6-Oxyindan-1-ones with dipeptide chains

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Through N-acylation of α- or β-amino acid units by 2-(3-oxo-2,3-dihydro-1H-inden-5-yloxy)acetic acid using the method of N-hydroxysuccinimide esters new dipeptide indan-1-one derivatives were obtained. In general, the direct interaction of the acetic carboxyl group of the substrate with the amino group of the α- or β-dipeptide is a more productive strategy than the sequential peptidic condensation of the two amino acids.

Introduction

Natural compounds with an indanone fragment, although relatively few in number, are very diverse both in functional groups present and in the biological activity. Among them (Figure 1), one can find toxic sesquiterpenes, named pterosins, contained in various fern species [1, 2] and usefull in diabet [3], osteoarthritis [4] and other diseases treatment; antibacterial polycondensed aromatic compounds such as indanonaftol B [5]; the biphenyl derivative 1 [6]; the dihydrofuranone derivative 2 [7]; as well as the carboxaldehyde derivative 3 with antitumor activity [8]. More generally, natural indanones or indanes can be considered as bio-inspiring or medicinal chemistry [9]. For example, indanone acetamides of type 4 were shown to exhibit promising antimicrobial and antifungal activity [10].

A remarkable indane drug, used in the treatment of neurodegenerative disorders, is Ladostigil (TV-3326), a reductive amination derivative of 6-hydroxyindan-1-one [11]. With the view to extending the scope of such bioactive compounds, methodological studies of the functionalization of the indanone core thus deserve particular attention.

Along this line, we previously reported on the functionalization of 6-hydroxyindan-1-one with amino acid fragments through an oxyacetic linker, showing that the method of
hydroxysuccinimide esters [12, 13] is more efficient than the carbonylimidazole condensation method [14].

The present report describes the beneficial use of hydroxysuccinimide esters for the synthesis of α- or β-dipeptide derivatives of 2-(3-oxo-2,3-dihydro-1H-inden-5-yloxy)acetic acid.

**Results and discussion**

Two possible strategies for the preparation of the α- or β-dipeptide targets can be distinguished: through either direct interaction of the indanone substrate with the terminal amino group of the preformed dipeptide, or sequential condensation of the two amino acids. The first method is obviously convenient but the second one can give more variety of products.

In order to explore the one-step strategy, the N-hydroxysuccinimide activated ester 6 was generated *in situ* from the acid 5 (Scheme 1), before addition of different dipeptides with a free amino function to obtain the target compounds 7a-i. TLC monitoring showed that the overall conversion was complete. Moderate to poor isolated yields were obtained in some cases (Scheme 1) because of the high solubility of the substance in the aqueous reaction medium (see Experimental part).

The two-step method was tested on tryptophan and methionine derivatives, the expected low solubility these substances *a priori* can help to avoid the losses during workup and allowing a more accurate evaluation of the reaction efficiency. So, the carboxylic group of compounds 8a,b (Scheme 2, the synthesis was described in ref. [14]) was converted into the corresponding N-hydroxysuccinimide activated ester 9. Without further purification, the latter was treated with another amino acid to give dipeptides 7j-n. The moderate overall yields of
products 7j-n were due to the low yields of the corresponding initial transformation 5→8 (see in ref. [14]), and the yield of the conversion 5→7 after two steps was only 26 % for dipeptide 7j, 33 % – for 7k, 25 % – for 7l, and 42 % – for 7m, 34 % – for 7n respectively.

All spectral data confirmed the structure of the products 7 (see Experimental part). The \(^1\)H NMR spectra in DMSO-d_{6} solutions did not allow detection of the COOH signals due to fast exchange; but the IR spectra displayed the corresponding wide intense absorption band of the O–H bond, along with a maximum absorption of the N–H bond near 3300 cm\(^{-1}\).

The syntheses were performed from optically pure amino acids, except the synthesis of 7l for which optically pure L-tryptophan and racemic DL-alanine were used. So, substance 7l was obtained as a mixture of equal amounts of two diastereomers, as shown by \(^1\)H NMR spectroscopy.

Scheme 2. Two-step synthesis of the \(\alpha\)-dipeptide derivatives 7j-m and \(\beta\)-dipetide derivative 7n from the acid 5 by consecutive reactions with two amino acids.
Conclusions

It was shown that the dipeptide derivatives of 2-(3-oxo-2,3-dihydro-1H-inden-5-yloxy)acetic acid can be obtained by either consecutive reactions of the two amino acids, or immediately from a pre-formed dipeptide precursor. Nonetheless, the one-step strategy appears more efficient: both more convenient and more productive. A more exact quantitative estimate can be obtained subsequently using parallel synthesis of series of identical dipeptides by these two methods.

The developed synthetic procedures can be useful for obtaining a number of new indanone amino acid derivatives in order to study their optical characteristics and biological activity.

Experimental part

The reaction progress and identities of the products were controlled with TLC on Merck F\textsubscript{254} plates using a chloroform:methanol (19:1, v/v) eluting system.

\textsuperscript{1}H and \textsuperscript{13}C NMR spectra were recorded on a Varian 400 spectrometer operating at 400 MHz for \textsuperscript{1}H and 100 MHz for \textsuperscript{13}C. NMR chemical shifts are reported in ppm, in the δ scale and are referenced using TMS as internal standard.

FTIR spectra were recorded on a Thermo Nicolet Nexus 470 spectrometer in KBr pellets.

Melting points were determined using a Leica Galen III Kofler-type melting point microscope, and were uncorrected.

The synthesis of 5 was performed using a previously described procedure \cite{14, 15}; for the synthesis of the amino acid derivatives 8, see ref. \cite{14}.

General procedure for N-acylation through the N-hydroxysuccinimide ester method. To a solution of the acid 5, 8a or 8b (1.5 mmol) and N-hydroxysuccinimide (0.23 g, 2 mmol) in absolute dioxane (10 mL) dicyclohexylcarbodiimide (0.41 g, 2 mmol) was added at room temperature under vigorous stirring. The mixture was stirred at room temperature for 2–3 h until an activated ester was formed (TLC monitoring); then a solution of the corresponding amino acid or dipeptide (1.75 mmol) and NaHCO\textsubscript{3} (0.25 g, 3 mmol) in water (10 mL) was added (the amino acids and dipeptide were been used in free amine form and not in protonated form). The reaction mixture was stirred at room temperature for 2–3 h (TLC monitoring). After the process was finished, the dicyclohexylurea precipitate was filtered off. The filtrate was poured into water (50 mL) and the solution was acidified (to pH 4–5) with dilute HCl. The precipitate formed was filtered off, recrystallized from a \textit{i}-PrOH:water 1:1 mixture.

\textit{N-}\{(1-oxoindan-6-yl)oxy\}acetyl\{glycyl\}glycine 7a. Yield 0.26 g, 0.81 mmol, 54 %. Mp 229–230°C. \textsuperscript{1}H NMR (DMSO-\textit{d}_6), δ (ppm):
2.63 (br. s, 2H, H$_2$-3), 3.00 (br. s, 2H, H$_2$-2), 3.65–3.85 (br. s, 2H, 2 NHCH$_2$), 4.59 (s, 2H, OCH$_2$CO), 7.10 (br. s, 1H, H-7), 7.33 (br. d, J=6.6 Hz, 1H, H-5), 7.50 (d, J=6.8 Hz, 1H, H-4), 8.23 (br. s, 1H, NH), 8.39 (br. s, 1H, NH).

$^{13}$C NMR (DMSO-$d_6$), $\delta$ (ppm): 25.1, 37.1, 41.1, 42.0, 67.6, 106.7, 123.8, 128.3, 138.2, 148.8, 157.7, 168.2, 169.4, 171.5, 206.2. IR (KBr), $\nu$ (cm$^{-1}$): 3289, 3099, 2934, 1714, 1671, 1633, 1569, 1492, 1438, 1288, 1253, 1070, 834, 746, 558.

$\text{N}-\{[1\text{-oxoindan-6-yl}\text{oxy}]\text{acetyl}\}\text{glycylalanine 7b.}$ Yield 0.24 g, 0.72 mmol, 48 %. Mp 202–203°C. $^1$H NMR (DMSO-$d_6$), $\delta$ (ppm): 1.25 (d, J=7.0 Hz, 3H, CHCH$_3$), 2.63 (br. s, 2H, H$_2$-3), 3.00 (br. s, 2H, H$_2$-2), 3.72–3.85 (br. s, 4H, NHCH$_2$), 4.16–4.25 (m, 1H, CHCH$_2$CH), 4.59 (s, 2H, OCH$_2$CO), 7.09 (br. s, 1H, H-7), 7.32 (br. d, J=8.0 Hz, 1H, H-5), 7.50 (d, J=8.0 Hz, 1H, H-4), 8.24 (d, J=7.0 Hz, 1H, NHCH), 8.32 (m, 1H, NHCH$_2$). $^{13}$C NMR (DMSO-$d_6$), $\delta$ (ppm): 17.6, 25.1, 37.0, 41.8, 48.0, 67.5, 106.8, 123.8, 128.2, 138.2, 148.8, 157.7, 168.1, 168.6, 174.4, 206.4. IR (KBr), $\nu$ (cm$^{-1}$): 3284, 3099, 2928, 1706, 1665, 1468, 1561, 1491, 1438, 1285, 1224, 1065, 835, 720, 559.

$\text{N}-\{[1\text{-oxoindan-6-yl}\text{oxy}]\text{acetyl}\}\text{glycylvaline 7c.}$ Yield 0.25 g, 0.69 mmol, 46 %. Mp 131–132°C. $^1$H NMR (DMSO-$d_6$), $\delta$ (ppm): 0.85 (br. s, 6H, CHCH(CH$_3$)$_2$), 1.98–2.09 (m, 1H, CHCH(CH$_3$)$_2$), 2.62 (br. s, 2H, H$_2$-3), 2.99 (br. s, 2H, H$_2$-2), 3.80–3.91 (br. s, 4H, NHCH$_2$), 4.11–4.20 (m, 1H, CHCH(CH$_3$)$_2$), 4.58 (s, 2H, OCH$_2$CO), 7.09 (br. s, 1H, H-7), 7.32 (br. d, J=6.0 Hz, 1H, H-5), 7.50 (d, J=6.0 Hz, 1H, H-4), 8.04 (d, J=6.8 Hz, 1H, NHCH), 8.32 (m, 1H, NHCH$_2$). $^{13}$C NMR (DMSO-$d_6$), $\delta$ (ppm): 18.3, 19.5, 25.1, 30.4, 37.0, 41.9, 57.7, 67.5, 106.6, 123.8, 128.2, 138.2, 148.8, 157.7, 168.1, 169.0, 173.4, 206.2. IR (KBr), $\nu$ (cm$^{-1}$): 3293, 3057, 2965, 2929, 1706, 1663, 1544, 1490, 1284, 1224, 1067, 837, 559.
CH(COOH)), 3.01 (br. t, J=5.2 Hz, 2H, H-2,3), 3.71 (dd, J=16.5 Hz, J=5.7 Hz, 1H, NH—CH₂—CONH), 3.81 (dd, J=16.5 Hz, J=5.7 Hz, 1H, NH—CH₂—CONH), 4.30–4.37 (m, 1H, CH₂–CH(COOH)), 4.58 (s, 2H, OCH₂CO), 6.64 (d, J=8.2 Hz, 2H, H-3',5' (4-HOC₆H₄)), 6.99 (d, J=8.2 Hz, 2H, H-2',6' (4-HOC₆H₄)), 7.11 (br. s, 1H, H-7), 7.33 (br. d, J=8.6 Hz, H-5), 7.50 (d, J=8.6 Hz, H-4), 8.15 (d, J=7.8 Hz, 1H, NHCH), 8.31 (t, J=5.7 Hz, 1H, NHCH₂). ¹³C NMR (DMSO-d₆), δ (ppm): 25.2, 36.6, 37.1, 41.9, 54.4, 67.5, 106.8, 115.4, 123.9, 127.9, 130.5, 138.2, 148.8, 156.3, 157.7, 168.1, 168.7, 173.4, 186.9, 206.4. IR (KBr), v (cm⁻¹): 3291, 2925, 1706, 1662, 1547, 1516, 1490, 1438, 1284, 1247, 1064, 835, 558.

N-[(1-oxoindan-6-yl)oxy]acetyl]alanvaline 7f. Yield 0.28 g, 0.75 mmol, 50 %. Mp 174–175°C. ¹H NMR (DMSO-d₆), δ (ppm): 0.81–0.87 (m, 6H, CHCH(CH₃)₂), 1.99–2.10 (m, 1H, CHCH(CH₃)₂), 1.25 (d, J=6.6 Hz, 3H, CHCH₃), 2.63 (m, 2H, H₂-3), 3.00 (m, 2H, H₂-2), 4.18 (br. t, J=6.5 Hz, 1H, CHCH(CH₃)₂), 4.59 (m, 3H, CHCH₃, OCH₂CO), 7.08 (br. s, 1H, H-7), 7.30 (br. d, J=8.2 Hz, H-5), 7.49 (d, J=8.2 Hz, H-4), 8.14 (d, J=7.0 Hz, 1H, NH), 8.19 (d, J=7.0 Hz, 1H, NH). ¹³C NMR (DMSO-d₆), δ (ppm): 18.0, 19.5, 25.1, 30.5, 37.0, 48.2, 57.3, 67.3, 106.3, 123.8, 128.2, 138.2, 148.7, 157.7, 167.2, 172.6, 173.3, 206.4. IR (KBr), v (cm⁻¹): 3277, 3068, 2967, 2934, 1740, 1701, 1654, 1549, 1491, 1443, 1267, 1227, 1077, 834, 676, 561.

N-[(1-oxoindan-6-yl)oxy]acetyl]alanyl-tryptophane 7h. Yield 0.35 g, 0.76 mmol, 51 %. Mp 118–119°C. ¹H NMR (DMSO-d₆), δ (ppm): 1.08 (d, J=6.0 Hz, 1H, CHCH₃), 1.23 (d, J=6.0 Hz, 1H, CHCH₃), 2.62 (br. s, 2H, H₂-3), 2.95–3.09 (m, 3H, H₂-2, CH₆(indol-3-yl)), 3.14–3.23 (m, 1H, CH₆(indol-3-yl)), 4.32–4.58 (m, 2H, 2NHCH₂CO), 4.57 (m, 2H, OCH₂CO), 6.97 (br. t, J=6.6 Hz, 1H, H-5' (indol-3-yl)), 7.01–7.09 (m, 2H, H-7, H-6' (indol-3-yl)), 7.14 (d, J=13.5 Hz, 1H, H-5), 7.27–7.34 (m, 2H, H-4, H-2' (indol-3-yl)), 7.47 (d, J=8.0 Hz, 1H, H-4' (indol-3-yl)), 7.50–7.55 (m, 1H, H-7' (indol-3-yl)), 8.10–8.19 (m, 1H, NH), 8.26 and 8.30 (two d, J=6.7 Hz, 1H, NH), 10.87 (br. s, 1H, NH (indol-3-yl)). ¹³C NMR (DMSO-d₆), δ (ppm): 18.8, 25.2, 27.4, 37.1, 48.1, 53.5, 67.4, 106.7,
110.2, 111.8, 118.6, 118.8, 121.3, 123.9, 124.1, 127.7, 128.3, 136.5, 138.2, 147.3, 148.8, 157.8, 167.3, 173.6, 206.4. IR (KBr), \( \nu \) (cm\(^{-1}\)): 3337, 3058, 2927, 1686, 1665, 1560, 1490, 1277, 1220, 1099, 745, 559.

\( N\)-(\(\{\)1-oxoindan-6-yl\}oxy)acetyl)alanyl-\( \beta \)-alanine \(7i\). Yield 0.27 g, 0.78 mmol, 52 %. Mp 117–118°C. \(^1\)H NMR (DMSO-\(d_6\)), \( \delta \) (ppm): 1.20 (d, \( J = 6.0 \) Hz, 3H, CH\(CH_3\)), 2.35 (br. t, \( J = 6.0 \) Hz, 2H, NHCH\(CH_2\)), 2.62 (br. s, 2H, H\(_2\)-3), 2.99 (br. s, 2H, H\(_2\)-2), 3.23 (br. t, \( J = 6.0 \) Hz, 2H, NHCH\(CH_2\)), 4.29 (br. t, \( J = 6.0 \) Hz, 1H, CH\(CH(CH_3)\)), 4.57 (s, 2H, OCH\(CH_2\)), 7.06 (br. s, 1H, H-7), 7.30 (br. d, \( J = 8.0 \) Hz, 1H, H-5), 7.48 (d, \( J = 8.0 \) Hz, 1H, H-4), 8.13 (br. s, 1H, NHCH\(H_2\)), 8.14 (br. d, \( J = 6.6 \) Hz, 1H, NH).

\(^{13}\)C NMR (DMSO-\(d_6\)), \( \delta \) (ppm): 18.9, 25.1, 34.2, 35.3, 37.0, 48.3, 67.3, 106.3, 123.9, 128.2, 138.2, 148.7, 157.7, 167.3, 172.3, 173.3, 206.5.

IR (KBr), \( \nu \) (cm\(^{-1}\)): 3291, 2929, 1719, 1693, 1664, 1627, 1546, 1492, 1286, 1227, 1075, 833.

\( N\)-(\(\{\)1-oxoindan-6-yl\}oxy)acetyl)-methionyltryptophan \(7j\). Yield 0.26 g, 0.50 mmol, 33 %. Mp 109–110°C. \(^1\)H NMR (DMSO-\(d_6\)), \( \delta \) (ppm): 1.67–2.10 (m, 5H, CH\(CH_2CH_2SCH_3\)), 2.62 (br. t, \( J = 5.4 \) Hz, 2H, H-2), 2.47 (m, 2H, CH\(H_2CH_2SCH_3\)), 2.98–3.13 (m, 3H, H\(_2\)-2, CH\(H_2\)(indol-3-yl)), 3.18–3.25 (m, NHCH\(H_2\)), 4.43–4.61 (m, 4H, OCH\(CH_2\), 2 NHCH\(CO\)), 6.94 (br. t, \( J = 7.4 \) Hz, 1H, H-5′ (indol-3-yl)), 7.01 (br. t, \( J = 7.4 \) Hz, 1H, H-6′ (indol-3-yl)), 7.05–7.13 (m, 2H, H-5,7), 7.24–7.32 (m, 2H, H-4, H-2′ (indol-3-yl)), 7.42 (d, \( J = 8.5 \) Hz, 1H, H-4′ (indol-3-yl)), 7.49–7.54 (m, 1H, H-7′ (indol-3-yl)), 8.05–8.21 and 8.32–8.41 (two m, 1.5 and 0.5 H, 2 NH), 10.74 (br. s, 1H, NH (indol-3-yl)). \(^{13}\)C NMR (DMSO-\(d_6\)), \( \delta \) (ppm): 15.0, 25.1, 29.7, 32.5, 36.9, 51.8, 53.4, 62.4, 67.2, 106.5, 110.0, 111.8, 118.5, 118.8, 121.3, 123.7, 124.0, 127.6, 128.3, 136.5, 138.2, 148.7, 157.7, 167.7, 171.0, 173.6, 206.4. IR (KBr), \( \nu \) (cm\(^{-1}\)): 3324, 3057, 2922, 1701, 1665, 1533, 1489, 1442, 1277, 1220, 1061, 837, 745, 560.

\( N\)-(\(\{\)1-oxoindan-6-yl\}oxy)acetyl)tryptophanylglycine \(7k\). Yield 0.39 g, 0.87 mmol, 58 %. Mp 139–140°C. \(^1\)H NMR (DMSO-\(d_6\)), \( \delta \) (ppm): 2.63 (br. s, 2H, OCH\(CH_2\)), 3.01–3.25 (m, 4H, H-2, CH\(H_2\)(indol-3-yl)), 3.73 (br. s, 2H, NHCH\(H_2\)), 4.40–4.52 (m, 2H, OCH\(CH_2\)), 6.93–7.05 (m, 2H, H-7, H-6′ (indol-3-yl)), 7.08–7.14 (m, 2H, H-5, H-2′ (indol-3-yl)), 7.30 (d, \( J = 7.0 \) Hz, 1H, H-4), 7.38 (d, \( J = 7.6 \) Hz, 1H, H-4′ (indol-3-yl)), 7.57 (d, \( J = 7.6 \) Hz, 1H, H-7′ (indol-3-yl)), 7.94 (d, \( J = 7.4 \) Hz, 1H, NH), 8.31–8.35 (m, 1H, NH (indol-3-yl)). \(^{13}\)C NMR (DMSO-\(d_6\)), \( \delta \) (ppm): 15.0, 25.1, 29.7, 32.5, 36.9, 51.8, 53.4, 62.4, 67.2, 106.5, 110.0, 111.8, 118.5, 118.8, 121.3, 123.7, 124.0, 127.6, 128.3, 136.5, 138.2, 148.7, 157.7, 167.7, 171.0, 173.6, 206.4. IR (KBr), \( \nu \) (cm\(^{-1}\)): 3313, 3057, 2927, 1711, 1664, 1541, 1489, 1437, 1278, 1221, 1063, 835, 795, 743, 559.
**N**-[(1-oxoindan-6-yl)oxy]acetyl]-
tryptophylanalanine 7I. Yield 0.30 g, 0.65 mmol, 43 %. Mp 139–141°C. \(^1\)H NMR (DMSO-\(d_6\), \(\delta\) (ppm): 1.18 (br. s, 1.5H, CH\(\beta\)CH), 1.29 (br. s, 1.5H, CH\(\alpha\)CH), 2.63 (br. s, 2H, H-2, H-3), 2.96–3.29 (m, 2H, H-2, CH\(\delta\)(indol-3-yl)), 4.10–4.29 (m, 1H, NH\(\beta\)CHCO), 4.42–4.72 (m, 3H, OCH\(\alpha\)CO, NH\(\beta\)CHCO), 6.91–7.23 (m, 5H, H-5, H-5', H-6, H-6', (indol-3-yl)), 7.30–7.37 (m, 2H, H-4), 7.42–7.49 (m, 1H, H-4' (indol-3-yl)), 7.56–7.66 (m, 1H, H-7 (indol-3-yl)), 8.00–8.19 (m, 1H, NH), 8.30–8.47 (m, 1H, NH), 10.82 (br. s, 1H, NH (indol-3-yl)). \(^1\)\(^3\)C NMR (DMSO-
\(d_6\), \(\delta\) (ppm): 17.2, 25.2, 28.1, 37.0, 48.2, 53.3, 67.4, 106.7, 109.9, 111.6, 118.6, 118.8, 121.2, 123.5, 124.2, 127.8, 128.2, 136.5, 138.2, 148.5, 157.4, 167.4, 171.2, 174.5, 206.4. IR (KBr), \(\nu\) (cm\(^{-1}\)): 3316, 3057, 2922, 2853, 1663, 1534, 1489, 1438, 1277, 1221, 1062, 871, 744, 559.

**N**-[(1-oxoindan-6-yl)oxy]acetyl]-
tryptophanyl-
\(\beta\)-alanine 7n. Yield 0.44 g, 0.95 mmol, 63 %. Mp 126–127°C. \(^1\)H NMR (DMSO-
\(d_6\), \(\delta\) (ppm): 2.32 (t, \(J=7.0\) Hz, 2H, NH\(\beta\)CH\(\alpha\)), 2.64 (br. t, \(J=5.6\) Hz, 2H, H-2), 2.95–3.06 (3H, m, H-2, CH\(\alpha\)(indol-3-yl)), 3.12 (dd, \(J=14.4\) Hz, \(J=5.0\) Hz, 1H, CH\(\beta\)(indol-3-yl)), 3.19–3.28 (m, 2H, NHCH\(\alpha\)CH), 4.45–4.57 (m, 3H, OCH\(\alpha\)CO, CH\(\alpha\)CH\(\beta\)(indol-3-yl), 6.94 (br. t, \(J=7.6\) Hz, 1H, H-5' (indol-3-yl)), 7.02–7.07 (m, 2H, H-7, H-6' (indol-3-yl)), 7.11 (br. s, 1H, H-2' (indol-3-yl)), 7.19 (dd, \(J=8.0\) Hz, \(J=2.4\) Hz, 1H, H-5), 7.31 (d, \(J=8.0\) Hz, 1H, H-4), 7.45 (d, \(J=7.6\) Hz, 1H, H-4' (indol-3-yl)), 7.58 (d, \(J=7.6\) Hz, 1H, H-7' (indol-3-yl)), 8.09 (d, \(J=8.0\) Hz, 1H, NH), 8.17 (br. t, \(J=5.0\) Hz, 1H, NH), 10.81 (s, 1H, NH (indol-3-yl)). \(^1\)\(^3\)C NMR (DMSO-
\(d_6\), \(\delta\) (ppm): 25.1, 28.3, 34.2, 35.4, 37.0, 53.6, 68.4, 67.4, 116.4, 117.1, 118.7, 118.9, 121.4, 123.8, 124.1, 127.7, 129.4, 129.8, 136.5, 138.2, 148.5, 157.7, 167.5, 171.7, 173.6, 206.3. IR (KBr), \(\nu\) (cm\(^{-1}\)): 3320, 3057, 2922, 2853, 1663, 1534, 1489, 1438, 1277, 1221, 1062, 871, 744, 559.

\(\alpha\)-acetyl]-
tryptophylmethionine 7m. Yield 0.57 g, 1.1 mmol, 73 %. Mp 111–112°C. \(^1\)H NMR (DMSO-
\(d_6\), \(\delta\) (ppm): 1.83–2.05 (m, 5H, CH\(\beta\)CH\(\beta\)SCH\(\beta\)SCH\(\beta\)), 2.17–2.32 (m, 1H, CH\(\beta\)CH\(\delta\)SCH\(\beta\)SCH\(\beta\)), 2.40–2.50 (m, 1H, CH\(\beta\)CH\(\delta\)SCH\(\beta\)SCH\(\beta\)), 2.63 (m, 2H, H-2, H-3), 2.96–3.08 (m, 3H, H-2, CH\(\delta\)(indol-3-yl)), 3.09–3.22 (m, 1H, CH\(\beta\)(indol-3-yl)), 4.23–4.30 (m, 0.5H, CH(CH\(\alpha\)CH\(\alpha\)SCH\(\alpha\)SCH\(\alpha\))), 4.32–4.39 (m, 0.5H, CH(CH\(\alpha\)CH\(\alpha\)SCH\(\alpha\)SCH\(\alpha\))), 4.44–4.59 (m, 2H, OCH\(\alpha\)CO), 4.59–4.73 (m, 1H, CH\(\alpha\)CH\(\alpha\)(indol-3-yl), 6.95 (br. t, \(J=7.6\) Hz, 1H, H-5' (indol-3-yl)), 7.01–7.08 (m, 2H, H-7, H-6' (indol-3-yl)), 7.12–7.22 (m, 2H, H-5, H-2' (indol-3-yl)), 7.31 (d, \(J=8.0\) Hz, 1H, H-4), 7.44 (d, \(J=8.0\) Hz, 1H, H-4' (indol-3-yl)), 7.62 (d, \(J=8.0\) Hz, 1H, H-7' (indol-3-yl)), 8.09 (d, \(J=8.0\) Hz, 0.5H, NH), 8.13 (d, \(J=8.0\) Hz, 0.5H, NH), 8.42–8.48 (m, 1H, NH (indol-3-yl)). \(^1\)\(^3\)C NMR (DMSO-
\(d_6\), \(\delta\) (ppm): 14.9, 25.1, 30.1, 31.2, 37.0, 51.6, 53.6, 66.8, 67.5, 106.9, 110.1, 111.8, 118.8, 118.9, 121.4, 123.7, 124.5, 127.9, 128.4, 136.5, 138.2, 148.7, 157.7, 167.5, 171.7, 173.6, 206.3. IR (KBr), \(\nu\) (cm\(^{-1}\)): 3320, 3057, 2922, 2853, 1663, 1534, 1489, 1438, 1277, 1221, 1062, 871, 744, 559.
IR (KBr), ν (cm⁻¹): 3297, 3058, 2926, 1701, 1665, 1560, 1534, 1438, 1279, 1222, 1186, 1063, 836, 743, 559.

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