***N*-{2-[4-Methyl-2-(1-oxoisochroman-3-yl)phenoxy]acetyl}-β-alanine (18e).** IR spectrum (KBr, ν, cm^{-1}): 3433 (br), 3366, 3077, 3046, 2949, 2918, 1726, 1629, 1610, 1550, 1502, 1466, 1432, 1406, 1350, 1285, 1230, 1167, 1120, 1090, 1068, 1001, 915, 816, 753, 721, 694. ^{1}H NMR spectrum (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 2.34 (5H, m, CH_3-5′, NHC<u>H</u>$_2$$CH_2$COOH), 3.19 (1H, dd, J = 16.8, 12.0, H-4α), 3.29–3.33 (3H, m, H-4β, $NHCH_2C\underline{H}_2$COOH), 4.48 (2H, s, CH_2O-2′), 6.02 (1H, dd, J = 12.0, 2.4, H-3), 6.83 (1H, d, J = 8.0, H-3′), 7.11 (1H, br.d, J = 8.0, H-4′), 7.33 (1H, br.s, H-6′), 7.40 (1H, d, J = 7.6, H-5), 7.46 (1H, t, J = 7.6, H-7), 7.62 (1H, t, J = 7.6, H-6), 7.93 (1H, br.t, J = 6.0, NH), 8.01 (1H, d, J = 7.6, H-8), 12.09 (1H, br.s, COOH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 20.1, 33.1, 33.6, 34.4, 67.3, 74.3, 112.2, 124.5, 126.9, 127.1, 127.5, 127.7, 129.3, 129.6, 130.0, 133.8, 139.7, 152.2, 164.8, 167.5, 172.7.

***N*-{2-[4-Methyl-2-(1-oxoisochroman-3-yl)phenoxy]acetyl}tyrosine (18g).** IR spectrum (KBr, ν, cm^{-1}): 3392 (br), 3038, 2926, 2745, 2540, 1726, 1707, 1637, 1542, 1517, 1502, 1460, 1450, 1345, 1276, 1230 (br), 1120, 1066, 1032, 1011, 916, 845, 810, 748, 720, 694, 605. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.28 (3H, s, CH_3-5′), 2.67–2.81 (1H, m, CH[$C\underline{H}_\alpha(4\text{-}HOC_6H_4)$]COOH), 2.92–2.97 (1H, m, CH[$C\underline{H}_\beta(4\text{-}HOC_6H_4)$]COOH), 3.17 (1H, m, H-4$\alpha$), 3.29 (1H, m, H-4$\beta$), 4.38 (1H, m, C<u>H</u>[$CH_2(4\text{-}HOC_6H_4)$]COOH), 4.47–4.58 (2H, m, CH_2O-2′), 5.90–5.99 (1H, m, H-3), 6.55–6.59 (2H, m, H-3″, 5″ ($4\text{-}HOC_6H_4$)), 6.72 (0.4H, d, J = 8.4, H-3′), 6.75 (0.6H, d, J = 8.4, H-3′), 6.87–6.91 (2H, m, H-2″, 6″ ($4\text{-}HOC_6H_4$)), 7.09 (1H, br.d, J = 8.4, H-4′), 7.33 (1H, br.s, H-6′), 7.40 (1H, t, H-5), 7.48 (1H, t, J = 7.2, H-7), 7.65 (1H, t, J = 7.2, H-6), 8.00 (1H, d, J = 7.2, H-8), 8.14 (1H, d, J = 7.2, NH), 9.22 (1H, br.s, 4-<u>H</u>OC_6H_4). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 20.9, 34.0, 36.4, 54.2, 67.8, 75.2, 113.0, 115.7, 125.4, 127.51, 127.8, 128.0, 128.1, 128.3, 128.5, 130.1, 130.4, 130.6, 130.8, 134.6, 140.4, 153.0, 156.6, 165.5, 168.2, 173.4.

***N*-{2-[4-Methyl-2-(1-oxoisochroman-3-yl)phenoxy]acetyl}tryptophan (18h).** IR spectrum (KBr, ν, cm^{-1}): 3411 (br), 3390, 3044, 2931 (br), 1720, 1711, 1631, 1535, 1502, 1460, 1432, 1349, 1290, 1274, 1233, 1117, 1069, 812, 747, 694. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 2.27 (3H, s, CH_3-5′), 3.07 (2H, m, H-4α, CH[C$\underline{H}_\alpha$(indol-3-yl)]COOH), 3.20–3.22 (2H, m, H-4β, CH[C$\underline{H}_\beta$(indol-3-yl)]COOH), 4.43–4.62 (3H, m, CH_2O-2′, C$\underline{H}$[CH_2(indol-3-yl)]COOH), 5.83 (0.4H, m, H-3), 5.54 (0.6H, br.d, J = 10.6, H-3), 6.70–6.78 (1H, m, H-3′), 6.93 (1H, br.t, J = 7.4, H-5″ (indol-3-yl)), 6.99–7.17 (3H, m, H-4′, 2″, 6″), 7.25–7.37 (3H, m, H-5, 6′, 4″), 7.43–7.53 (2H, m, H-7, 7″), 7.65 (1H, br.t, J = 7.2, H-6), 7.98 (1H, br.s, H-8), 8.14 (1H, br.s, NH), 10.79 (1H, s, NH (indol-3-yl)). ^{13}C NMR spectrum (100 MHz, DMSO-d_6, δ, ppm): 21.0, 27.6, 33.9, 53.4, 67.8, 74.2, 110.4, 112.1, 113.0, 118.8, 119.0, 121.6, 124.2, 125.4, 127.5, 127.7, 127.9, 128.3, 128.5, 130.1, 130.3, 130.7, 134.6, 136.8, 140.4, 153.0, 165.5, 168.2, 173.7.

***N*-{2-[4-Methyl-2-(1-oxoisochroman-3-yl)phenoxy]acetyl}methionine (18i).** IR spectrum (KBr, ν, cm^{-1}): 3394 (br), 3068, 3036, 2918 (br), 2560 (br), 1726 (br), 1693, 1606, 1535, 1502, 1461, 1441, 1350, 1277, 1228, 1163, 1117, 1085, 1070, 1031, 912, 807, 748, 693. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 1.83–2.01 (5H, m, CH[CH_2C$\underline{H}_2$SC$\underline{H}_3$]COOH), 2.28–2.34 (5H, m, CH_3-5′, CH[C$\underline{H}_2$$CH_2$$SCH_3$]COOH), 3.15 (1H, m, H-4$\alpha$), 3.33 (1H, m, H-4$\beta$), 4.34 (1H, m, C$\underline{H}$[$(CH_2)_2SCH_3$]COOH), 4.52–4.70 (2H, m, CH_2O-2′), 5.59–6.05 (1H, m, H-3), 6.90 (1H, br.d, J = 8.0, H-3′), 7.13 (1H, br.d, J = 8.0, H-4′), 7.35 (1H, br.s, H-6′), 7.40–7.43 (1H, m, H-5), 7.48 (1H, t, J = 7.6, H-7), 7.66 (1H, t, J = 7.6, H-6), 7.99 (1H, d, J = 7.6, H-8), 8.24 (1H, br.t, J = 8.4, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 15.2, 21.0, 30.3, 31.1, 33.8, 34.0, 51.4, 68.0, 75.3, 113.0, 125.4, 127.7, 127.9, 128.3, 128.5, 130.1, 130.3, 130.8, 134.6, 140.5, 153.0, 165.6, 168.6, 173.7.

***N*-{2-[4-Methyl-2-(1-oxoisochroman-3-yl)phenoxy]acetyl}citrulline (18k).** IR spectrum (KBr, ν, cm^{-1}): 3503, 3442, 3407, 3356, 3037, 2926 (br), 2863, 1731, 1713, 1669, 1608, 1561, 1530, 1503, 1461, 1444, 1354, 1284, 1230, 1130, 1120, 1070, 1016, 806, 752, 692. ^{1}H NMR spectrum* (400 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm, J/Hz): 1.34 (2H, m, CH[CH_2C$\underline{H}_2$$CH_2NHCONH_2$]COOH), 1.60 (1H, m, CH[C$\underline{H}_\alpha$$(CH_2)_2NHCONH_2$]COOH), 1.74 (1H, m, CH[C$\underline{H}_\beta$$(CH_2)_2NHCONH_2$]COOH), 2.34 (3H, s, CH_3-5′), 2.91 (2H, m, CH[$(CH_2)_2$C$\underline{H}_2NHCONH_2$]COOH), 3.18 (1H, m, H-4α), 3.32 (2H, m, H-4β), 4.24 (1H, m, C$\underline{H}$[$(CH_2)_3NHCONH_2$]COOH), 4.59 (2H, m, CH_2O-2′), 5.24 (2H, br.s, NHCON$\underline{H}_2$), 5.85 (1H, br.s, N$\underline{H}$$CONH_2$), 6.00 (1H, dt, J = 10.4, 1.6, H-3), 6.86 (1H, d, J = 8.4, H-3′), 7.11 (1H, br.d, J = 8.4, H-4′), 7.34 (1H, br.s, H-6′), 7.40 (1H, d, J = 7.6, H-5), 7.45 (1H, t, J = 7.6, H-7), 7.62 (1H, t, J = 7.6, H-6), 8.00 (1H, d, J = 7.6, H-8), 8.13 (1H, br.t, J = 6.0, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6–CCl_4 1:1, δ, ppm): 20.1, 26.4, 28.2, 33.0, 33.2, 51.4, 67.1, 74.5, 112.3, 124.5, 126.8, 127.0, 127.5, 127.7, 129.3, 129.5, 130.0, 133.8, 139.7, 152.3, 158.6, 164.8, 167.5, 173.1.

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