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Convenient synthesis of 1-aryl-9*H*-β-carboline-3-carbaldehydes and their transformation into dihydropyrimidinone derivatives by Biginelli reaction

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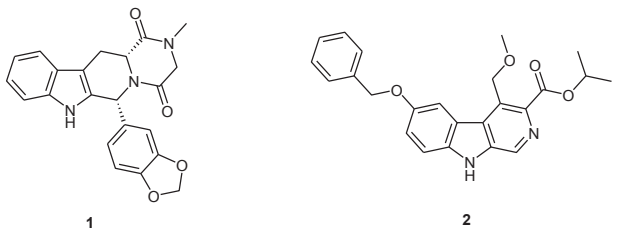
ABSTRACT

In the present work, a practical synthesis of 1-aryl-β-carboline-3-carbaldehydes as versatile building blocks and their application in Biginelli reaction is reported. The starting material of the four-step synthesis is racemic tryptophan methyl ester. The procedure involves a Pictet–Spengler cyclization, a dehydrogenation, an ester reduction, and an alcohol oxidation step. The β-carboline-3-carbaldehydes were further transformed using a Biginelli reaction into derivatives containing a pharmacologically significant dihydropyrimidine ring at position-3.

1. Introduction

The β-carbolines constitute an important class of natural and synthetic indole alkaloids.[1] β-Carbolines and their saturated counterparts such as dihydro-β-carbolines and tetrahydro-β-carbolines can be found in plants, mammalians, marine invertebrates, foods, drinks, and fruits.[2] Both simple and complicated β-carboline derivatives exhibit significant biological and pharmaceutical activities including antimicrobial,[3] antimalarial,[4] antithrombotic,[5] parasiticidal,[6] anti-HIV,[7] anti-Alzheimer,[8] and antifungal effects.[9] Moreover, tadalafil (**1**, Scheme 1) is a commercially available drug for the treatment of erectile dysfunction.[10] Another important representative of the β-carboline family is the anxiolytic drug abecarnil (**2**), a partial agonist acting selectively at the benzodiazepine site of the γ-aminobutyric acid A ($GABA_A$) receptor.[11]

In recent years the synthesis and biological activity of 1,3-disubstituted β-carbolines have been extensively studied.[12] We have previously reported the synthesis of novel fused tetracyclic β-carboline derivatives such as oxadiazolo-pyridoindoles, triazolo-pyridoindoles, and azetopyridoindoles.[13] In the present paper we focus on the synthesis of new 1,3-disubstituted β-carbolines containing a dihydropyrimidinone druglike scaffold at the C-3 position. A retrosynthetic analysis of the planned heterocyclic compounds **3** is outlined in Scheme 2. The final step was envisaged as a Biginelli reaction of 1-aryl-9*H*-β-carboline-3-carbaldehydes **4**. Only a few examples of similar aldehyde derivatives are known in the literature: Cao et al. reported the synthesis and study of the in vitro cytotoxic activity of some 9-substituted 1-(3,4,5-trimethoxyphenyl)-β-carboline-3-carbaldehydes,[14] but their application in Biginelli reaction is not reported. We planned to elaborate an improved process for the synthesis of aldehydes **4** and to extend it to various 1-aryl groups, starting from esters **5** by dehydration of the C-ring and subsequent transformation of the ester group to a formyl moiety. Synthesis of **5** was anticipated by the esterification of racemic tryptophan (**6**) followed by the



Scheme 1.

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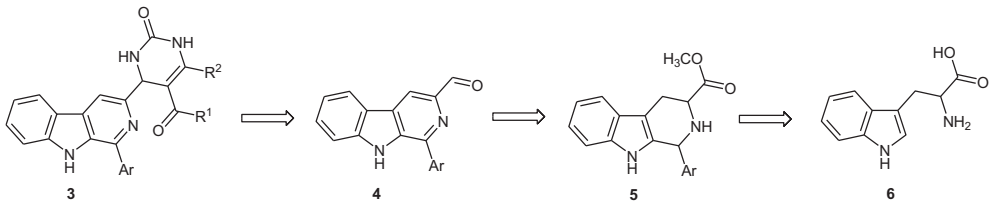


Scheme 2.

Pictet–Spengler reaction of racemic tryptophan methyl ester with the appropriate aromatic aldehydes.

2. Results and discussion

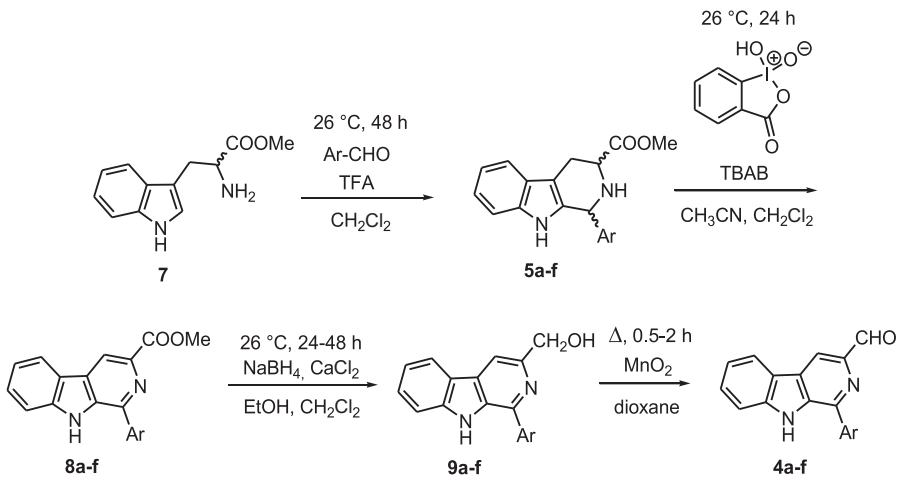
The starting material of the synthesis of 1-aryl-β-carboline-3-carbaldehydes (**4**) was racemic tryptophan (**6**). This compound was esterified using the literature method (thionyl chloride, methanol, room temperature, 24 h) and the ester (**7**) was isolated in 89% yield.[15] This intermediate was subjected to a Pictet–Spengler reaction with six different aromatic aldehydes (Scheme 3). The catalyst was trifluoroacetic acid and dichloromethane was used as the solvent.[10a,12f] The reaction was carried out at room temperature in order to avoid possible side products and the decomposition caused by heating of the solution. The tetrahydro-β-carboline esters (**5**) were prepared in good to excellent yields (66–96%) as diastereomeric mixtures. The next step of the synthesis was the aromatization of the C ring of the β-carboline skeleton. Three methods found in the literature were tried. The reaction with elemental sulfur in xylene[12d–e,16] or with 10% Pd/C in xylene[17] produced the aromatic ester in a yield of 50–60%. The best reagent was 2-iodoxybenzoic acid (IBX) that gave 74–83% yield.[18] Although some of lithium containing reagents ($LiAlH_4$, $LiBH_4$) are known for the reduction of **8** esters to alcohols **9**,[14c,17,19] and a patent application mentions $NaBH_4$ too,[20] we applied $CaCl_2$-activated $NaBH_4$ that has been used successfully in our laboratory.[21] The solvent was a mixture of dichloromethane and ethanol at room temperature. The products **9** were isolated in almost quantitative yields (93–98%). Alcohols **9** were oxidized by using activated manganese dioxide (MnO_2)[17] to give the expected aldehydes **4** in a yield of 60–87%. Accordingly the synthesis of the expected key intermediates **4** was accomplished in a total yield of 30–57% (Table 1). The reactions were followed by thin layer chromatography (TLC) and HPLC–MS. The identification and characterization of the substrates was performed with IR and NMR spectroscopy and high-resolution mass spectrometry. Among the synthesized β-carboline derivatives alcohols **9a**,**b**,**d**,**e** and all the aldehydes (**4a**–**f**) are new.

Table 1
Yields of the reaction sequence leading to 1-aryl-9*H*-β-carboline-3-carbaldehydes (**4**)

Entry		Ar	Yield of **5** (%)	Yield of **8** (%)	Yield of **9** (%)	Yield of **4** (%)	Overall yield **7**→**4** (%)
1	**a**	Ph	96	77	98	79	57
2	**b**	4-MeO–C_6H_4	66	78	96	86	43
3	**c**	4-Cl–C_6H_4	74	83	95	87	51
4	**d**	4-O_2N–C_6H_4	68	78	95	60	30
5	**e**	1,3-Benzodioxol-5-yl	86	81	93	69	45
6	**f**	2-Thienyl	78	74	97	84	47

The aldehyde key intermediates (**4**) were successfully reacted in a Biginelli reaction (Scheme 4) with urea (**10**) and four different β-dioxo compounds [pentane-2,4-dione (**11a**), ethyl acetoacetate (**11b**), ethyl isobutyrylacetate (**11c**), and ethyl benzoylacetate (**11d**)]. The reaction was catalyzed by $NiCl_2 \cdot 6H_2O$ and the solvent was boiling ethanol containing a catalytic amount of concd aq hydrochloric acid solution.[22] The reaction did not take place when *N*-bromosuccinimide[23] was applied as the catalyst. The reactions were followed by TLC and HPLC–MS until the starting material disappeared or the conversion was measured constant. The isolated 2-oxo-1,2,3,4-tetrahydropyrimidine (**12a**–**v**) derivatives have not been described before.

Only a few target compounds were prepared in a yield exceeding 80%, in most cases the Biginelli products were obtained in medium yields (ca. 40–75%). A possible explanation for the moderate yield is a side-reaction, the product of which was successfully isolated in 47% yield in one case when **4c** was treated with ethyl benzoylacetate (**11d**) and urea (Scheme 5). Obviously, aldehyde **4c** and **11d** gave a Knoevenagel-type by-product [**13**, (*E*) isomer], which latter is unable to react with urea to give target compound **12l**.



Scheme 3.

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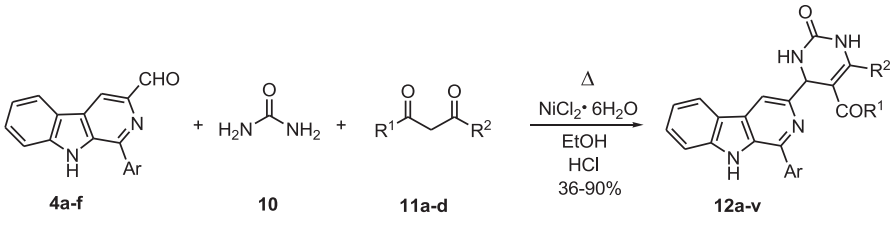
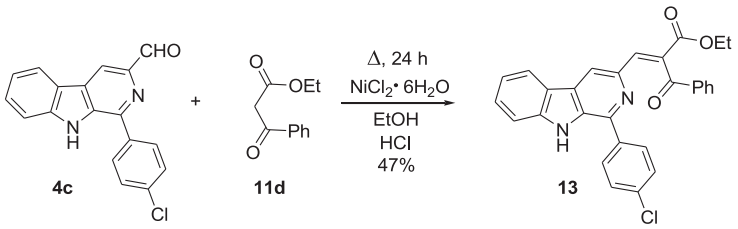


Scheme 4.



Scheme 5.

3. Conclusions

A four-step versatile synthesis of new 1-aryl-β-carboline-3-carbaldehydes is reported starting from the easily available racemic tryptophan methyl ester through a Pictet–Spengler cyclization with an aromatic aldehyde as the first step. Among the known possibilities for the dehydrogenation of the tetrahydro-β-carboline esters thus obtained, the application of IBX provided the highest yields in our hands. For the reduction of the aromatic ester function to the corresponding alcohol, the use of $Ca(BH_4)_2$ generated in situ from $CaCl_2$ and $NaBH_4$ proved to be a versatile method and the oxidation to the corresponding carbaldehydes was achieved by using activated MnO_2. Due to the applicability of the formyl moiety in various chemical reactions, these new aldehydes are versatile intermediates in organic and medicinal chemistry. In the present work the aldehydes were taken into a three-component Biginelli reaction with urea and β-keto esters. Accordingly, a series of new, potentially bioactive β-carbolinyl-dihydropyrimidinone derivatives were synthesized. In one case a Knoevenagel-type side-reaction was observed.

4. Experimental section

4.1. General

Commercially available reagents were purchased from Sigma–Aldrich and were used without further purification. All melting points were measured with a Kofler–Boëtius micro-apparatus and were not corrected. ^1H and ^{13}C NMR spectra were recorded with a Varian Unity Inova 500 spectrometer (500 and 125 MHz for ^1H and ^{13}C NMR spectra, respectively) or with a Bruker Avance III spectrometer (400 and 100 MHz for ^1H and ^{13}C NMR spectra, respectively). DMSO-d_6 was used as the solvent and TMS was used as the internal standard. The FTIR spectra of KBr pellets or neat samples were recorded with a Bruker Vector 22 spectrometer. Mass spectra were recorded on a Bruker Maxis Impact Q-TOF spectrometer coupled to a Dionex UltiMate 3000 RRLC (Rapid Resolutions Liquid Chromatograph) system. The chromatographic column used was a Waters Acquity BEH C18 column with dimensions of 2.1×50 mm. A gradient elution of 5 min was used at a flow rate of 0.5 mL/min [initial: 10% acetonitrile (ACN), 0.01 M ammonium acetate (AmAc); 5 min: 90% ACN, 0.01 M AmAc]. The reactions were monitored by analytical TLC on silica gel 60 PF_{254} and LC–MS chromatography. Analytical samples of new compounds were obtained by crystallization.

4.2. General procedure for the synthesis of tetrahydro-β-carboline carboxylate derivatives. Preparation of compounds 5a–f

Racemic tryptophan methyl ester (7) (41.3 mmol, 9.0 g) and the appropriate aldehyde (1.1 equiv, 45.4 mmol, 4.6 mL of benzaldehyde, 5.5 mL of 4-methoxybenzaldehyde, 6.4 g of 4-chlorobenzaldehyde, 6.9 g of 4-nitrobenzaldehyde, 4.2 g of thiophene-2-carbaldehyde, 6.8 g of benzo[*d*][1,3]dioxol-5-carbaldehyde) were dissolved in dichloromethane (100 mL) and cooled to 0 °C with an ice bath. To this solution was added dropwise TFA (6.4 mL), and the mixture was stirred at 26 °C until the starting material disappeared. The reaction mixture was then basified with 10% $NaHCO_3$ (150 mL) and extracted with dichloromethane (2×30 mL). The organic layer was washed with water (30 mL), dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by recrystallization to give the esters **5** as diastereomers. Spectroscopic data of the products are in accord with the literature (**5a**,[24a] **5b**,[24b] **5c**,[24c] **5d**,[24b] **5e**,[24d] **5f**[24e]).

4.3. General procedure for the dehydrogenation of tetrahydro-β-carboline carboxylate derivatives. Preparation of β-carboline carboxylates 8a–f

To a solution of tetrahydro-β-carboline carboxylate diastereomeric mixtures (**5a**–**f**) [26.1 mmol, 8.0 g methyl-1-phenyl- (**5a**), 8.8 g methyl-1-(4-methoxyphenyl)- (**5b**), 8.9 g methyl-1-(4-chlorophenyl)- (**5c**), 9.2 g methyl-1-(4-nitrophenyl)- (**5d**), 9.1 g methyl-1-(1,3-benzodioxol-5-yl)- (**5e**), 8.2 g methyl-1-thiophene-2-yl-2,3,4,9-tetrahydro-1*H*-β-carboline-3-carboxylate (**5f**)] in dichloromethane (100 mL) and acetonitrile (100 mL) at 26 °C were added TBAB (0.5 equiv, 13.1 mmol, 4.2 g) and IBX (2 equiv,

52.2 mmol, 14.6 g). The reaction mixture was stirred until the starting material disappeared. The reaction mixture was diluted with saturated $Na_2S_2O_3$ (100 mL) and 25% aq NH_3 (30 mL) and extracted with dichloromethane/methanol 7:3 (3×100 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and the residue purified by flash chromatography (silica gel 60 PF_{254}) using hexane/dichloromethane and dichloromethane/methanol as the eluents to afford esters **8a**–**f**. Spectroscopic data of the products are in accord with the literature (**8a**,**b**,**d**,[18] **8c**,[24a] **8e**,[25a] **8f**[25b]).

4.4. General procedure for the synthesis of (β-carbolin-3-yl) methanol derivatives. Preparation of compounds 9a–f

To a solution of β-carboline carboxylate derivatives [18.2 mmol, 5.5 g methyl-1-phenyl- (**8a**), 6.1 g methyl 1-(4-methoxyphenyl)- (**8b**), 6.1 g methyl 1-(4-chlorophenyl)- (**8c**), 6.3 g methyl 1-(4-nitrophenyl)- (**8d**), 6.3 g methyl 1-(1,3-benzodioxol-5-yl)- (**8e**), 5.6 g methyl 1-(thiophene-2-yl)-9*H*-β-carboline-3-carboxylate (**8f**)] and crushed $CaCl_2$ (2 equiv, 36.4 mmol, 4.0 g) in dichloromethane (100 mL) and ethanol (100 mL) $NaBH_4$ (5 equiv, 90.9 mmol, 3.5 g) was added in small portions at 26 °C. The reaction mixture was stirred until the starting material disappeared, it was then concentrated in vacuo and quenched with dichloromethane/methanol (1:1, 250 mL). Then 1 M aq solution of hydrochloric acid (80 mL) and 1 M NaOH (80 mL) were added. The mixture was separated and extracted with dichloromethane/methanol 7:3 (3×100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by recrystallization. Spectroscopic data of products **9c** and **9f** are in accord with the literature.[25b] Alcohols **9a**,**b**,**d**,**e** are new compounds and they are characterized below.

*4.4.1. (1-Phenyl-9H-β-carbolin-3-yl)methanol (**9a**).* Yield: 4.90 g (98%), white crystals, mp 176–177 °C (*i*-PrOH). IR (KBr, cm^{-1}): 3266, 1699, 1416, 1243, 1056, 734. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.57 (br s, 1H, NH), 8.27–8.25 (m, 1H, ArH), 8.21 (s, 1H, ArH), 8.04–8.00 (m, 2H, ArH), 7.67–7.65 (m, 1H, ArH), 7.59–7.56 (m, 2H, ArH), 7.53–7.51 (m, 2H), 7.25 (t, *J*=7.3 Hz, 1H, ArH), 5.39 (t, *J*=5.7 Hz, 1H, OH), 4.79 (d, *J*=5.6 Hz, 2H, CH_2) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 150.8 (C═), 141.6 (C═), 140.9 (C═), 138.5 (C═), 132.1 (C═), 130.2 (C═), 128.8 (HC═), 128.7 (HC═), 128.5 (HC═), 128.1 (HC═), 121.6 (HC═), 121.1 (C═), 119.5 (HC═), 112.5 (HC═), 110.3 (HC═), 64.8 (CH_2) ppm. HRMS calcd for $C_{18}H_{15}N_2O$ $[M+H]^+$ 275.1179; found 275.1184.

*4.4.2. [1-(4-Methoxyphenyl)-9H-β-carbolin-3-yl]methanol (**9b**).* Yield: 5.80 g (96%), white crystals, mp 176–177 °C (MeCN). IR (KBr, cm^{-1}): 3156, 1654, 1515, 1246, 738. ^1H NMR (DMSO-d_6, 400 MHz): δ 11.38 (br s, 1H, NH), 8.27–8.23 (m, 1H, ArH), 8.11 (s, 1H, ArH), 8.02–7.98 (m, 2H, ArH), 7.65–7.62 (m, 1H, ArH), 7.55–7.51 (m, 1H, ArH), 7.26–7.22 (m, 1H, ArH), 7.18–7.15 (m, 2H, ArH), 5.39 (t, *J*=5.7 Hz, 1H, OH), 4.78 (d, *J*=5.7 Hz, 2H, CH_2), 3.87 (s, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 100 MHz): δ 159.7 (O–C═), 150.7 (C═), 141.6 (C═), 140.9 (C═), 131.9 (C═), 131.0 (C═), 130.1 (C═), 129.9 (HC═), 128.1 (HC═), 121.6 (HC═), 121.2 (C═), 119.5 (HC═), 114.2 (HC═), 112.5 (HC═), 109.8 (HC═), 64.9 (CH_2), 55.5 (CH_3) ppm. HRMS calcd for $C_{19}H_{17}N_2O_2$ $[M+H]^+$ 305.1285; found 305.1291.

*4.4.3. [1-(4-Nitrophenyl)-9H-β-carbolin-3-yl]methanol (**9d**).* Yield: 5.50 g (95%), yellow crystals, mp 257–259 °C (DMF/EtOH). IR (KBr, cm^{-1}): 3351, 3097, 1628, 1523, 1353, 783. ^1H NMR (DMSO-d_6, 400 MHz): δ 12.35 (br s, 1H, NH), 8.65 (br s, 1H, ArH), 8.52 (d, *J*=9.4 Hz, 2H, ArH), 8.48 (d, *J*=8.0 Hz, 1H, ArH), 8.31 (d, *J*=7.8 Hz, 2H, ArH), 7.76–7.70 (m, 2H, ArH), 7.42–7.38 (m, 1H, ArH), 4.97 (s, 2H, CH_2), 4.0 (br s, 1H, OH together with water) ppm. ^{13}C NMR (DMSO-d_6, 100 MHz): δ 148.5 (C═), 147.2 (O_2N–C═), 143.9 (C═), 135.8 (C═), 133.7 (C═), 132.5 (C═), 131.4 (HC═), 130.9 (HC═), 124.0 (HC═), 123.1 (HC═), 121.1 (HC═), 120.2 (HC═), 113.8 (HC═), 113.0 (HC═), 61.5 (CH_2) ppm. HRMS calcd for $C_{18}H_{14}N_3O_3$ $[M+H]^+$ 320.1030; found 320.1034.

*4.4.4. [1-(1,3-Benzodioxol-5-yl)-9H-β-carbolin-3-yl]methanol (**9e**).* Yield: 5.39 g (93%), yellow crystals, mp 205–207 °C (DMF/H_2O). IR (KBr, cm^{-1}): 3154, 3090, 2905, 1666, 1502, 1244, 1041, 741. ^1H NMR (DMSO-d_6, 400 MHz): δ 11.37 (br s, 1H, NH), 8.25 (d, *J*=7.8 Hz, 1H, ArH), 8.11 (s, 1H, ArH), 7.64–7.62 (m, 1H, ArH), 7.57–7.51 (m, 3H, ArH), 7.24 (t, *J*=7.4 Hz, 1H, ArH), 7.14 (d, *J*=8.5 Hz, 1H, ArH), 6.14 (s, 2H, O–CH_2–O), 5.35 (t, *J*=5.8 Hz, 1H, OH), 4.77 (d, *J*=5.7 Hz, 2H, CH_2) ppm. ^{13}C NMR (DMSO-d_6, 100 MHz): δ 150.6 (C═), 147.7 [two signals: 147.74 (O–C═), 147.70 (O–C═)], 141.6 (C═), 140.5 (C═), 132.6 (C═), 131.8 (C═), 130.2 (C═), 128.1 (HC═), 122.5 (HC═), 121.6 (HC═), 121.1 (C═), 119.5 (HC═), 112.5 (HC═), 110.0 (HC═), 108.7 (HC═), 108.6 (HC═), 101.4 (O–CH_2–O), 64.9 (CH_2) ppm. HRMS calcd for $C_{19}H_{15}N_2O_3$ $[M+H]^+$ 319.1077; found 319.1093.

4.5. General procedure for the oxidation of (β-carbolin-3-yl) methanol derivatives. Preparation of aldehydes 4a–f

The (β-carbolin-3-yl)methanol derivative [15.9 mmol, 4.4 g 1-phenyl- (**9a**), 4.9 g 1-(4-methoxyphenyl)- (**9b**), 4.9 g 1-(4-chlorophenyl)- (**9c**), 5.1 g 1-(4-nitrophenyl)- (**9d**), 5.1 g 1-(1,3-benzodioxol-5-yl)- (**9e**), 4.5 g [1-(thiophene-2-yl)-9*H*-β-carboline-3-yl]methanol (**9f**)] was suspended in dioxane (200 mL) and activated manganese dioxide (10 equiv, 159.3 mmol, 13.9 g) was added. The reaction mixture was refluxed until the starting material disappeared. The suspension was filtered and concentrated at reduced pressure. Pure products were obtained by recrystallization. Compounds **4a**–**f** are new.

*4.5.1. 1-Phenyl-9H-β-carbolin-3-carbaldehyde (**4a**).* Yield 3.40 g (79%), light brown crystals, mp 313–314 °C (decomp., dioxane/EtOH). IR (KBr, cm^{-1}): 3362, 1683, 1585, 1285. ^1H NMR (DMSO-d_6, 400 MHz): δ 12.17 (br s, 1H, NH), 10.18 (s, 1H, CHO), 8.88 (s, 1H, ArH), 8.75–8.73 (m, 1H, ArH), 8.07 (d, *J*=7.4 Hz, 2H, ArH), 7.76–7.71 (m, 1H, ArH), 7.69–7.58 (m, 4H, ArH), 7.38–7.35 (m, 1H, ArH) ppm. ^{13}C NMR (DMSO-d_6, 100 MHz): δ 193.1 (CHO), 143.7 (C═), 142.7 (C═), 141.8 (C═), 137.2 (C═), 131.6 (C═), 129.4 (C═), 129.3 (HC═), 129.0 (HC═), 128.7 (HC═), 128.5 (HC═), 122.3 (HC═), 121.5 (C═), 120.8 (HC═), 113.9 (HC═), 112.9 (HC═) ppm. HRMS calcd for $C_{18}H_{13}N_2O$ $[M+H]^+$ 273.1022; found 273.1028.

*4.5.2. 1-(4-Methoxyphenyl)-9H-β-carboline-3-carbaldehyde (**4b**).* Yield 4.00 g (83%), pale yellow crystals, mp 242–244 °C (MeCN). IR (KBr, cm^{-1}): 3286, 1675, 1511, 1245, 1024, 844, 752. ^1H NMR (DMSO-d_6, 400 MHz): δ 12.01 (br s, 1H, NH), 10.17 (s, 1H, CHO), 8.78 (s, 1H, ArH), 8.46–8.43 (m, 1H, ArH), 8.07–8.03 (m, 2H, ArH), 7.75–7.72 (m, 1H, ArH), 7.65–7.61 (m, 1H, ArH), 7.38–7.34 (m, 1H, ArH), 7.24–7.20 (m, 2H, ArH), 3.90 (s, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 100 MHz): δ 193.3 (CHO), 160.2 (MeO–C═), 143.4 (C═), 142.7 (C═), 141.7 (C═), 135.4 (C═), 130.1 (HC═), 129.9 (HC═), 129.3 (C═), 129.0 (C═), 122.3 (HC═), 121.6 (C═), 120.8 (HC═), 114.4 (HC═), 113.6 (HC═), 113.1 (HC═), 55.6 (CH_3) ppm. HRMS calcd for $C_{19}H_{15}N_2O_2$ $[M+H]^+$ 303.1128; found 303.1137.

*4.5.3. 1-(4-Chlorophenyl)-9H-β-carboline-3-carbaldehyde (**4c**).* Yield 4.30 g (87%), pale yellow crystals, mp 267–268 °C (dioxane). IR (KBr, cm^{-1}): 3291, 1683, 1561, 1286, 737. ^1H NMR (DMSO-d_6, 400 MHz): δ 12.06 (br s, 1H, NH), 10.17 (s, 1H, CHO), 8.83 (s, 1H, ArH), 8.45 (d, *J*=7.8 Hz, 1H, ArH), 8.11–8.06 (m, 2H, ArH), 7.73–7.70 (m, 3H, ArH), 7.64 (t, *J*=7.6 Hz, 1H, ArH), 7.37 (t, *J*=7.4 Hz, 1H, ArH) ppm. ^{13}C NMR (DMSO-d_6, 100 MHz): δ 193.0 (CHO), 143.4 (C═), 141.8 (C═), 141.4 (C═), 136.2 (C═), 135.5 (C═), 134.0 (C═),

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130.5 (Cl–C=), 129.6 (HC=), 129.1 (C=), 128.9 (HC=), 122.3 (HC=), 121.5 (C=), 120.9 (HC=), 114.2 (HC=), 113.0 (HC=) ppm. HRMS calcd for $C_{18}H_{12}ClN_2O$ $[M+H]^+$ 307.0633; found 307.0637.

*4.5.4. 1-(4-Nitrophenyl)-9H-β-carboline-3-carbaldehyde (**4d**).* Yield 3.00 g (60%), yellow crystals, mp 305–306 °C (DMF). IR (KBr, cm^{-1}): 3284, 1684, 1510, 1347, 1237. ^1H NMR (DMSO-d_6, 500 MHz): δ 12.12 (br s, 1H, NH), 10.15 (s, 1H, CHO), 8.86 (s, 1H, ArH), 8.47–8.43 (m, 3H, ArH), 8.33–8.31 (m, 2H, ArH), 7.71–7.69 (m, 1H, ArH), 7.65–7.62 (m, 1H, ArH), 7.38–7.34 (m, 1H, ArH) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 192.8 (CHO), 147.7 (O_2N–C=), 143.6 (C=), 143.5 (C=), 141.9 (C=), 140.0 (C=), 135.8 (C=), 130.2 (C=), 130.0 (HC=), 129.4 (HC=), 124.0 (HC=), 122.4 (HC=), 121.4 (C=), 121.0 (HC=), 114.8 (HC=), 113.0 (HC=) ppm. HRMS calcd for $C_{18}H_{12}N_3O_3$ $[M+H]^+$ 318.0873; found 318.0864.

*4.5.5. 1-(1,3-Benzodioxol-5-yl)-9H-β-carboline-3-carbaldehyde (**4e**).* Yield 3.70 g (69%), light brown crystals, mp 264–266 °C (decomp., dioxane). IR (KBr, cm^{-1}): 3278, 1679, 1559, 1313, 1290, 1124. ^1H NMR (DMSO-d_6, 500 MHz): 11.99 (br s, 1H, NH), 10.16 (s, 1H, CHO), 8.77 (s, 1H, ArH), 8.43 (d, *J*=7.6 Hz, 1H, ArH), 7.74–7.72 (m, 1H, ArH), 7.64–7.61 (m, 3H, ArH), 7.37–7.34 (m, 1H, ArH), 7.19 (d, *J*=8.1 Hz, 1H, ArH), 6.18 (s, 2H, O–CH_2–O) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 193.0 (CHO), 148.1 (O–C=), 147.7 (O–C=), 143.1 (C=), 142.2 (C=), 141.6 (C=), 135.2 (C=), 131.3 (C=), 129.2 (C=), 128.8 (HC=), 122.8 (HC=), 122.1 (HC=), 121.4 (C=), 120.6 (HC=), 113.5 (HC=), 112.9 (HC=), 108.7 (HC=), 108.6 (HC=), 101.5 (O–CH_2–O) ppm. HRMS calcd for $C_{19}H_{13}N_2O_3$ $[M+H]^+$ 317.0921; found 317.0922.

*4.5.6. 1-Thiophen-2-yl-9H-β-carboline-3-carbaldehyde (**4f**).* Yield 3.70 g (84%), pale yellow crystals, mp 300–302 °C (decomp., dioxane). IR (KBr, cm^{-1}): 3299, 1675, 1589, 1241. ^1H NMR (DMSO-d_6, 500 MHz): 11.99 (br s, 1H, NH), 10.13 (s, 1H, CHO), 8.77 (s, 1H, ArH), 8.44 (d, *J*=7.9 Hz, 1H, ArH), 8.19–8.18 (m, 1H, ArH), 7.84–7.80 (m, 2H, ArH), 7.68–7.65 (m, 1H, ArH), 7.40–7.37 (m, 2H, ArH) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 192.6 (CHO), 142.9 (C=), 142.1 (C=), 141.8 (C=), 136.9 (C=), 133.4 (C=), 130.0 (C=), 129.2 (HC=), 129.1 (HC=), 128.7 (HC=), 127.1 (HC=), 122.2 (C=), 121.5 (HC=), 121.1 (HC=), 113.8 (HC=), 113.2 (HC=) ppm. HRMS calcd for $C_{16}H_{11}N_2OS$ $[M+H]^+$ 279.0587; found 279.0596.

4.6. General procedure for the synthesis of β-carbolinyl-dihydropyrimidinone derivatives. Preparation of compounds 12a–v

A suspension of β-carbolin-3-carbaldehyde derivatives [1.32 mmol, 0.36 g 1-phenyl- (**4a**), 0.40 g 1-(4-methoxyphenyl)- (**4b**), 0.41 g 1-(4-chlorophenyl)- (**4c**), 0.39 g 1-(4-nitrophenyl)- (**4d**), 0.42 g 1-(1,3-benzodioxol-5-yl)- (**4e**), 0.37 g 1-(thiophene-2-yl)-9*H*-β-carboline-3-carbaldehyde (**4f**)], urea (**10**) (1.5 equiv, 1.97 mmol, 0.12 g), the appropriate β-keto ester [1.32 mmol, 0.13 mL pentane-2,4-dione (**11a**), 0.17 mL ethyl acetoacetate (**11b**), 0.21 mL ethyl isobutyrylacetate (**11c**), 0.23 mL ethyl benzoylacetate (**11d**)], $NiCl_2 \cdot 6H_2O$ catalyst (0.25 equiv, 0.07 g), and concd aq HCl solution (five drops) in EtOH (20 mL) was heated under reflux until the starting material disappeared or the conversion did not grow. After cooling, the reaction mixture was concentrated. Water (30 mL) was added and the mixture was extracted with chloroform/methanol 7:3 (3×50 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel 60 PF_{254}) with dichloromethane/methanol 97:3 eluent. Compounds **12a**–**v** are new.

*4.6.1. 5-Acetyl-6-methyl-4-(1-phenyl-9H-β-carbolin-3-yl)-3,4-dihydropyrimidin-2(1H)-one (**12a**).* Yield 0.33 g (63%), white crystals, mp 272–273 °C (EtOH/$CHCl_3$/DMF). IR (KBr, cm^{-1}): 3637, 3232, 3111, 1700, 1623, 1466, 1233. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.51 (br s, 1H, NH), 9.17 (br s, 1H, NH), 8.24 (d, *J*=7.9 Hz, 1H, ArH), 8.08–8.06 (m, 2H, ArH), 7.95 (s, 1H, ArH), 7.80 (br s, 1H, NH), 7.68–7.50 (m, 5H, ArH), 7.25 (t, *J*=7.4 Hz, 1H, ArH), 5.56 (m, 1H, CH), 2.27 (m, 6H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.0 (Me–C=O), 152.9 (HN–CO–NH), 151.6 (C=), 147.5 (C=), 141.7 (C=), 141.2 (C=), 138.4 (C=), 132.2 (C=), 130.2 (C=), 128.8 (HC=), 128.7 (HC=), 128.5 (HC=), 128.3 (HC=), 121.6 (HC=), 121.0 (C=), 119.7 (HC=), 112.6 (HC=), 110.4 (HC=), 109.8 (C=), 56.2 (CH), 30.5 (CH_3), 18.9 (CH_3) ppm. HRMS calcd for $C_{24}H_{21}N_4O_2$ $[M+H]^+$ 397.1659; found 397.1656.

*4.6.2. Ethyl 6-methyl-2-oxo-4-(1-phenyl-9H-β-carbolin-3-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12b**).* Yield 0.42 g (74%), pale yellow crystals, mp 174–176 °C (EtOH). IR (KBr, cm^{-1}): 3422, 3302, 3105, 1697, 1633, 1451, 1238, 1096. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.48 (br s, 1H, NH), 9.15 (s, 1H, NH), 8.24 (d, *J*=7.8 Hz, 1H, ArH), 8.08 (m, 2H, ArH), 7.91 (s, 1H, ArH), 7.66–7.59 (m, 4H, ArH, NH), 7.56–7.51 (m, 2H, ArH), 7.25 (t, *J*=7.4 Hz, 1H, ArH), 5.46 (d, *J*=3.0 Hz, 1H, CH), 4.03–4.01 (m, 2H, CH_2), 2.27 (s, 3H, CH_3), 1.11 (t, *J*=7.2 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.8 (EtO–C=O), 153.1 (HN–CO–NH), 151.6 (C=), 148.5 (HN–C=), 141.7 (C=), 141.1 (C=), 138.5 (C=), 132.3 (C=), 130.0 (C=), 128.8 [two signals: 128.83 (HC=), 128.78 (HC=)], 128.5 (HC=), 128.3 (C=), 121.5 (HC=), 121.1 (C=), 119.7 (HC=), 112.6 (HC=), 110.3 (HC=), 99.2 (C=), 59.2 (CH_2), 55.9 (CH), 18.0 (CH_3), 14.3 (CH_3) ppm. HRMS calcd for $C_{25}H_{23}N_4O_3$ $[M+H]^+$ 427.1765; found 427.1766.

*4.6.3. Ethyl 6-(1-methylethyl)-2-oxo-4-(1-phenyl-9H-β-carbolin-3-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12c**).* Yield 0.44 g (74%), white crystals, mp 257–258 °C (EtOH). IR (KBr, cm^{-1}): 3413, 3256, 2973, 1676, 1627, 1455, 1264, 1091. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.50 (br s, 1H, NH), 8.81 (br s, 1H, NH), 8.21 (d, *J*=7.9 Hz, 1H, ArH), 8.12–8.10 (m, 2H, ArH), 7.90–7.89 (m, 1H, ArH), 7.68–7.51 (m, 6H, ArH, NH), 7.26 (t, *J*=7.5 Hz, 1H, ArH), 5.45 (d, *J*=3.2 Hz, 1H, CH), 4.17 (sp, *J*=6.9 Hz, 1H, CH), 4.01 (q, *J*=7.0 Hz, 2H, CH_2), 1.18 (d, *J*=7.1 Hz, 3H, CH_3), 1.17 (d, *J*=6.9 Hz, 3H, CH_3), 1.10 (t, *J*=6.4 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.8 (EtO–C=O), 156.5 (HN–C=), 153.4 (HN–CO–NH), 151.6 (C=), 141.7 (C=), 141.2 (C=), 138.4 (C=), 132.3 (C=), 130.0 (C=), 128.8 (HC=), 128.7 (HC=), 128.4 (HC=), 128.3 (HC=), 121.3 (HC=), 121.1 (C=), 119.7 (HC=), 112.7 (HC=), 110.2 (HC=), 98.3 (C=), 59.2 (CH_2), 56.0 (CH), 27.1 (CH), 19.3 (CH_3), 19.2 (CH_3), 14.2 (CH_3) ppm. HRMS calcd for $C_{27}H_{27}N_4O_3$ $[M+H]^+$ 455.2078; found 455.2072.

*4.6.4. Ethyl 2-oxo-6-phenyl-4-(1-phenyl-9H-β-carbolin-3-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12d**).* Yield 0.46 g (71%), white crystals, mp 288–289 °C (EtOH/$CHCl_3$). IR (KBr, cm^{-1}): 3404, 3341, 3081, 1670, 1494, 1238. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.69 (br s, 1H, NH), 9.21 (br s, 1H, NH), 8.29–8.26 (m, 1H, ArH), 8.12 (d, *J*=7.5 Hz, 2H, ArH), 8.10 (s, 1H, ArH), 7.74 (br s, 1H, NH), 7.69–7.67 (m, 2H, ArH), 7.62–7.59 (m, 2H, ArH), 7.54–7.52 (m, 1H, ArH), 7.41–7.35 (m, 5H, ArH), 7.29–7.26 (m, 1H, ArH), 5.54 (d, *J*=3.1 Hz, 1H, CH), 3.74–3.71 (m, 2H, CH_2), 0.74 (t, *J*=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.5 (EtO–C=O), 152.8 (HN–CO–NH), 151.7 (C=), 149.2 (HN–C=), 141.7 (C=), 140.4 (C=), 138.2 (C=), 135.7 (C=), 132.7 (C=), 130.8 (C=), 129.2 (C=), 128.8 [two signals: 128.84 (HC=), 128.79 (HC=)], 128.5 [two signals: 128.54 (HC=), 128.51 (HC=)], 127.8 (HC=), 121.6 (HC=), 121.0 (C=), 119.8 (HC=), 111.7 (HC=), 110.9 (HC=), 100.3 (C=), 59.0 (CH_2), 56.3 (CH), 13.6 (CH_3) ppm. HRMS calcd for $C_{30}H_{25}N_4O_3$ $[M+H]^+$ 489.1935; found 489.1916.

*4.6.5. 5-Acetyl-4-[1-(4-methoxyphenyl)-9H-β-carbolin-3-yl]-6-methyl-3,4-dihydropyrimidin-2(1H)-one (**12e**).* Yield 0.52 g (90%),

yellow crystals, mp 270–272 °C (decomp., EtOH). IR (KBr, cm^{-1}): 3404, 3237, 2929, 1699, 1609, 1148. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.44 (br s, 1H, NH), 9.13 (br s, 1H, NH), 8.23–8.21 (m, 1H, ArH), 8.03 (d, J=8.8 Hz, 2H, ArH), 7.88 (s, 1H, ArH), 7.79 (br s, 1H, NH), 7.65–7.63 (m, 1H, ArH), 7.55–7.54 (m, 1H, ArH), 7.24 (t, J=7.9 Hz, 1H, ArH), 7.16 (d, J=8.8 Hz, 2H, ArH), 5.56 (d, J=3.3 Hz, 1H, CH), 3.88 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 2.26 (s, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.0 (Me–C=O), 159.8 (O–C=), 152.9 (HN–CO–NH), 151.5 (C=), 147.3 (C=), 141.7 (C=), 141.2 (C=), 131.9 (C=), 130.9 (C=), 130.0 (C=), 129.8 (HC=), 128.2 (HC=), 121.5 (HC=), 121.0 (C=), 119.6 (HC=), 114.3 (HC=), 112.6 (HC=), 109.9 (HC=), 109.3 (C=), 56.2 (CH), 55.5 (CH_3), 30.4 (CH_3), 18.9 (CH_3) ppm. HRMS calcd for $C_{25}H_{23}N_4O_3$ $[M+H]^+$ 427.1765; found 427.1768.

*4.6.6. Ethyl 4-[1-(4-methoxyphenyl)-9H-β-carbolin-3-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12f**).* Yield 0.40 g (67%), white crystals, mp 220–221 °C (MeCN). IR (KBr, cm^{-1}): 3242, 1700, 1650, 1444, 1227, 1095, 694. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.45 (br s, 1H, NH), 9.18 (d, J=1.7 Hz, 1H, NH), 8.22 (d, J=7.9 Hz, 1H, ArH), 8.05 (d, J=8.7 Hz, 2H, ArH), 7.86 (s, 1H, ArH), 7.66–7.64 (m, 2H, ArH, NH), 7.54 (t, J=7.6 Hz, 1H, ArH), 7.25 (t, J=7.5 Hz, 1H, ArH), 7.16–7.14 (m, 2H, ArH), 5.45 (d, J=3.1 Hz, 1H, CH), 4.05–4.00 (m, 2H, CH_2), 3.88 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 1.12 (t, J=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.9 (EtO–C=O), 159.8 (O–C=), 153.1 (HN–CO–NH), 151.5 (C=), 148.4 (C=), 141.6 (C=), 141.1 (C=), 132.0 (C=), 131.0 (C=), 129.8 (HC=), 128.1 (HC=), 121.4 (HC=), 121.1 (C=), 119.6 (HC=), 114.2 (HC=), 112.6 (HC=), 109.6 (HC=), 99.3 (C=), 59.1 (CH_2), 55.9 (CH), 55.5 (CH_3), 18.0 (CH_3), 14.3 (CH_3) ppm. HRMS calcd for $C_{26}H_{25}N_4O_4$ $[M+H]^+$ 457.1870; found 457.1873.

*4.6.7. Ethyl 4-[1-(4-methoxyphenyl)-9H-β-carbolin-3-yl]-6-(1-methylethyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12g**).* Yield 0.37 g (57%), white crystals, mp 301–302 °C (decomp., DMF). IR (KBr, cm^{-1}): 3360, 3213, 3123, 1677, 1622, 1099. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.43 (br s, 1H, NH), 8.78 (br s, 1H, NH), 8.19–8.17 (m, 1H, ArH), 8.07 (d, J=8.7 Hz, 2H, ArH), 7.82 (s, 1H, ArH), 7.66–7.60 (m, 2H, ArH, NH), 7.55–7.52 (m, 1H, ArH), 7.26–7.23 (m, 1H, ArH), 7.13 (d, J=3.1 Hz, 2H, ArH), 5.43 (d, J=3.1 Hz, 1H, CH), 4.16 (sp, J=7.0 Hz, 1H, CH), 4.00 (q, J=7.0 Hz, 2H, CH_2), 3.88 (s, 3H, CH_3), 1.18 (d, J=7.3 Hz, 3H, CH_3), 1.16 (d, J=7.1 Hz, 3H, CH_3), 1.09 (t, J=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.8 (EtO–C=O), 159.8 (O–C=), 156.4 (C=), 153.4 (HN–CO–NH), 151.4 (C=), 141.6 (C=), 141.2 (C=), 131.9 (C=), 131.0 (C=), 129.8 [two signals: 129.80 (C=), 129.76 (HC=)], 128.1 (HC=), 121.3 (HC=), 121.1 (C=), 119.6 (HC=), 114.1 (HC=), 112.6 (HC=), 109.5 (HC=), 98.3 (C=), 59.3 (CH_2), 55.9 (CH), 55.5 (CH_3), 27.1 (CH), 19.4 (CH_3), 19.2 (CH_3), 14.2 (CH_3) ppm. HRMS calcd for $C_{28}H_{29}N_4O_4$ $[M+H]^+$ 485.2183; found 485.2179.

*4.6.8. Ethyl 4-[1-(4-methoxyphenyl)-9H-β-carbolin-3-yl]-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12h**).* Yield 0.30 g (44%), white crystals, mp 270–271 °C (EtOH). IR (KBr, cm^{-1}): 3315, 3199, 3081, 1691, 1669, 1497, 1241, 754. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.47 (br s, 1H, NH), 9.21 (br s, 1H, NH), 8.26 (d, J=7.9 Hz, 1H, ArH), 8.11 (d, J=8.8 Hz, 2H, ArH), 7.97 (s, 1H, ArH), 7.75 (br s, 1H, NH), 7.66 (d, J=8.2 Hz, 1H, ArH), 7.55 (t, J=7.4 Hz, 1H, ArH), 7.40–7.36 (m, 3H, ArH), 7.34–7.32 (m, 2H, ArH), 7.26 (t, J=7.4 Hz, 1H, ArH), 7.15 (d, J=8.7 Hz, 2H, ArH), 5.52 (d, J=3.2 Hz, 1H, CH), 3.88 (s, 3H, O–CH_3), 3.74–3.72 (m, 2H, CH_2), 0.74 (t, J=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.6 (EtO–C=O), 159.8 (MeO–C=), 152.9 (HN–CO–NH), 151.2 (C=), 148.9 (HN–C=), 141.7 (C=), 141.2 (C=), 135.7 (C=), 132.1 (C=), 131.0 (C=), 129.9 (C=), 129.8 (HC=), 128.8 (HC=), 128.5 (HC=), 128.2 (HC=), 127.8 (HC=), 121.5 (HC=), 121.1 (C=), 119.6 (HC=), 114.2 (HC=), 112.7 (HC=), 109.8 (HC=), 100.6 (C=), 59.0 (CH_2), 56.4 (CH), 55.5 (O–CH_3), 13.6 (CH_3) ppm. HRMS calcd for $C_{31}H_{27}N_4O_4$ $[M+H]^+$ 519.2027; found 519.2025.

*4.6.9. 5-Acetyl-4-[1-(4-chlorophenyl)-9H-β-carbolin-3-yl]-6-methyl-3,4-dihydropyrimidin-2(1H)-one (**12i**).* Yield 0.43 g (75%), pale yellow crystals, mp 285–287 °C (MeCN). IR (KBr, cm^{-1}): 3637, 3235, 3158, 1709, 1588, 1242, 747. ^1H NMR (DMSO-d_6, 500 MHz): 11.54 (br s, 1H, NH), 9.15 (br s, 1H, NH), 8.26–8.24 (m, 1H, ArH), 8.10–8.07 (m, 2H, ArH), 7.96 (s, 1H, ArH), 7.81 (br s, 1H, NH), 7.67–7.65 (m, 2H, ArH), 7.65–7.63 (m, 1H, ArH), 7.57–7.54 (m, 1H, ArH), 7.28–7.25 (m, 1H, ArH), 5.57 (d, J=3.3 Hz, 1H, CH), 2.28 (s, 3H, CH_3), 2.26 (s, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 194.9 (Me–C=O), 152.9 (HN–CO–NH), 151.7 (C=), 147.6 (C=), 141.8 (C=), 139.8 (C=), 137.2 (C=), 133.4 (Cl–C=), 132.2 (C=), 130.5 (C=), 130.2 (HC=), 128.8 (HC=), 128.5 (HC=), 121.7 (HC=), 121.0 (C=), 119.8 (HC=), 112.6 (HC=), 110.4 (HC=), 109.8 (C=), 56.1 (CH), 30.5 (CH_3), 18.9 (CH_3) ppm. HRMS calcd for $C_{24}H_{20}ClN_4O_2$ $[M+H]^+$ 431.1269; found 431.1269.

*4.6.10. Ethyl 4-[1-(4-chlorophenyl)-9H-β-carbolin-3-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12j**).* Yield 0.46 g (76%), white crystals, mp 286–288 °C (decomp., MeCN). IR (KBr, cm^{-1}): 3389, 3236, 3106, 1707, 1450, 1229, 1092. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.52 (br s, 1H, NH), 9.15 (br d, J=1.8 Hz, 1H, NH), 8.26–8.24 (m, 1H, ArH), 8.12–8.10 (m, 2H, ArH), 7.93 (s, 1H, ArH), 7.66–7.63 (m, 4H, ArH, NH), 7.57–7.54 (m, 1H, ArH), 7.28–7.25 (m, 1H, ArH), 5.45 (d, J=3.2 Hz, 1H, CH), 4.03–4.01 (m, 2H, CH_2), 2.27 (s, 3H, CH_3), 1.12 (t, J=7.3 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.8 (EtO–C=O), 153.1 (HN–CO–NH), 151.7 (C=), 148.5 (C=), 141.7 (C=), 139.8 (C=), 137.2 (C=), 133.4 (C=), 132.3 (C=), 130.2 [two signals: 130.22 (Cl–C=), 130.18 (HC=)], 128.8 (HC=), 128.4 (HC=), 121.6 (HC=), 121.0 (C=), 119.8 (HC=), 112.6 (HC=), 110.6 (HC=), 99.2 (C=), 59.2 (CH_2), 55.9 (CH), 18.0 (CH_3), 14.3 (CH_3) ppm. HRMS calcd for $C_{25}H_{22}ClN_4O_3$ $[M+H]^+$ 461.1375; found 461.1377.

*4.6.11. Ethyl 4-[1-(4-chlorophenyl)-9H-β-carbolin-3-yl]-6-(1-methylethyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12k**).* Yield 0.67 g (84%), pale yellow crystals, mp 278–279 °C (EtOH/$CHCl_3$). IR (KBr, cm^{-1}): 3375, 3213, 3124, 1704, 1686, 1621, 1228, 1093. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.53 (br s, 1H, NH), 8.80 (br s, 1H, NH), 8.22–8.20 (m, 1H, ArH), 8.14–8.12 (m, 2H, ArH), 7.91 (s, 1H, ArH), 7.65–7.63 (m, 4H, ArH, NH), 7.57–7.54 (m, 1H, ArH), 7.28–7.25 (m, 1H, ArH), 5.45 (d, J=3.1 Hz, 1H, CH), 4.17 (sp, J=7.0 Hz, 1H, CH), 3.99 (q, J=7.0 Hz, 2H, CH_2), 1.17 (d, J=6.7 Hz, 3H, CH_3), 1.16 (d, J=6.8 Hz, 3H, CH_3), 1.08 (t, J=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.8 (EtO–C=O), 156.6 (C=), 153.4 (HN–CO–NH), 151.7 (C=), 141.7 (C=), 139.8 (C=), 137.2 (C=), 133.4 (Cl–C=), 132.2 (C=), 130.3 (C=), 130.2 (HC=), 128.7 (HC=), 128.4 (HC=), 121.4 (HC=), 121.0 (C=), 119.8 (HC=), 112.6 (HC=), 110.5 (HC=), 98.2 (C=), 59.3 (CH_2), 55.9 (CH), 27.1 (CH), 19.4 (CH_3), 19.2 (CH_3), 14.2 (CH_3) ppm. HRMS calcd for $C_{27}H_{26}ClN_4O_3$ $[M+H]^+$ 489.1688; found 489.1679.

*4.6.12. Ethyl 4-[1-(4-chlorophenyl)-9H-β-carbolin-3-yl]-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12l**).* Yield 0.25 g (36%), white crystals, mp 266–268 °C (EtOH/$CHCl_3$). IR (KBr, cm^{-1}): 3342, 3202, 1691, 1666, 1493, 1252, 746. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.57 (br s, 1H, NH), 9.21 (br s, 1H, NH), 8.30–8.28 (m, 1H, ArH), 8.16 (d, J=8.6 Hz, 2H, ArH), 8.06 (s, 1H, ArH), 7.76 (br s, 1H, NH), 7.67–7.64 (m, 3H, ArH), 7.59–7.57 (m, 1H, ArH), 7.41–7.39 (m, 4H, ArH), 7.34–7.33 (m, 1H, ArH), 7.30–7.26 (m, 1H, ArH), 5.54 (d, J=3.2 Hz, 1H, CH), 3.74–3.72 (m, 2H, CH_2), 0.74 (t, J=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.5 (EtO–C=O), 152.8 (HN–CO–NH), 151.4 (C=), 149.0 (HN–C=), 141.8 (C=), 139.9

(C=), 137.2 (C=), 135.6 (C=), 133.4 (C=), 132.4 (C=), 130.4 (Cl–C=), 130.2 (C=), 128.8 [two signals: 128.80 (HC=), 128.77 (HC=)], 128.5 [two signals: 128.54 (HC=), 128.49 (HC=)], 127.8 (HC=), 121.6 (HC=), 121.0 (C=), 119.8 (HC=), 112.6 (HC=), 110.8 (HC=), 100.5 (C=), 59.1 (CH_2), 56.3 (CH), 13.6 (CH_3) ppm. HRMS calcd for $C_{30}H_{24}N_4O_3$ $[M+H]^+$ 523.1531; found 523.1528.

*4.6.13. 5-Acetyl-6-methyl-4-[1-(4-nitrophenyl)-9H-β-carbolin-3-yl]-3,4-dihydropyrimidin-2(1H)-one (**12m**).* Yield 0.39 g (70%), yellow crystals, mp 270 °C (decomp., EtOH/CH_2Cl_2). IR (KBr, cm^{-1}): 3394, 3247, 3113, 1711, 1624, 1344, 1236. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.71 (br s, 1H, NH), 9.18 (br s, 1H, NH), 8.43 (d, *J*=8.8 Hz, 2H, ArH), 8.35 (d, *J*=8.9 Hz, 2H, ArH), 8.30–8.28 (m, 1H, ArH), 8.06 (s, 1H, ArH), 7.84 (br s, 1H, NH), 7.66–7.65 (m, 1H, ArH), 7.60–7.57 (m, 1H, ArH), 7.30–7.27 (m, 1H, ArH), 5.60 (d, *J*=3.2 Hz, 1H, CH), 2.30 (s, 3H, CH_3), 2.26 (s, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 194.8 (Me–C=O), 152.9 (HN–CO–NH), 152.0 (C=), 147.8 (O_2N–C=), 147.3 (C=), 144.6 (C=), 141.9 (C=), 138.4 (C=), 132.7 (C=), 131.1 (C=), 129.6 (HC=), 128.8 (HC=), 123.9 (HC=), 121.8 (HC=), 120.9 (C=), 120.0 (HC=), 112.6 (HC=), 111.5 (HC=), 109.8 (C=), 56.1 (CH), 30.5 (CH_3), 19.0 (CH_3) ppm. HRMS calcd for $C_{24}H_{20}N_5O_4$ $[M+H]^+$ 442.1510; found 442.1507.

*4.6.14. Ethyl 6-methyl-4-[1-(4-nitrophenyl)-9H-β-carbolin-3-yl]-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12n**).* Yield 0.37 g (59%), yellow crystals, mp 300–303 °C (DMF). IR (KBr, cm^{-1}): 3219, 3115, 2974, 1708, 1665, 1344, 1232, 1100. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.69 (br s, 1H, NH), 9.18 (br s, 1H, NH), 8.42 (d, *J*=8.6 Hz, 2H, ArH), 8.36 (d, *J*=8.5 Hz, 2H, ArH), 8.29 (d, *J*=7.7 Hz, 1H, ArH), 8.03 (s, 1H, ArH), 7.69–7.65 (m, 2H, ArH, NH), 7.60–7.57 (m, 1H, ArH), 7.30–7.27 (m, 1H, ArH), 5.48 (d, *J*=2.1 Hz, 1H, CH), 4.04–4.01 (m, 2H, CH_2), 2.28 (s, 3H, CH_3), 1.12 (t, *J*=7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.8 (EtO–C=O), 153.1 (HN–CO–NH), 152.1 (C=), 148.7 (O_2N–C=), 147.3 (C=), 144.6 (C=), 141.9 (C=), 138.4 (C=), 132.8 (C=), 130.8 (C=), 129.5 (HC=), 128.8 (HC=), 123.9 (HC=), 121.7 (HC=), 120.9 (C=), 120.0 (HC=), 112.6 (HC=), 111.7 (HC=), 99.1 (C=), 59.2 (CH_2), 55.9 (CH), 18.0 (CH_3), 14.3 (CH_3) ppm. HRMS calcd for $C_{25}H_{22}N_5O_5$ $[M+H]^+$ 472.1615; found 472.1617.

*4.6.15. 5-Acetyl-4-[1-(1,3-benzodioxol-5-yl)-9H-β-carbolin-3-yl]-6-methyl-3,4-dihydropyrimidin-2(1H)-one (**12o**).* Yield 0.26 g (43%), pale yellow crystals, mp 295–297 °C (decomp., DMF/H_2O). IR (KBr, cm^{-1}): 3402, 3238, 3096, 2932, 1704, 1664, 1468, 1236, 1097. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.46 (br s, 1H, NH), 9.17 (br s, 1H, NH), 8.22 (d, *J*=6.9 Hz, 1H, ArH), 7.90 (s, 1H, ArH), 7.81 (br s, 1H, NH), 7.66–7.61 (m, 3H, ArH), 7.57–7.54 (t, *J*=7.5 Hz, 1H, ArH), 7.24 (t, *J*=7.4 Hz, 1H, ArH), 7.14 (d, *J*=8.0 Hz, 1H, ArH), 6.15 (s, 2H, O–CH_2–O), 5.55 (d, *J*=3.0 Hz, 1H, CH), 2.27 (s, 3H, CH_3), 2.26 (s, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.0 (Me–C=O), 153.0 (HN–CO–NH), 151.7 (C=), 147.9 [two signals: 147.89 (O–C=), 147.86 (O–C=)], 147.5 (C=), 141.7 (C=), 140.9 (C=), 132.6 (C=), 131.9 (C=), 130.1 (C=), 128.3 (HC=), 122.4 (HC=), 121.6 (HC=), 121.0 (C=), 119.6 (HC=), 112.7 (HC=), 109.6 (C=), 108.8 (HC=), 108.5 (HC=), 101.4 (O–CH_2–O), 56.1 (CH), 30.5 (CH_3), 18.9 (CH_3) ppm. HRMS calcd for $C_{25}H_{21}N_4O_4$ $[M+H]^+$ 441.1557; found 441.1558.

*4.6.16. Ethyl 4-[1-(1,3-benzodioxol-5-yl)-9H-β-carbolin-3-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12p**).* Yield 0.29 g (47%), pale yellow crystals, mp 273–275 °C (EtOH/THF). IR (KBr, cm^{-1}): 3402, 3239, 3097, 2933, 1704, 1664, 1491, 1236, 1097. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.46 (br s, 1H, NH), 9.21 (br s, 1H, NH), 8.23 (d, *J*=7.8 Hz, 1H, ArH), 7.87 (s, 1H, ArH), 7.66–7.62 (m, 4H, ArH, NH), 7.54 (t, *J*=7.6 Hz, 1H, ArH), 7.25 (t, *J*=7.5 Hz, 1H, ArH), 7.14 (d, *J*=7.8 Hz, 1H, ArH), 6.15 (s, 2H, O–CH_2–O), 5.42 (d, *J*=2.7 Hz, 1H, CH), 4.07–3.99 (m, 2H, CH_2), 2.26 (s, 3H, CH_3), 1.13 (t, *J*=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.9 (EtO–C=O), 153.3 (HN–CO–NH), 151.4 (C=), 148.6 (HN–C=), 147.9 [two signals: 147.93 (O–C=), 147.87 (O–C=)], 141.7 (C=), 140.9 (C=), 132.7 (C=), 132.0 (C=), 130.0 (C=), 128.3 (HC=), 122.4 (HC=), 121.5 (HC=), 121.1 (C=), 119.7 (HC=), 112.7 (HC=), 109.9 (HC=), 108.8 (HC=), 108.5 (HC=), 101.5 (O–CH_2–O), 99.2 (C=), 59.2 (CH_2), 55.9 (CH), 18.0 (CH_3), 14.4 (CH_3) ppm. HRMS calcd for $C_{26}H_{23}N_4O_5$ $[M+H]^+$ 471.1663; found 471.1663.

*4.6.17. Methyl 4-[1-(1,3-benzodioxol-5-yl)-9H-β-carbolin-3-yl]-6-(1-methylethyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12q**).* Yield 0.43 g (67%), pale yellow crystals, mp 275–276 °C (DMF/H_2O). IR (KBr, cm^{-1}): 3338, 3208, 3061, 2962, 1694, 1622, 1224, 1097. ^1H NMR (DMSO-d_6, 500 MHz): 11.47 (br s, 1H, NH), 8.87 (br s, 1H, NH), 8.21 (d, *J*=7.5 Hz, 1H, ArH), 7.84 (s, 1H, ArH), 7.66–7.64 (m, 4H, ArH, NH), 7.54 (t, *J*=7.5 Hz, 1H, ArH), 7.28–7.25 (m, 1H, ArH), 7.12 (d, *J*=8.3 Hz, 1H, ArH), 6.14 (s, 2H, O–CH_2–O), 5.41 (s, 1H, CH), 4.17 (sp, *J*=6.5 Hz, 1H, CH), 3.54 (s, 3H, CH_3), 1.18–1.16 (m, 6H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 166.3 (MeO–C=O), 156.8 (HN–C=), 153.4 (HN–CO–NH), 151.1 (C=), 147.8 [two signals: 147.84 (O–C=), 147.80 (O–C=)], 141.6 (C=), 140.9 (C=), 132.6 (C=), 131.9 (C=), 130.0 (C=), 128.2 (HC=), 122.3 (HC=), 121.4 (HC=), 121.0 (C=), 119.6 (HC=), 112.6 (HC=), 109.6 (HC=), 108.7 (HC=), 108.4 (HC=), 101.4 (O–CH_2–O), 98.0 (C=), 55.7 (CH), 51.0 (O–CH_3), 27.1 (CH), 19.3 (CH_3), 19.2 (CH_3) ppm. HRMS calcd for $C_{27}H_{25}N_4O_5$ $[M+H]^+$ 485.1819; found 485.1819.

*4.6.18. Ethyl 4-[1-(1,3-benzodioxol-5-yl)-9H-β-carbolin-3-yl]-2-oxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12r**).* Yield: 0.32 g (45%), light brown crystals, mp 274–275 °C (DMF/H_2O). IR (KBr, cm^{-1}): 3344, 3203, 2982, 1693, 1667, 1492, 1242, 741. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.47 (br s, 1H, NH), 9.21 (br s, 1H, NH), 8.25 (d, *J*=8.0 Hz, 1H, ArH), 7.98 (s, 1H, ArH), 7.74 (br s, 1H, NH), 7.68–7.65 (m, 3H, ArH), 7.55 (t, *J*=7.7 Hz, 1H, ArH), 7.43–7.41 (m, 5H, ArH), 7.26 (t, *J*=7.5 Hz, 1H, ArH), 7.13 (d, *J*=7.5 Hz, 1H, ArH), 6.13 (s, 2H, O–CH_2–O), 5.50 (d, *J*=3.2 Hz, 1H, CH), 3.75–3.71 (m, 2H, CH_2), 0.74 (t, *J*=5.5 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.9 (EtO–C=O), 152.9 (HN–CO–NH), 151.0 (C=), 148.9 (HN–C=), 147.9 (O–C=), 147.8 (O–C=), 141.6 (C=), 140.9 (C=), 135.6 (C=), 132.7 (C=), 132.0 (C=), 130.1 (C=), 128.8 (HC=), 128.5 (HC=), 128.2 (HC=), 127.8 (HC=), 122.4 (HC=), 121.5 (HC=), 121.1 (C=), 119.7 (HC=), 112.7 (HC=), 110.1 (HC=), 108.8 (HC=), 108.4 (HC=), 101.4 (O–CH_2–O), 100.5 (C=), 59.0 (CH_2), 56.3 (CH), 13.6 (CH_3) ppm. HRMS calcd for $C_{31}H_{25}N_4O_5$ $[M+H]^+$ 533.1819; found 533.1810.

*4.6.19. 5-Acetyl-6-methyl-4-(1-thiophen-2-yl-9H-β-carbolin-3-yl)-3,4-dihydropyrimidin-2(1H)-one (**12s**).* Yield 0.31 g (60%), pale yellow crystals, mp 304–305 °C (decomp., MeCN/$CHCl_3$/DMF). IR (KBr, cm^{-1}): 3336, 3300, 3109, 1674, 1620, 1446, 1239. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.45 (br s, 1H, NH), 9.17 (br s, 1H, NH), 8.22 (d, *J*=7.8 Hz, 1H, ArH), 8.09 (d, *J*=3.5 Hz, 1H, ArH), 7.93 (s, 1H, ArH), 7.81 (br s, 1H, NH), 7.73–7.70 (m, 2H, ArH), 7.61–7.55 (m, 1H, ArH), 7.33–7.28 (m, 2H, ArH), 5.52 (d, *J*=3.3 Hz, 1H, CH), 2.32 (s, 3H, CH_3), 2.26 (s, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 194.8 (Me–C=O), 152.8 (HN–CO–NH), 151.4 (C=), 147.3 (HN–C=), 143.9 (C=), 141.8 (C=), 135.8 (C=), 130.6 (C=), 130.0 (C=), 128.6 (HC=), 128.5 (HC=), 125.8 (HC=), 121.5 (HC=), 120.9 (C=), 120.0 (HC=), 112.8 (HC=), 110.0 (HC=), 109.9 (C=), 55.8 (CH), 30.4 (CH_3), 18.9 (CH_3) ppm. HRMS calcd for $C_{22}H_{19}N_4O_2S$ $[M+H]^+$ 403.1223; found 403.1221.

*4.6.20. Ethyl 6-methyl-2-oxo-4-(1-thiophen-2-yl-9H-β-carbolin-3-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12t**).* Yield 0.45 g (81%), pale yellow crystals, mp 285–287 °C (EtOH/$CHCl_3$). IR (KBr, cm^{-1}): 3374, 3241, 3113, 1707, 1659, 1436, 1223, 1085. ^1H NMR (DMSO-d_6, 500 MHz): δ 11.42 (br s, 1H, NH), 9.19 (br s, 1H, NH), 8.26–8.23 (m, 1H, ArH), 8.09 (d, *J*=3.7 Hz, 1H, ArH), 7.88 (s, 1H, ArH),

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7.72–7.70 (m, 2H, ArH), 7.61 (br s, 1H, NH), 7.59–7.57 (m, 1H, ArH), 7.32 (t, J=4.3 Hz, 1H, ArH), 7.29–7.28 (m, 1H, ArH), 5.39 (d, J=2.9 Hz, 1H, CH), 4.03–4.01 (m, 2H, CH_2), 2.28 (s, 3H, CH_3), 1.12 (t, J=7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.3 (EtO–C=O), 152.9 (HN–CO–NH), 151.4 (C=), 148.6 (C=), 144.1 (C=), 141.8 (C=), 135.9 (C=), 130.3 (C=), 130.1 (C=), 128.5 (HC=), 125.6 (HC=), 121.5 (HC=), 121.0 (C=), 120.0 (HC=), 112.8 (HC=), 110.4 (HC=), 99.2 (C=), 59.1 (CH_2), 55.7 (CH), 18.0 (CH_3), 14.3 (CH_3) ppm. HRMS calcd for $C_{23}H_{21}N_4O_3S$ $[M+H]^+$ 433.1329; found 433.1329.

*4.6.21. Ethyl 6-(1-methylethyl)-2-oxo-4-(1-thiophen-2-yl-9H-β-carbolin-3-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12u**).* Yield 0.34 g (55%), pale yellow crystals, mp 299–301 °C (EtOH/$CHCl_3$/DMF). IR (KBr, cm^{-1}): 3326, 1674, 1625, 1455, 1226, 1101. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.43 (br s, 1H, NH), 8.80 (br s, 1H, NH), 8.22–8.20 (m, 1H, ArH), 8.10–8.09 (m, 1H, ArH), 7.87 (s, 1H, ArH), 7.73–7.71 (m, 2H, ArH), 7.60–7.56 (m, 2H, ArH, NH), 7.32–7.26 (m, 2H, ArH), 5.40 (d, J=2.4 Hz, 1H, CH), 4.18 (sp, J=7.1 Hz, 1H, CH), 4.00 (q, J=7.1 Hz, 2H, CH_2), 1.21 (d, J=7.1 Hz, 3H, CH_3), 1.17 (d, J=7.0 Hz, 3H, CH_3), 1.11 (t, J=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.7 (EtO–C=O), 156.6 (HN–C=), 153.3 (HN–CO–NH), 151.5 (C=), 144.1 (C=), 141.8 (C=), 136.2 (C=), 130.3 (C=), 130.1 (C=), 128.5 (HC=), 128.4 (HC=), 125.6 (HC=), 121.4 (HC=), 121.0 (C=), 120.0 (HC=), 112.8 (HC=), 110.5 (HC=), 98.1 (C=), 59.2 (CH_2), 55.8 (CH), 27.0 (CH), 19.4 (CH_3), 14.2 (CH_3) ppm. HRMS calcd for $C_{25}H_{25}N_4O_3S$ $[M+H]^+$ 461.1642; found 461.1640.

*4.6.22. Ethyl 2-oxo-6-phenyl-4-(1-thiophen-2-yl-9H-β-carbolin-3-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**12v**).* Yield 0.53 g (81%), pale yellow crystals, mp 291–292 °C (MeCN/$CHCl_3$/DMF). IR (KBr, cm^{-1}): 3339, 3106, 1699, 1678, 1647, 1454, 1243, 1107. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.48 (br s, 1H, NH), 9.24 (br s, 1H, NH), 8.28–8.27 (m, 1H, ArH), 8.13 (d, J=3.2 Hz, 1H, ArH), 8.00 (s, 1H, ArH), 7.74–7.72 (m, 3H, ArH, NH), 7.60–7.57 (m, 1H, ArH), 7.39–7.37 (m, 5H, ArH), 7.32 (t, J=3.2 Hz, 1H, ArH), 7.31–7.28 (m, 1H, ArH), 5.49 (d, J=2.9 Hz, 1H, CH), 3.77–3.71 (m, 2H, CH_2), 0.73 (t, J=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 165.4 (EtO–C=O), 152.7 (HN–CO–NH), 151.2 (C=), 149.2 (HN–C=), 144.1 (C=), 141.8 (C=), 136.2 (C=), 135.8 (C=), 130.4 (C=), 130.2 (C=), 128.7 (HC=), 128.6 (HC=), 128.5 (HC=), 127.7 (HC=), 125.7 (HC=), 121.6 (HC=), 121.1 (C=), 120.1 (HC=), 112.8 (HC=), 110.7 (HC=), 100.4 (C=), 59.0 (CH_2), 56.3 (CH), 13.6 (CH_3) ppm. HRMS calcd for $C_{28}H_{23}N_4O_3S$ $[M+H]^+$ 495.1485; found 495.1480.

*4.6.23. Ethyl (2E)-3-[1-(4-chlorophenyl)-9H-β-carbolin-3-yl]-2-(phenylcarbonyl)prop-2-enoate (**13**).* The compound was isolated as a by-product during the preparation of **12l**. Yield 0.30 g (47%), pale yellow crystals, mp 301–302 °C (MeCN). IR (KBr, cm^{-1}): 3369, 1715, 1672, 1627, 1227. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 11.79 (br s, 1H, NH), 8.60 (s, 1H, ArH), 8.27–8.25 (m, 1H, ArH), 8.11 (s, 1H, CH), 7.90–7.89 (m, 2H, ArH), 7.65–7.64 (m, 1H, ArH), 7.60–7.55 (m, 2H, ArH), 7.46–7.42 (m, 4H, ArH), 7.39 (d, J=8.8 Hz, 2H, ArH), 7.34–7.31 (m, 1H, ArH), 4.21 (q, J=7.1 Hz, 2H, CH_2), 1.18 (t, J=7.1 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMSO-d_6, 125 MHz): δ 194.0 (Ph–C=O), 164.9 [C(O)–OEt], 141.5 (C=), 141.0 [two signals: 141.04 (HC=), 141.03 (C=)], 140.4 (C=), 137.0 (C=), 135.8 (C=), 133.6 (C=), 133.0 (C=), 132.9 (Cl–C=), 130.2 (HC=), 130.0 (C=), 129.8 (C=), 128.8 (HC=), 128.7 (HC=), 128.6 (HC=), 128.5 (HC=), 121.8 (HC=), 121.1 (HC=), 120.6 (C=), 119.1 (HC=), 112.9 (HC=), 61.0 (CH_2), 14.2 (CH_3) ppm. HRMS calcd for $C_{29}H_{22}ClN_2O_3$ $[M+H]^+$ 481.1313; found 481.1311.

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