6-Oxyindan-1-ones with amino acid fragments

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New indan-1-one derivatives (8 examples) with amino acid fragments were synthesized through the N-acylation of the amino acids by 2-(3-oxo-2,3-dihydro-1*H*-inden-5-yloxy)acetic acid using the method of activated *N*-hydroxysuccinimide esters. To obtain corresponding methyl esters (2 examples) two ways were possible: the *N*-acylation of the amino acid methyl esters by 2-(3-oxo-2,3-dihydro-1-inden-5-yloxy)acetic acid through the activated imidazole derivatives or methylation of the carboxylic function of preformed *N*-{[(1-oxoindan-6-yl)oxy]acetyl}amino acids.

Introduction

Compounds containing an indane fragment are objectively widely represented in nature. The variability of such structures is provided by different types of substituents, not only in the benzene ring, but also those presented in positions 1-3: this fragment of the molecule can be saturated or can hold a double bond, or functional groups mainly hydroxy or keto groups.

Among natural indanes, probably, the class of pterosins is most meticulously studied (**Figure 1**). These sesquiterpenes, contained in various fern species, have interested researchers for their bioactivity [1, 2], but, unfortunately, many of the pterosins are highly toxic. So, it is not surprising that in recent years there have been a lot of experiments to creation bioactive substances with an indane fragment devoid of this shortcoming, and many tries had been successful [3–5].

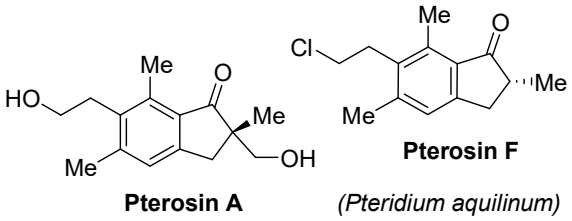


Figure 1. Pterosins – naturally occurring indan-1-ones.

In particular, it has been interesting and beneficial for medicinal chemistry to combine the indane cycle with the amino acid residue in structures of varying complexity. Among these molecules (**Figure 2**) we can find anti-hypertensive agent **1** [3], compound **2** with anti-diabetic activity [4], and antipsoriasis agent **3** [5]. That is why the purpose of the present work

was to obtain new amino acid derivatives of indane.

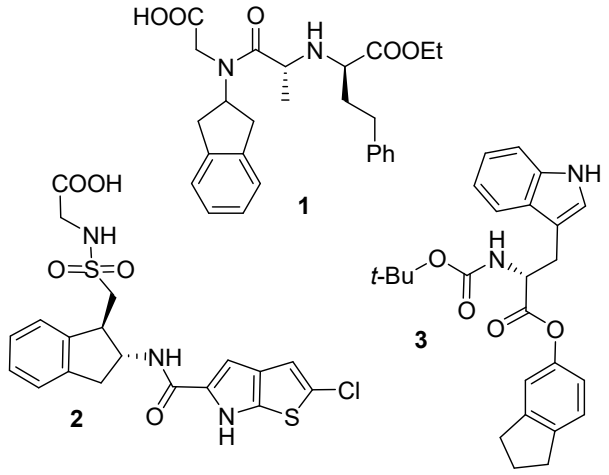
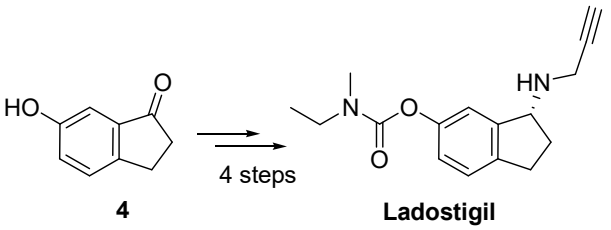


Figure 2. Bioactive indane derivatives with amino acid fragments.

As a base object for modification we chose 6-hydroxyindan-1-one **4**. Firstly, its molecule contains a phenolic OH group, convenient for connection of the amino acid residue *via* an amide bond with a hydroxylacetic linker; furthermore, exactly the indan-1-one system is observed in natural high-bioactive pterosins (**Figure 1**). In addition, indanones are a convenient material for conversion into a variety of related derivatives: indanes, hydroxy- and aminoindanes.

Studies of 6-hydroxyindan-1-on began in the 1920s with the works of Ingold and Piggott [6], and while in subsequent years the number of publications devoted to derivatives of the indane series has increased significantly [7]; and in some studies the synthetic possibilities of this molecule was been shown. For example, the using of 6-hydroxyindan-1-one **4** proved to be convenient for the preparation of Ladostigil (TV-3326) (**Scheme 1**), such substance demonstrates excellent results in the treatment of neurodegenerative disorders (Parkinsonism, Alzheimer's disease) [8].

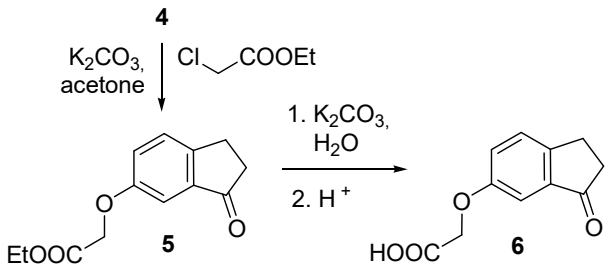


Scheme 1. 6-Hydroxyindan-1-one in Ladostigil synthesis

Known at first only as a synthetic compound, indanone **4** was recently isolated in nature: beside the pyridine alkaloids, polyphenols and cinnamic acids, this compound was isolated from the plant *Scrophularia ningpoensis*, known in traditional Chinese medicine due to myocardioprotective properties [9].

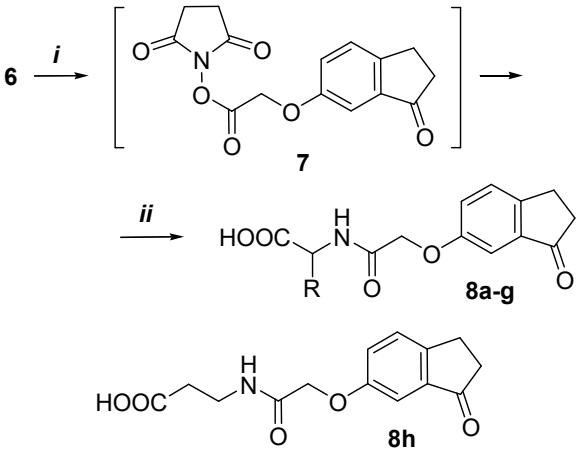
Results and discussion

Modification of indanone **4** with a hydroxyacetic fragment was carried out according to a scheme analogous to that described in the early publication [10] (**Scheme 2**); however for hydrolysis of ester **5** not acid but basic medium was used. (It had been noted that water solution of potash was implemented for such reaction; and using of aqueous alkali isn't recommended because the indanone system tends to condense in an alkaline medium [11]).



Scheme 2. The synthesis of 2-(3-oxo-2,3-dihydro-1*H*-inden-5-yloxy)acetic acid

To create the amide bond of acid **6** with the NH_2 group of amino acids, the classical method of activated *N*-hydroxysuccinimide esters was used [12, 13] (**Scheme 3**). This method makes it possible to obtain acylating agents (succinimide esters **7**) and to acylate the NH_2 group of the amino acid thought consecutive addition of reagents as "one-pot" synthesis; and the process conditions are mild, which is very important in case of acid **6** modification.

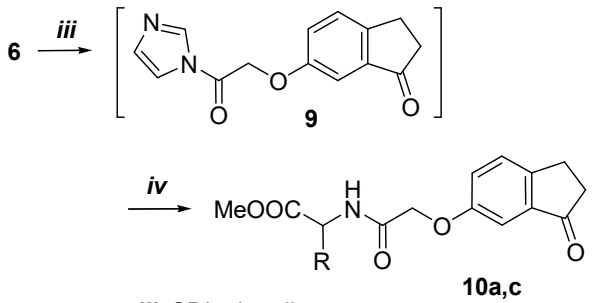


i: 1. DCC, abs. dioxane, rt; 2. *N*-hydroxysuccinimide
ii: 1. amino acid, $NaHCO_3$, dioxane : water 1:1, rt; 2. HCl

Scheme 3. The *N*-acylation of the amino acids by 2-(3-oxo-2,3-dihydro-1*H*-inden-5-yloxy)acetic acid thought the method of *N*-hydroxysuccinimide esters (R see **Table 1**).

The benefits of *N*-hydroxysuccinimide esters using became more apparent by a comparison it with another method we tried. Namely, some amino acid derivatives of indanone were obtained in reaction of methyl esters of amino acids and the activated imidazole derivative of acid **6** [13] (**Scheme 4**).

The reactions wich were presented on **Scheme 4** also carried out in a "one-pot" variation; and the yields of methyl esters **10a,c** can be considered suitable, but they are lower to the yields of products **8a,c**.

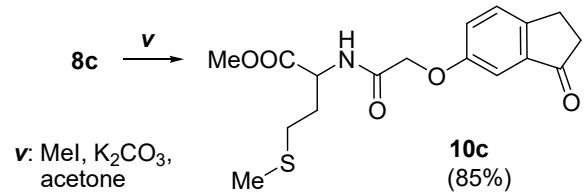


iii: CDI, abs. dioxane, rt;
iv: $H_2NCH(R)COOMe{\cdot}HCl$, Et_3N, 60°C

Scheme 4. The *N*-acylation of the amino acids methyl esters by 2-(3-oxo-2,3-dihydro-1*H*-inden-5-yloxy)acetic acid thought the activated imidazole derivatives (R see **Table 1**).

An alternative tactic to the obtaining of compounds **10a,c** could be implemented for the next way: the preparation of the amino acid derivative **8** through the stage of *N*-hydroxy-succinimide ester, and following methylation of the carboxylic function with methyl iodide. To compare the efficiency of this procedure with the reactions on **Scheme 4**, the methionine derivative **10c** (**Scheme 4**) was also obtained by

methylation of the corresponding derivative **8c** (**Scheme 5**).



Scheme 5. Synthesis of ester **10c** by methylation of acid **8c**.

Table 1. List, yields and melting points of the products **8, 10**

Pro-duct	*Initial amino acid* (R)	m.p., °C	Yeild, %
8a	*Gly* (H)	196–197	57
8b	*Nle* (*n*-Bu)	133–134	28
8c	*Met* ($CH_2CH_2SCH_3$)	71–72	80
8d	*Phe* (Bn)	142–143	56
8e	*Tyr* ($CH_2(4\text{-}OHC_6H_4)$)	197–198	26
8f	*Trp* (CH_2(indol-3-yl))	148–149	57
8g	*Cyt* ($(CH_2)_3NHC(NH)NH_2$)	185 dec.	61
8h	*β-Ala*	195–196	48
10a	*Gly* (H)	64–65	43
10c	*Met* ($CH_2CH_2SCH_3$)	89–90	52*/ 85**

* Scheme 4

** Scheme 5

In this case, the total yield of the substance **10c** from the initial acid **6** after two stages was 68%, which is higher than the yield following the **Scheme 4** using (52%). Therefore a strategy based on the production of amino acid derivatives of indanone type **8** should be considered most suitable not only because these products can be obtained easily and in high yields, but also because compounds **8** can be very convenient raw materials for the synthesis of the corresponding methyl esters **10**.

Experimental part

Reaction flow and identity of obtained compounds was controlled with TLC on Merck F_{254} plates using chloroform : methanol (19:1, *v*/*v*) system as eluents.

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

IR spectra were recorded on a Perkin Elmer BX II spectrometer in KBr pellets.

Melting points were determined using a *Kofler*-type Leica Galen III micro hot stage microscope and uncorrected.

General procedure for *N*-acylation of the amino acid by acid 6 through the method of *N*-hydroxysuccinimide esters. To a solution of 0.21 g (1 mmol) of acid **6** and 0.13 g (1.1 mmol) of *N*-hydroxysuccinimide in 10 ml of absolute dioxane at room temperature and with vigorous stirring 0.23 g (1.1 mmol) of dicyclohexylcarbodiimide was added. The reaction mixture was stirred at room

temperature for 2–3 h until an activated ester was formed (TLC monitoring); then a solution of 1.1 mmol of the corresponding amino acid and 0.14 g (1.67 mmol) of $NaHCO_3$ in 10 ml of water was added. The reaction mixture was stirred at room temperature for 2–3 h (TLC monitoring); and after the process was finished the dicyclohexylurea precipitate was filtered off. The filtrate was poured into 50 ml of water and the solution was acidified (pH 4–5) with dilute HCl. The precipitate formed was filtered off, recrystallized from mixture *i*-PrOH – water 1:1.

N-{[(1-oxoindan-6-yl)oxy]acetyl}-glycine **8a**. ^{1}H NMR (DMSO-d_6): 2.62 (br. s, 2H, H_2-3), 3.00 (br. s, 2H, H_2-2), 3.82 (br. s, 2H, NH$\underline{CH_2}$), 4.59 (s, 2H, OCH_2CO), 7.10 (br. s, 1H, H-7), 7.33 (br. d, *J*=8.0 Hz, 1H, H-5), 7.49 (d, *J*=8.0 Hz, 1H, H-4), 8.48 (br. s, 1H, NH). ^{13}C NMR (DMSO-d_6): 25.3, 37.2, 41.1, 67.6, 107.0, 124.2, 128.5, 138.4, 149.1, 157.8, 168.6, 171.7, 206.8. IR (KBr, ν, cm^{-1}): 3529, 3445, 3288, 1729, 1664, 1552, 1494, 1311, 1222, 1071, 836.

N-{[(1-oxoindan-6-yl)oxy]acetyl}norleucine **8b**. ^{1}H NMR (DMSO-d_6 : CCl_4 1:1): 0.89 (m, 3H, NHCH[$(CH_2)_3\underline{CH_3}$]), 1.28 (m, 4H, NHCH[$CH_2(\underline{CH_2})_2CH_3$]), 1.67 (m, 1H, [$\underline{CH_\alpha}(CH_2)_2CH_3$]), 1.77 (m, 1H, NHCH[$\underline{CH_\beta}$–$(CH_2)_2CH_3$]), 2.64 (br. t, *J*=4.3 Hz, 2H, H_2-3), 3.07 (br. t, *J*=4.3 Hz, 2H, H_2-2), 4.27 (m, 1H, NH$\underline{CH}$[*n*-Bu]), 4.54 (d, *J*=14.6 Hz, 1H, $OCH_\alpha CO$), 4.59 (d, *J*=14.6 Hz, 1H, $OCH_\beta CO$), 7.11 (d, *J*=2.2 Hz, 1H, H-7), 7.30 (dd, ^3J=8.0 Hz, ^4J=2.2 Hz, H-5), 7.46 (d, *J*=8.0 Hz, H-4), 8.09 (m, 1H, NH), 12.57 (br. s, 1H, COOH). ^{1}H NMR ($CDCl_3$): 0.90 (m, 3H, NHCH[$(CH_2)_3\underline{CH_3}$]), 1.34 (m, 4H, NHCH[$CH_2(\underline{CH_2})_2CH_3$]), 1.80 (m, 1H, [$\underline{CH_\alpha}(CH_2)_2CH_3$]), 1.97 (m, 1H, NHCH[$\underline{CH_\beta}$–$(CH_2)_2CH_3$]), 2.75 (br. t, *J*=5.0 Hz, 2H, H_2-3), 3.11 (br. t, *J*=5.0 Hz, 2H, H_2-2), 4.58 (s, 2H, OCH_2CO), 4.72 (m, 1H, NH$\underline{CH}$[*n*-Bu]), 7.00 (br. d, *J*=7.2 Hz, 1H, NH), 7.28 (m, 2H, H-5,7), 7.45 (d, *J*=8.4 Hz, 1H, H-4). ^{13}C NMR ($CDCl_3$): 13.8, 22.3, 25.2, 27.3, 37.0, 51.7, 56.6, 67.5, 107.3, 123.6, 127.9, 138.4, 149.2, 156.8, 168.0, 171.3, 206.7. IR (KBr, ν, cm^{-1}): 3380, 2958, 1700, 1540, 1274, 1220, 1187, 1062, 836.

N-{[(1-oxoindan-6-yl)oxy]acetyl}-methionine **8c**. ^{1}H NMR (DMSO-d_6 : CCl_4 1:1): 1.91–2.08 (m, 5H, NHCH[$CH_2\underline{CH_2}S\underline{CH_3}$]), 2.43 (m, 2H, NHCH[$\underline{CH_2}CH_2SCH_3$]), 2.64 (m, 2H, H_2-3), 3.07 (m, 2H, H_2-2), 4.42 (m, 1H, NH$\underline{CH}$[$(CH_2)_2SCH_3$]), 4.55 (m, 2H, OCH_2CO), 7.12 (br. s, 1H, H-7), 7.29 (br. d, *J*=8.2 Hz, H-5), 7.44 (d, *J*=8.2 Hz, H-4), 8.17 (br. d, *J*=7.0 Hz, 1H, NH). ^{13}C NMR (DMSO-d_6): 15.2, 25.4, 30.4, 31.0, 37.3, 51.3, 67.5, 106.8, 124.3, 128.4, 138.4, 149.0, 158.0, 168.4, 173.7, 206.5. IR (KBr, ν, cm^{-1}): 3501, 3400, 2935, 1670, 1519, 1446, 1309, 1256, 1208, 1063, 839.

N-{[(1-oxoindan-6-yl)oxy]acetyl}-phenylalanine **8d**. ^{1}H NMR ($CDCl_3$): 2.75 (br. t, *J*=5.2 Hz, 2H, H_2-3), 3.11 (br. t, *J*=5.2 Hz, 2H, H_2-2), 3.20 (dd, ^2J=14.2 Hz, ^3J=6.4 Hz, 1H, NHCH[$\underline{CH_\alpha}$Ph]), 3.26 (dd, ^2J=14.2 Hz,

^3J=6.4 Hz, 1H, NHCH[$\underline{CH}_\beta$Ph]), 4.50 (d, J=15.0 Hz, 1H, OCH_αCO), 4.55 (d, J=15.0 Hz, 1H, OCH_βCO), 4.98 (q, J=6.4 Hz, 1H, NH$\underline{CH}$[Bn]), 6.95 (br. d, J=8.2 Hz, 1H, NH), 7.13–7.19 (m, 5H, Ph), 7.28 (m, 2H, H-5,7), 7.42 (d, J=8.0 Hz, 1H, H-4). ^{1}H NMR (DMSO-d_6): 2.60–2.68 (m, 2H, H_2-3), 2.92–3.05 (m, 3H, H_2-2, NHCH[$\underline{CH}_\alpha$Ph]), 3.26 (dd, ^2J=13.2 Hz, ^3J=3.6 Hz, 1H, NHCH[$\underline{CH}_\beta$Ph]), 4.45–4.61 (m, 3H, OCH_2CO, NH$\underline{CH}$[Bn], 7.05 (br. s, 1H, H-7), 7.11–7.29 (m, 6H, H-5, Ph), 7.47 (d, J=8.2 Hz, 1H, H-4), 8.31 (br. s, 1H, NH), 12.87 (br. s, 1H, COOH). ^{13}C NMR (DMSO-d_6): 25.4, 37.0, 37.2, 53.9, 67.4, 106.9, 124.1, 127.1, 128.5, 128.9, 129.7, 138.1×2, 138.4×2, 149.0, 157.9, 168.2, 173.3, 206.6. IR (KBr, ν, cm^{-1}): 3412, 3266, 2930, 1673 br, 1544, 1490, 1306, 1278, 1222, 1186, 1069, 845, 693.

N-{[(1-oxoindan-6-yl)oxy]acetyl}-tyrosine **8e**. ^{1}H NMR (DMSO-d_6): 2.64 (br. t, J=5.2 Hz, 2H, H_2-3), 2.86 (m, 1H, NHCH[$\underline{CH}_\alpha$(4-HOC_6H_4)]), 2.95 (m, 1H, NHCH[$\underline{CH}_\beta$(4-HOC_6H_4)]), 3.01 (br. t, J=5.2 Hz, 2H, H_2-2), 4.41 (m, 1H, NH$\underline{CH}$[CH_2–(4-HOC_6H_4)]), 4.54 (m, 2H, OCH_2CO), 6.60 (d, J=8.3 Hz, 2H, H-3′,5′ (4-HOC_6H_4)), 6.96 (d, J=8.3 Hz, 2H, H-2′,6′ (4-HOC_6H_4)), 7.05 (br. s, 1H, H-7), 7.24 (br. d, J=8.2 Hz, H-5), 7.47 (d, J=8.2 Hz, H-4), 8.22 (d, J=8.0 Hz, 1H, NH), 9.23 (br. s, 1H, 4-$\underline{HO}C_6H_4$). ^{13}C NMR (DMSO-d_6): 25.4, 36.3, 37.3, 54.2, 67.5, 106.9, 115.6×2, 124.0, 128.1, 128.5, 130.7×2, 138,4, 149.0, 156.5, 157.9, 168.1, 173.4, 201.7. IR (KBr, ν, cm^{-1}): 3384, 2918, 1720, 1703, 1630, 1544, 1491, 1438, 1278, 1205, 1063, 914, 836, 794.

N-{[(1-oxoindan-6-yl)oxy]acetyl}-tryptophan **8f**. ^{1}H NMR (DMSO-d_6): 2.64 (br. t, J=4.5 Hz, 2H, H_2-3), 3.02 (br. t, J=4.5 Hz, 2H, H_2-2), 3.12–3.31 (m, 2H, NHCH[$\underline{CH_2}$(indol-3-yl)]), 4.49–4.65 (m, 3H, OCH_2CO, NH$\underline{CH}$[CH_2(indol-3-yl)]), 6.97 (br. t, J=7.8 Hz, 1H, H-5′ (indol-3-yl)), 7.00–7.11 (m, 2H, H-2′,6′), 7.14 (br. s, 1H, H-7), 7.22 (br. d, J=7.8 Hz, H-5), 7.36 (d, J=7.8 Hz, 1H, H-4′ (indol-3-yl)), 7.46 (d, J=7.8 Hz, H-4), 7.56 (d, J=7.8 Hz, 1H, H-7′ (indol-3-yl)), 7.96 (m, 1H, NH), 10.79 (s, 1H, NH (indol-3-yl)). ^{13}C NMR (DMSO-d_6): 25.4, 27.5, 37.3, 53.5, 67.5, 107.1, 110.3, 112.1, 118.8, 119.1, 121.6, 124.0, 124.4, 127.9, 128.5, 136.7, 138.4, 149.0, 157.8, 168.0, 173.8, 206.7. IR (KBr, ν, cm^{-1}): 3406, 3339, 1700 br, 1535, 1278, 1222, 1186, 1065, 833, 745.

N-{[(1-oxoindan-6-yl)oxy]acetyl}-citrulline **8g**. ^{1}H NMR (DMSO-d_6 : CCl_4 1:1): 1.37–1.46 (m, 2H, NHCH[$CH_2\underline{CH_2}CH_2$–$NHCONH_2$]), 1.61–1.71 (m, 1H, NHCH[$\underline{CH}_\alpha(CH_2)_2NHCONH_2$]), 1.75–1.85 (m, 1H, NHCH[$\underline{CH}_\beta(CH_2)_2NHCONH_2$]), 2.64 (br. t, J=4.5 Hz, 2H, H_2-3), 2.95–3.01 (m, 2H, NHCH[$(CH_2)_2\underline{CH_2}NHCONH_2$]), 3.06 (br. t, J=4.5 Hz, 2H, H_2-2), 4.25–4.32 (m, 1H, NH$\underline{CH}$[$(CH_2)_3NHCONH_2$]), 4.56 (s, 2H, OCH_2CO), 5.93 (br. s, 1H, $\underline{NH}CONH_2$), 7.10 (d,

J=2.2 Hz, 1H, H-7), 7.29 (dd, ^3J=8.3 Hz, ^4J=2.2 Hz, H-5), 7.44 (d, *J*=8.3 Hz, H-4), 8.21 (d, *J*=7.6 Hz, 1H, NH). ^{13}C NMR ($CDCl_3$): 25.2, 27.2, 28.8, 37.1, 52.0, 67.3, 106.7, 124.0, 128.3, 138.3, 148.8, 157.9, 159.2, 168.0, 173.7, 206.5. IR (KBr, ν, cm^{-1}): 3373, 3317, 2936, 2880, 1700, 1595, 1440, 1261, 1057, 845.

N-{[(1-oxoindan-6-yl)oxy]acetyl}-*β*-alanine **8h**. ^{1}H NMR (DMSO-d_6 : CCl_4 1:1): 2.41 (br. t, *J*=6.6 Hz, 2H, $NHCH_2\underline{CH_2}$), 2.63 (br. t, *J*=4.3 Hz, 2H, H_2-3), 3.05 (br. t, *J*=4.3 Hz, 2H, H_2-2), 3.31–3.40 (m, 2H, $NH\underline{CH_2}CH_2$), 4.46 (s, 2H, OCH_2CO), 7.08 (br. s, 1H, H-7), 7.27 (br. d, *J*=8.3 Hz, H-5), 7.44 (d, *J*=8.3 Hz, H-4), 8.05 (br. t, *J*=6.0 Hz, 1H, NH). ^{13}C NMR ($CDCl_3$): 25.2, 34.2, 35.0, 37.1, 67.6, 106.8, 124.0, 128.4, 138.3, 148.8, 157.8, 167.9, 173.3, 206.5. IR (KBr, ν, cm^{-1}): 3333, 2924, 1712, 1650, 1564, 1488, 1427, 1284, 1191, 1063, 845.

General procedure for *N*-acylation of the amino acid methyl esters by acid 6 through the activated imidazole derivatives. A solution of 0.21 g (1 mmol) of acid **6** and 0.2 g (1.25 mmol) 1,1'-carbonyldiimidazole in 10 ml of absolute dioxane vigorous stirring at room temperature for 2–2.5 h. To the resulting activated imidazole derivative 1.1 mmol of the corresponding ester of amino acid (hydrochloride) and 0.17 ml (1.25 mmol) of Et_3N were added. The reaction mixture was stirred at 50°C for 2–3 h, then cooled and poured into 50 ml of water and. The slowly-formed precipitate was filtered off, recrystallized from mixture *i*-PrOH – water 1:1.

Methyl ester of *N*-{[(1-oxoindan-6-yl)-oxy]acetyl}glycine **10a**. ^{1}H NMR ($CDCl_3$): 2.75 (br. t, *J*=5.6 Hz, 2H, H_2-3), 3.11 (br. t, *J*=5.6 Hz, 2H, H_2-2), 3.80 (s, 3H, COOMe), 4.17 (d, *J*=5.8 Hz, 2H, $NH\underline{CH_2}COOH$), 4.59 (s, 2H, OCH_2CO), 7.08 (m, 1H, NH), 7.24 (d, *J*=2.7 Hz, 1H, H-7), 7.27 (dd, ^3J=8.3 Hz, ^4J=2.7 Hz, H-5), 7.45 (d, *J*=8.3 Hz, 1H, H-4). ^{13}C NMR ($CDCl_3$): 25.2, 37.0, 40.8, 52.5, 67.5, 107.0, 123.6, 127.9, 138.5, 149.2, 156.9, 168.0, 169.9, 206.5. IR (KBr, ν, cm^{-1}): 3546, 3451, 3322, 3036, 2913, 1731, 1706, 1662, 1552, 1490, 1446, 1245, 1071, 984, 834.

Methyl ester of *N*-{[(1-oxoindan-6-yl)-oxy]acetyl}methionine **10c**. ^{1}H NMR ($CDCl_3$): 2.01–2.13 (m, 4H, $NHCH[CH_2\underline{CH_\alpha}S\underline{CH_3}]$), 2.19–2.27 (m, 1H, $NHCH[CH_2\underline{CH_\beta}SCH_3]$), 2.52 (t, *J*=7.3 Hz, 2H, $NHCH[\underline{CH_2}CH_2SCH_3]$), 2.75 (br. t, *J*=5.6 Hz, 2H, H_2-3), 3.11 (br. t, *J*=5.6 Hz, 2H, H_2-2), 3.79 (s, 3H, COOMe), 4.53–4.61 (m, 2H, OCH_2CO), 4.80–4.86 (m, 1H, $NH\underline{CH}[(CH_2)_2SCH_3]$), 7.24 (d, *J*=2.0 Hz, 1H, H-7), 7.25–7.30 (2H+$CHCl_3$, m, H-5, NH), 7.45 (d, *J*=8.5 Hz, 1H, H-4). ^{1}H NMR (DMSO-d_6): 1.85–2.06 (m, 5H, $NHCH[CH_2\underline{CH_2}S\underline{CH_3}]$), 2.34–2.50 (m, 2H, $NHCH[\underline{CH_2}CH_2SCH_3]$), 2.64 (br. t, *J*=5.6 Hz, 2H, H_2-3), 3.01 (br. t, *J*=5.6 Hz, 2H, H_2-2), 3.62 (s, 3H, COOMe), 4.41–4.50 (m, 1H, $NH\underline{CH}[(CH_2)_2SCH_3]$), 4.56–4.69 (m, 2H, OCH_2CO), 7.07 (br. s, 1H, H-7), 7.31 (br. d, *J*=8.2 Hz, H-5), 7.51 (d, *J*=8.2 Hz, H-4), 8.59

(d, J=7.7 Hz, 1H, NH). ^{13}C NMR (DMSO-d_6): 25.4, 30.5, 37.3, 51.2, 67.4, 106.7, 124.4, 128.5, 138.4, 149.0, 158.0, 168.6, 172.6, 206.7. IR (KBr, ν, cm^{-1}): 3417, 3064, 2952, 2913, 1731, 1712, 1688, 1614, 1524, 1488, 1443, 1362, 1250, 1166, 1057, 990, 903, 831.

General procedure for methylation of COOH group of acids 8. To a solution of 0.75 mmol of acid **8** in 10 ml of acetone 0.22 g (1.6 mmol) of dried and powdered K_2CO_3 and 0.1 ml (1.6 mmol) of MeI were added. The reaction mixture was refluxed with vigorous stirring 1.5–2 h. After the process was finished (TLC monitoring) the solution of product was separated from inorganic precipitate, and evaporated in vacuum. The residue was recrystallized from mixture *i*-PrOH – water 1:1.

Conclusions

So it was shown that the *N*-acylation of amino acids by 2-(3-oxo-2,3-dihydro-1*H*-inden-5-yloxy)acetic acid can be easily made using the method of *N*-hydroxysuccinimide esters; and it performed the creation of new indan-1-one derivatives with various amino acid fragments possible. For synthesis of appropriate methyl esters not reaction between 2-(3-oxo-2,3-dihydro-1*H*-inden-5-yloxy)acetic acid activated imidazole derivative and amino acids methyl esters but the methylation of the carboxylic function of preformed *N*-{[(1-oxoindan-6-yl)-oxy]acetyl}amino acids can be used.

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