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MODIFIED COUMARINS. 5. AMINO-ACID DERIVATIVES OF 3-HYDROXY-7,8,9,10-TETRAHYDROBENZO[*c*]CHROMEN-6-ONE

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Peptide-chemistry methods (symmetric anhydrides and activated esters) and the Mannich reaction were used to prepare various conjugates of amino acids with 7,8,9,10-tetrahydrobenzo[c]chromen-6-one in which the amino acids are bound to the coumarin by the C- or N-terminus.

Key words: coumarins, 7,8,9,10-tetrahydrobenzo[c]chromen-6-one, amino-acid derivatives, Mannich reaction, synthesis.

One alternative for constructing new biologically active compounds is to synthesize analogs of natural bioregulators in order to increase the pharmacological activity, in particular, by forming several active centers in the molecule. An advantage of such compounds is that their structures are similar to the biochemical structures of a living organism and cause significantly less side effects. Coumarins are commonly used as a basis for constructing pharmacologically active compounds because of the high biological activity of natural coumarins. On the other hand, one can suppose that the combination in one molecule of coumarin and amino-acid fragments might lead to compounds with new physiological properties in view of the importance of the latter to the life processes of living organisms.

It is known that more than 30 types of pharmacological activity have been found for compounds with the coumarin core. In particular, 7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one derivatives include compounds that have antiallergic [1] and anti-inflammatory [2] activity; that act as CNS stimulants [3], neuroprotectors and anticonvulsive agent [4],antidepressants and antiallergens [5], insecticides [6], depressants, anticonvulsants, analgetics, antipyretics, and anti-inflammatory agents [7]; and that cure hypoxia [8].

Therefore, our goal was to modify derivatives of 7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one by judiciously introducing into them amino-acid units. The starting hydroxycoumarin **1** was prepared in high yield by Pechmann condensation of resorcinol and ethyl-2-hydroxycyclohexanecarboxylate in the presence of H_2SO_4 (72%) [9].

The amino-acid unit was introduced into the coumarin by three methods. The first method was based on Mannich aminomethylation. C-aminomethylation was effected by heating a mixture of **1**, the corresponding amino acid, and an equivalent amount of formalin in aqueous alcohol [10]. The aminomethyl group added to the 4-position of the 7,8,9,10-tetrahydrobenzo[*c*]chromen-6-one. Derivatives of alanine (**2**), 2-aminobutanoic acid (**3**), valine (**4**), norvaline (**5**), leucine (**6**), isoleucine (**7**), norleucine (**8**), and phenylalanine (**9**) were prepared this way. The structures of these Mannich bases were confirmed by quantitative elemental analysis and PMR spectroscopy. The PMR spectra of **2**-**9** were recorded in CF_3CO_2H. The region of coumarin aromatic protons was simplified owing to a lack of coupling by H-4. Aromatic protons in the 1- and 2-positions resonated as doublets with spin—spin coupling constants (SSCC) 8.8 Hz at 7.8 and 7.2 ppm, respectively. The PMR spectra also contained signals for the amino-acid protons and 2H signals at 4.9-5.0 ppm for the methylene group.

The second method was based on formation of an ester of the amino acid and phenolic compounds. The most suitable and convenient method for synthesizing 7-O-aminoacylcoumarins is the reaction of 7-hydroxycoumarins and symmetric anhydrides of N-substituted amino acids because the reaction proceeds under mild conditions and yields no side products [11, 12].

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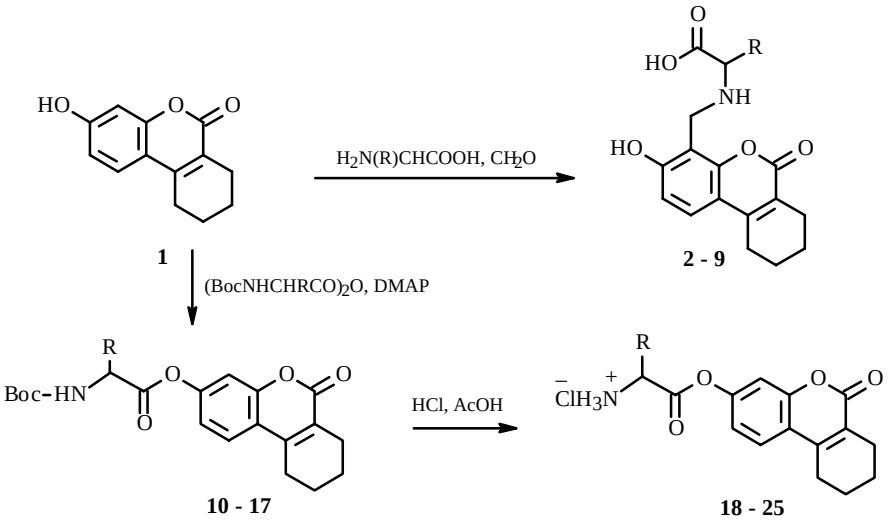


2, 11, 19: R = CH_3; **3:** R = CH_2CH_3; **4, 12, 20:** R = $CH(CH_3)_2$; **5:** R = $CH_2CH_2CH_3$;
6, 13, 21: R = $CH_2CH(CH_3)_2$; **7, 14, 22:** R = $CH(CH_3)CH_2CH_3$; **8:** R = $CH_2CH_2CH_2CH_3$;
9, 16, 24: R = CH_2Ph; **10, 18:** R = H; **15, 23:** R = $CH_2CH_2SCH_3$; **17, 25:** R = Ph

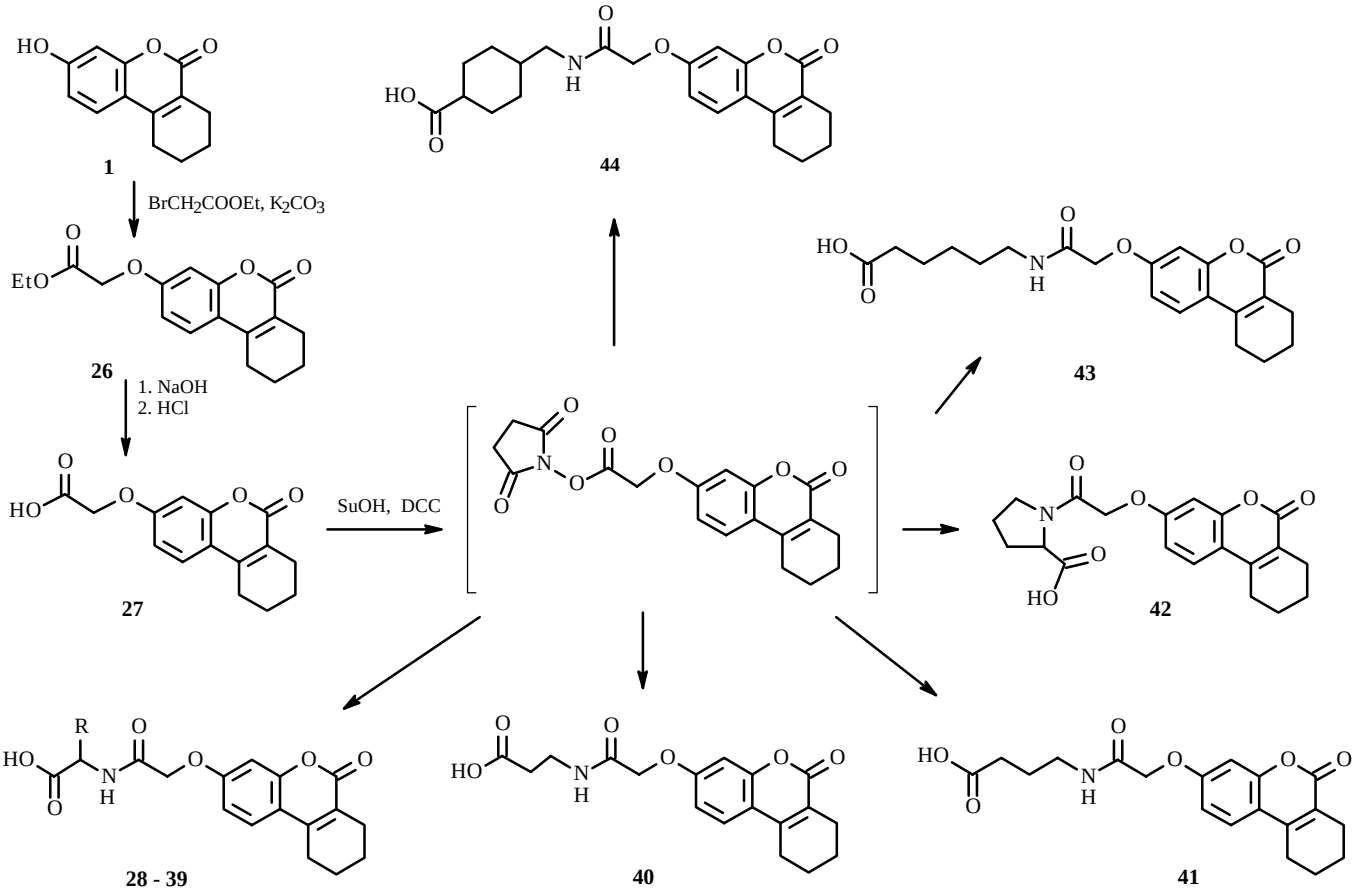
Symmetric anhydrides of N-substituted amino acids were prepared by reacting dicyclohexylcarbodiimide (DCC) with two equivalents of N-substituted amino acid in absolute THF at 0°C. The amino group was blocked using the *t*-butyloxycarbonyl (Boc) protecting group. Acylation of **1** by symmetric anhydrides $(BocNHCHRCO)_2O$ was carried out in absolute THF in the presence of a catalytic amount of 4-dimethylaminopyridine (DMAP) at 0°C. The reaction yielded N-substituted 7-O-aminoacylcoumarins **10**-**17**. These molecules included glycine (**10**), alanine (**11**), valine (**12**), leucine (**13**), isoleucine (**14**), methionine (**15**), phenylalanine (**16**), and α-phenylglycine (**17**). The PMR spectra of **10**-**16** contained signals for the coumarin ring, amino-acid unit, and protecting group. A strong 9H singlet of the Boc group was observed at 1.4-1.5 ppm. The signal of the amide appeared at 5.0-5.2 ppm.

The protecting group was removed from **10**-**17** using acidolysis by dry HCl in glacial acetic acid (3 M) at 0°C. The structures of **18**-**25** were proved by quantitative elemental analysis and PMR spectroscopy. The PMR spectra of **18**-**25** in DMSO-d_6 lacked signals for the protecting group. Signals of the amine hydrochloride appeared at 8.9-9.1 ppm.

The third method was based on activated esters. Alkylation of **1** in acetone in the presence of potash by ethylbromoacetate yielded the ethyl ester **26**, saponification of which by NaOH in aqueous propan-2-ol with subsequent acidolysis gave the corresponding acid **27**. N-Hydroxysuccinimide esters were used as the activated esters. These are typically highly reactive and do not racemize the products [13]. The N-hydroxysuccinimide ester was prepared by reacting **27** and N-hydroxysuccinimide using DCC as the condensing agent [11, 14].

N-[2-(4-Oxo-1,2,3,4-tetrahydrocyclopenta[*c*]chromen-7-yloxy)acetyl]amino acids (**28**-**44**) were prepared by condensation of the activated ester and sodium salts of the amino acids in water:dioxane (1:1) at room temperature with subsequent acidolysis of the resulting salts. These syntheses introduced into the coumarin glycine (**28**), alanine (**29**), valine (**30**), norvaline (**31**), leucine (**32**), isoleucine (**33**), norleucine (**34**), methionine (**35**), phenylalanine (**36**), α-phenylglycine (**37**), citrulline (**39**), proline (**42**), asparagine (**38**), 3-aminopropanoic (**40**), 4-aminobutanoic (**41**), 6-aminohexanoic (**43**), and *trans*-4-aminomethylcyclohexanecarboxylic (**44**) acids.

The structures of the amino-acid derivatives **26**-**37** were proved by quantitative analysis and PMR spectroscopy. The PMR spectra of **26**-**37** contained signals for the amide proton at 8.20-8.50 ppm, coumarin protons, and the amino-acid unit.



28: R = H; **29:** R = CH_3; **30:** R = $CH(CH_3)_2$; **31:** R = $CH_2CH_2CH_3$; **32:** R = $CH_2CH(CH_3)_2$; **33:** R = $CH(CH_3)CH_2CH_3$; **34:** R = $CH_2CH_2CH_2CH_3$; **35:** R = $CH_2CH_2SCH_3$; **36:** R = CH_2Ph; **37:** R = Ph; **38:** R = CH_2COOH; **39:** R = $CH_2CH_2CH_2NHCONH_2$

EXPERIMENTAL

The course of the reactions and the purity of the products were monitored by TLC on Merck 60 F254 plates using $CHCl_3$—CH_3OH (9:1 and 95:5). IR spectra were recorded on a Nicolet FTIR Nexus 475 spectrometer; PMR, on Varian VXR-300 and Mercury-400 spectrometers at 300 and 400 MHz, respectively, with TMS internal standard. Elemental analyses of all compounds agreed with those calculated.

Starting 7,8,9,10-tetrahydro-3-hydroxy-6H-dibenzo[*b*,*d*]pyran-6-one (**1**) was prepared by the literature method [9].

Mannich Bases 2-9. A warm solution of hydroxycoumarin (**1**, 1.08 g, 5 mmole) in EtOH (30 mL) was treated with a solution of the appropriate amino acid (5 mmole) in water (20 mL) and formalin (5 mmole, 0.45 mL, 35%). The reaction mixture was held at 80-90°C for 6-8 h. The resulting precipitate was filtered off and crystallized from EtOH (50%).

N-[(7,8,9,10-Tetrahydro-3-hydroxy-6-oxo-6H-dibenzo[*b*,*d*]-pyran-4-yl)methyl]-alanine (2). Yield 28%, mp 255-256°C, $C_{17}H_{19}NO_5$. IR spectrum (KBr, cm^{-1}): 3150, 2937, 2610, 1704, 1603, 1572, 1473, 1396, 1384, 1363, 1296, 1185, 1090, 1045. PMR spectrum (400 MHz, TFA, δ, ppm, J/Hz): 1.96 (3H, d, J = 6.8, CH_3-3′), 1.99 (4H, m, CH_2-8, CH_2-9), 2.69 (2H, m, CH_2-10), 2.97 (2H, m, CH_2-7), 4.51 (1H, q, H-2′), 4.91 (2H, br.s, CH_2-4), 7.20 (1H, d, J = 8.8, H-2), 7.87 (1H, d, J = 8.8, H-1).

2-[[(7,8,9,10-Tetrahydro-3-hydroxy-6-oxo-6H-dibenzo[*b*,*d*]pyran-4-yl)methyl]amino]-butanoic Acid (3). Yield 49%, mp 265-266°C, $C_{18}H_{21}NO_5$. IR spectrum (KBr, cm^{-1}): 3159, 2938, 2535, 1704, 1602, 1581, 1473, 1386, 1342, 1332, 1316, 1293, 1267, 1184, 1091. PMR spectrum (300 MHz, TFA, δ, ppm, J/Hz): 1.25 (3H, t, J = 7.2, CH_3-4′), 2.02 (4H, m, CH_2-

8, CH_2-9), 2.37 (2H, m, CH_2-3′), 2.69 (2H, m, CH_2-10), 2.96 (2H, m, CH_2-7), 4.45 (1H, m, H-2′), 4.98 (2H, br.s, CH_2-4), 7.18 (1H, d, J = 9.0, H-2), 7.88 (1H, d, J = 9.0, H-1).

N-[(7,8,9,10-Tetrahydro-3-hydroxy-6-oxo-6H-dibenzo[*b,d*]pyran-4-yl)methyl]-valine (4). Yield 58%, mp 245-246°C, $C_{19}H_{23}NO_5$. IR spectrum (KBr, cm^{-1}): 2937, 2541, 1703, 1603, 1562, 1382, 1332, 1323, 1295, 1090. PMR spectrum (400 MHz, TFA, δ, ppm, J/Hz): 1.22 (3H, d, J = 6.8, CH_3-4′), 1.29 (3H, d, J = 6.8, CH_3-3′), 1.99 (4H, m, CH_2-8, CH_2-9), 2.65 (1H, m, H-3′), 2.69 (2H, m, CH_2-10), 2.99 (2H, m, CH_2-7), 4.26 (1H, d, J = 3.6, H-2′), 4.94 (2H, br.s, CH_2-4), 7.20 (1H, d, J = 8.8, H-2), 7.87 (1H, d, J = 8.8, H-1).

N-[(7,8,9,10-Tetrahydro-3-hydroxy-6-oxo-6H-dibenzo[*b,d*]pyran-4-yl)methyl]-norvaline (5). Yield 49%, mp 260-261°C, $C_{19}H_{23}NO_5$. IR spectrum (KBr, cm^{-1}): 2967, 2535, 1704, 1603, 1567, 1505, 1469, 1435, 1383, 1365, 1335, 1317, 1302, 1268, 1244, 1184, 1093. PMR spectrum (300 MHz, TFA, δ, ppm, J/Hz): 1.10 (3H, t, J = 7.2, CH_3-5′), 1.66 (2H, m, CH_2-4′), 2.01 (4H, m, CH_2-8, CH_2-9), 2.68 (2H, m, CH_2-10), 2.98 (2H, m, CH_2-7), 3.07 (2H, m, CH_2-3′), 4.55 (1H, m, H-2′), 4.97 (2H, br.s, CH_2-4), 7.20 (1H, d, J = 9.0, H-2), 7.86 (1H, d, J = 9.0, H-1).

N-[(7,8,9,10-Tetrahydro-3-hydroxy-6-oxo-6H-dibenzo[*b,d*]pyran-4-yl)methyl]-leucine (6). Yield 43%, mp 246-247°C, $C_{20}H_{25}NO_5$. IR spectrum (KBr, cm^{-1}): 2938, 2537, 1704, 1604, 1577, 1473, 1376, 1355, 1309, 1292, 1267, 1183, 1092. PMR spectrum (400 MHz, TFA, δ, ppm, J/Hz): 1.07 (3H, d, J = 6.8, CH_3-5′), 1.11 (3H, d, J = 6.8, CH_3-4′), 1.96-2.05 (5H, m, CH_2-8, CH_2-9, H-4′), 2.09 (2H, m, CH_2-3′), 2.69 (2H, m, CH_2-10), 2.99 (2H, m, CH_2-7), 4.26 (1H, t, J = 6.8, H-2′), 4.94 (2H, d, J = 4.0, CH_2-4), 7.20 (1H, d, J = 8.8, H-2), 7.87 (1H, d, J = 8.8, H-1).

N-[(7,8,9,10-Tetrahydro-3-hydroxy-6-oxo-6H-dibenzo[*b,d*]pyran-4-yl)methyl]-isoleucine (7). Yield 52%, mp 256-257°C, $C_{20}H_{25}NO_5$. IR spectrum (KBr, cm^{-1}): 2937, 2533, 1703, 1602, 1561, 1504, 1471, 1451, 1383, 1334, 1319, 1295, 1268, 1245, 1183, 1089. PMR spectrum (300 MHz, TFA, δ, ppm, J/Hz): 1.08 (3H, t, J = 7.2, CH_3-5′), 1.17 (3H, d, J = 6.9, CH_3-3′), 1.5-1.65 (3H, m, H-3′, CH_3-4′), 1.98 (4H, m, CH_2-8, CH_2-9), 2.67 (2H, m, CH_2-10), 2.99 (2H, m, CH_2-7), 4.36 (1H, m, H-2′), 4.95 (2H, br.s, CH_2-4), 7.20 (1H, d, J = 9.0, H-2), 7.88 (1H, d, J = 9.0, H-1).

N-[(7,8,9,10-Tetrahydro-3-hydroxy-6-oxo-6H-dibenzo[*b,d*]pyran-4-yl)methyl]-norleucine (8). Yield 56%, mp 247-248°C, $C_{20}H_{25}NO_5$. IR spectrum (KBr, cm^{-1}): 2934, 2578, 1704, 1604, 1569, 1505, 1470, 1384, 1368, 1335, 1317, 1296, 1267, 1094. PMR spectrum (300 MHz, TFA, δ, ppm, J/Hz): 1.02 (3H, t, J = 7.2, CH_3-6′), 1.50-1.65 (4H, m, CH_2-4′, CH_2-5′), 2.00 (4H, m, CH_2-8, CH_2-9), 2.69 (2H, m, CH_2-10), 2.95 (2H, m, CH_2-7), 3.02 (2H, m, CH_2-3′), 4.42 (1H, m, H-2′), 4.95 (2H, br.s, CH_2-4), 7.19 (1H, d, J = 9.0, H-2), 7.87 (1H, d, J = 9.0, H-1).

N-[(7,8,9,10-Tetrahydro-3-hydroxy-6-oxo-6H-dibenzo[*b,d*]pyran-4-yl)methyl]-phenylalanine (9). Yield 64%, mp 243-244°C, $C_{23}H_{23}NO_5$. IR spectrum (KBr, cm^{-1}): 2937, 2537, 1705, 1607, 1577, 1474, 1451, 1417, 1390, 1375, 1308, 1291, 1267, 1095, 1082. PMR spectrum (400 MHz, TFA, δ, ppm, J/Hz): 2.01 (4H, m, CH_2-8, CH_2-9), 2.68 (2H, m, CH_2-10), 2.98 (2H, m, CH_2-7), 3.33 (1H, dd, J = 9.6, J = 10.4, CH_2-3′a), 3.68 (1H, dd, J = 9.6, J = 10.4, CH_2-3′b), 4.47 (1H, m, H-2′), 4.87 (2H, dd, J = 13.6, J = 14.0, CH_2-4), 7.18 (3H, m, H-2, H-2″, H-6″), 7.34 (3H, m, H-3″, H-4″, H-5″), 7.85 (1H, d, J = 8.8, H-1).

N-Protected 3-O-Aminoacyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-ones 10-16. A cooled solution (0°C) of the appropriate N-Boc-amino acid (9 mmole) in absolute THF (20 mL) was treated with DCC (0.93 g, 4.5 mmole). The reaction mixture was stirred vigorously for 20-30 min at 0°C. The resulting precipitate of dicyclohexylurea was filtered off. The mother liquor was treated with 7-hydroxycoumarin (**1**, 0.86 g, 4 mmole) in absolute THF (20 mL) and DMAP (20 mg). The reaction mixture was held for 30-45 min at room temperature with vigorous stirring (completion of the reaction was determined by TLC). Solvent was evaporated in vacuum. The solid was dissolved in ethylacetate (50 mL) and washed successively with $NaHCO_3$ (5%, 2×25 mL), water (25 mL), and saturated NaCl (25 mL). The organic layer was dried over anhydrous $MgSO_4$. Solvent was removed in vacuum. The solid was crystallized from propan-2-ol.

3-O-(N-*t*-Butyloxycarbonylglycyl)-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-one (10). Yield 73%, mp 140-142°C, $C_{20}H_{23}NO_6$. PMR spectrum (300 MHz, DMSo-d_6, δ, ppm, J/Hz): 1.40 [9H, s, $(CH_3)_3C$], 1.73 (4H, m, CH_2-8, CH_2-9), 2.42 (2H, m, CH_2-10), 2.78 (2H, m, CH_2-7), 4.01 (2H, d, J = 5.7, CH_2-2′), 7.12 (1H, dd, $J_{2,4}$ = 2.1, $J_{2,1}$ = 8.4, H-2), 7.18 (1H, d, J = 2.1, H-4), 7.45 (1H, t, J = 5.4, CONH), 7.75 (1H, d, J = 8.4, H-1).

3-O-(N-*t*-Butyloxycarbonylalanyl)-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-one (11). Yield 82%, mp 111-112°C, $C_{21}H_{25}NO_6$. PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.45 [9H, s, $(CH_3)_3C$], 1.57 (3H, d, J = 7.5, CH_3-3′), 1.84 (4H, m , CH_2-8, CH_2-9), 2.57 (2H, m, CH_2-10), 2.74 (2H, m, CH_2-7), 4.55 (1H, m, H-2′), 5.06 (1H, m, CONH), 7.05 (1H, dd, $J_{2,4}$ = 2.1, $J_{2,1}$ = 8.7, H-2), 7.11 (1H, d, J = 2.1, H-4), 7.56 (1H, d, J = 8.4, H-1).

3-O-(N-*t*-Butyloxycarbonylvalyl)-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-one (12). Yield 71%, mp 88-89°C, $C_{23}H_{29}NO_6$. PMR spectrum (300 MHz, $(CD_3)_2CO$, δ, ppm, J/Hz): 1.11 (3H, d, J = 6.6, CH_3-4′), 1.15 (3H, d, J = 6.6, CH_3-3′),

1.45 [9H, s, $(CH_3)_3C$], 1.77 (4H, m, CH_2-8, CH_2-9), 2.36 (1H, m, H-3′), 2.40 (2H, m, CH_2-10), 2.78 (2H, m, CH_2-7), 4.31 (1H, m, H-2′), 6.58 (1H, m, CONH), 6.92 (1H, d, J = 2.4, H-4), 6.98 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.65 (1H, d, J = 9.0, H-1).

3-O-(N-*t*-Butyloxycarbonylleucyl)-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-one (13). Yield 67%, mp 84-85°C, $C_{24}H_{31}NO_6$. PMR spectrum (300 MHz, $(CD_3)_2CO$, δ, ppm, J/Hz): 1.03 (6H, d, J = 5.7, CH_3-5′, CH_3-4′), 1.45 [9H, s, $(CH_3)_3C$], 1.75 (4H, m, CH_2-8, CH_2-9), 1.87 (3H, m, CH_2-3″, H-4″), 2.41 (2H, m, CH_2-10), 2.79 (2H, m, CH_2-7), 4.54 (1H, m, H-2′), 6.51 (1H, m, CONH), 6.91 (1H, d, J = 2.4, H-4), 6.96 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.64 (1H, d, J = 9.0, H-1).

3-O-(N-*t*-Butyloxycarbonylisoleucyl)-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-one (14). Yield 64%, mp 78-80°C, $C_{24}H_{31}NO_6$. PMR spectrum (300 MHz, $(CD_3)_2CO$, δ, ppm, J/Hz): 0.99 (3H, t, J = 5.7, CH_3-5″), 1.10 (3H, d, J = 6.9, CH_3-3′), 1.44 (1H, m, CH_2-4′a), 1.47 [9H, s, $(CH_3)_3C$], 1.66 (1H, m, CH_2-4′b), 1.77 (4H, m, CH_2-8, CH_2-9), 2.10 (1H, m, H-3′), 2.40 (2H, m, CH_2-10), 2.77 (2H, m, CH_2-7), 4.36 (1H, m, H-2′), 6.57 (1H, m, CONH), 6.92 (1H, d, J = 2.4, H-4), 6.98 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.66 (1H, d, J = 9.0, H-1).

3-O-(N-*t*-Butyloxycarbonylmethionyl)-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-one (15). Yield 73%, mp 73-74°C, $C_{23}H_{29}NO_6S$. PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.47 [9H, s, $(CH_3)_3C$], 1.86 (4H, m, CH_2-8, CH_2-9), 2.15 (3H, s, SCH_3), 2.36 (2H, m, CH_2-4′), 2.58 (2H, m, CH_2-10), 2.66 (2H, m, CH_2-3″), 2.78 (2H, m, CH_2-7), 4.67 (1H, m, H-2′), 5.19 (1H, m, CONH), 7.07 (1H, dd, $J_{2,4}$ = 2.1, $J_{2,1}$ = 8.7, H-2), 7.12 (1H, d, J = 2.1, H-4), 7.57 (1H, d, J = 8.7, H-1).

3-O-(N-*t*-Butyloxycarbonylphenylalanyl)-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-one (16). Yield 81%, mp 140-141°C, $C_{27}H_{29}NO_6$. PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.46 [9H, s, $(CH_3)_3C$], 1.85 (4H, m, CH_2-8, CH_2-9), 2.57 (2H, m, CH_2-10), 2.77 (2H, m, CH_2-7), 3.22 (2H, m, CH_2-3′), 4.81 (1H, m, H-2′), 5.05 (1H, m, CONH), 7.05 (1H, dd, $J_{2,4}$ = 2.1, $J_{2,1}$ = 8.7, H-2), 7.11 (1H, d, J = 2.1, H-4), 7.26 (2H, m, H-2″, H-6″), 7.34 (3H, m, H-3″, H-4″, H-5″), 7.55 (1H, d, J = 8.4, H-1).

3-O-(N-*t*-Butyloxycarbonylphenylglycyl)-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-one (17). Yield 75%, mp 145-147°C, $C_{26}H_{27}NO_6$. PMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.46 [9H, s, $(CH_3)_3C$], 1.84 (4H, m, CH_2-8, CH_2-9), 2.57 (2H, m, CH_2-10), 2.75 (2H, m, CH_2-7), 5.54 (2H, m, H-2′, CONH), 6.95 (1H, dd, $J_{2,4}$ = 2.1, $J_{2,1}$ = 8.7, H-2), 6.99 (1H, d, J = 2.1, H-4), 7.35-7.50 (5H, m, Ph-2′), 7.56 (1H, d, J = 8.4, H-1).

Hydrochlorides of 3-O-Aminoacyl-7,8,9,10-tetrahydro-6H-benzo[*b,d*]pyran-6-ones 18-25. A solution of 7-O-Boc-aminoacylcoumarin **10-17** (2 mmole) in absolute THF (10 mL) was treated with dry HCl in glacial acetic acid (10 mL, 3 M) and held for 45-60 min at 0°C. The completion of the reaction was monitored by TLC. The reaction mixture was diluted with absolute ether (100 mL) and held for 30 min at 0°C. The precipitate was filtered off and dried.

3-O-Glycyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-one Hydrochloride (18). Yield 81%, mp 225°C (dec.), $C_{15}H_{16}ClNO_4$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.75 (4H, m, CH_2-8, CH_2-9), 2.40 (2H, m, CH_2-10), 2.78 (2H, m, CH_2-7), 4.16 (2H, m, CH_2-2′), 7.01 (1H, dd, $J_{2,4}$ = 2.1, $J_{2,1}$ = 8.4, H-2), 7.12 (1H, d, J = 2.1, H-4), 7.75 (1H, d, J = 8.4, H-1), 8.80 (3H, br.s, NH_3^+).

3-O-Alanyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-one Hydrochloride (19). Yield 89%, mp 220°C (dec.), $C_{16}H_{18}ClNO_4$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.62 (3H, d, J = 7.2, CH_3-3′), 1.78 (4H, m, CH_2-8, CH_2-9), 2.39 (2H, m, CH_2-10), 2.77 (2H, m, CH_2-7), 4.43 (1H, m, H-2′), 6.94 (1H, d, J = 2.4, H-4), 6.99 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.68 (1H, d, J = 9.0, H-1), 8.91 (3H, br.s, NH_3^+).

3-O-Valyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-one Hydrochloride (20). Yield 76%, mp 230°C (dec.), $C_{18}H_{22}ClNO_4$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.11 (3H, d, J = 6.9, CH_3-4′), 1.15 (3H, d, J = 6.9, CH_3-3′), 1.77 (4H, m, CH_2-8, CH_2-9), 2.40 (3H, m, CH_2-10, H-3′), 2.78 (2H, m, CH_2-7), 4.18 (1H, m, H-2′), 6.93 (1H, d, J = 2.4, H-4), 6.98 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.67 (1H, d, J = 9.0, H-1), 9.01 (3H, br.s, NH_3^+).

3-O-Leucyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-one Hydrochloride (21). Yield 73%, mp 235°C (dec.), $C_{19}H_{24}ClNO_4$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.88 (3H, d, J = 5.7, CH_3-5′), 0.94 (3H, d, J = 5.7, CH_3-4′), 1.59 (2H, m, CH_2-3′), 1.75 (4H, m, CH_2-8, CH_2-9), 1.82 (1H, m, H-4′), 2.38 (2H, m, CH_2-10), 2.75 (2H, m, CH_2-7), 4.29 (1H, m, H-2″), 6.95 (1H, d, J = 2.4, H-4), 7.00 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.68 (1H, d, J = 9.0, H-1), 8.95 (3H, br.s, NH_3^+).

3-O-Isoleucyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-one Hydrochloride (22). Yield 79%, mp 230°C (dec.), $C_{19}H_{24}ClNO_4$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.00 (3H, t, J = 5.7, CH_3-5″), 1.12 (3H, d, J = 6.9, CH_3-3′), 1.44 (1H, m, CH_2-4′a), 1.69 (1H, m, CH_2-4′b), 1.75 (4H, m, CH_2-8, CH_2-9), 2.13 (1H, m, H-3′), 2.39 (2H, m, CH_2-10), 2.78 (2H, m, CH_2-7), 4.25 (1H, m, H-2′), 6.91 (1H, d, J = 2.4, H-4), 6.97 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.65 (1H, d, J = 9.0, H-1), 8.96 (3H, br.s, NH_3^+).

3-O-Methionyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-one Hydrochloride (23). Yield 65%, mp 220°C (dec.),

$C_{18}H_{22}ClNO_4S$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.82 (4H, m, CH_2-8, CH_2-9), 2.11 (3H, s, SCH_3), 2.34 (2H, m, CH_2-4′), 2.58 (2H, m, CH_2-10), 2.80 (4H, m, CH_2-7, CH_2-3″), 4.46 (1H, m, H-2′), 7.07 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 8.7, H-1), 9.00 (3H, br.s, NH_3^+).

3-O-Phenylalanyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-one Hydrochloride (24). Yield 87%, mp 245°C (dec.), $C_{22}H_{22}ClNO_4$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.75 (4H, m, CH_2-8, CH_2-9), 2.40 (2H, m, CH_2-10), 2.77 (2H, m, CH_2-7), 3.30 (1H, m, CH_2-3″a), 3.41 (1H, m, CH_2-3″b), 4.57 (1H, m, H-2′), 6.92 (1H, d, J = 2.4, H-4), 6.99 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.32 (5H, m, Ph-3′), 7.69 (1H, d, J = 9.0, H-1), 9.14 (3H, br.s, NH_3^+).

3-O-Phenylglycyl-7,8,9,10-tetrahydro-6H-dibenzo[*b,d*]pyran-6-one Hydrochloride (25). Yield 79%, mp 250°C (dec.), $C_{21}H_{20}ClNO_4$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.77 (4H, m, CH_2-8, CH_2-9), 2.39 (2H, m, CH_2-10), 2.78 (2H, m, CH_2-7), 5.58 (1H, m, H-2′), 6.92 (1H, d, J = 2.4, H-4), 6.99 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.37-7.45 (5H, m, Ph-2′), 7.69 (1H, d, J = 9.0, H-1), 9.05 (3H, br.s, NH_3^+).

Ethyl-2-[(7,8,9,10-tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetate (26). A hot solution of **1** (10.8 g, 50 mmole) in absolute acetone (100 mL) was treated with freshly calcined potash (20.7 g, 150 mmole), stirred vigorously and heated (50-56°C), and treated with ethylchloroacetate (6.1 mL, 55 mmole). The reaction mixture was held for 2 h with vigorous stirring (course of the reaction was monitored by TLC). After the reaction was finished, the reaction mixture was poured into H_2SO_4 solution (500 mL, 1 N). The resulting precipitate was filtered off and crystallized from propan-2-ol (75%). Yield 92%, mp 137-138°C, $C_{17}H_{18}O_5$. IR spectrum (KBr, cm^{-1}): 2947, 1765, 1706, 1612, 1509, 1394, 1267, 1209, 1166, 1101, 1078, 1026, 826. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.22 (3H, t, J = 7.2, CH_3-2″), 1.73 (4H, m, CH_2-8, CH_2-9), 2.37 (2H, m, CH_2-10), 2.73 (2H, m, CH_2-7), 4.18 (2H, q, CH_2-1″), 4.89 (2H, s, CH_2-2′), 6.92 (1H, d, J = 2.4, H-4), 6.94 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.2, H-2), 7.58 (1H, d, J = 9.2, H-1).

2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetic Acid (27). A solution of **26** (11.8 g, 40 mmole) in propan-2-ol (100 mL) was treated with NaOH (100 mL, 1 N). The mixture was boiled for 2 h (course of the reaction was monitored by TLC). After the reaction was finished, the reaction mixture was treated with H_2SO_4 (200 mL, 1 N). The resulting precipitate was filtered off and crystallized from propan-2-ol (50%). Yield 85%, mp 170°C, $C_{15}H_{14}O_5$. IR spectrum (KBr, cm^{-1}): 2943, 1752, 1705, 1698, 1613, 1510, 1430, 1391, 1297, 1255, 1230, 1168, 1103, 1070, 825. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.74 (4H, m, CH_2-8, CH_2-9), 2.38 (2H, m, CH_2-10), 2.73 (2H, m, CH_2-7), 4.80 (2H, s, CH_2-2′), 6.91 (1H, d, J = 2.4, H-4), 6.93 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.2, H-2), 7.59 (1H, d, J = 9.2, H-1), 12.99 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]amino Acids 28-44. A cooled solution of **27** (1.04 g, 4 mmole) and N-hydroxysuccinimide (0.51 g, 4.4 mmole) in absolute dioxane (20 mL) was treated with DCC (0.83 g, 4 mmole). The mixture was held for 2 h with vigorous stirring (course of the reaction was monitored by TLC). The precipitate of dicyclohexylurea was filtered off. The N-hydroxysuccinimide ester was treated with a solution of the appropriate amino acid (4.4 mmole) and NaOH (0.18 g, 4.4 mmole) in water (20 mL). The reaction mixture was stirred for 3-4 h (course of the reaction was monitored by TLC). After the reaction was finished, the reaction mixture was treated with water (100 mL) and acidified to pH 4. The precipitate was filtered off and crystallized from propan-2-ol (50%).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]glycine (28). Yield 61%, mp 229-231°C, $C_{17}H_{17}NO_6$. IR spectrum (KBr, cm^{-1}): 3346, 2945, 1709, 1621, 1559, 1426, 1296, 1264, 1219, 1165, 1105, 1040. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.73 (4H, m, CH_2-8, CH_2-9), 2.40 (2H, m, CH_2-10), 2.76 (2H, m, CH_2-7), 3.83 (2H, d, J = 6.0, CH_2-2″), 4.65 (2H, s, CH_2-1′), 6.96 (1H, d, J = 2.4, H-4), 7.00 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.64 (1H, d, J = 9.0, H-1), 8.45 (1H, t, CONH), 12.40 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6*H*-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]alanine (29). Yield 67%, mp 212-213°C, $C_{18}H_{19}NO_6$. IR spectrum (KBr, cm^{-1}): 3391, 2938, 1721, 1714, 1623, 1545, 1511, 1422, 1293, 1161, 1149, 1103, 1030. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.33 (3H, d, J = 7.5, CH_3-3″), 1.73 (4H, m, CH_2-8, CH_2-9), 2.40 (2H, m, CH_2-10), 2.77 (2H, m, CH_2-7), 4.31 (1H, m, H-2″), 4.64 (2H, s, CH_2-1′), 6.95 (1H, d, J = 2.4, H-4), 7.00 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.63 (1H, d, J = 9.0, H-1), 8.43 (1H, d, J = 7.2, CONH), 12.66 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]valine (30). Yield 54%, mp 177-179°C, $C_{20}H_{23}NO_6$. IR spectrum (KBr, cm-^{1}): 3375, 2958, 1719, 1711, 1644, 1617, 1513, 1427, 1397, 1283, 1265, 1235, 1170, 1099. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.91 (6H, d, J = 6.9, CH_3-4″, CH_3-3″), 1.74 (4H, m, CH_2-8, CH_2-9), 2.11 (1H, m, H-3″), 2.40 (2H, m, CH_2-10), 2.78 (2H, m, CH_2-7), 4.21 (1H, m, H-2″), 4.73 (2H, s, CH_2-1′), 6.90 (1H, d, J = 2.4, H-4), 7.01 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.59 (1H, d, J = 9.0, H-1), 8.43 (1H, d, J = 8.4, CONH), 12.78 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]norvaline (31). Yield 68%, mp 172-

174°C, $C_{20}H_{23}NO_6$. IR spectrum (KBr, cm^{-1}): 3381, 2954, 1715, 1621, 1546, 1510, 1428, 1388, 1296, 1265, 1231, 1165, 1104, 1064. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.87 (3H, t, CH_3-5″), 1.33 (2H, m, CH_2-4″), 1.73 (6H, CH_2-8, CH_2-9, CH_2-3″), 2.39 (2H, m, CH_2-10), 2.73 (2H, m, CH_2-7), 4.30 (1H, m, H-2″), 4.67 (2H, s, CH_2-1′), 6.91 (1H, d, J = 2.4, H-4), 6.95 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.58 (1H, d, J = 9.0, H-1), 8.35 (1H, d, J = 8.1, CONH), 12.50 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]leucine (32). Yield 52%, mp 160°C, $C_{21}H_{25}NO_6$. IR spectrum (KBr, cm^{-1}): 3333, 2944, 1728, 1706, 1614, 1569, 1510, 1431, 1392, 1284, 1264, 1233, 1171, 1158, 1097, 1029. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.82 (3H, d, J = 5.7, C_3-5″), 0.88 (3H, d, J = 5.7, CH_3-4″), 1.59 (3H, m, CH_2-3″, H-4″), 1.73 (4H, m, CH_2-8, CH_2-9), 2.40 (2H, m, CH_2-10), 2.77 (2H, m, CH_2-7), 4.29 (1H, m, H-2″), 4.66 (2H, s, CH_2-1′), 6.92 (1H, d, J = 2.4, H-4), 6.97 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.63 (1H, d, J = 9.0, H-1), 8.37 (1H, d, J = 8.1, CONH), 12.50 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]isoleucine (33). Yield 48%, mp 163°C, $C_{21}H_{25}NO_6$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.84 (3H, t, CH_3-5″), 0.87 (3H, d, J = 5.7, CH_3-3″), 1.20 (1H, m, CH_2-4″a), 1.44 (1H, m, CH_2-4″b), 1.73 (4H, m, CH_2-8, CH_2-9), 1.84 (1H, m, H-3″), 2.40 (2H, m, CH_2-10), 2.76 (2H, m, CH_2-7), 4.26 (1H, m, H-2″), 4.70 (2H, s, CH_2-1′), 6.91 (1H, d, J = 2.4, H-4), 6.95 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.62 (1H, d, J = 9.0, H-1), 8.17 (1H, d, J = 7.5, CONH), 12.72 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]norleucine (34). Yield 82%, mp 167-169°C, $C_{21}H_{25}NO_6$. IR spectrum (KBr, cm^{-1}): 3378, 2935, 1716, 1622, 1545, 1510, 1426, 1389, 1295, 1265, 1221, 1165, 1103. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.86 (3H, t, CH_3-6″), 1.26 (4H, m, CH_2-5″, CH_2-4″), 1.74 (6H, m, CH_2-8, CH_2-9, CH_2-3″), 2.38 (2H, m, CH_2-10), 2.73 (2H, m, CH_2-7), 4.27 (1H, m, H-2″), 4.68 (2H, s, CH_2-1′), 6.91 (1H, d, J = 2.4, H-4), 6.95 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.58 (1H, d, J = 9.0, H-1), 8.35 (1H, d, J = 7.8, CONH), 12.50 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]methionine (35). Yield 49%, mp 129°C, $C_{20}H_{23}NO_6S$. IR spectrum (KBr, cm^{-1}): 3322, 2936, 1744, 1719, 1619, 1541, 1510, 1434, 1393, 1281, 1261, 1223, 1168, 1103. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.74 (4H, m, CH_2-8, CH_2-9), 1.97 (2H, m, CH_2-4″), 2.03 (3H, s, SCH_3), 2.40 (2H, m, CH_2-10), 2.45 (2H, m, CH_2-3″), 2.76 (2H, m, CH_2-7), 4.42 (1H, m, H-2″), 4.67 (2H, s, CH_2-1′), 6.93 (1H, d, J = 2.4, H-4), 6.97 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.62 (1H, d, J = 9.0, H-1), 8.42 (1H, d, J = 7.5, CONH), 12.40 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]phenylalanine (36). Yield 79%, mp 192-194°C, $C_{24}H_{23}NO_6$. IR spectrum (KBr, cm^{-1}): 3411, 2937, 1708, 1667, 1621, 1546, 1509, 1436, 1389, 1297, 1265, 1221, 1192, 1160, 1103, 1031. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.74 (4H, m, CH_2-8, CH_2-9), 2.41 (2H, m, CH_2-10), 2.76 (2H, m, CH_2-7), 2.98 (1H, dd, J = 14.1, J = 14.4, CH_2-3″a), 3.11 (1H, dd, J = 14.1, J = 14.4, CH_2-3″b), 4.53 (1H, m, H-2″), 4.59 (2H, s, CH_2-1′), 6.85 (1H, d, J = 2.4, H-4), 6.91 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.21 (5H, m, Ph-3″), 7.59 (1H, d, J = 9.0, H-1), 8.35 (1H, d, J = 8.4, CONH), 12.40 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]phenylglycine (37). Yield 71%, mp 185°C, $C_{23}H_{21}NO_6$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.72 (4H, m, CH_2-8, CH_2-9), 2.39 (2H, m, CH_2-10), 2.72 (2H, m, CH_2-7), 4.75 (2H, s, CH_2-1′), 5.43 (1H, d, J = 7.5, H-2″), 6.92 (1H, d, J = 2.4, H-4), 6.96 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.33-7.42 (5H, m, Ph-2″), 7.58 (1H, d, J = 9.0, H-1), 8.85 (1H, d, J = 7.2, CONH), 12.60 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]aspargic Acid (38). Yield 46%, mp 198-199°C, $C_{19}H_{19}NO_8$. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.74 (4H, m, CH_2-8, CH_2-9), 2.40 (2H, m, CH_2-10), 2.76 (4H, m, CH_2-7, CH_2-3″), 4.64 (1H, m, H-2″), 4.66 (2H, s, CH_2-1′), 6.92 (1H, d, J = 2.4, H-4), 6.96 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.65 (1H, d, J = 9.0, H-1), 8.43 (1H, d, J = 7.5, CONH), 12.40 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]citrulline (39). Yield 60%, mp 143-146°C, $C_{21}H_{25}N_2O_7$. IR spectrum (KBr, cm^{-1}): 3391, 2949, 1691, 1659, 1613, 1570, 1536, 1512, 1431, 1396, 1355, 1288, 1264, 1244, 1172, 1105. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.39 (2H, m, CH_2-4″), 1.76 (6H, m, CH_2-8, CH_2-9, CH_2-3″), 2.40 (2H, m, CH_2-10), 2.77 (2H, m, CH_2-7), 2.95 (2H, m, CH_2-5″), 4.24 (1H, m, H-2″), 4.66 (2H, s, CH_2-1′), 5.40 (2H, s, NH_2), 5.96 (1H, t, J = 5.6, NH), 6.94 (1H, d, J = 2.4, H-4), 6.98 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 8.8, H-2), 7.64 (1H, d, J = 8.8, H-1), 8.45 (1H, d, J = 8.0, CONH), 12.72 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]-β-alanine (40). Yield 88%, mp 207°C, $C_{18}H_{19}NO_6$. IR spectrum (KBr, cm^{-1}): 3290, 2944, 1700, 1654, 1610, 1556, 1511, 1435, 1394, 1284, 1262, 1213, 1178, 1101, 1040. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.75 (4H, m, CH_2-8, CH_2-9), 2.40 (2H, m, CH_2-10), 2.44 (2H, m, CH_2-2″), 2.76 (2H, m, CH_2-7), 3.36 (2H, m, CH_2-3″), 4.58 (2H, s, CH_2-1′), 6.94 (1H, d, J = 2.4, H-4), 6.98 (1H, dd, $J_{2,4}$ = 2.4,

$J_{2,1}$ = 9.0, H-2), 7.63 (1H, d, J = 9.0, H-1), 8.18 (1H, t, J = 4.8, CONH), 12.26 (1H, br.s, COOH).

4-[(2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl)amino]butanoic Acid (41). Yield 68%, mp 171-172°C, $C_{19}H_{21}NO_6$. IR spectrum (KBr, cm^{-1}): 3379, 2942, 1722, 1704, 1614, 1561, 1509, 1429, 1392, 1283, 1265, 1206, 1171, 1098, 1063. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.72 (6H, m, CH_2-8, CH_2-9, CH_2-3″), 2.22 (2H, t, CH_2-2″), 2.39 (2H, m, CH_2-10), 2.74 (2H, m, CH_2-7), 3.15 (2H, m, CH_2-4″), 4.58 (2H, s, CH_2-1′), 6.92 (1H, d, J = 2.4, H-4), 6.97 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.62 (1H, d, J = 9.0, H-1), 8.19 (1H, t, J = 5.4, CONH), 12.05 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]proline (42). Yield 65%, mp 105-107°C, $C_{20}H_{21}NO_6$. IR spectrum (KBr, cm^{-1}): 3434, 2936, 1709, 1612, 1510, 1456, 1430, 1393, 1283, 1262, 1226, 1168, 1101, 1038. PMR spectrum (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.72 (4H, m, CH_2-8, CH_2-9), 1.83-2.19 (4H, m, CH_2-3″, CH_2-4″), 2.39 (2H, m, CH_2-10), 2.75 (2H, m, CH_2-7), 3.43 (1H, m, CH_2-5″a), 3.61 (1H, m, CH_2-5″b), 4.92 (2H, s, CH_2-1′), 6.91 (1H, d, J = 2.4, H-4), 6.95 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 8.8, H-2), 7.60 (1H, d, J = 8.8, H-1), 12.63 (1H, br.s, COOH).

4-[(2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl)amino]hexanoic Acid (43). Yield 63%, mp 182-183°C, $C_{21}H_{25}NO_6$. IR spectrum (KBr, cm^{-1}): 3368, 2944, 1732, 1714, 1639, 1619, 1565, 1429, 1391, 1287, 1267, 1228, 1166, 1105, 1061. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 1.22 (2H, m, CH_2-4″), 1.44 (4H, m, CH_2-3″, CH_2-5″), 1.74 (4H, m, CH_2-8, CH_2-9), 2.15 (2H, t, J = 7.5, CH_2-2″), 2.40 (2H, m, CH_2-10), 2.77 (2H, m, CH_2-7), 3.42 (2H, m, CH_2-6″), 4.57 (2H, s, CH_2-1′), 6.94 (1H, d, J = 2.4, H-4), 6.98 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.64 (1H, d, J = 9.0, H-1), 8.11 (1H, t, J = 5.4, CONH), 11.94 (1H, br.s, COOH).

N-[2-[(7,8,9,10-Tetrahydro-6-oxo-6H-dibenzo[*b,d*]pyran-3-yl)oxy]acetyl]-*trans*-4-aminomethylcyclohexane-carboxylic Acid (44). Yield 71%, mp 219-221°C, $C_{23}H_{27}NO_6$. IR spectrum (KBr, cm^{-1}): 3354, 2930, 1714, 1678, 1646, 1619, 1563, 1510, 1450, 1432, 1392, 1365, 1295, 1266, 1228, 1161, 1105, 1058. PMR spectrum (300 MHz, DMSO-d_6, δ, ppm, J/Hz): 0.88 and 1.18 (4H, two m, CH_2-3‴, CH_2-5‴), 1.25 (1H, m, H-4‴), 1.60-1.80 (8H, m, CH_2-8, CH_2-9, CH_2-2‴, CH_2-6‴), 2.10 (1H, m, H-1‴), 2.41 (2H, m, CH_2-10), 2.74 (2H, m, CH_2-7), 2.98 (2H, t, J = 7.2, CH_2-1″), 4.60 (2H, s, CH_2-1′), 6.93 (1H, d, J = 2.4, H-4), 6.97 (1H, dd, $J_{2,4}$ = 2.4, $J_{2,1}$ = 9.0, H-2), 7.64 (1H, d, J = 9.0, H-1), 8.10 (1H, t, J = 5.7, CONH), 11.90 (1H, br.s, COOH).

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