Convenient Synthesis of a Library of Lactam-Fused β-Carbolines via the Ugi Reaction[1]

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Dedicated to Dr. Vijay Nair on the occasion of his 70th birthday

Abstract: We present a convenient synthesis of a chemical library of lactam-fused β-carbolines via a Ugi four-center three-component reaction employing [1-formyl-3-(methoxycarbonyl)-9*H*-pyrido[3,4-*b*]indol-9-yl]acetic acid or (1-formyl-9*H*-pyrido[3,4-*b*]indol-9-yl)acetic acid, amines and isonitriles.

Key words: Ugi reaction, multicomponent reactions, β-carbolines

The β-carboline scaffold represents a core unit of several alkaloids and pharmaceutical agents. In particular, the annulated β-carboline-containing compounds and natural products are of high medicinal importance as these analogues are known to display a number of bioactivities such as antimicrobial, antifungal, antiparasitic and anticancer activity.[3] In our project related to the development of general protocols for accessing annulated β-carbolines from 1-formyl-9*H*-β-carboline, we have reported the synthesis of canthines, canthin-6-ones, homofascaplysin, harmicine mimics and several β-carboline-fused heterocycles using Morita–Baylis–Hillman (MBH), cycloaddition, carbonyl–ene or RCM-based approaches.[4] In a continuation of our studies under the program, we now report the synthesis of new lactam-fused β-carbolines via an isonitrile-based multicomponent reaction (IMCR) employing [1-formyl-3-(methoxycarbonyl)-9*H*-pyrido[3,4-*b*]indol-9-yl]acetic acid and (1-formyl-9*H*-pyrido[3,4-*b*]indol-9-yl)acetic acid as the bifunctional starting materials.

Over the last several years, multicomponent reactions (MCRs) including IMCRs have become increasingly important in organic and medicinal chemistry because they allow the synthesis of highly sophisticated polyfunctional molecules with a wide structural and functional diversity combined with excellent combinatorial efficacy.[5] Among IMCRs, the modified Ugi four-center three-component reaction (U-4C-3CR) based on the use of bifunctional components has been a popular strategy for obtaining six- and seven-membered fused heterocycles. Amidst such bifunctional substrates, prototypes incorporating an acid and an aldehyde or keto group are reported to be highly successful. Zhang and co-workers demonstrated the utility of several commercially available starting materials incorporating an aldehyde and an acid group for the synthesis of a variety of lactams via this route.[6] Ivachtchenko and co-workers elegantly exploited this protocol for the synthesis of an array of annulated systems.[7] More recently, adopting a similar approach, Ghandi and co-workers reported the synthesis of 3-oxo-1,2,3,4-tetrahydropyrazino[1,2-*a*]benzimidazole-1-carboxamides.[8] Taking a cue from these reports, we decided to investigate the potential of a β-carboline-based bifunctional substrate for the Ugi reaction. In principle, installing an acetic acid subunit at N-9 of 1-formyl-9*H*-β-carboline would offer a substrate which could serve as a reactant in the Ugi reaction to produce new annulated β-carbolines. Such lactam-fused β-carbolines have not been previously reported in the literature.

The synthesis of the key bifunctional β-carbolines **5** and **8** was accomplished from **1** and **2**, respectively, as outlined in Scheme 1. Initially, the aldehyde **3** that was obtained from the acetal **1** was subjected to a substitution reaction with *tert*-butyl bromoacetate to furnish **4**. Trifluoroacetic acid promoted chemoselective hydrolysis of the *tert*-butyl ester group in **4** afforded the required starting material **5**. At this stage, it occurred to us to first carry out the substitution reaction of **1** with *tert*-butyl bromoacetate and then perform the acid hydrolysis to generate **5** as this would reduce the number of steps involved for the synthesis of **5**. Accordingly, acetal **1** was treated with *tert*-butyl bromoacetate in the presence of cesium carbonate to give diester **6** in more than 95% yield. Trifluoroacetic acid promoted hydrolysis of the *tert*-butyl ester coupled with unmasking of the acetal in **6** afforded the required aldehyde–acid substrate **5** in 84% yield. Likewise, treatment of acetal **2** with *tert*-butyl bromoacetate gave ester **7** which on treatment with trifluoroacetic acid afforded the required material **8** in 81% yield.

The optimization study for determining the reaction conditions for the Ugi reaction was initiated with **5**. Compound **5** was treated with commercially available 4-tolylsulfonylmethyl isocyanide (TosMIC) and aniline in methanol at room temperature (Scheme 2; R^2 = Ph, R^3 = 4-Ts). It was satisfying to observe that the reaction was complete in 12 hours and was typically characterized by the separation of a solid product in the reaction mixture. Isolation and spectroscopic characterization of the separated solid indicated it to be the desired lactam-annulated carboline **5Ja**. This result provoked us to investigate

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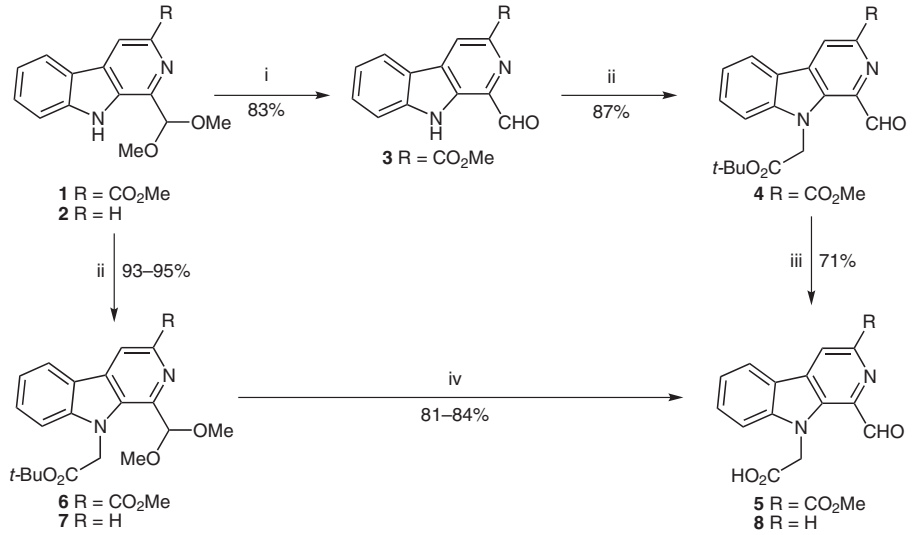
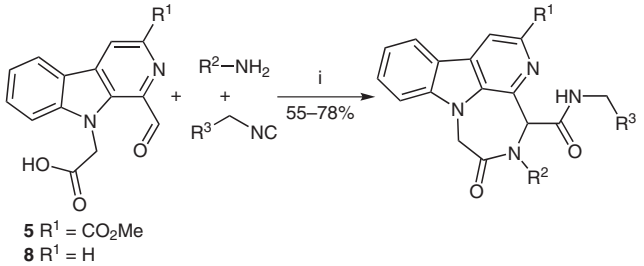


Scheme 1 *Reagents and conditions*: (i) AcOH–H_2O (2:3, v/v), 100 °C, 45 min; (ii) $BrCH_2CO_2t$-Bu, Cs_2CO_3, anhyd DMF, r.t., 45 min; (iii) TFA–H_2O (100:1, v/v), r.t., 12 h; (iv) TFA–H_2O (100:1, v/v), 90 °C, 1.5 h.

this strategy for the synthesis of a chemical library of lactam-fused carbolines. Aiming at this objective, we performed reactions of **5** and **8** with TosMIC and several amines (Figure 1) in parallel fashion. Gratifyingly, in all reactions solids separated out, which were collected by filtration and washed with cold methanol to afford the analytically pure products **5Aa–5La**, **8Aa**, **8Ea** and **8La** in moderate to good yields. Product which was dissolved in the methanol during filtration was easily retrieved via processing of the filtrate followed by purification via short-column chromatography. In general, it was observed that 75–80% of the isolated yield of each product was obtained via filtration, while the remaining 20–25% of the product was recovered from the filtrate. It was found that the best yields of the products were isolated when anilines or benzylamine was employed as the amine component. Methyl glycinate (HCl salt neutralized with Et_3N before addition) and 3-aminopropanol gave the products in moderate yields only, whereas yields of products from other amines ranged between the two limits.

Next, to expand the structural diversity accessible via the developed approach, reactions with alternative isonitriles were investigated. One of the isonitriles was generated from a glycine ester, whereas the other isonitriles were obtained from the allylamines synthesized from the MBH adducts, as reported earlier[9] (Figure 1). The double bond stereochemistry of the isonitriles **c** and **d** was *Z*, whereas



Scheme 2 *Reagents and conditions*: (i) MeOH, r.t., 3–12 h.

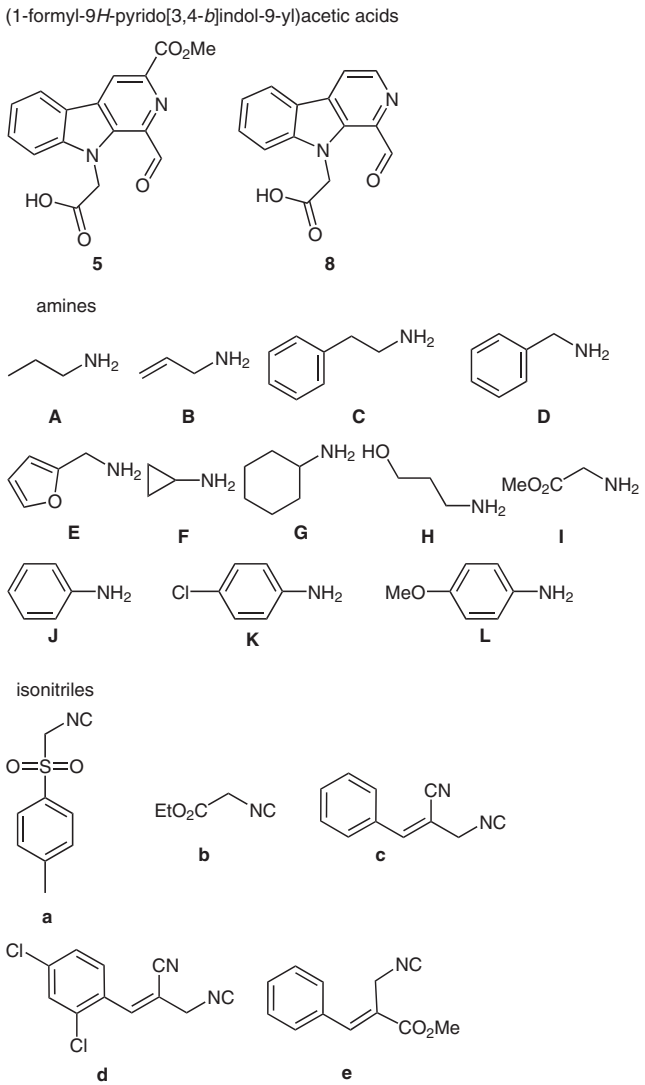


Figure 1 Diversity elements

that of **e** was *E*. Accordingly, **5** and **8** were treated with several amines and these alternative isonitriles in parallel format. It was pleasing to discover that, in contrast to TosMIC, reactions with these isonitriles were complete in three to four hours to yield the required products as solids, which were isolated by simple filtration. Similar to earlier observations, here, too, the anilines and benzylamine gave the products in best yields. The various products generat-

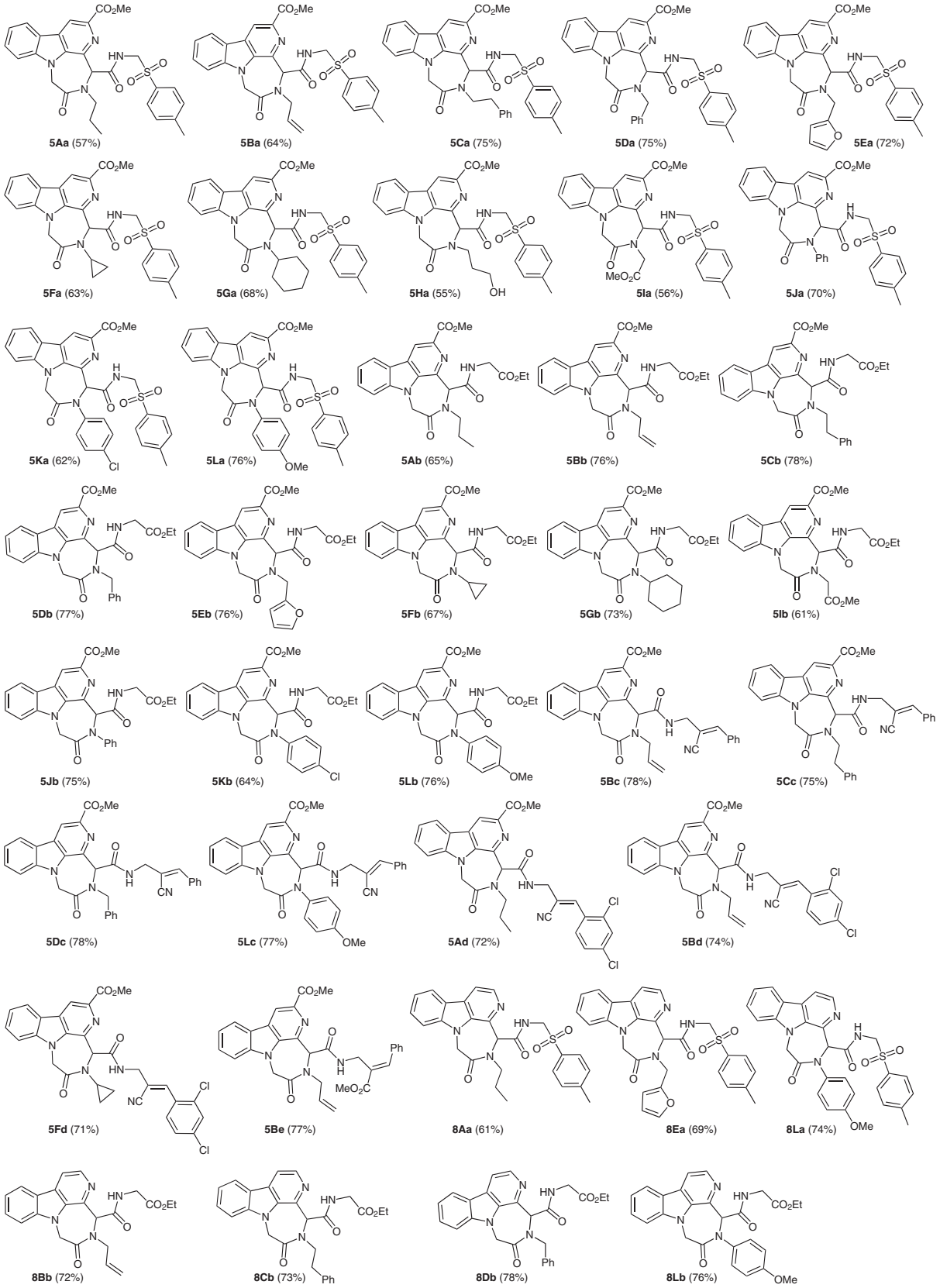


Figure 2 Structures of the isolated products (% yields)

ed during the present study along with the isolated yields are illustrated in Figure 2. These results show that this approach is general and works well with a wide range of substrates.

In conclusion, a small library of lactam-fused β-carbolines was prepared by using a β-carboline-based bifunctional scaffold, which can be readily produced from 1-formyl-9*H*-β-carboline. The simplicity of the synthetic protocol and ready availability of diverse starting materials make this an attractive strategy for obtaining new β-carboline-fused prototypes via combinatorial techniques.

Melting points were determined in capillary tubes on a Precision hot-stage apparatus containing silicon oil and are uncorrected. IR spectra were recorded using a Perkin Elmer RX 1 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on either a Bruker 300-MHz or a Bruker 200-MHz FT spectrometer, using TMS as an internal standard (chemical shifts in δ values, *J* in Hz). Mass spectra were recorded as ES-MS or DART on Micromass Quattro-II or JEOL-AccuTOF JMS-T100LC mass spectrometers, respectively. The HRMS spectra were recorded as EI-HRMS on a JEOL system or as DART-HRMS (recorded as ES+) on a JEOL-AccuTOF JMS-T100LC mass spectrometer equipped with a DART (Direct Analysis in Real Time) source. Elemental analyses were performed on a Carlo Erba 1108 microanalyzer or an Elementar Vario EL III microanalyzer. Hexanes refers to the fraction with bp 65–70 °C. Due to the poor solubility of compounds **5Ja**, **5Ib** and **8Lb**, the corresponding ^{13}C NMR spectra could not be recorded.

Methyl 9-(*tert*-Butoxycarbonylmethyl)-1-(dimethoxymethyl)-9*H*-β-carboline-3-carboxylate (6); Typical Procedure

To a stirred soln of acetal **1** (5.60 g, 18.6 mmol) in anhyd DMF (80 mL), Cs_2CO_3 (8.49 g, 26.1 mmol) was added at r.t. After 15 min, *tert*-butyl bromoacetate (3.63 mL, 22.3 mmol) in anhyd DMF (10 mL) was added dropwise and the reaction was allowed to continue for an additional 45 min at r.t. On completion of the reaction, as monitored by TLC, the contents were poured into H_2O (250 mL) under stirring with a glass rod. The resulting solid was collected by filtration and dried over P_2O_5 in a dessicator under reduced pressure to obtain **6** as a yellowish white solid; yield: 7.35 g (95%).

Mp 141–143 °C; R_f = 0.48 (hexanes–EtOAc, 75:25).

IR (KBr): 1713 (CO_2CH_3), 1750 (CO_2t-Bu) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, 3 × CH_3), 3.48 (s, 6 H, 2 × OCH_3), 4.05 (s, 3 H, OCH_3), 5.55 (s, 2 H, NCH_2), 5.70 (s, 1 H, CH), 7.35–7.40 (m, 2 H, ArH), 7.64 (t, *J* = 7.2 Hz, 1 H, ArH), 8.20 (d, *J* = 7.8 Hz, 1 H, ArH), 8.91 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.2, 48.6, 52.8, 55.9, 81.8, 110.2, 110.4, 118.5, 121.2, 121.5, 121.7, 129.3, 131.6, 136.0, 141.1, 143.1, 166.5, 168.0.

MS (ES$^+$): *m*/*z* = 415.0 [M$^+$ + 1].

Anal. Calcd for $C_{22}H_{26}N_2O_6$ (414.1791): C, 63.76; H, 6.32; N, 6.76. Found: C, 63.57; H, 6.42; N, 6.93.

Methyl 9-(*tert*-Butoxycarbonylmethyl)-1-formyl-9*H*-β-carboline-3-carboxylate (4)

Light yellow solid; yield: 0.40 g (87% from **3**); mp 204–205 °C; R_f = 0.47 (hexanes–EtOAc, 70:30).

IR (KBr): 1701 (CHO), 1748 (CO_2CH_3 and CO_2t-Bu) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.43 (s, 9 H, 3 × CH_3), 4.11 (s, 3 H, OCH_3), 5.58 (s, 2 H, NCH_2), 7.41–7.50 (m, 2 H, ArH), 7.71 (dt, *J* = 1.1, 12.3 Hz, 1 H, ArH), 8.24 (d, *J* = 7.7 Hz, 1 H, ArH), 9.05 (s, 1 H, ArH), 10.32 (s, 1 H, CHO).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.9, 49.3, 52.9, 82.7, 110.2, 120.7, 121.1, 121.6, 122.1, 130.0, 133.2, 136.9, 137.3, 143.0, 165.5, 167.3, 193.8.

MS (ES$^+$): *m*/*z* = 369.1 [M$^+$ + 1].

Anal. Calcd for $C_{20}H_{20}N_2O_5$ (368.1372): C, 65.21; H, 5.47; N, 7.60. Found: C, 65.05; H, 5.32; N, 7.76.

***tert*-Butyl [1-(Dimethoxymethyl)-β-carbolin-9-yl]acetate (7)**

White solid; yield: 5.72 g (93%); mp 130–131 °C; R_f = 0.36 (hexanes–EtOAc, 75:25).

IR (KBr): 1756 (CO_2t-Bu) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 (s, 9 H, 3 × CH_3), 3.47 (s, 6 H, 2 × OCH_3), 5.48 (s, 2 H, NCH_2), 5.61 (s, 1 H, CH), 7.28–7.34 (m, 2 H, ArH), 7.60 (t, *J* = 8.1 Hz, 1 H, ArH), 8.01 (d, *J* = 5.2 Hz, 1 H, ArH), 8.13 (d, *J* = 7.8 Hz, 1 H, ArH), 8.39 (d, *J* = 5.1 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.1, 48.3, 53.5, 55.7, 81.6, 109.8, 110.1, 115.6, 120.4, 121.4, 128.9, 131.6, 134.5, 137.0, 140.7, 142.7, 168.4.

MS (ES$^+$): *m*/*z* = 357.1 [M$^+$ + 1].

Anal. Calcd for $C_{20}H_{24}N_2O_4$ (356.1736): C, 67.40; H, 6.79; N, 7.86. Found: C, 67.36; H, 6.74; N, 7.59.

[1-Formyl-3-(methoxycarbonyl)-9*H*-β-carbolin-9-yl]acetic Acid (5); Typical Procedure

A mixture of acetal **6** (6.70 g, 16.2 mmol), TFA (75 mL) and H_2O (0.7 mL) was heated at 90 °C for 1.5 h. After completion of the reaction, as monitored by TLC, the contents were poured into H_2O (300 mL) under stirring and left for 7 h. The separated solid was collected by filtration and dried over P_2O_5 under reduced pressure to afford **5** as a brown solid; yield: 4.25 g (84%).

Mp 143–145 °C; R_f = 0.12 ($CHCl_3$–MeOH, 90:10).

IR (KBr): 1710 (CHO and CO_2CH_3), 3460 (CO_2H) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.99 (s, 3 H, OCH_3), 5.63 (s, 2 H, NCH_2), 7.47 (t, *J* = 7.3 Hz, 1 H, ArH), 7.68–7.84 (m, 2 H, ArH), 8.54 (d, *J* = 7.5 Hz, 1 H, ArH), 9.22 (s, 1 H, ArH), 10.14 (s, 1 H, CHO).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 48.5, 52.6, 111.2, 120.5, 120.9, 122.1, 130.2, 132.6, 136.1, 136.8, 137.1, 142.9, 165.0, 170.2, 193.5.

MS (ES$^+$): *m*/*z* = 313.2 [M$^+$ + 1].

Anal. Calcd for $C_{16}H_{12}N_2O_5$ (312.0746): C, 61.54; H, 3.87; N, 8.97. Found: C, 61.35; H, 3.96; N, 8.67.

(1-Formyl-9*H*-β-carbolin-9-yl)acetic Acid (8)

Brown solid; yield: 2.30 g (81%); mp 157–158 °C; R_f = 0.27 ($CHCl_3$–MeOH, 90:10).

IR (KBr): 1708 (CHO), 3071 (CO_2H) cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 5.61 (s, 2 H, NCH_2), 7.40 (t, *J* = 7.2 Hz, 1 H, ArH), 7.66–7.77 (m, 2 H, ArH), 8.37 (d, *J* = 7.8 Hz, 1 H, ArH), 8.54 (d, *J* = 4.9 Hz, 1 H, ArH), 8.66 (d, *J* = 4.8 Hz, 1 H, ArH), 10.13 (s, 1 H, CHO).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 48.2, 110.9, 119.4, 120.3, 121.2, 121.8, 129.6, 132.0, 135.2, 137.7, 138.8, 142.6, 170.3, 194.2.

MS (ES$^+$): *m*/*z* = 255 [M$^+$ + 1].

Anal. Calcd for $C_{14}H_{10}N_2O_3$ (254.0691): C, 66.14; H, 3.96; N, 11.02. Found: C, 66.35; H, 4.02; N, 11.21.

[1-Formyl-3-(methoxycarbonyl)-9*H*-β-carbolin-9-yl]acetic Acid (5) from Ester 4

A mixture of *tert*-butyl ester **4** (0.37 g, 1 mmol), TFA (14 mL) and H_2O (0.014 mL) was stirred at r.t. for 12 h. After completion of the

reaction, as monitored by TLC, the contents were poured into H_2O (30 mL) under stirring and left for 1 h. The separated solid was collected by filtration and dried over P_2O_5 under reduced pressure to afford **5** as a brown solid; yield: 0.23 g (71%); mp 143–145 °C; R_f = 0.12 ($CHCl_3$–MeOH, 90:10).

Methyl 6-Oxo-5-propyl-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Aa); Typical Procedure for the Intramolecular Ugi Reaction

To a soln of acid **5** (0.25 g, 0.80 mmol) in MeOH (2 mL), *n*-$PrNH_2$ (0.066 mL, 0.80 mmol) was added and the mixture was stirred for 5 min. Then, TosMIC (0.16 g, 0.80 mmol) was added and stirring was continued for 12 h at r.t. After completion of the reaction, as monitored by TLC, the separated solid was collected by filtration and washed with cold MeOH (3 × 1 mL) and Et_2O (2 × 1 mL). The white solid (0.21 g) so obtained was the required product and was analytically pure. Further product was recovered from the filtrate by concentration under reduced pressure to furnish an oily residue which was treated with H_2O (20 mL) and extracted with EtOAc (30 mL). The separated organic layer was dried (Na_2SO_4) and concentrated to yield an oily residue. Purification of this residue via short silica gel (60–120 mesh) column chromatography (hexanes–EtOAc, 70:30) afforded **5Aa** as a white solid (0.04 g); total yield: 0.25 g (57%).

Mp 218–220 °C; R_f = 0.66 (hexanes–EtOAc, 40:60).

IR (KBr): 1660 (CONH), 1711 (CO_2CH_3), 3451 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.3 Hz, 3 H, $NCH_2CH_2CH_3$), 1.33–1.59 (m, 2 H, $NCH_2CH_2CH_3$), 1.94 (s, 3 H, CH_3), 3.35–3.44 (m, 1 H, $NCHHCH_2CH_3$), 3.48–3.60 (m, 1 H, $NCHHCH_2CH_3$), 4.12 (s, 3 H, OCH_3), 4.23–4.35 (m, 2 H, NCH_2), 4.86 (d, *J* = 15.0 Hz, 1 H, NHCHH), 5.14 (dd, *J* = 9.3, 14.1 Hz, 1 H, NHCHH), 5.50 (s, 1 H, CH), 6.46 (d, *J* = 8.0 Hz, 2 H, ArH), 7.01 (d, *J* = 8.0 Hz, 2 H, ArH), 7.48 (t, *J* = 7.5 Hz, 1 H, ArH), 7.57 (d, *J* = 8.5 Hz, 1 H, ArH), 7.77 (t, *J* = 7.6 Hz, 1 H, ArH), 8.19 (br s, 1 H, NH), 8.29 (d, *J* = 7.8 Hz, 1 H, ArH), 8.95 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.2, 21.0, 21.3, 50.1, 52.7, 53.1, 60.1, 67.6, 110.4, 118.3, 121.2, 122.0, 122.5, 128.5, 129.3, 130.1, 133.4, 135.4, 137.0, 138.9, 141.6, 144.8, 166.1, 167.5, 168.1.

MS (ES^+): *m*/*z* = 549.1 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{28}H_{29}N_4O_6S$: 549.1808; found: 549.1809.

Methyl 5-Allyl-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ba)

White solid; yield: 0.28 g (64%); mp 214–216 °C; R_f = 0.66 (hexanes–EtOAc, 40:60).

IR (KBr): 1653 (CONH), 1702 (CON), 1727 (CO_2CH_3), 3433 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.89 (s, 3 H, CH_3), 3.92–4.07 (m, 1 H, NCH*H*), 4.12 (s, 3 H, OCH_3), 4.18–4.39 (m, 3 H, NC*H*H and =CH_2), 4.91 (d, *J* = 15.2 Hz, 1 H, NHCH*H*), 5.11–5.24 (m, 3 H, NHC*H*H and NCH_2), 5.48 (s, 1 H, CH), 5.61–5.80 (m, 1 H, =CH), 6.42 (d, *J* = 8.0 Hz, 2 H, ArH), 6.98 (d, *J* = 8.2 Hz, 2 H, ArH), 7.46–7.60 (m, 2 H, ArH), 7.73–7.81 (m, 1 H, ArH), 8.30 (d, *J* = 8.0 Hz, 1 H, ArH), 8.50 (br s, 1 H, NH), 8.95 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.1, 49.9, 52.7, 52.9, 60.0, 66.4, 110.2, 118.1, 119.4, 121.0, 121.9, 122.4, 128.4, 129.1, 130.0, 130.1, 131.9, 133.3, 135.3, 136.9, 138.5, 141.4, 144.6, 165.9, 167.7, 167.9.

MS (ES^+): *m*/*z* = 547.1 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{28}H_{27}N_4O_6S$: 547.1651; found: 547.1665.

Methyl 6-Oxo-5-(2-phenylethyl)-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ca)

White solid; yield: 0.36 g (75%); mp 230–232 °C; R_f = 0.75 (hexanes–EtOAc, 40:60).

IR (KBr): 1656 (CONH), 1690 (CON), 1736 (CO_2CH_3), 3468 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, CH_3), 2.64–2.71 (m, 1 H, NCH_2CHH), 2.79–2.88 (m, 1 H, NCH_2CHH), 3.62–3.69 (m, 1 H, $NCHHCH_2$), 3.81–3.88 (m, 1 H, $NCHHCH_2$), 4.12 (s, 3 H, OCH_3), 4.22 (dd, *J* = 3.8, 14.2 Hz, 1 H, NCH*H*), 4.34 (d, *J* = 15.2 Hz, 1 H, NC*H*H), 4.85 (d, *J* = 14.9 Hz, 1 H, NHCH*H*), 5.08 (dd, *J* = 9.4, 14.3 Hz, 1 H, NHC*H*H), 5.36 (s, 1 H, CH), 6.43 (d, *J* = 7.9 Hz, 2 H, ArH), 6.98–7.05 (m, 7 H, ArH), 7.49 (t, *J* = 7.8 Hz, 1 H, ArH), 7.57 (d, *J* = 8.1 Hz, 1 H, ArH), 7.77 (t, *J* = 8.1 Hz, 1 H, ArH), 8.06 (br s, 1 H, NH), 8.30 (d, *J* = 7.8 Hz, 1 H, ArH), 8.92 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.1, 34.0, 49.9, 53.0, 53.4, 60.0, 68.4, 110.2, 118.1, 121.0, 121.9, 122.4, 126.4, 128.3, 128.4, 128.8, 129.1, 130.0, 133.2, 135.2, 136.7, 138.0, 138.5, 141.4, 144.7, 165.9, 167.5, 167.9.

MS (ES^+): *m*/*z* = 611.1 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{33}H_{31}N_4O_6S$: 611.1964; found: 611.2008.

Methyl 5-Benzyl-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Da)

White solid; yield: 0.36 g (75%); mp 209–211 °C; R_f = 0.77 (hexanes–EtOAc, 40:60).

IR (KBr): 1660 (CONH), 1711 (CON and CO_2CH_3), 3463 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, CH_3), 4.08 (s, 4 H, OCH_3 and NCH*H*), 4.46–4.62 (m, 2 H, NCH_2), 4.83–5.05 (m, 3 H, NC*H*H and $NHCH_2$), 5.50 (s, 1 H, CH), 6.38 (d, *J* = 7.5 Hz, 2 H, ArH), 6.93 (d, *J* = 7.7 Hz, 2 H, ArH), 7.22–7.26 (m, 5 H, ArH), 7.49 (t, *J* = 6.9 Hz, 1 H, ArH), 7.60 (d, *J* = 8.2 Hz, 1 H, ArH), 7.77 (d, *J* = 7.0 Hz, 1 H, ArH), 8.30 (d, *J* = 7.5 Hz, 2 H, ArH and NH), 8.92 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.1, 50.1, 53.0, 53.5, 59.9, 66.7, 110.3, 118.2, 121.2, 122.0, 122.5, 128.0, 128.4, 128.5, 128.7, 129.1, 130.1, 130.2, 133.3, 135.4, 135.5, 136.9, 138.5, 141.5, 144.6, 165.9, 167.7, 168.1.

MS (ES^+): *m*/*z* = 597.2 [M^+ + 1].

Anal. Calcd for $C_{32}H_{28}N_4O_6S$ (596.1730): C, 64.42; H, 4.73; N, 9.39. Found: C, 64.72; H, 4.54; N, 9.03.

Methyl 5-(Furan-2-ylmethyl)-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ea)

White solid; yield: 0.34 g (72%); mp 208–210 °C; R_f = 0.47 (hexanes–EtOAc, 50:50).

IR (KBr): 1632 (CONH), 1716 (CON and CO_2CH_3), 3451 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, CH_3), 4.11 (s, 3 H, OCH_3), 4.19 (dd, *J* = 4.2, 14.2 Hz, 1 H, NCH*H*), 4.37 (d, *J* = 15.8 Hz, 1 H, NC*H*H), 4.50 (d, *J* = 15.4 Hz, 1 H, NCH*H*), 4.87–4.94 (m, 2 H, NC*H*H and NHCH*H*), 5.08 (dd, *J* = 9.3, 14.1 Hz, 1 H, NHC*H*H), 5.70 (s, 1 H, CH), 6.28 (s, 2 H, ArH), 6.39 (d, *J* = 7.9 Hz, 2 H, ArH), 6.96 (d, *J* = 8.1 Hz, 2 H, ArH), 7.26 (s, 1 H, ArH), 7.48 (t, *J* = 7.4 Hz, 1 H, ArH), 7.57 (d, *J* = 8.8 Hz, 1 H, ArH), 7.76 (t, *J* = 7.5 Hz, 1 H, ArH), 8.29 (d, *J* = 7.9 Hz, 1 H, ArH), 8.40 (br s, 1 H, NH), 8.93 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.2, 46.0, 49.9, 53.1, 60.0, 66.9, 109.8, 110.3, 110.7, 118.2, 121.2, 122.0, 122.5, 128.5, 129.2, 130.0, 130.2, 133.4, 135.4, 137.0, 138.4, 141.6, 142.9, 144.7, 149.3, 166.0, 167.6, 167.8.

MS (ES^+): *m*/*z* = 587.3 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{30}H_{27}N_4O_7S$: 587.1600; found: 587.1568.

Methyl 5-Cyclopropyl-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Fa)

White solid; yield: 0.27 g (63%); mp 218–220 °C; R_f = 0.57 (hexanes–EtOAc, 40:60).

IR (KBr): 1670 (CONH), 1687 (CON), 1740 (CO_2CH_3), 3350 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.52–0.65 (m, 2 H, CH_2), 0.74–0.95 (m, 2 H, CH_2), 1.90 (s, 3 H, CH_3), 2.75–2.84 (m, 1 H, NCH), 4.12 (s, 3 H, OCH_3), 4.21–4.31 (m, 2 H, NCH_2), 4.87 (d, *J* = 15.5 Hz, 1 H, NHC*H*), 5.18 (dd, *J* = 9.2, 14.1 Hz, 1 H, NHC*H*H), 5.72 (s, 1 H, CH), 6.42 (d, *J* = 8.1 Hz, 2 H, ArH), 6.99 (d, *J* = 8.2 Hz, 2 H, ArH), 7.45–7.58 (m, 2 H, ArH), 7.77 (t, *J* = 8.3 Hz, 1 H, ArH), 8.29 (d, *J* = 7.8 Hz, 1 H, ArH), 8.50 (br s, 1 H, NH), 8.94 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 7.8, 9.9, 21.2, 34.4, 50.3, 53.1, 60.1, 69.4, 110.3, 118.2, 121.2, 122.0, 122.5, 128.6, 129.2, 130.1, 130.2, 133.3, 135.3, 137.0, 138.8, 141.6, 144.7, 166.1, 168.3, 170.0.

MS (ES^+): *m*/*z* = 547.1 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{28}H_{27}N_4O_6S$: 547.1651; found: 547.1699.

Methyl 5-Cyclohexyl-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ga)

White solid; yield: 0.32 g (68%); mp 185–186 °C; R_f = 0.84 (hexanes–EtOAc, 40:60).

IR (KBr): 1656 (CONH), 1708 (CON and CO_2CH_3), 3347 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08–1.15 (m, 2 H, CH_2), 1.32 (br s, 4 H, 2 × CH_2), 1.62–1.77 (m, 4 H, 2 × CH_2), 1.96 (s, 3 H, CH_3), 4.11 (s, 3 H, OCH_3), 4.28 (t, *J* = 11.8 Hz, 2 H, NCH_2), 4.60 (br s, 1 H, NCH), 4.86 (d, *J* = 15.1 Hz, 1 H, NHC*H*), 5.13 (dd, *J* = 8.0, 11.7 Hz, 1 H, NHC*H*H), 5.60 (s, 1 H, CH), 6.48 (d, *J* = 7.2 Hz, 2 H, ArH), 7.01 (d, *J* = 7.6 Hz, 2 H, ArH), 7.49 (d, *J* = 7.5 Hz, 1 H, ArH), 7.58 (d, *J* = 7.6 Hz, 1 H, ArH), 7.75 (d, *J* = 6.2 Hz, 1 H, ArH), 8.11 (br s, 1 H, NH), 8.28 (d, *J* = 7.4 Hz, 1 H, ArH), 8.93 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.3, 25.3, 25.6, 29.6, 30.7, 50.3, 53.0, 55.2, 60.1, 61.8, 110.3, 118.3, 121.2, 121.9, 122.5, 128.5, 129.3, 130.0, 133.4, 135.5, 137.2, 139.3, 141.6, 144.8, 166.0, 167.4, 168.6.

MS (ES^+): *m*/*z* = 589.2 [M^+ + 1].

Anal. Calcd for $C_{31}H_{32}N_4O_6S$ (588.2043): C, 63.25; H, 5.48; N, 9.52. Found: C, 63.08; H, 5.39; N, 9.68.

Methyl 5-(3-Hydroxypropyl)-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ha)

White solid; yield: 0.25 g (55%); mp 198–200 °C; R_f = 0.35 (hexanes–EtOAc, 25:75).

IR (KBr): 1657 (CONH), 1712 (CON and CO_2CH_3), 3414 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.71 (m, 2 H, $NCH_2CH_2CH_2$), 1.94 (s, 3 H, CH_3), 3.51–3.54 (m, 4 H, NCH*H*CH_2CH_2O*H*), 3.85–3.92 (m, 1 H, NC*H*HCH_2CH_2), 4.08 (s, 3 H, OCH_3), 4.31 (dd, *J* = 4.4, 14.2 Hz, 1 H, NCH*H*), 4.54 (d, *J* = 15.1 Hz, 1 H, NC*H*H), 4.91 (d, *J* = 15.2 Hz, 1 H, NHCH*H*), 5.07 (dd, *J* = 8.5, 14.0 Hz, 1 H, NHC*H*H), 5.61 (s, 1 H, CH), 6.52 (d, *J* = 7.9 Hz, 2 H, ArH), 7.06 (d, *J* = 8.1 Hz, 2 H, ArH), 7.49 (t, *J* = 7.5 Hz, 1 H, ArH), 7.57 (d, *J* = 8.2 Hz, 1 H, ArH), 7.77 (t, *J* = 7.6 Hz, 1 H, ArH), 8.30 (d, *J* = 7.9 Hz, 1 H, ArH), 8.66 (br s, 1 H, NH), 8.94 (d, *J* = 6.6 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 20.7, 45.0, 49.0, 60.1, 66.1, 109.0, 110.4, 115.3, 120.3, 120.6, 122.4, 128.1, 129.0, 129.2, 133.4, 133.7, 138.4, 138.9, 140.6, 142.9, 144.3, 149.9, 167.5, 168.3.

MS (ES^+): *m*/*z* = 565.2 [M^+ + 1].

Anal. Calcd for $C_{28}H_{28}N_4O_7S$ (564.1679): C, 59.56; H, 5.00; N, 9.92. Found: C, 59.62; H, 5.24; N, 9.85.

Methyl 5-(Methoxycarbonylmethyl)-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ia)

White solid; yield: 0.26 g (56%); mp 164–165 °C; R_f = 0.24 (hexanes–EtOAc, 40:60).

IR (KBr): 1660 (CONH), 1702 (CON and CO_2CH_3), 3456 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, CH_3), 3.71 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 4.24 (d, *J* = 17.8 Hz, 1 H, NCH*H*), 4.47 (d, *J* = 17.7 Hz, 1 H, NC*H*H), 4.68–4.90 (m, 3 H, NCH*H* and $NHCH_2$), 5.04 (d, *J* = 15.4 Hz, 1 H, NC*H*H), 5.52 (s, 1 H, CH), 6.90 (d, *J* = 8.0 Hz, 2 H, ArH), 7.38–7.47 (m, 3 H, ArH), 7.54 (d, *J* = 8.4 Hz, 1 H, ArH), 7.72 (t, *J* = 7.5 Hz, 1 H, ArH), 8.25 (d, *J* = 7.9 Hz, 1 H, ArH), 8.92 (s, 1 H, ArH), 9.21 (t, *J* = 6.1 Hz, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.4, 49.3, 51.2, 52.8, 52.9, 60.5, 68.3, 110.0, 118.5, 121.3, 121.8, 122.4, 128.7, 129.7, 129.8, 129.9, 133.9, 135.5, 136.9, 138.3, 141.4, 145.0, 166.1, 167.6, 168.2, 170.7.

MS (ES^+): *m*/*z* = 579.3 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{28}H_{27}N_4O_8S$: 579.1550; found: 579.1614.

Methyl 6-Oxo-5-phenyl-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ja)

White solid; yield: 0.33 g (70%); mp 187–189 °C; R_f = 0.73 (hexanes–EtOAc, 40:60).

IR (KBr): 1668 (CONH), 1714 (CON and CO_2CH_3), 3387 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.97 (s, 3 H, CH_3), 4.10 (s, 3 H, OCH_3), 4.30 (dd, *J* = 4.4, 14.2 Hz, 1 H, NCH*H*), 4.51 (d, *J* = 15.2 Hz, 1 H, NC*H*H), 5.02 (d, *J* = 15.2 Hz, 1 H, NHCH*H*), 5.12–5.30 (m, 1 H, NHC*H*H), 5.80 (s, 1 H, CH), 6.50 (d, *J* = 8.0 Hz, 2 H, ArH), 7.05 (d, *J* = 7.9 Hz, 4 H, ArH), 7.26–7.35 (m, 3 H, ArH), 7.52 (t, *J* = 7.6 Hz, 1 H, ArH), 7.62 (d, *J* = 8.5 Hz, 1 H, ArH), 7.80 (t, *J* = 8.0 Hz, 1 H, ArH), 8.34 (d, *J* = 7.7 Hz, 1 H, ArH), 8.45–8.49 (m, 1 H, NH), 8.99 (s, 1 H, ArH).

MS (ES^+): *m*/*z* = 583.1 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{31}H_{27}N_4O_6S$: 583.1651; found: 583.1606.

Methyl 5-(4-Chlorophenyl)-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ka)

White solid; yield: 0.30 g (62%); mp 238–240 °C; R_f = 0.77 (hexanes–EtOAc, 40:60).

IR (KBr): 1657 (CONH), 1686 (CON), 1741 (CO_2CH_3), 3449 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.00 (s, 3 H, CH_3), 4.06 (s, 3 H, OCH_3), 4.23–4.50 (m, 2 H, NCH_2), 4.98–5.20 (m, 2 H, NHCH_2), 5.78 (s, 1 H, CH), 6.52 (d, *J* = 7.7 Hz, 2 H, ArH), 7.05–7.06 (m, 4 H, ArH), 7.29 (d, *J* = 8.3 Hz, 2 H, ArH), 7.46–7.63 (m, 2 H, ArH), 7.78 (t, *J* = 7.42 Hz, 1 H, ArH), 8.15 (br s, 1 H, NH), 8.32 (d, *J* = 11.6 Hz, 1 H, ArH), 8.98 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.3, 50.1, 53.0, 60.0, 70.3, 110.3, 118.4, 121.2, 122.1, 122.6, 128.3, 128.5, 129.3, 129.8, 130.2, 130.5, 133.4, 133.9, 135.3, 137.4, 138.1, 141.6, 142.3, 144.8, 165.8, 167.6, 168.0.

MS (ES^+): *m*/*z* = 617.1 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{31}H_{26}ClN_4O_6S$: 617.1262; found: 617.1259.

Methyl 5-(4-Methoxyphenyl)-6-oxo-4-[(4-tolylsulfonylmethyl)carbamoyl]-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5La)

White solid; yield: 0.37 g (76%); mp 164–166 °C; R_f = 0.62 (hexanes–EtOAc, 40:60).

IR (KBr): 1673 (CONH), 1713 (CON and CO_2CH_3), 3416 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.96 (s, 3 H, CH_3), 3.49 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 4.28 (dd, *J* = 4.1, 14.2 Hz, 1 H, NCH*H*), 4.47 (d, *J* = 15.2 Hz, 1 H, NC*H*H), 5.00 (d, *J* = 15.1 Hz, 1 H, NHCH*H*), 5.17 (dd, *J* = 9.2, 14.0 Hz, 1 H, NHC*H*H), 5.77 (s, 1 H, CH), 6.48 (d, *J* = 7.9 Hz, 2 H, ArH), 6.84 (d, *J* = 8.8 Hz, 2 H, ArH), 6.96–7.05 (m, 4 H, ArH), 7.51 (t, *J* = 7.5 Hz, 1 H, ArH), 7.62 (d, *J* = 8.4 Hz, 1 H, ArH), 7.79 (t, *J* = 7.7 Hz, 1 H, ArH), 8.33 (d, *J* = 7.9 Hz, 1 H, ArH), 8.41 (d, *J* = 4.1 Hz, 1 H, NH), 8.98 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.3, 50.2, 53.1, 60.0, 70.4, 110.4, 118.5, 121.2, 122.1, 122.6, 126.7, 128.2, 128.5, 129.3, 129.7, 130.2, 130.5, 133.4, 135.3, 137.3, 138.3, 141.7, 143.9, 144.8, 166.0, 167.7, 168.1.

MS (ES^+): *m*/*z* = 613.1 [M^+ + 1].

Anal. Calcd for $C_{32}H_{28}N_4O_7S$ (612.1679): C, 62.73; H, 4.61; N, 9.14. Found: C, 62.83; H, 4.58; N, 9.09.

Methyl 4-[(Ethoxycarbonylmethyl)carbamoyl]-6-oxo-5-propyl-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ab)

White solid; yield: 0.24 g (65%); mp 218–220 °C; R_f = 0.32 (hexanes–EtOAc, 30:70).

IR (KBr): 1671 (CON and CONH), 1708 (CO_2CH_3), 1743 ($CO_2C_2H_5$), 3321 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.4 Hz, 3 H, $NCH_2CH_2CH_3$), 1.14 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.48–1.59 (m, 2 H, $NCH_2CH_2CH_3$), 3.61 (br s, 2 H, $NCH_2CH_2CH_3$), 3.94–4.11 (m, 7 H, OCH_3, OCH_2CH_3 and NCH_2), 5.14 (d, *J* = 15.2 Hz, 1 H, NHCH*H*), 5.27 (d, *J* = 15.1 Hz, 1 H, NHC*H*H), 5.65 (s, 1 H, CH), 6.87 (br s, 1 H, NH), 7.40 (t, *J* = 7.4 Hz, 1 H, ArH), 7.60 (d, *J* = 8.4 Hz, 1 H, ArH), 7.69 (t, *J* = 7.6 Hz, 1 H, ArH), 8.19 (d, *J* = 7.7 Hz, 1 H, ArH), 8.87 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.2, 14.1, 21.2, 42.0, 50.3, 52.6, 52.8, 61.6, 67.8, 110.3, 118.5, 121.2, 121.6, 122.3, 129.8, 129.9, 135.4, 137.0, 139.3, 141.6, 166.1, 167.3, 168.8, 169.0.

MS (ES^+): *m*/*z* = 467.3 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{24}H_{27}N_4O_6$: 467.1930; found: 467.1924.

Methyl 5-Allyl-4-[(ethoxycarbonylmethyl)carbamoyl]-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Bb)

White solid; yield: 0.28 g (76%); mp 219–220 °C; R_f = 0.37 (hexanes–EtOAc, 30:70).

IR (KBr): 1675 (CON and CONH), 1711 (CO_2CH_3), 1740 ($CO_2C_2H_5$), 3356 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 3.86–4.29 (m, 9 H, OCH_3, OCH_2CH_3, NCH_2 and $=CH_2$), 4.41 (dd, *J* = 5.5, 15.2 Hz, 1 H, NCH*H*), 5.15–5.34 (m, 3 H, NHCH_2 and NC*H*H), 5.64 (s, 1 H, CH), 5.80–5.89 (m, 1 H, =CH), 7.08 (br s, 1 H, NH), 7.41 (t, *J* = 7.4 Hz, 1 H, ArH), 7.59 (d, *J* = 8.5 Hz, 1 H, ArH), 7.69 (t, *J* = 7.3 Hz, 1 H, ArH), 8.19 (d, *J* = 8.0 Hz, 1 H, ArH), 8.85 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 42.0, 50.2, 52.8, 61.6, 66.6, 110.3, 118.4, 119.3, 121.2, 121.6, 122.2, 129.8, 129.9, 132.4, 135.5, 136.9, 139.1, 141.6, 166.0, 167.7, 168.6, 169.0.

MS (ES^+): *m*/*z* = 465.3 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{24}H_{25}N_4O_6$: 465.1774; found: 465.1795.

Methyl 4-[(Ethoxycarbonylmethyl)carbamoyl]-6-oxo-5-(2-phenylethyl)-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Cb)

White solid; yield: 0.33 g (78%); mp 128–130 °C; R_f = 0.37 (hexanes–EtOAc, 30:70).

IR (KBr): 1647 (CONH), 1671 (CON), 1690 (CO_2CH_3), 1734 ($CO_2C_2H_5$), 3350 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.78–3.02 (m, 2 H, NCH_2CH_2), 3.72–3.86 (m, 1 H, NCH*H*CH_2), 3.90–4.10 (m, 8 H, NC*H*HCH_2, OCH_2CH_3, OCH_3 and NCH_2), 5.13 (d, *J* = 15.2 Hz, 1 H, NHCH*H*), 5.26 (d, *J* = 15.2 Hz, 1 H, NHC*H*H), 5.56 (s, 1 H, CH), 6.86 (br s, 1 H, NH), 7.04–7.07 (m, 5 H, ArH), 7.40 (t, *J* = 7.6 Hz, 1 H, ArH), 7.59 (d, *J* = 8.3 Hz, 1 H, ArH), 7.69 (t, *J* = 7.4 Hz, 1 H, ArH), 8.19 (d, *J* = 7.8 Hz, 1 H, ArH), 8.83 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 34.1, 42.0, 50.2, 52.8, 53.5, 61.6, 68.6, 110.3, 118.4, 121.1, 121.6, 122.2, 126.3, 128.3, 128.8, 129.7, 129.8, 135.4, 136.8, 138.3, 139.1, 141.5, 166.0, 167.4, 168.7, 169.0.

MS (ES^+): *m*/*z* = 529.3 [M^+ + 1].

HRMS (ESI^+): *m*/*z* calcd for $C_{29}H_{28}N_4NaO_6$: 551.1907; found: 551.1958.

Methyl 5-Benzyl-4-[(ethoxycarbonylmethyl)carbamoyl]-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Db)

White solid; yield: 0.32 g (77%); mp 215–216 °C; R_f = 0.37 (hexanes–EtOAc, 30:70).

IR (KBr): 1668 (CON and CONH), 1704 (CO_2CH_3), 1728 ($CO_2C_2H_5$), 3331 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 3.72–3.88 (m, 2 H, NCH_2), 3.98–4.16 (m, 5 H, OCH_3 and OCH_2CH_3), 4.82 (d, *J* = 15.1 Hz, 1 H, NCH*H*), 4.95 (d, *J* = 15.1 Hz, 1 H, NC*H*H), 5.24 (d, *J* = 15.2 Hz, 1 H, NHCH*H*), 5.41 (d, *J* = 15.2 Hz, 1 H, NHC*H*H), 5.63 (s, 1 H, CH), 6.86 (s, 1 H, NH), 7.26 (m, 5 H, ArH), 7.40 (t, *J* = 7.6 Hz, 1 H, ArH), 7.61 (d, *J* = 8.2 Hz, 1 H, ArH), 7.70 (t, *J* = 7.7 Hz, 1 H, ArH), 8.19 (d, *J* = 7.8 Hz, 1 H, ArH), 8.83 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 41.7, 50.2, 52.6, 53.5, 61.5, 66.9, 110.3, 118.4, 121.2, 121.6, 122.3, 127.9, 128.3, 128.8, 129.8, 129.9, 135.6, 136.1, 136.8, 139.1, 141.6, 165.8, 168.1, 168.4, 168.9.

MS (ES$^+$): m/z = 515.2 [M$^+$ + 1].

HRMS (ESI$^+$): m/z calcd for $C_{28}H_{26}N_4NaO_6$: 537.1750; found: 537.1801.

Methyl 4-[(Ethoxycarbonylmethyl)carbamoyl]-5-(furan-2-ylmethyl)-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Eb)

White solid; yield: 0.31 g (76%); mp 143–145 °C; R_f = 0.38 (hexanes–EtOAc, 55:45).

IR (KBr): 1681 (CON and CONH), 1701 (CO_2CH_3), 1732 ($CO_2C_2H_5$), 3331 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.15 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 3.91 (d, J = 5.6 Hz, 2 H, NCH_2), 4.01–4.13 (m, 5 H, OCH_3 and OCH_2CH_3), 4.69 (d, J = 15.4 Hz, 1 H, NCHH), 5.20 (d, J = 15.4 Hz, 1 H, NCHH), 5.16–5.42 (m, 2 H, $NHCH_2$), 5.82 (s, 1 H, CH), 6.29–6.38 (m, 2 H, ArH), 7.08 (t, J = 5.3 Hz, 1 H, NH), 7.27–7.43 (m, 2 H, ArH), 7.57–7.72 (m, 2 H, ArH), 8.18 (d, J = 7.9 Hz, 1 H, ArH), 8.84 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 42.0, 46.0, 50.1, 52.7, 61.5, 66.9, 109.8, 110.3, 110.7, 118.4, 121.2, 121.6, 122.2, 129.7, 129.8, 135.5, 136.8, 139.0, 141.5, 142.9, 149.7, 166.0, 167.6, 168.5, 169.2.

MS (ES$^+$): m/z = 505.4 [M$^+$ + 1].

HRMS (ESI$^+$): m/z calcd for $C_{26}H_{25}N_4O_7$: 505.1723; found: 505.1701.

Methyl 5-Cyclopropyl-4-[(ethoxycarbonylmethyl)carbamoyl]-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Fb)

White solid; yield: 0.25 g (67%); mp 237–238 °C; R_f = 0.32 (hexanes–EtOAc, 30:70).

IR (KBr): 1671 (CON and CONH), 1706 (CO_2CH_3), 1737 ($CO_2C_2H_5$), 3346 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72–0.76 (m, 2 H, CH_2), 0.89–0.97 (m, 2 H, CH_2), 1.14 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 3.01–3.03 (m, 1 H, CH), 3.86–4.11 (m, 7 H, OCH_3, OCH_2CH_3 and NCH_2), 5.01–5.21 (m, 2 H, $NHCH_2$), 5.88 (s, 1 H, CH), 7.02 (br s, 1 H, NH), 7.39 (t, J = 7.5 Hz, 1 H, ArH), 7.58 (d, J = 8.3 Hz, 1 H, ArH), 7.68 (t, J = 7.5 Hz, 1 H, ArH), 8.18 (d, J = 7.8 Hz, 1 H, ArH), 8.85 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.1, 9.5, 14.1, 34.5, 42.0, 50.5, 52.7, 61.6, 69.5, 110.3, 118.4, 121.1, 121.6, 122.2, 129.8, 129.9, 135.3, 136.9, 139.3, 141.6, 166.0, 169.0, 169.1, 169.6.

MS (ES$^+$): m/z = 465.2 [M$^+$ + 1].

HRMS (ESI$^+$): m/z calcd for $C_{24}H_{25}N_4O_6$: 465.1774; found: 465.1781.

Methyl 5-Cyclohexyl-4-[(ethoxycarbonylmethyl)carbamoyl]-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Gb)

White solid; yield: 0.29 g (73%); mp 214–216 °C; R_f = 0.51 (hexanes–EtOAc, 60:40).

IR (KBr): 1658 (CONH), 1675 (CON), 1704 (CO_2CH_3), 1724 ($CO_2C_2H_5$), 3379 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 1.26–1.47 (m, 6 H, 3 × CH_2), 1.63–1.72 (m, 2 H, CH_2), 1.85 (br s, 1 H, CHH), 2.02 (br s, 1 H, CHH), 3.86–4.11 (m, 7 H, OCH_2CH_3, OCH_3 and NCH_2), 4.70 (br s, 1 H, NCH), 5.14 (d, J = 15.2 Hz, 1 H, NHCHH), 5.26 (d, J = 15.2 Hz, 1 H, NHCHH), 5.73 (s, 1 H, CH), 6.82 (t, J = 5.4 Hz, 1 H, NH), 7.38 (t, J = 6.6 Hz, 1 H, ArH), 7.59 (d, J = 8.2 Hz, 1 H, ArH), 7.68 (t, J = 7.6 Hz, 1 H, ArH), 8.18 (d, J = 7.7 Hz, 1 H, ArH), 8.84 (s, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 25.3, 25.6, 25.7, 29.9, 31.0, 42.1, 50.5, 52.8, 55.2, 61.6, 62.0, 110.3, 118.5, 121.2, 121.5, 122.3, 129.7, 135.5, 137.1, 140.0, 141.5, 166.1, 167.2, 169.0, 169.3.

MS (ES$^+$): m/z = 507.3 [M$^+$ + 1].

Anal. Calcd for $C_{27}H_{30}N_4O_6$ (506.2165): C, 64.02; H, 5.97; N, 11.06. Found: C, 64.19; H, 5.78; N, 11.01.

Methyl 4-[(Ethoxycarbonylmethyl)carbamoyl]-5-(methoxycarbonylmethyl)-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ib)

White solid; yield: 0.24 g (61%); mp >250 °C; R_f = 0.35 (hexanes–EtOAc, 20:80).

IR (KBr): 1652 (CONH), 1674 (CON), 1703 (CO_2CH_3), 1746 ($CO_2C_2H_5$), 3334 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.0 Hz, 3 H, OCH_2CH_3), 3.83 (s, 3 H, OCH_3), 3.94–4.33 (m, 8 H, OCH_2CH_3, NCH_2, OCH_3, and NCHH), 4.78 (d, J = 17.9 Hz, 1 H, NCHH), 5.22 (d, J = 15.4 Hz, 1 H, NHCHH), 5.54 (d, J = 16.0 Hz, 2 H, NHCHH and CH), 7.38 (d, J = 15.3 Hz, 1 H, ArH), 7.53–7.70 (m, 2 H, ArH), 8.19 (d, J = 8.0 Hz, 1 H, ArH), 8.88 (s, 1 H, ArH), 9.03 (br s, 1 H, NH).

MS (ES$^+$): m/z = 497.2 [M$^+$ + 1].

Anal. Calcd for $C_{24}H_{24}N_4O_8$ (496.1594): C, 58.06; H, 4.87; N, 11.29. Found: C, 58.13; H, 4.96; N, 11.06.

Methyl 4-[(Ethoxycarbonylmethyl)carbamoyl]-6-oxo-5-phenyl-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Jb)

White solid; yield: 0.30 g (75%); mp 193–195 °C; R_f = 0.42 (hexanes–EtOAc, 30:70).

IR (KBr): 1657 (CONH), 1669 (CON), 1707 (CO_2CH_3), 1738 ($CO_2C_2H_5$), 3303 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 3.88–4.11 (m, 7 H, OCH_2CH_3, OCH_3 and NCH_2), 5.29 (d, J = 15.2 Hz, 1 H, NHCHH), 5.47 (d, J = 15.2 Hz, 1 H, NHCHH), 5.97 (s, 1 H, CH), 7.13 (br s, 1 H, NH), 7.24–7.45 (m, 6 H, ArH), 7.63–7.74 (m, 2 H, ArH), 8.22 (d, J = 7.8 Hz, 1 H, ArH), 8.89 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 42.1, 50.6, 52.8, 61.6, 70.6, 110.4, 118.6, 121.3, 121.8, 122.3, 126.9, 128.0, 129.7, 129.9, 130.2, 135.5, 137.0, 139.0, 141.7, 144.1, 166.0, 167.6, 168.8, 169.0.

MS (ES$^+$): m/z = 501.2 [M$^+$ + 1].

HRMS (ESI$^+$): m/z calcd for $C_{27}H_{24}N_4NaO_6$: 523.1594; found: 523.1654.

Methyl 5-(4-Chlorophenyl)-4-[(ethoxycarbonylmethyl)carbamoyl]-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Kb)

White solid; yield: 0.27 g (64%); mp 213–214 °C; R_f = 0.46 (hexanes–EtOAc, 40:60).

IR (KBr): 1665 (CON and CONH), 1702 (CO_2CH_3), 1742 ($CO_2C_2H_5$), 3284 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 3.93–4.13 (m, 7 H, OCH_2CH_3, OCH_3 and NCH_2), 5.28 (d, J = 15.4 Hz, 1 H, NHCHH), 5.43 (d, J = 15.3 Hz, 1 H, NHCHH), 5.92 (s, 1 H, CH), 7.11 (t, J = 5.6 Hz, 1 H, NH), 7.20–7.45 (m, 5 H, ArH), 7.62–7.74 (m, 2 H, ArH), 8.22 (d, J = 7.9 Hz, 1 H, ArH), 8.89 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 42.1, 50.5, 52.8, 61.7, 70.5, 110.4, 118.6, 121.3, 121.9, 122.4, 128.5, 129.8, 130.0, 130.3, 133.8, 135.4, 137.1, 138.7, 141.7, 142.5, 166.0, 167.7, 168.7, 168.9.

MS (ES$^+$): m/z = 535.2 [M$^+$ + 1].

Anal. Calcd for $C_{27}H_{23}ClN_4O_6$ (534.1306): C, 60.62; H, 4.33; N, 10.47. Found: C, 60.45; H, 4.42; N, 10.59.

Methyl 4-[(Ethoxycarbonylmethyl)carbamoyl]-5-(4-methoxyphenyl)-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Lb)

White solid; yield: 0.32 g (76%); mp 226–228 °C; R_f = 0.35 (hexanes–EtOAc, 30:70).

IR (KBr): 1661 (CONH), 1675 (CON), 1703 (CO_2CH_3), 1728 ($CO_2C_2H_5$), 3316 (NH) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.14 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 3.79 (s, 3 H, OCH_3), 3.88–4.11 (m, 7 H, OCH_2CH_3, OCH_3 and NCH_2), 5.28 (d, *J* = 15.5 Hz, 1 H, NHCH*H*), 5.42 (d, *J* = 15.5 Hz, 1 H, NHC*H*H), 5.94 (s, 1 H, CH), 6.88 (d, *J* = 8.4 Hz, 2 H, ArH), 6.98 (s, 1 H, NH), 7.18 (d, *J* = 8.6 Hz, 2 H, ArH), 7.42 (t, *J* = 7.7 Hz, 1 H, ArH), 7.63–7.74 (m, 2 H, ArH), 8.23 (d, *J* = 7.9 Hz, 1 H, ArH), 8.90 (s, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 42.0, 50.5, 52.7, 55.6, 61.6, 70.9, 110.4, 114.8, 118.6, 121.2, 121.7, 122.3, 128.0, 129.9, 130.1, 135.4, 137.0, 137.1, 139.0, 141.7, 159.0, 166.0, 167.8, 168.8, 169.0.

MS (ES^+): *m*/*z* = 531.3 [M^+ + 1].

Anal. Calcd for $C_{28}H_{26}N_4O_7$ (530.1801): C, 63.39; H, 4.94; N, 10.56. Found: C, 63.71; H, 4.56; N, 10.25.

(*Z*)-Methyl 5-Allyl-4-[(2-cyano-3-phenylallyl)carbamoyl]-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Bc)

White solid; yield: 0.33 g (78%); mp 226–228 °C; R_f = 0.24 (hexanes–EtOAc, 40:60).

IR (KBr): 1660 (CONH), 1681 (CON), 1695 (CO_2CH_3), 3374 (NH) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.05–4.18 (m, 6 H, OCH_3, $=CH_2$ and NCH*H*), 4.46–4.52 (m, 1 H, NC*H*H), 5.18–5.30 (m, 3 H, NCH_2 and NHCH*H*), 5.40 (d, *J* = 15.3 Hz, 1 H, NHC*H*H), 5.64 (s, 1 H, CH), 5.78–5.91 (m, 1 H, =CH), 6.93 (s, 1 H, ArH), 7.26–7.42 (m, 4 H, ArH and =CH), 7.55–7.60 (m, 3 H, ArH), 7.69 (t, *J* = 8.4 Hz, 1 H, ArH), 8.19 (d, *J* = 8.2 Hz, 1 H, ArH), 8.56 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 43.8, 50.6, 52.9, 53.0, 66.9, 107.6, 110.3, 117.4, 118.3, 119.4, 121.2, 121.6, 122.3, 128.9, 129.8, 130.1, 130.7, 132.4, 132.8, 135.5, 136.8, 139.0, 141.7, 144.7, 166.2, 168.0, 168.7.

MS (ES^+): *m*/*z* = 520.2 [M^+ + 1].

Anal. Calcd for $C_{30}H_{25}N_5O_4$ (519.1907): C, 69.35; H, 4.85; N, 13.48. Found: C, 69.59; H, 4.72; N, 13.43.

(*Z*)-Methyl 4-[(2-Cyano-3-phenylallyl)carbamoyl]-6-oxo-5-(2-phenylethyl)-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Cc)

White solid; yield: 0.35 g (75%); mp 158–160 °C; R_f = 0.66 (hexanes–EtOAc, 40:60).

IR (KBr): 1659 (CONH), 1692 (CON and CO_2CH_3), 3321 (NH) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.78–2.86 (m, 1 H, NCH_2CH*H*), 2.88–3.00 (m, 1 H, NCH_2CH*H*), 3.72–3.82 (m, 1 H, NCH*H*CH_2), 4.00–4.06 (m, 5 H, OCH_3, NC*H*HCH_2 and NCH*H*), 4.17–4.24 (m, 1 H, NC*H*H), 5.14 (d, *J* = 15.1 Hz, 1 H, NHCH*H*), 5.31 (d, *J* = 15.2 Hz, 1 H, NHC*H*H), 5.55 (s, 1 H, CH), 6.91 (s, 1 H, ArH), 7.05 (s, 5 H, ArH), 7.29–7.42 (m, 4 H, ArH and =CH), 7.53–7.60 (m, 3 H, ArH), 7.69 (t, *J* = 7.5 Hz, 1 H, ArH), 8.19 (d, *J* = 7.9 Hz, 1 H, ArH), 8.33 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 43.8, 50.4, 52.9, 53.5, 68.8, 107.5, 110.3, 118.3, 121.1, 121.6, 122.3, 126.4, 128.4, 128.9, 129.8, 130.8, 132.7, 135.4, 136.8, 138.2, 138.9, 141.6, 144.9, 166.1, 167.6, 168.7.

MS (ES^+): *m*/*z* = 584.3 [M^+ + 1].

Anal. Calcd for $C_{35}H_{29}N_5O_4$ (583.2220): C, 72.03; H, 5.01; N, 12.00. Found: C, 72.15; H, 5.23; N, 12.09.

(*Z*)-Methyl 5-Benzyl-4-[(2-cyano-3-phenylallyl)carbamoyl]-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Dc)

White solid; yield: 0.36 g (78%); mp 235–236 °C; R_f = 0.53 (hexanes–EtOAc, 40:60).

IR (KBr): 1655 (CONH), 1692 (CON and CO_2CH_3), 3377 (NH) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.96 (t, *J* = 5.4 Hz, 2 H, NCH_2), 4.01 (s, 3 H, OCH_3), 4.61 (d, *J* = 14.9 Hz, 1 H, NCH*H*), 5.15 (d, *J* = 14.9 Hz, 1 H, NC*H*H), 5.26 (d, *J* = 15.5 Hz, 1 H, NHCH*H*), 5.49 (d, *J* = 15.8 Hz, 1 H, NHC*H*H), 5.65 (s, 1 H, CH), 6.80 (s, 1 H, ArH), 7.13–7.43 (m, 9 H, ArH and =CH), 7.54–7.72 (m, 4 H, ArH), 8.19 (d, *J* = 7.6 Hz, 1 H, ArH), 8.84 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 43.6, 50.6, 52.8, 53.6, 67.1, 107.3, 110.4, 117.5, 118.3, 121.2, 121.6, 122.2, 128.1, 128.6, 128.9, 129.8, 130.0, 130.7, 132.8, 135.6, 135.9, 136.7, 138.9, 141.7, 144.8, 166.1, 168.2, 168.4.

MS (ES^+): *m*/*z* = 570.2 [M^+ + 1].

Anal. Calcd for $C_{34}H_{27}N_5O_4$ (569.2063): C, 71.69; H, 4.78; N, 12.30. Found: C, 71.85; H, 4.93; N, 12.12.

(*Z*)-Methyl 4-[(2-Cyano-3-phenylallyl)carbamoyl]-5-(4-methoxyphenyl)-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Lc)

White solid; yield: 0.36 g (77%); mp 153–155 °C; R_f = 0.18 (hexanes–EtOAc, 40:60).

IR (KBr): 1669 (CONH), 1686 (CON), 1708 (CO_2CH_3), 3388 (NH) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, OCH_3), 4.03–4.09 (m, 4 H, OCH_3 and NCH*H*), 4.29 (dd, *J* = 6.1, 14.9 Hz, 1 H, NC*H*H), 5.30 (t, *J* = 7.8 Hz, 1 H, NHCH*H*), 5.46–5.53 (m, 1 H, NHC*H*H), 5.94 (d, *J* = 7.3 Hz, 1 H, CH), 6.89 (t, *J* = 9.7 Hz, 2 H, ArH), 7.15–7.42 (m, 8 H, ArH and =CH), 7.55 (d, *J* = 6.2 Hz, 1 H, ArH), 7.63 (d, *J* = 8.6 Hz, 1 H, ArH), 7.71 (t, *J* = 8.2 Hz, 1 H, ArH), 8.22 (d, *J* = 8.0 Hz, 1 H, ArH), 8.89 (d, *J* = 4.2 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 43.8, 50.8, 52.9, 55.6, 71.1, 107.6, 110.5, 114.9, 118.5, 121.2, 121.8, 122.3, 128.0, 128.9, 129.4, 130.0, 130.4, 130.8, 132.7, 136.9, 137.2, 138.9, 141.8, 144.7, 145.6, 159.0, 166.2, 168.1, 168.8.

MS (ES^+): *m*/*z* = 586.1 [M^+ + 1].

Anal. Calcd for $C_{34}H_{27}N_5O_5$ (585.2012): C, 69.73; H, 4.65; N, 11.96. Found: C, 69.84; H, 4.76; N, 11.89.

(*Z*)-Methyl 4-{[2-Cyano-3-(2,4-dichlorophenyl)allyl]carbamoyl}-6-oxo-5-propyl-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Ad)

White solid; yield: 0.34 g (72%); mp 135–136 °C; R_f = 0.44 (hexanes–EtOAc, 40:60).

IR (KBr): 1658 (CONH), 1689 (CON), 1721 (CO_2CH_3), 3439 (NH) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.1 Hz, 3 H, $NCH_2CH_2CH_3$), 1.54–1.66 (m, 2 H, $NCH_2CH_2CH_3$), 3.57–3.66 (m, 2 H, $NCH_2CH_2CH_3$), 4.06–4.14 (m, 4 H, OCH_3 and NCH*H*), 4.26–4.33 (m, 1 H, NC*H*H), 5.16 (d, *J* = 14.8 Hz, 1 H, NHCH*H*), 5.37 (d, *J* = 14.7 Hz, 1 H, NHC*H*H), 5.68 (s, 1 H, CH), 7.15 (s, 1 H, NH),

7.21–7.43 (m, 3 H, =CH and ArH), 7.59 (d, J = 8.5 Hz, 2 H, ArH), 7.67–7.76 (m, 2 H, ArH), 8.19 (d, J = 5.2 Hz, 1 H, ArH), 8.86 (s, 1 H, ArH).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 10.8, 20.9, 49.4, 51.2, 52.2, 66.6, 110.6, 113.6, 116.8, 118.2, 120.6, 121.2, 122.7, 127.9, 128.6, 129.4, 130.4, 130.5, 133.9, 134.9, 135.4, 136.6, 139.3, 139.6, 140.9, 165.7, 166.2, 169.2.

MS (ES$^+$): m/z = 590.2 [M$^+$ + 1].

HRMS (ESI$^+$): m/z calcd for $C_{30}H_{26}Cl_2N_5O_4$: 590.1362; found: 590.1376.

(*Z*)-Methyl 5-Allyl-4-{[2-cyano-3-(2,4-dichlorophenyl)allyl]carbamoyl}-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Bd)

White solid; yield: 0.35 g (74%); mp 186–188 °C; R_f = 0.47 (hexanes–EtOAc, 40:60).

IR (KBr): 1659 (CONH), 1692 (CON and CO_2CH_3), 3420 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.05 (s, 3 H, OCH_3), 4.12–4.31 (m, 3 H, NCH_2 and NC*H*H), 4.46–4.51 (m, 1 H, NC*H*H), 5.18–5.41 (m, 4 H, NHCH_2 and =CH_2), 5.66 (s, 1 H, CH), 5.83–5.85 (m, 1 H, =CH), 7.14–7.42 (m, 4 H, NH, =CH and ArH), 7.60–7.98 (m, 4 H, ArH), 8.18 (d, J = 7.2 Hz, 1 H, ArH), 8.84 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 43.3, 50.5, 52.9, 53.0, 66.9, 110.3, 111.7, 116.5, 118.4, 119.5, 121.2, 121.7, 122.3, 127.7, 129.6, 129.8, 129.9, 130.2, 132.4, 134.9, 135.5, 136.9, 137.0, 139.0, 139.4, 141.7, 166.1, 167.9, 168.7.

MS (ES$^+$): m/z = 588.4 [M$^+$ + 1].

HRMS (ESI$^+$): m/z calcd for $C_{30}H_{23}Cl_2N_5NaO_4$: 610.1025; found: 610.1020.

(*Z*)-Methyl 4-{[2-Cyano-3-(2,4-dichlorophenyl)allyl]carbamoyl}-5-cyclopropyl-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Fd)

White solid; yield: 0.33 g (71%); mp 228–230 °C; R_f = 0.46 (hexanes–EtOAc, 40:60).

IR (KBr): 1666 (CONH), 1701 (CON and CO_2CH_3), 3332 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.70–0.79 (m, 2 H, CH_2), 0.85–1.01 (m, 2 H, CH_2), 2.98–3.06 (m, 1 H, NCH), 4.06–4.18 (m, 4 H, OCH_3 and NC*H*H), 4.29–4.41 (m, 1 H, NC*H*H), 5.19 (dd, J = 15.4, 18.2 Hz, 2 H, NHCH_2), 5.92 (s, 1 H, CH), 7.14–7.44 (m, 5 H, =CH and ArH), 7.55–7.77 (m, 2 H, ArH), 8.18 (d, J = 7.7 Hz, 1 H, ArH), 8.84 (s, 1 H, ArH).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 7.7, 9.0, 33.9, 42.5, 52.2, 68.8, 75.3, 76.1, 110.7, 113.6, 116.8, 118.3, 120.6, 121.3, 122.6, 127.9, 128.8, 129.4, 130.4, 130.5, 133.9, 134.7, 135.4, 136.7, 139.1, 141.0, 165.7, 168.3, 169.1.

MS (ES$^+$): m/z = 588.4 [M$^+$ + 1].

HRMS (ESI$^+$): m/z calcd for $C_{30}H_{23}Cl_2N_5NaO_4$: 610.1025; found: 610.1047.

(*E*)-Methyl 5-Allyl-4-{[2-(methoxycarbonyl)-3-phenylallyl]carbamoyl}-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-2-carboxylate (5Be)

White solid; yield: 0.34 g (77%); mp 203–204 °C; R_f = 0.47 (hexanes–EtOAc, 40:60).

IR (KBr): 1666 (CONH), 1677 (CON), 1725 (CO_2CH_3), 3406 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.61 (s, 3 H, OCH_3), 4.06–4.21 (m, 4 H, OCH_3 and NC*H*H), 4.26–4.50 (m, 3 H, NC*H*H and NCH_2), 5.12–5.29 (m, 4 H, NHCH_2 and =CH_2), 5.54 (s, 1 H, CH), 5.76–5.95 (m, 1 H, =CH), 7.08 (s, 1 H, NH), 7.27–7.44 (m, 6 H, ArH), 7.57–7.74 (m, 3 H, =CH and ArH), 8.20 (d, J = 7.7 Hz, 1 H, ArH), 8.86 (s, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 37.2, 50.4, 52.2, 52.9, 53.0, 66.9, 110.3, 118.3, 119.4, 121.2, 121.6, 122.3, 127.4, 128.7, 129.4, 129.8, 130.0, 132.4, 134.0, 135.4, 137.1, 139.3, 141.6, 142.9, 166.1, 167.5, 167.6, 167.7.

MS (ES$^+$): m/z = 553.3 [M$^+$ + 1].

Anal. Calcd for $C_{31}H_{28}N_4O_6$ (552.2009): C, 67.38; H, 5.11; N, 10.14. Found: C, 67.52; H, 5.01; N, 10.06.

6-Oxo-5-propyl-*N*-(4-tolylsulfonylmethyl)-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-4-carboxamide (8Aa)

White solid; yield: 0.29 g (61%); mp 226–228 °C; R_f = 0.44 (hexanes–EtOAc, 40:60).

IR (KBr): 1656 (CONH), 1689 (CON), 3451 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, J = 6.8 Hz, 3 H, $NCH_2CH_2CH_3$), 1.42–1.57 (m, 2 H, $NCH_2CH_2CH_3$), 1.94 (s, 3 H, CH_3), 3.41–3.53 (m, 2 H, $NCH_2CH_2CH_3$), 3.99 (d, J = 15.1 Hz, 1 H, NCH*H*), 4.24 (d, J = 13.6 Hz, 1 H, NC*H*H), 4.76 (d, J = 15.2 Hz, 1 H, NHCH*H*), 5.15 (dd, J = 9.9, 13.0 Hz, 1 H, NHC*H*H), 5.36 (s, 1 H, CH), 6.39 (d, J = 7.5 Hz, 2 H, ArH), 6.95 (d, J = 7.7 Hz, 2 H, ArH), 7.41–7.53 (m, 3 H, ArH), 7.70 (d, J = 7.1 Hz, 1 H, ArH), 8.07 (d, J = 5.0 Hz, 1 H, NH), 8.24 (d, J = 7.6 Hz, 1 H, ArH), 8.49 (d, J = 4.4 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 11.2, 21.1, 21.3, 49.9, 52.7, 59.7, 67.6, 109.9, 115.6, 121.0, 121.1, 122.5, 128.5, 129.4, 129.7, 130.5, 133.0, 134.2, 138.7, 139.2, 141.4, 144.9, 167.7, 168.5.

MS (ES$^+$): m/z = 491.3 [M$^+$ + 1].

Anal. Calcd for $C_{26}H_{26}N_4O_4S$ (490.1675): C, 63.66; H, 5.34; N, 11.42. Found: C, 63.34; H, 5.56; N, 11.35.

5-(Furan-2-ylmethyl)-6-oxo-*N*-(4-tolylsulfonylmethyl)-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-4-carboxamide (8Ea)

White solid; yield: 0.36 g (69%); mp 214–216 °C; R_f = 0.35 (hexanes–EtOAc, 40:60).

IR (KBr): 1662 (CONH), 1693 (CON), 3377 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, CH_3), 3.95 (d, J = 15.0 Hz, 1 H, NCH*H*), 4.15 (dd, J = 3.4, 14.2 Hz, 1 H, NC*H*H), 4.70 (d, J = 3.4 Hz, 2 H, NCH_2), 4.80 (d, J = 22.4 Hz, 1 H, NHCH*H*), 5.13 (dd, J = 10.1, 14.2 Hz, 1 H, NHC*H*H), 5.56 (s, 1 H, CH), 6.25–6.26 (m, 2 H, ArH), 6.33 (d, J = 8.0 Hz, 2 H, ArH), 6.90 (d, J = 8.1 Hz, 2 H, ArH), 7.41 (t, J = 7.5 Hz, 2 H, ArH), 7.52 (d, J = 8.5 Hz, 1 H, ArH), 7.72 (t, J = 8.2 Hz, 1 H, ArH), 8.06 (d, J = 5.2 Hz, 1 H, ArH), 8.23 (d, J = 7.9 Hz, 1 H, ArH), 8.49 (d, J = 5.2 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 20.9, 30.8, 52.3, 58.3, 66.5, 110.7, 118.3, 120.6, 121.4, 122.8, 128.2, 128.8, 129.4, 129.6, 134.2, 134.9, 136.6, 139.0, 141.0, 144.6, 165.6, 166.5, 168.8.

MS (ES$^+$): m/z = 529.2 [M$^+$ + 1].

Anal. Calcd for $C_{28}H_{24}N_4O_5S$ (528.1467): C, 63.62; H, 4.58; N, 10.60. Found: C, 63.34; H, 4.86; N, 10.25.

5-(4-Methoxyphenyl)-6-oxo-*N*-(4-tolylsulfonylmethyl)-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluorene-4-carboxamide (8La)

White solid; yield: 0.40 g (74%); mp 243–245 °C; R_f = 0.38 (hexanes–EtOAc, 40:60).

IR (KBr): 1664 (CONH), 1685 (CON), 3483 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.96 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 4.09 (d, J = 15.0 Hz, 1 H, NCH*H*), 4.22 (dd, J = 3.7, 14.3

Hz, 1 H, NC*H*H), 4.89 (d, *J* = 15.1 Hz, 1 H, NHCH*H*), 5.19 (dd, *J* = 9.8, 14.1 Hz, 1 H, NHC*H*H), 5.64 (s, 1 H, CH), 6.40 (d, *J* = 7.8 Hz, 2 H, ArH), 6.85 (d, *J* = 8.9 Hz, 2 H, ArH), 6.96 (d, *J* = 8.2 Hz, 2 H, ArH), 7.03 (d, *J* = 8.9 Hz, 2 H, ArH), 7.44 (t, *J* = 7.3 Hz, 2 H, ArH), 7.56 (d, *J* = 8.2 Hz, 1 H, ArH), 7.74 (t, *J* = 7.5 Hz, 1 H, ArH), 8.12 (d, *J* = 5.2 Hz, 1 H, NH), 8.28 (d, *J* = 7.9 Hz, 1 H, ArH), 8.52 (d, *J* = 5.2 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.4, 50.1, 55.6, 59.8, 70.9, 110.1, 114.9, 115.6, 121.2, 122.6, 127.9, 128.6, 129.4, 129.8, 130.7, 133.1, 134.3, 137.3, 138.5, 139.4, 141.5, 144.9, 159.1, 168.1, 168.6.

MS (ES^+): *m*/*z* = 555.2 [M^+ + 1].

Anal. Calcd for $C_{30}H_{26}N_4O_5S$ (554.1624): C, 64.97; H, 4.73; N, 10.10. Found: C, 65.07; H, 4.84; N, 10.02.

Ethyl [(5-Allyl-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluoren-4-ylcarbonyl)amino]acetate (8Bb)
White solid; yield: 0.32 g (72%); mp 141–143 °C; R_f = 0.38 (hexanes–EtOAc, 40:60).

IR (KBr): 1662 (CONH), 1691 (CON), 1743 ($CO_2C_2H_5$), 3378 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 3.96 (d, *J* = 5.5 Hz, 2 H, NCH_2), 4.09 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 4.14–4.44 (m, 2 H, NCH_2), 5.14–5.51 (m, 4 H, =CH_2 and $NHCH_2$), 5.75 (s, 1 H, CH), 5.72–5.92 (m, 1 H, =CH), 6.77 (t, *J* = 5.2 Hz, 1 H, NH), 7.28–7.36 (m, 1 H, ArH), 7.52–7.68 (m, 2 H, ArH), 7.97 (d, *J* = 5.3 Hz, 1 H, ArH), 8.13 (d, *J* = 7.9 Hz, 1 H, ArH), 8.41 (d, *J* = 5.3 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 41.9, 50.1, 52.6, 61.6, 66.5, 109.8, 115.4, 119.3, 120.6, 120.9, 122.2, 129.3, 130.1, 132.6, 134.2, 138.8, 139.1, 141.2, 168.0, 169.0.

MS (ES^+): *m*/*z* = 407.4 [M^+ + 1].

Anal. Calcd for $C_{22}H_{22}N_4O_4$ (406.1641): C, 65.01; H, 5.46; N, 13.78. Found: C, 65.15; H, 5.59; N, 13.66.

Ethyl {[6-Oxo-5-(2-phenylethyl)-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluoren-4-ylcarbonyl]amino}acetate (8Cb)
White solid; yield: 0.34 g (73%); mp 168–170 °C; R_f = 0.63 (hexanes–EtOAc, 40:60).

IR (KBr): 1662 (CONH), 1689 (CON), 1742 ($CO_2C_2H_5$), 3378 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.80–2.86 (m, 1 H, NCH_2CHH), 2.92–2.98 (m, 1 H, NCH_2CHH), 3.64–3.73 (m, 1 H, $NCHHCH_2$), 3.94 (d, *J* = 5.4 Hz, 2 H, NCH_2), 4.05–4.16 (m, 3 H, OCH_2CH_3 and $NCHHCH_2$), 5.09 (s, 2 H, $NHCH_2$), 5.39 (s, 1 H, CH), 6.68 (s, 1 H, NH), 7.05–7.06 (m, 5 H, ArH), 7.32 (t, *J* = 7.2 Hz, 1 H, ArH), 7.54 (d, *J* = 8.4 Hz, 1 H, ArH), 7.64 (t, *J* = 7.5 Hz, 1 H, ArH), 7.94 (d, *J* = 5.3 Hz, 1 H, ArH), 8.13 (d, *J* = 7.9 Hz, 1 H, ArH), 8.34 (d, *J* = 5.3 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 34.2, 41.9, 50.1, 53.4, 61.7, 68.8, 109.8, 115.3, 120.6, 120.9, 122.2, 126.3, 128.3, 128.8, 129.3, 130.0, 134.1, 138.4, 138.6, 139.1, 141.2, 167.8, 169.0, 169.1.

MS (ES^+): *m*/*z* = 471.2 [M^+ + 1].

Anal. Calcd for $C_{27}H_{26}N_4O_4$ (470.1954): C, 68.92; H, 5.57; N, 11.91. Found: C, 68.86; H, 5.64; N, 11.83.

Ethyl [(5-Benzyl-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluoren-4-ylcarbonyl)amino]acetate (8Db)
White solid; yield: 0.31 g (78%); mp 148–150 °C; R_f = 0.44 (hexanes–EtOAc, 40:60).

IR (KBr): 1655 (CONH), 1692 (CON), 1741 ($CO_2C_2H_5$), 3391 (NH) cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 3.87 (d, *J* = 5.5 Hz, 2 H, NCH_2), 4.06 (q, *J* = 7.2 Hz, 2 H, OCH_2CH_3), 4.70 (d, *J* = 15.1 Hz, 1 H, NHCH*H*), 5.09 (d, *J* = 15.0 Hz, 1 H, NHC*H*H), 5.21 (s, 2 H, NCH_2), 5.48 (s, 1 H, CH), 6.60 (s, 1 H, NH), 7.22–7.26 (m, 5 H, ArH), 7.33 (t, *J* = 7.2 Hz, 1 H, ArH), 7.57 (d, *J* = 8.4 Hz, 1 H, ArH), 7.65 (t, *J* = 7.1 Hz, 1 H, ArH), 7.93 (d, *J* = 5.3 Hz, 1 H, ArH), 8.13 (d, *J* = 7.9 Hz, 1 H, ArH), 8.31 (d, *J* = 5.3 Hz, 1 H, ArH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.3, 41.8, 50.2, 53.3, 61.6, 66.9, 109.9, 115.3, 120.6, 121.0, 122.2, 127.9, 128.4, 128.8, 129.3, 130.0, 134.2, 136.1, 138.7, 139.1, 141.2, 168.4, 168.8, 169.0.

MS (ES^+): *m*/*z* = 457.4 [M^+ + 1].

Anal. Calcd for $C_{26}H_{24}N_4O_4$ (456.1798): C, 68.41; H, 5.30; N, 12.27. Found: C, 68.36; H, 5.16; N, 12.49.

Ethyl {[5-(4-Methoxyphenyl)-6-oxo-4,5,6,7-tetrahydro-3,5,7a-triazacyclohepta[*jk*]fluoren-4-ylcarbonyl]amino}acetate (8Lb)
White solid; yield: 0.32 g (76%); mp 243–245 °C; R_f = 0.32 (hexanes–EtOAc, 40:60).

IR (KBr): 1668 (CONH), 1691 (CON), 1747 ($CO_2C_2H_5$), 3309 (NH) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 3.79 (s, 3 H, OCH_3), 3.98–4.01 (m, 2 H, NCH_2), 4.09 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 5.19–5.30 (m, 2 H, $NHCH_2$), 5.79 (s, 1 H, CH), 6.74 (br s, 1 H, NH), 6.88 (d, *J* = 8.9 Hz, 2 H, ArH), 7.21 (d, *J* = 8.9 Hz, 2 H, ArH), 7.35 (t, *J* = 7.0 Hz, 1 H, ArH), 7.58 (d, *J* = 8.3 Hz, 1 H, ArH), 7.66 (t, *J* = 7.3 Hz, 1 H, ArH), 8.00 (d, *J* = 5.3 Hz, 1 H, ArH), 8.16 (d, *J* = 7.8 Hz, 1 H, ArH), 8.42 (d, *J* = 5.3 Hz, 1 H, ArH).

MS (ES^+): *m*/*z* = 473.5 [M^+ + 1].

Anal. Calcd for $C_{26}H_{24}N_4O_5$ (472.1747): C, 66.09; H, 5.12; N, 11.86. Found: C, 66.16; H, 5.03; N, 11.96.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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