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Tetrahedron
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Tetrahedron 62 (2006) 9931–9941

Annulated 1,2,3,4-tetrahydro-β-carbolines by intramolecular Mannich-type amino- and amidoalkylations of *N*(9)-(ω-nitroalkyl)-3,4-dihydro-β-carbolines

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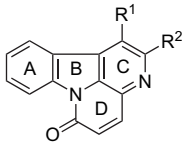
Received 14 April 2006; revised 14 July 2006; accepted 3 August 2006
Available online 24 August 2006

Abstract—2-[1-(ω-Nitroalkyl)-1*H*-indol-3-yl]ethylformamides **11** were transformed to the corresponding 9-(ω-nitroalkyl)-4,9-dihydro-3*H*-β-carbolines **5** and through a diastereoselective intramolecular aminoalkylation to the annulated tetrahydro-β-carbolines **13**, in high yields. Intramolecular *N*-acyliminium cyclisation of compounds **5** afforded the tetracyclic diazacycloalkano[*jk*]fluorenes in two diastereoisomeric forms **18** and **19** with moderate selectivity. Conjugate addition reactions performed on compounds **18** and **19** led to pentacyclic indolo[3,2,1-*de*]pyrido[3,2,1-*jk*]naphthyridinone **26a** or diazabenzo[*a*]naphtho[2,1,8-*cde*]azulenone **26b**.

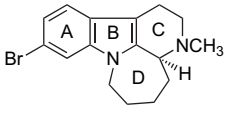
1. Introduction

The β-carboline nucleus is found in a plethora of naturally occurring and synthetic biologically active compounds.[1] β-Carboline alkaloids have been shown to bind with high affinity to serotonin receptors in the central nervous system and are also of biological importance in many other processes.[2,3]

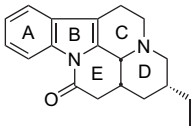
The structurally diverse annulated β-carboline alkaloids have received considerable attention over the years for both their medicinal properties and intriguing molecular structures. Canthin-6-ones (**1**) are representative members of the canthine[4] family and posses a tetracyclic indolo-[3,2,1-*de*][1,5]naphthyridine skeleton. Members of this family have been shown to exhibit a wide range of pharmacological activities including antifungal, antiviral and antitumor properties.[5] Arborescidine B (**2**) and other alkaloids with related structures,[6] isolated from the marine tunicate *Pseudodistoma arborescens*, are characterised by a peculiar tetracyclic skeleton that incorporates an azepino ring fused to a tetrahydro-β-carboline unit. The pentacyclic alkaloids belonging to the tacamine[7] and vinca-eburna[8] groups, which include tacamonine[7b] (**3**) and eburnamonine (**4**), are potent cerebral vasodilators, exhibit a gastroprotective action and a protective effect against brain damage caused by ischemia.[9]



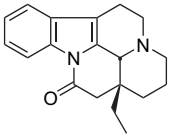
1 Canthin-6-ones



2 Arborescidine B



3 Tacamonine



4 Eburnamonine

Pictet–Spengler or Bichler–Napieralsky cyclisations are the synthetic methods most frequently used to construct the tetracyclic ABCD canthine or arborescidine-type skeletons.[4,5a,c,d,10] An elegant strategy to access the canthine skeleton, developed by Snyder[11] in 1992 and improved by Lindsley[4] in 2003, is based on an inverse electron demand Diels–Alder reaction of a triazine tethered indole, utilising indole as the dienophile. Another methodology for the construction of a precursor of akagerine, a member of the arborescidine family, developed by Bennasar et al.,[12] is based on the nucleophilic addition of indole-containing enolates to *N*-alkylpyridinium salts followed by acid promoted cyclisation of the resulting 1,4-dihydropyridine derivatives.

Numerous synthetic approaches to the tacamine- or vinca-eburna-type skeleton have been reported. In 1995, a novel strategy for the construction of the pentacyclic framework of the eburnamonines was developed by Grieco,[13] featuring

Keywords: *N*(9)-Nitroalkyl-3,4-dihydro-β-carbolines; Annulated 1,2,3,4-tetrahydro-β-carbolines; Intramolecular Mannich-type amino- and amidoalkylation.
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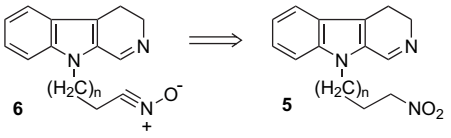
0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.08.020

an intramolecular imino Diels–Alder reaction of a vinylindole imine. But the most common synthetic entry to these alkaloids is based on an ABCD→ABCDE construction in which the E ring is formed late in the synthesis. The vast majority of the synthesis construct the ABCD tetracyclic system via a Pictet–Spengler[14] or Bichler–Napieralsky[15] cyclisation starting from 3-(2-aminoethyl)indole derivatives. Another strategy applied for the synthesis of the properly substituted tetracyclic indoloquinolizidine moieties was the annulation reaction of a 3,4-dihydro-β-carboline.[16] Limited examples have been published in which the 1,2-unsaturated β-carboline moiety is directly derivatized by nucleophilic addition reactions. These almost exclusively involve the introduction of an allyl group. Martin, Yamaguchi and others reported that when 3,4-dihydro-β-carboline was subjected to addition of nucleophiles in the presence of acyl halides, 1,2,3,4-tetrahydro-β-carboline derivatives were formed.[17] In these reactions *N*-acylated iminium salts, formed in situ, were trapped by silyl enol ethers or organotin reagents.

To the best of our knowledge and despite the amount of research concerning the intermolecular alkylation reactions of the *N*(2)-acyliminiun salts of 3,4-dihydro-β-carboline, the intramolecular mode of the reaction starting from *N*(9)-substituted 3,4-dihydro-β-carbolines has not received analogous attention. For this reason and in connection with our continuing interest[18] about indole chemistry we investigated the intramolecular alkylations of *N*(9)-(ω-nitroalkyl)-3,4-dihydro-β-carbolines **5** and we report our results herein.

2. Results and discussion

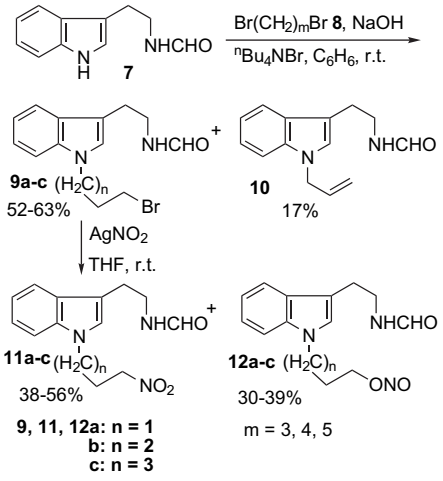
In the course of our efforts to study intramolecular 1,3-cycloaddition reactions on the carbon–nitrogen double bond of 3,4-dihydro-β-carbolines **6**, bearing a nitrile oxide tethered to the indole nitrogen, we attempted the synthesis of *N*(9)-(ω-nitroalkyl)-3,4-dihydro-β-carbolines **5** (Scheme 1).[19]



Scheme 1. Attempted approach to nitrile oxides **6**.

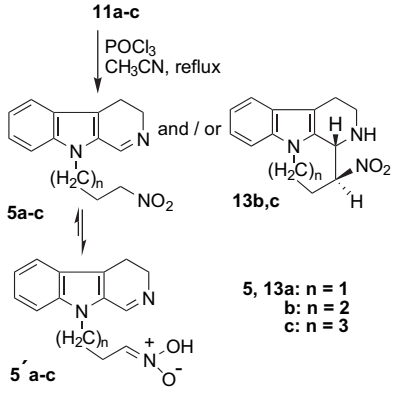
Nitroalkyl groups could be transformed to the corresponding nitrile oxide derivatives upon treatment with phenyl isocyanate in the presence of triethylamine.[19]

We planned to prepare the desired dihydro-β-carbolines **5** via a Bichler–Napieralsky condensation of the corresponding N_a-ω-nitroalkyl-tryptamine derivatives **11** (Scheme 3). For the synthesis of compounds **11** the sequence illustrated in Scheme 2 was followed. Indolyl-ethylformamide **7** was derivatized to the corresponding N_a-ω-bromoalkyl-tryptamine derivatives **9a–c** upon treatment[19] with aqueous NaOH and the proper α,ω-dibromoalkane **8** under mild phase transfer catalysis conditions, in 52–63% yields. The *N*-ω-bromoethylation of the amide **7** was inefficient[19,20] leading to extremely low yield of the desired product. The chain-length dependence of the yield has been observed in analogous reactions of carbazole.[20] From the bromoalkylation reaction of **7** with 1,3-dibromoethane, derivative **10** was also isolated (yield 17%). Nitroalkyl derivatives **11a–c** were prepared from N_a-ω-bromoalkyl-tryptamines **9a–c** upon treatment with $AgNO_2$, in 38–56% yield.[19] In all cases they were accompanied by the corresponding nitrites **12a–c** (yield 30–39%) from which they were separated by column chromatography.



Scheme 2. Preparation of nitroalkyl-indolyl-ethylformamides **11**.

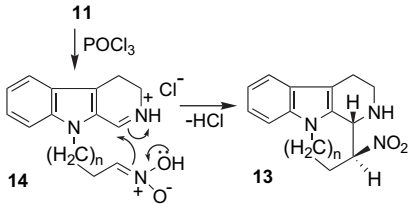
Bichler–Napieralsky cyclisations were attempted by refluxing a solution of the nitro compound **11** and $POCl_3$ in acetonitrile.[21] After removal of acetonitrile, hydrochloric acid was added to solubilise the crude reaction mixture, which was then basified by addition of concentrated ammonia solution. The products were isolated either by filtration or column chromatography. In some cases ammonia addition was omitted and the products were isolated from the acidic reaction mixture. To our surprise, besides the expected nitroalkyl-dihydro-β-carbolines **5a–c**, the tetracyclic compounds **13b** and **c** were also isolated (Scheme 3). In the case of **11a** only the nitroalkyl-dihydro-β-carboline **5a** was isolated from the acidic reaction mixture, in 71% yield. Upon addition of concentrated ammonia solution, a complex mixture of products occurred in which a tetracyclic product analogous to **13** was not detected. On the other hand, the tetracyclic products **13b** and **c** were isolated (yields 90 and 87%)



Scheme 3. Bichler–Napieralsky cyclisations of ω-nitroalkyl-dihydro-β-carbolines **11**.

from the Bichler–Napieralsky cyclisation reactions of the open chain compounds **11b** and **c**, respectively, when the reaction mixture was basified with ammonia. When the acidic trituration was applied, the product of the reaction of **11b** was nitrobutyl-dihydro-β-carboline **5b** (yield 86%) analogous to that obtained from the reaction of **11a**. In contrast, the corresponding nitropentyl-dihydro-β-carboline **5c** was obtained in very low yield (12%) from the acidic reaction mixture of **11c**. In this case, the main reaction product was the tetracyclic diazacycloocta[*jk*]fluorene **13c**, isolated in 72% yield. Probably, the length of the *N*-alkyl group has influence on the formation of products **5** and/or **13**. The nitroalkyl-dihydro-β-carbolines **5** were found to exist in their enol tautomers **5′** in dimethylsulfoxide-d_6 used for the measurement of the NMR spectra. Moreover, a degree of solvation (with H_2O or/and MeOH) of these nitroalkyl-dihydro-β-carbolines **5** is indicated by the existence of intense peaks in the region δ 3.20–3.68 in the ^{1}H NMR spectra.

Compounds **13** can be considered as products of an intramolecular Mannich-type alkylation and result through an internal nucleophilic attack of the carbon atom α- to the nitro group on the electrophilic iminium carbon atom of salt **14** (Scheme 4). This is the obvious pathway in all cases when the reaction is carried out in an acidic environment. When products were isolated from the basic mixture, the participation of a stronger carbanionic nucleophile, to reinforce the formation of products **13**, cannot be excluded.



Scheme 4. Proposed reaction pathway for the formation of compounds **13**.

Structure elucidation of compounds **13** was based on their analytical and spectroscopic data, which are in agreement with literature data for annulated tetrahydro-β-carbolines with similar structures.[22] The signals for C-3a (δ 52.2–54.5) and C-4 (δ 90.3–91.3) in the ^{13}C NMR spectra as well as for 3a-H (δ 4.49–4.56) and 4-H (δ 4.65–4.85) in the ^{1}H NMR spectra are of diagnostic importance.

Tetracyclic compounds **13** were isolated as single diastereoisomers. The trans-stereochemistry of the newly formed ring junction was established by evaluation of the ^{1}H–^{1}H spin–spin coupling constants ($^3J_{\text{H-3a,H-4}}$=10.5 Hz for **13b**; $^3J_{\text{H-3a,H-4}}$=10.4 Hz for **13c**). In addition, NOE experiments on compound **13c** showed an enhancement between 3a-H (δ 4.56) and 8-H_a (δ 4.00) as well as between 4-H (δ 4.86) and 2-H_b (δ 3.28), as depicted in Figure 1. However, enhancements between 4-H and 3a-H or 8-H_a were not observed.

The stereochemical outcome of the cyclisation could be anticipated from a diastereoselective attack of the electrophilic iminium ion carbon on the nucleophilic carbon species. Under the reaction conditions, the more stable product, in

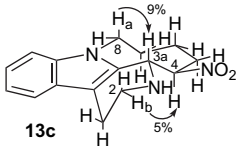
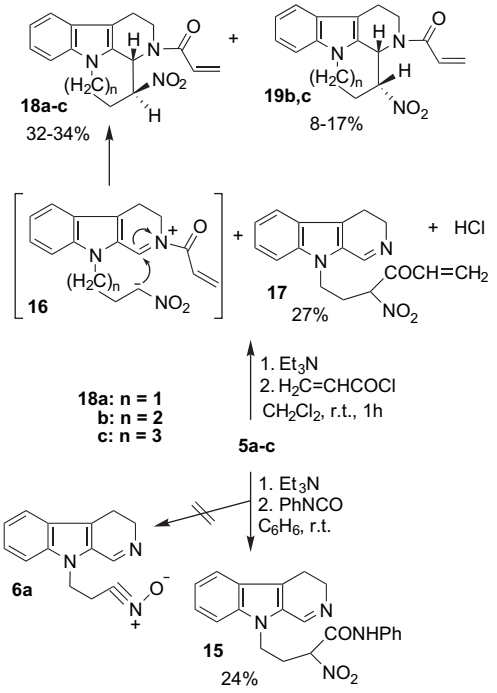


Figure 1. Prominent NOE interactions.

which 3a-H and 4-H are positioned trans to each other, is probably formed.

Treatment of nitropropyl-dihydro-β-carboline **5a** with PhNCO and Et_3N led to compound **15** instead of the corresponding initial target, nitrile oxide **6a** (Scheme 5). On the other hand, the formation of tetracyclic compounds **13**, which resemble the ABCD framework of canthines and arborescidines, indicates the interesting chemical behaviour of nitroalkyl-dihydro-β-carbolines **5** to undergo promptly intramolecular Mannich-type alkylations. Thus we decided to extend our study to analogous reactions and investigate the intramolecular amidoalkylation of ω-nitroalkyl-dihydro-β-carbolines **5** towards products analogous to **13**.[23]



Scheme 5. Reactions of ω-nitroalkyl-dihydro-β-carbolines **5** with acryloyl chloride and phenyl isocyanate.

N-Acylated quaternary salts of ω-nitroalkyl-dihydro-β-carbolines **5** were formed in situ and cyclised to mixtures of tetracyclic derivatives **18** and **19**, in 33–51% total yields, by treating a dichloromethane solution of the starting material **5** with acryloyl chloride in the presence of 2 equiv of Et_3N (Scheme 5). The relatively low calculated yields of the reactions could to some extent be attributed to the solvation of the dihydro-β-carbolines **5** indicated from their NMR spectra, as it has previously been mentioned. The cyclisation reactions in ratios **18b**:**19b** and **18c**:**19c** 2:1 and 4:1, respectively afforded the separable by column chromatography diastereomeric products **18** and **19**. However, only one isomer, the trans-diastereoisomer **18a**, was detected and

isolated in 33% yield from the reaction of dihydro-β-carboline **5a**.

Cyclisation products **18** and **19** are probably derived through an intramolecular nucleophilic attack of the carbanionic centre of the intermediate **16** to the electrophilic carbon of the *N*-acyliminium ion. The moderate diastereoselectivity of the cyclisations could be explained on terms of similar thermodynamic stability of the two stereoisomers, probably due to the presence of the added *N*-acryloyl substituent. It is possible that the size of the ring to be formed is of crucial importance to the diastereoselectivity of the reaction.

Besides the cyclised product **18a**, the acyl derivative **17** was also formed, in 27% yield, from the reaction of nitropropyl-dihydro-β-carboline **5a**. As previously mentioned, compound **15**, structurally similar with **17**, was the only product isolated (24% yield) from the reaction of the same dihydro-β-carboline **5a** with phenyl isocyanate. The NMR spectra of compounds **15** and **17**, both in the aromatic and the methylene proton regions, appear similar to that of their precursor carbolines **5**, indicating the predominance of their enol tautomer in solution.

Structural assignment of compounds **18** and **19** was mainly based on their NMR spectra, which are in accordance with those of the corresponding nonacylated compounds **13**. Namely, characteristic peaks for C-3a, C-4 and the carbonyl carbon atoms in their ^{13}C NMR spectra appear at δ 49.7–53.3, 83.2–89.9 and 166.5–168.0, respectively. In the ^{1}H NMR spectra, almost all the methylenic protons are differentiated, indicating the presence of asymmetric carbons and the characteristic peaks for the acryloyl substituent appear in the region δ 5.73–6.72. The chemical shifts for the 4-H (δ 4.78–5.00) of the trans-diastereoisomers **18a–c** appear at values comparable to those of the compounds **13**. In contrast, the corresponding signal for the cis-diastereoisomers **19b** and **c** appears at lower field values (δ 5.39–5.46). Signals for the 3a-H of both stereoisomers **18** and **19** (δ 5.94–6.72) are shifted downfield, compared to the corresponding protons of compounds **13**, presumably deshielded by the *N*-acryloyl substituent.

The trans configuration of products **18** was to some extent indicated by the similar chemical shifts of 3a-H and 4-H compared to that of the corresponding protons of the nonacylated analogs **13**, as well as by the magnitude of the coupling constants[22,24] (^{3}J=10.4–10.5 Hz) between these protons. The corresponding coupling constant in the spectrum of **19b** is clearly smaller and the signals for 3a-H and 4-H appear as broad singlets.

Attempts to confirm the stereochemistry of compounds **18b** and **c** by NOE analysis were unsuccessful due to complexity of their ^{1}H NMR spectra and the small chemical shift differences $\Delta\delta$ in the crucial region δ 3.40–6.70. In contrast, NOE experiments on compound **18a** were more informative. With saturation of 2-Ha (δ 3.31) a 5% increase in the signal intensity of 4-H (δ 4.78) was observed, whereas saturation of 4-H caused an 8% increase in the signal intensity of 2-Ha (Fig. 2). Significant increase in the signal intensity of 3a-H (δ 5.97) was not observed in either case. On the other hand, saturation of 3a-H caused increase in the signal intensity of 2-Hb (δ 4.28) and no change in the signal intensity of 4-H. For all these reasons, the trans stereochemistry of compound **18a** could be deduced.

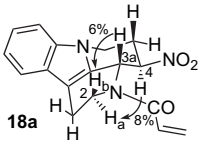
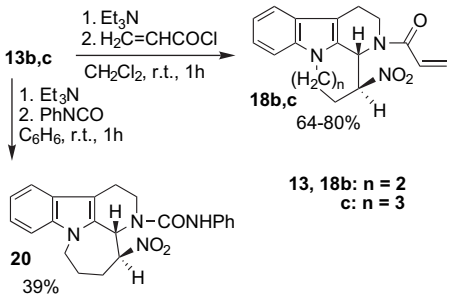


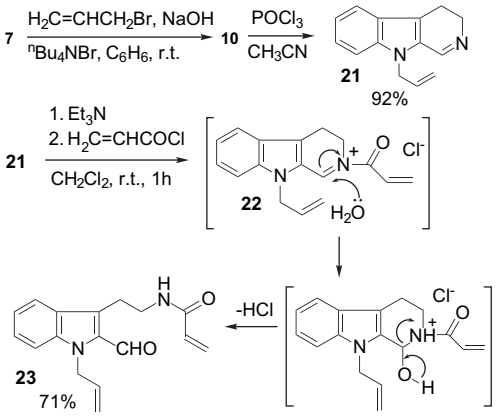
Figure 2. Prominent NOE correlations.

Furthermore, the stereochemistry of tetracyclic products **18** was undoubtedly retained on N-acylation of compounds **13b** and **c**, with confirmed trans configuration. The latter afforded **18b** and **c** or **20**, respectively, upon treatment with acryloyl chloride or phenyl isocyanate in the presence of Et_3N–CH_2Cl_2 (Scheme 6). As the acylation reactions are not carried out on the asymmetric carbon centres, changes in the trans configuration are not expected. The acid[24,25a,b] or base-catalyzed[22,26a,b] epimerization of β-carboline-type alkaloids, including yohimbane or tacamine-type alkaloids, is well known. Base mediated epimerization has been achieved using MeONa–MeOH, pyridine or aqueous NaOH at room temperature or under reflux for several hours and it is supposed to proceed through exchange of the proton at C-3a with the base. As it will be discussed later, triethylamine is a rather weak base to cause epimerization by abstracting 3a-H.



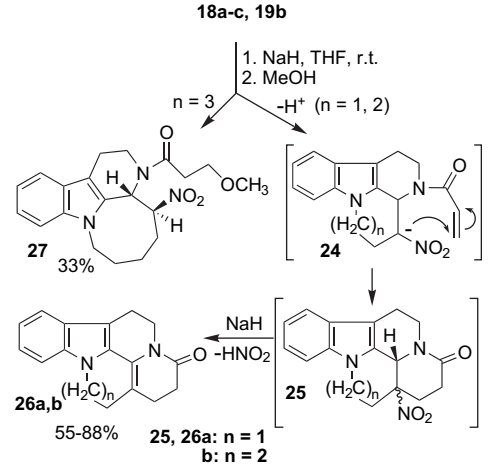
Scheme 6. Acylation of diazacycloalkano[*jk*]fluorenes **13**.

To examine the scope of the above mentioned intramolecular amidoalkylation with substrates carrying an alkenyl instead of the nitroalkyl substituent, we tried the reaction of allyl-dihydro-β-carboline **21** (Scheme 7). Compound **21** derived from the Bichler–Napieralski reaction of the allyl-amide **10**, the by-product of the bromoalkylation reaction of indolyl-ethylformamide **7** mentioned before. Compound **10** was also independently prepared (yield 69%) from the direct allylation of the amide **7** upon treatment with allylbromide under phase transfer catalysis conditions. To our disappointment, instead of the desired cyclisation product, aldehyde **23** was produced in 71% yield. Product **23** was probably formed through dihydro-pyridine ring opening caused by hydrolysis of the *N*-acyliminium salt **22** during the work up. This result is perhaps indicative of the insufficient nucleophilic strength of the π-bond to promote cyclisation, at least under mild conditions. Analogous ring opening of dihydro-β-carbolines has been reported in the literature.[27]



Scheme 7. Reaction of the allyl-dihydro-β-carboline **21** with acryloyl chloride and Et_3N.

Tetracyclic compounds **18** and **19** possess a conjugate acceptor tethered to the ABCD skeleton of the eburna's or vinca's. Thus cyclisation reactions, performed by treatment of **18** and **19** with excess NaH in dry THF solution, proceeded cleanly to produce the pentacyclic indolo-quinolizinones **26** (Scheme 8). The reaction of **18a** afforded indolo-quinolizinone **26a** in 88% yield while both diastereoisomers **18b** or **19b** led to **26b** in 60 or 55% yields, respectively. Indolo-quinolizinones **26** are intramolecular alkylation products and are formed by conjugate addition of the initially formed enolate **24** to the acryloyl group, followed by HNO_2 elimination from the intermediate **25** (Scheme 8).



Scheme 8. Reactions of compounds **18** and **19** with NaH.

The fact that the cyclisation of compounds **18** and **19** to the corresponding pentacyclic products **25** or **26** requires a base, the strength of NaH, perhaps confirms our previously mentioned hypothesis that epimerization during the Et_3N mediated acylation process of **13** (Scheme 6) does not take place. If triethylamine could abstract a proton from **18** to access the enolate **24**, the outcome of the reaction would be the formation of a pentacyclic product such as **25** or **26**.

The analogous annulation reaction attempted with compound **18c** led to tetracyclic product **27** (yield 33%) instead of the corresponding **25** or **26**. Compound **27** is a product of conjugate addition of methanol, used during the work up to decompose the excess of NaH, to the acryloyl group. The deviation of this reaction from the common route could probably be attributed to steric factors that impede the cyclisation process. Based on the coupling constant of the doublet peak for 3a-H (J=10.5 Hz), the trans configuration could be assigned to compound **27**.

3. Conclusions

In conclusion, we have presented the synthesis of *N*(2)-acryloyl-diazacycloalkano[*jk*]fluorenes **18**, **19** from 9-(ω-nitroalkyl)-4,9-dihydro-1*H*-β-carbolines **5** and acryloyl chloride, through a diastereoselective intramolecular N-acyliminium cyclisation. Synthesis of annulated 1,2,3,4-tetrahydro-β-carbolines **13** with similar structure has also been achieved in a single diastereoisomeric form and in high yields through a tandem Bichler–Napieralsky—intramolecular aminoalkylation process starting from 2-[1-(ω-nitroalkyl)-1*H*-indol-3-yl]ethylformamides **11**. Possessing an intriguing tetracyclic framework, compounds **13**, as well as their *N*-acylated derivatives **18**, **19**, are promising starting materials for indole alkaloids synthesis through derivatization of the tetrahydropyridine ring nitrogen atom and/or the α- to NO_2 active methine group. Transformation of diazacycloalkano[*jk*]fluorenes **18**, **19** to annulated indolo-quinolizinones **26**, through internal conjugate addition, constitutes a successful application. Improvement of the diastereoselectivity of the reactions by using chiral tryptamine substrates or chiral acylating agents is under investigation.

4. Experimental

4.1. General procedure for the preparation of 2-[1-(ω-bromoalkyl)-1*H*-indol-3-yl]ethylformamides 9 and 2-(1-allyl-1*H*-indol-3-yl)ethylformamide (10)

To a stirred solution of 2-(indol-3-yl)ethylformamide[21b] (**7**) (1.880 g, 10 mmol) in benzene (50 mL) an aqueous solution of NaOH (50% w/w) (10 g) and after 15 min $^nBu_4NBr$ (3.480 g, 10.8 mmol) were added, followed by an excess (30 mmol) of the proper α,ω-dibromoalkane **8** or allylbromide. The mixture was stirred at room temperature for 1–1.5 h or until the consumption of the starting 2-(indol-3-yl)ethylformamide **7**, monitored by TLC. The organic layer was separated, washed with water, dried (Na_2SO_4) and evaporated under reduced pressure. Column chromatography of the residue (silica gel, light petroleum ether–ethyl acetate 1:4 as eluant) afforded 2-[1-(ω-bromoalkyl)-1*H*-indol-3-yl]ethylformamides **9** or 2-(1-allyl-1*H*-indol-3-yl)ethylformamide (**10**). Compound **10** was also isolated (0.390 g, 17%) from the reaction of 1,3-dibromopropane (**8a**) in addition to the bromoalkyl derivative **9a**.

4.1.1. 2-[1-(3-Bromopropyl)-1*H*-indol-3-yl]ethylformamide (9a). Oil (1.610 g, 52%); IR (liquid film) cm^{-1} 3280, 1650; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.01 (s, 1H), 7.56 (d, J=7.7 Hz, 1H), 7.32 (d, J=8.2 Hz, 1H), 7.21 (t, J=7.7 Hz, 1H), 7.10 (t, J=7.3 Hz, 1H), 6.96 (s, 1H), 6.04 (br s, 1H), 4.21 (t, J=6.4 Hz, 2H), 3.65–3.49 (m, 2H), 3.25 (t, J=6.1 Hz, 2H), 2.94 (t, J=6.9 Hz, 2H), 2.36–2.22 (m,

2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.3, 136.1, 127.8, 125.6, 121.8, 119.1, 118.8, 111.5, 109.3, 43.7, 38.3, 32.5, 30.4, 24.9; MS *m/z* (%) 310/308 (M^+, 13), 265/263 (23), 252/250 (100), 228 (22), 183 (34), 170 (99), 143 (25), 115 (29). Anal. Calcd for $C_{14}H_{17}N_2OBr$: C, 54.38; H, 5.54; N, 9.06. Found: C, 54.30; H, 5.31; N, 8.80.

4.1.2. 2-[1-(4-Bromobutyl)-1*H*-indol-3-yl]ethylformamide (9b). Oil (2.040 g, 63%); IR (liquid film) cm^{-1} 3280, 1650; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.00 (s, 1H), 7.56 (d, *J*=7.9 Hz, 1H), 7.27 (d, *J*=7.9 Hz, 1H), 7.19 (t, *J*=7.6 Hz, 1H), 7.07 (t, *J*=7.3 Hz, 1H), 6.89 (s, 1H), 6.17 (s, 1H), 4.03 (t, *J*=6.8 Hz, 2H), 3.63–3.50 (m, 2H), 3.29 (t, *J*=6.1 Hz, 2H), 2.92 (t, *J*=7.0 Hz, 2H), 1.98–1.88 (m, 2H), 1.88–1.68 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.2, 136.2, 127.6, 125.4, 121.6, 118.9, 118.7, 111.3, 109.2, 45.0, 38.2, 32.9, 29.7, 28.6, 24.9; MS *m/z* (%) 324/322 (M^+, 23), 279/277 (48), 266/264 (100), 184 (44), 130 (86), 115 (34). Anal. Calcd for $C_{15}H_{19}N_2OBr$: C, 55.74; H, 5.92; N, 8.67. Found: C, 55.94; H, 5.76; N, 8.46.

4.1.3. 2-[1-(5-Bromopentyl)-1*H*-indol-3-yl]ethylformamide (9c). Oil (1.820 g, 54%); IR (liquid film) cm^{-1} 3280, 1650; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (s, 1H), 7.57 (d, *J*=7.9 Hz, 1H), 7.30 (d, *J*=8.0 Hz, 1H), 7.21 (t, *J*=7.3 Hz, 1H), 7.10 (t, J=7.3 Hz, 1H), 6.93 (s, 1H), 5.86 (br s, 1H), 4.06 (t, *J*=7.0 Hz, 2H), 3.65–3.55 (m, 2H), 3.35 (t, *J*=6.7 Hz, 2H), 2.96 (t, *J*=6.7 Hz, 2H), 1.88–1.75 (m, 4H), 1.48–1.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.1, 136.3, 127.7, 125.7, 121.7, 118.9, 118.8, 111.2, 109.4, 45.9, 38.4, 33.3, 32.1, 29.3, 25.5, 25.0; MS *m/z* (%) 338/336 (M^+, 55), 293/291 (81), 280/278 (96), 257 (17), 198 (59), 156 (85), 130 (100), 115 (44). Anal. Calcd for $C_{16}H_{21}N_2OBr$: C, 56.98; H, 6.28; N, 8.31. Found: C, 56.70; H, 6.59; N, 8.19.

4.1.4. 2-(1-Allyl-1*H*-indol-3-yl)ethylformamide (10). (1.570 g, 69%) From the reaction of allylbromide as a colourless oil; IR (liquid film) cm^{-1} 3260, 1640; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.11 (s, 1H), 7.59 (d, *J*=8.2 Hz, 1H), 7.31 (d, *J*=8.2 Hz, 1H), 7.22 (t, *J*=7.7 Hz, 1H), 7.12 (t, *J*=7.3 Hz, 1H), 6.95 (s, 1H), 6.09–5.89 (m, 1H), 5.65 (br s, 1H), 5.28 (d, *J*=10 Hz, 1H), 5.10 (d, *J*=17 Hz, 1H), 4.68 (d, *J*=4.6 Hz, 2H), 3.65 (t, *J*=6.4 Hz, 2H), 2.99 (t, *J*=6.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.7, 136.3, 133.3, 127.7, 125.6, 121.5, 118.9, 118.6, 117.0, 111.3, 109.5, 48.4, 38.4, 24.8; MS *m/z* (%) 228 (M^+, 86), 183 (78), 170 (100), 142 (80), 130 (86), 116 (56). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.54; H, 6.97; N, 12.01.

4.2. General procedure for the preparation of 2-[1-(ω-nitroalkyl)-1*H*-indol-3-yl]ethylformamides 11 and ω-{3-[2-(formylamino)ethyl]-1*H*-indol-1-yl}alkyl nitrites 12

To a solution of the proper 2-[1-(ω-bromoalkyl)-1*H*-indol-3-yl]ethylformamide **9** (5 mmol) in dry THF (50 mL) silver nitrite (2.695 g, 17.5 mmol) was added and the mixture, protected from light, was stirred at room temperature for 2 d or until all the starting material was consumed. After filtration of the silver salts and evaporation of the solvent, the residue was repeatedly subjected to column chromatography (silica gel, light petroleum ether–ethyl acetate 2:5 as eluant) to afford the corresponding nitro compounds **11** and nitrites **12** in order of eluance.

4.2.1. 2-[1-(3-Nitropropyl)-1*H*-indol-3-yl]ethylformamide (11a). Oil (0.620 g, 45%); IR (liquid film) cm^{-1} 3290, 1660, 1540, 1370; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.07 (s, 1H), 7.58 (d, *J*=7.9 Hz, 1H), 7.32–7.20 (m, 2H), 7.12 (t, *J*=7.3 Hz, 1H), 6.89 (s, 1H), 5.98 (br s, 1H), 4.30–4.16 (m, 4H), 3.57 (m, 2H), 2.94 (t, *J*=6.7 Hz, 2H), 2.47–2.45 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.2, 136.1, 127.9, 125.6, 122.2, 119.4, 119.1, 112.3, 109.1, 72.3, 42.6, 38.2, 27.5, 25.0. MS *m/z* (%) 275 (M^+, 29), 231 (47), 217 (45), 184 (22), 171 (55), 143 (100), 115 (35). Anal. Calcd for $C_{14}H_{17}N_3O_3$: C, 61.08; H, 6.22; N, 15.26. Found: C, 60.98; H, 6.55; N, 15.07.

4.2.2. 2-[1-(4-Nitrobutyl)-1*H*-indol-3-yl]ethylformamide (11b). Oil (0.550 g, 38%); IR (liquid film) cm^{-1} 3280, 1660, 1540, 1370; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.13 (s, 1H), 7.59 (d, *J*=7.9 Hz, 1H), 7.37–7.20 (m, 2H), 7.13 (t, *J*=7.0 Hz, 1H), 6.94 (s, 1H), 5.66 (br s, 1H), 4.30 (t, *J*=6.1 Hz, 2H), 4.15 (t, *J*=6.1 Hz, 2H), 3.74–3.60 (m, 2H), 2.99 (t, *J*=6.7 Hz, 2H), 2.09–1.86 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.3, 136.3, 127.8, 125.5, 122.0, 119.3, 119.0, 111.8, 109.3, 74.9, 45.1, 38.3, 26.9, 25.1, 24.7; MS *m/z* (%) 289 (M^+, 31), 244 (100), 231 (65), 184 (71), 170 (70), 143 (18), 115 (7). Anal. Calcd for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.62; N, 14.52. Found: C, 62.08; H, 6.48; N, 14.38.

4.2.3. 2-[1-(5-Nitropentyl)-1*H*-indol-3-yl]ethylformamide (11c). Oil (0.850 g, 56%); IR (liquid film) cm^{-1} 3280, 1660, 1540, 1380; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (s, 1H), 7.58 (d, *J*=7.9 Hz, 1H), 7.29 (d, *J*=7.9 Hz, 1H), 7.21 (t, *J*=7.0 Hz, 1H), 7.10 (t, *J*=7.0 Hz, 1H), 6.92 (s, 1H), 5.81 (br s, 1H), 4.31 (t, *J*=7.0 Hz, 2H), 4.08 (t, *J*=6.7 Hz, 2H), 3.68–3.58 (m, 2H), 2.96 (t, *J*=6.7 Hz, 2H), 2.02–1.80 (two overlapping m, 4H), 1.44–1.30 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.3, 136.4, 127.9, 125.7, 121.9, 119.1, 119.0, 111.5, 109.3, 75.3, 45.7, 38.4, 29.4, 26.8, 25.1, 23.7; MS *m/z* (%) 303 (M^+, 49), 257 (58), 245 (47), 184 (78), 170 (100), 143 (98), 115 (90). Anal. Calcd for $C_{16}H_{21}N_3O_3$: C, 63.35; H, 6.98; N, 13.85. Found: C, 63.43; H, 7.00; N, 13.44.

4.2.4. 3-{3-[2-(Formylamino)ethyl]-1*H*-indol-1-yl}propyl nitrite (12a). Oil (0.535 g, 39%); IR (liquid film) cm^{-1} 3260, 3040, 1660, 1620; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.03 (s, 1H), 7.57 (d, *J*=7.9 Hz, 1H), 7.30–7.16 (m, 2H), 7.10 (t, *J*=7.9 Hz, 1H), 6.90 (s, 1H), 6.12 (br s, 1H), 4.28 (t, *J*=6.1 Hz, 2H), 4.16 (t, *J*=6.7 Hz, 2H), 3.64–3.52 (m, 2H), 2.93 (t, *J*=6.7 Hz, 2H), 2.17 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.2, 136.3, 128.0, 125.5, 122.3, 119.4, 119.1, 112.2, 109.1, 69.8, 42.2, 38.4, 27.4, 25.1; MS *m/z* (%) 275 (M^+, 20), 245 (54), 229 (39), 215 (27), 201 (46), 184 (49), 170 (67), 143 (50), 129 (100). Anal. Calcd for $C_{14}H_{17}N_3O_3$: C, 61.08; H, 6.22; N, 15.26. Found: C, 61.01; H, 6.39; N, 15.14.

4.2.5. 4-{3-[2-(Formylamino)ethyl]-1*H*-indol-1-yl}butyl nitrite (12b). Oil (0.520 g, 36%); IR (liquid film) cm^{-1} 3290, 3040, 1660, 1620; ^{1}H NMR ($CDCl_3$, 300 MHz), δ 8.06 (s, 1H), 7.57 (d, *J*=7.8 Hz, 1H), 7.40–7.21 (m, 2H), 7.09 (t, *J*=7.4 Hz, 1H), 6.91 (s, 1H), 5.94 (br s, 1H), 4.34 (t, *J*=6.3 Hz, 2H), 4.08 (t, *J*=6.9 Hz, 2H), 3.70–3.55

(m, 2H), 2.94 (t, J=6.9 Hz, 2H), 2.05–1.90 (m, 2H), 1.85–1.65 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.2, 136.3, 127.8, 125.5, 121.8, 119.1, 118.9, 111.6, 109.3, 72.5, 45.4, 38.3, 26.5, 25.1, 24.2; MS *m/z* (%) 289 (M^+, −), 260 (59), 214 (30), 202 (68), 184 (33), 170 (100), 143 (86), 130 (71), 115 (8). Anal. Calcd for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.62; N, 14.52. Found: C, 62.08; H, 6.48; N, 14.38.

4.2.6. 5-{3-[2-(Formylamino)ethyl]-1*H*-indol-1-yl}pentyl nitrite (12c). Oil (0.455 g, 30%); IR (liquid film) cm^{-1} 3290, 3040, 1660, 1620; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.12 (s, 1H), 7.59 (d, J=8.0 Hz, 1H), 7.31 (d, J=7.3 Hz, 1H), 7.23 (t, J=7.9 Hz, 1H), 7.12 (t, J=7.3 Hz, 1H), 6.93 (s, 1H), 5.62 (br s, 1H), 4.40 (t, J=6.4 Hz, 2H), 4.09 (t, J=6.7 Hz, 2H), 3.71–3.59 (m, 2H), 3.00 (t, J=6.7 Hz, 2H), 1.96–1.80 (m, 2H), 1.78–1.64 (m, 2H), 1.53–1.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.3, 136.3, 127.8, 125.7, 121.8, 119.0, 118.9, 111.3, 109.3, 72.8, 45.8, 38.4, 29.7, 26.4, 25.1, 23.2; MS *m/z* (%) 303 (M^+, 24), 289 (45), 273 (45), 229 (98), 215 (78), 202 (39), 185 (78), 170 (65), 157 (100), 143 (78), 115 (62). Anal. Calcd for $C_{16}H_{21}N_3O_3$: C, 63.35; H, 6.98; N, 13.85. Found: C, 63.65; H, 7.15; N, 14.17.

4.3. *Bischler–Napieralski* reactions of 2-[1-(ω-nitroalkyl)-1*H*-indol-3-yl]ethylformamides 11 and 2-(1-allyl-1*H*-indol-3-yl)ethylformamide (10)

4.3.1. Procedure A: preparation of 9-(ω-nitroalkyl)-4,9-dihydro-3*H*-β-carbolines 5 and 9-allyl-4,9-dihydro-3*H*-β-carboline (21). To a stirred solution of the proper 2-[1-(ω-nitroalkyl)-1*H*-indol-3-yl]ethylformamide **11** (1 mmol) or 2-(1-allyl-1*H*-indol-3-yl)ethylformamide (**10**) (0.228 g, 1 mmol) in acetonitrile (10 mL), kept at 0 °C, a solution of $POCl_3$ (0.184 g, 1.2 mmol) in CH_3CN (5 mL) was added dropwise and the mixture was stirred for 15 min at this temperature and then refluxed for 1 h. The solvent was removed in vacuo and hydrochloric acid 1 N was added to the residue until resolution occurred. Undissolved impurities were removed by filtration and the acidic solution was extracted (3×20 mL) with CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4) and evaporated under reduced pressure. The residue was subjected to column chromatography (silica gel, ethyl acetate–methanol 4:1 as eluant) to afford 9-(ω-nitroalkyl)-4,9-dihydro-3*H*-β-carbolines **5a**,**b** or 9-allyl-4,9-dihydro-3*H*-β-carboline (**21**). Analytical pure samples of the dihydro-β-carbolines **5** or **21**, eluted from the column by methanol containing solvent, could not be obtained due to their insolubility in all common solvents. ^{1}H and ^{13}C NMR spectra show the existence of a substantial quantity of MeOH and/or H_2O. In the case of 2-[1-(5-nitropentyl)-1*H*-indol-3-yl]ethylformamide (**11c**), dihydro-β-carboline **5c** was precipitated upon trituration of the residue with CH_2Cl_2–petroleum ether and was isolated by filtration (0.034 g, 12% yield). By concentration of the filtrate, (±)-(3a*R*,4*S*)-4-nitro-2,3,3a,4,5,6,7,8-octahydro-1*H*-3,8a-diazacycloocta[*jk*]fluorene (**13c**) (0.205 g, 72%) was obtained in almost pure form.

4.3.1.1. 9-(3-Nitropropyl)-4,9-dihydro-3*H*-β-carboline (5a). Orange-coloured amorphous solid (0.183 g, 71%), mp 188–190 °C; IR (nujol) cm^{-1} 1650, 1545, 1375; ^{1}H NMR ($CDCl_3$–DMSO-d_6, 300 MHz) δ 8.22 (s, 1H), 7.76 (d, J=7.9 Hz, 1H), 7.49 (d, J=8.5 Hz, 1H), 7.34 (t, J=7.8 Hz, 1H), (t, J=7.5 Hz, 1H), 4.31 (t, J=6.7 Hz, 2H), 3.68–3.23 [br, solvents (MeOH, H_2O)], 3.02 (t, J=7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$–DMSO-d_6, 75 MHz) δ 142.8, 138.1, 129.0, 127.9, 125.4, 121.1, 120.1, 119.9, 118.1, 110.1, 51.9 (MeOH), 43.0, 39.8 (overlapping), 23.1, 21.7; MS *m/z* (%) 257 (M^+, 30), 227 (80), 211 (100), 181 (78), 168 (23), 115 (15). ESIHRMS *m/z* calcd for $C_{14}H_{15}N_3O_2$+H (MH^+) 258.12370, found 258.12399.

4.3.1.2. 9-(4-Nitrobutyl)-4,9-dihydro-3*H*-β-carboline (5b). Orange-coloured amorphous solid (0.233 g, 86%), mp 192–195 °C; IR (KBr) cm^{-1} 1639, 1548, 1383, 1345; ^{1}H NMR ($CDCl_3$–DMSO-d_6, 300 MHz) δ 8.52 (br, 2H), 8.29 (s, 1H), 7.80 (d, J=8.2 Hz, 1H), 7.42–7.29 (m, 2H), 7.11 (t, J=7.3 Hz, 1H), 4.32 (t, J=7.2 Hz, 2H), 3.58 and 3.54 (two s, MeOH), 3.39 (t, J=7.7 Hz, 2H), 3.20 (t, J=5.5 Hz, 2H), 3.12–3.01 (m, 2H), 2.37–2.24 (br, 2H); ^{13}C NMR ($CDCl_3$–DMSO-d_6, 300 MHz) δ 145.1, 137.9, 126.3, 125.5, 124.5, 120.1, 119.9, 119.1, 118.9, 108.5, 51.9 (MeOH), 43.8, 39.2, 29.2, 22.8, 21.4; MS *m/z* (%) 271 (M^+, 59), 243 (27), 225 (32), 196 (100), 181 (30), 168 (26), 115 (15). ESIHRMS *m/z* calcd for $C_{15}H_{17}N_3O_2$+H (MH^+) 272.13935, found 272.13961.

4.3.1.3. 9-(5-Nitropentyl)-4,9-dihydro-3*H*-β-carboline (5c). Orange-coloured amorphous solid, mp 250–252 °C; IR (KBr) cm^{-1} 1640, 1546, 1381; ^{1}H NMR ($CDCl_3$–DMSO-d_6, 300 MHz) δ 8.32 and 8.27 (overlapping br s and s, 3H), 7.75 (d, J=7.9 Hz, 1H), 7.40 (d, J=7.9 Hz, 1H), 7.31 (t, J=7.9 Hz, 1H), 7.14 (t, J=7.9 Hz, 1H), 4.30–4.14 (m, 2H), 3.68–3.20 (m, 2H, overlapping with the peak of H_2O), 3.20–3.01 (m, 2H), 3.01–2.88 (m, 2H), 2.06–1.88 (m, 2H), 1.88–1.68 (m, 2H); ^{13}C NMR ($CDCl_3$–DMSO-d_6, 75 MHz) δ 149.4, 136.6, 127.9, 125.6, 123.1, 119.9, 118.8, 118.0, 114.5, 108.3, 41.0, 38.6, 26.6, 26.4, 21.4, 19.5; MS *m/z* (%) 285 (M^+, 30), 210 (17), 183 (100), 181 (96), 168 (57). ESIHRMS *m/z* calcd for $C_{16}H_{19}N_3O_2$+H (MH^+) 286.15500, found 286.15481.

4.3.1.4. (±)-(3a*R*,4*S*)-4-Nitro-2,3,3a,4,5,6,7,8-octahydro-1*H*-3,8a-diazacycloocta[*jk*]fluorene (13c). Yellowish oil; IR (liquid film) cm^{-1} 3305, 1544, 1384, 1343; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, J=7.3 Hz, 1H), 7.30 (d, J=7.9 Hz, 1H), 7.23 (t, J=7.0 Hz, 1H), 7.12 (t, J=7.3 Hz, 1H), 4.86 (dt, J_1=10.4 Hz, J_2=3.7 Hz, 1H), 4.56 (d, J=10.4 Hz, 1H), 4.42 (dd, J_1=15.3 Hz, J_2=3.7 Hz, 1H), 4.00 (dt, J_1=15.3 Hz, J_2=3.7 Hz, 1H), 3.28 (tt, J_1=14.0, J_2=4.3 Hz, 1H), 3.22 (dd, J_1=14.0 Hz, J_2=7.9 Hz, 1H), 2.77 (dd, J_1=7.9 Hz, J_2=3.7 Hz, 2H), 2.38–2.08 (m, 3H), 1.99 (tdd, J_1=13.4 Hz, J_2=8.5 Hz, J_3=4.9 Hz, 1H), 1.91–1.62 (m, 2H), 0.92–0.73 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.6, 132.1, 126.9, 122.2, 119.3, 118.6, 109.2, 108.9, 91.3, 52.2, 40.0, 37.9, 28.7, 28.5, 22.3, 19.2; MS *m/z* (%) 285 (M^+, 97), 258 (66), 239 (24), 199 (100), 181 (51), 170 (80), 115 (64). Anal. Calcd for $C_{16}H_{19}N_3O_2$: C, 67.35; H, 6.71; N, 14.73. Found: C, 67.76; H, 6.72; N, 14.38.

4.3.1.5. 9-Allyl-4,9-dihydro-3*H*-β-carboline (21). Brown viscous oil (0.193 g, 92%); IR (liquid film) cm^{-1} 1644, 1620; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.50 (s, 1H), 7.58 (d, J=7.7 Hz, 1H), 7.32–7.29 (m, 2H), 7.16 (t, J=8.1 Hz, 1H), 5.99–5.90 (m, 1H), 5.17 (d, J=10.3 Hz, 1H), 4.97 (d, J=17.3 Hz, 1H), 4.85–4.80 (m, 2H), 3.91 (t, J=8.7 Hz, 2H), 2.91 (t, J=8.7 Hz, 2H);

^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.5, 138.0, 132.9, 125.1, 124.8, 120.3, 117.2, 110.3, 47.8, 45.6, 19.2; MS *m/z* (%) 211 (M+1, 39), 210 (M^+, 100), 182 (16), 169 (27), 168 (45), 142 (15), 115 (25), 41 (25); Anal. Calcd for $C_{14}H_{14}N_2$: C, 79.97; H, 6.71; N, 13.32. Found: C, 79.51; H, 6.59; N, 13.70.

4.3.2. Procedure B: preparation of diazacycloalkano[*jk*]-fluorenes 13. The process described previously (Section 4.3.1) was followed up to the point of addition of hydrochloric acid and removal of the undissolved impurities by filtration. The filtrate was then turned basic by addition of aqueous NH_4OH solution (25% w/w) causing the precipitation of yellow-coloured diazacycloalkano[*jk*]fluorenes **13b** and **c**. The solids were separated by filtration, washed repeatedly with water and dried in a dessicator. They were purified by column chromatography (silica gel, ethyl acetate–methanol 4:1 as eluant). The reaction of 2-[1-(3-nitropropyl)-1*H*-indol-3-yl]ethylformamide **11a** afforded a complicate mixture in which the corresponding tetracyclic compound **13** was not detected. The crude reaction product was used in the reaction with phenyl isocyanate (Section 4.5) without further purification.

4.3.2.1. (±)-(3a*R*,4*S*)-4-Nitro-1,2,3,3a,4,5,6,7-octahydro-3,7a-diazacyclohepta[*jk*]fluorene (13b). Yellow crystals (0.244 g, 90%), mp 174–177 °C (CH_2Cl_2–petroleum ether); IR (nujol) cm^{-1} 3300, 1540, 1370; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, J=7.8 Hz, 1H), 7.31−7.17 (m, 2H), 7.10 (t, J=7.0 Hz, 1H), 4.65 (dt, J_1=10.5 Hz, J_2=2.9 Hz, 1H), 4.54 (dd, J_1=14.1 Hz, J_2=4.6 Hz, 1H), 4.49 (d, J=10.5 Hz, 1H), 3.78 (t, J=14.1 Hz, 1H), 3.14 (tt, J_1=13.1 Hz, J_2=4.8 Hz, 1H), 3.07 (tt, J_1=13.1 Hz, J_2=4.8 Hz, 1H), 2.84–2.62 (m, 2H), 2.59–2.10 (m, 3H), 1.89 (br s, 1H), 1.69–1.51 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.8, 131.3, 126.2, 121.9, 119.2, 118.5, 111.0, 108.6, 90.3, 54.5, 43.9, 40.4, 33.7, 26.6, 22.5; MS *m/z* 271 (M^+, 54), 241 (35), 225 (78), 196 (100), 183 (53), 169 (98), 115 (52). Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.13; H, 6.18; N, 15.63.

4.3.2.2. (±)-(3a*R*,4*S*)-4-Nitro-2,3,3a,4,5,6,7,8-octahydro-1*H*-3,8a-diazacycloocta[*jk*]fluorene (13c). 0.248 g, 87%.

4.4. General procedure for the reactions of 9-(ω-nitroalkyl)-4,9-dihydro-3*H*-β-carbolines 5 and 9-allyl-4,9-dihydro-3*H*-β-carboline (21) with acryloyl chloride and Et_3N

Triethylamine (0.101 g, 1 mmol) was added to a solution of the proper 9-(ω-nitroalkyl)-4,9-dihydro-3*H*-β-carboline **5** (0.5 mmol) or 9-allyl-4,9-dihydro-3*H*-β-carboline (**21**) (0.105 g, 0.5 mmol) in CH_2Cl_2 (10 mL). After stirring for 15 min acryloyl chloride (0.068 g, 0.75 mmol) was added and the mixture was stirred at 25 °C for 2 h or until the consumption of the starting dihydro-β-carboline. The reaction mixture was transferred to a separatory funnel and washed with water (10 mL). The aqueous layer was extracted with CH_2Cl_2 (2×30 mL) and the combined organic layers dried over Na_2SO_4. Solvent was removed in vacuo and column chromatography (silica gel, light petroleum ether–ethyl acetate 4:1 as eluant) of the residue afforded the corresponding compounds **18**, **19** or the acrylamide **23**. In the case of 9-(3-nitropropyl)-4,9-dihydro-β-carboline **5a**, besides **18a** compound **17** was also isolated.

4.4.1. Reaction of 9-(3-nitropropyl)-4,9-dihydro-3*H*-β-carboline (5a) with acryloyl chloride. Column chromatography afforded in order of elution.

4.4.1.1. (±)-1-{(3a*R*,4*S*)-4-Nitro-1,2,3a,4,5,6-hexahydro-3*H*-indolo[3,2,1-*de*][1,5]naphthyridin-3-yl}-2-propen-1-one (18a). Light yellow crystals (0.052 g, 33%), mp 147–149 °C (CH_2Cl_2–CH_3CO_2Et); IR (KBr) cm^{-1} 1651, 1639, 1557, 1385, 1331; ^{1}H NMR ($CDCl_3$, 300 MHz, 25 °C) δ 7.52 (d, J=7.3 Hz, 1H), 7.33 (d, J=7.9 Hz, 1H), 7.26 (t, J=7.3 Hz, 1H), 7.17 (t, J=7.3 Hz, 1H), 6.65 (dd, J_1=17.0 Hz, J_2=10.4 Hz, 1H), 6.35 (d, J=17.0 Hz, 1H), 6.02 (br, 1H), 5.78 (d, J=10.4 Hz, 1H), 4.77 (dt, J_1=8.9 Hz, J_2=4.6 Hz, 1H), 4.40 (dt, J_1=11.3 Hz, J_2=5.2 Hz, 1H), 4.28 (br, 1H), 3.87 (ddd, J_1=11.3 Hz, J_2=9.8 Hz, J_3=5.2 Hz, 1H), 3.37 (br, 1H), 3.05–2.75 (m, 3H), 2.49 (ddd, J_1=14.6 Hz, J_2=9.8 Hz, J_3=4.9 Hz, 1H); ^{1}H NMR ($CDCl_3$, 300 MHz, 50 °C) δ 7.49 (d, J=7.9 Hz, 1H), 7.29 (d, J=7.9 Hz, 1H), 7.23 (t, J=7.3 Hz, 1H), 7.15 (t, J=7.0 Hz, 1H), 6.60 (dd, J_1=10.7 Hz, J_2=16.5 Hz, 1H), 6.29 (d, J=16.5 Hz, 1H), 5.97 (br d, J=8.6 Hz, 1H), 5.73 (d, J=10.7 Hz, 1H), 4.78 (dt, J_1=9.1 Hz, J_2=5.5 Hz, 1H), 4.38 (dt, J_1=11.6 Hz, J_2=5.5 Hz, 1H), 4.28 (br, 1H), 3.87 (ddd, J_1=13.4 Hz, J_2=9.1 Hz, J_3=5.5 Hz, 1H), 3.31 (br, 1H), 2.98–2.71 (m, 3H), 2.46 (ddd, J_1=14.6 Hz, J_2=9.1 Hz, J_3=4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, 25 °C) δ 167.9, 138.3, 130.5, 129.3, 127.7, 122.4, 120.5, 118.7, 110.0, 83.0, 53.1 (br), 43.9 (br), 40.7, 29.0, 22.6; ^{13}C NMR ($CDCl_3$, 75 MHz, 50 °C) δ 168.0, 138.5, 130.6, 128.8, 128.0, 122.5, 120.6, 118.8, 110.0, 83.2, 53.3, 43.6 (br), 40.7, 29.3, 22.7; MS *m/z* (%) 311 (M^+, 8), 265 (46), 236 (53), 211 (100), 182 (40). Anal. Calcd for $C_{17}H_{17}N_3O_3$: C, 65.58; H, 5.50; N, 13.50. Found: C, 65.51; H, 5.54; N, 13.50.

4.4.1.2. 6-(3,4-Dihydro-9*H*-β-carbolin-9-yl)-4-nitro-1-hexen-3-one (17). Oil (0.042 g, 27%); IR (liquid film) cm^{-1} 1661, 1620, 1551, 1385; ^{1}H NMR ($CDCl_3$–DMSO-d_6, 300 MHz) δ 8.16–8.02 (br, 1H), 8.05 (s, 1H), 7.68 (d, J=7.9 Hz, 1H), 7.38 (d, J=7.9 Hz, 1H), 7.31 (t, J=7.6 Hz, 1H), 7.09 (t, J=7.6 Hz, 1H), 6.14 (d, J=6.4 Hz, 2H), 5.51 (t, J=6.4 Hz, 1H), 4.28 (t, J=7.0 Hz, 2H), 3.51–3.38 (m, 2H), 3.23 (t, J=7.0 Hz, 2H), 3.11 (t, J=8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$–DMSO-d_6, 75 MHz) δ 164.8, 141.7, 137.9, 131.2, 128.6, 128.0, 125.2, 124.4, 121.1, 120.7, 119.7, 109.6, 39.8, 39.2, 23.5, 23.0; MS *m/z* (%) 312 (M+1, 36), 295 (100), 240 (50), 228 (95), 182 (46), 168 (44). Anal. Calcd for $C_{17}H_{17}N_3O_3$: C, 65.58; H, 5.50; N, 13.49. Found: C, 65.33; H, 5.37; N, 13.11.

4.4.2. Reaction of 9-(4-nitrobutyl)-4,9-dihydro-3*H*-β-carboline (5b) with acryloyl chloride. Diastereoisomers **18b** and **19b** were obtained from the column in order of elution.

4.4.2.1. (±)-1-[(3a*R*,4*S*)-4-Nitro-1,3a,4,5,6,7-hexahydro-3,7a-diazacyclohepta[*jk*]fluoren-3(2*H*)-yl]-2-propen-1-one (18b). Oil (0.055 g, 34%); IR (liquid film) cm^{-1} 1651, 1614, 1552, 1371, 1346; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: Mixture of rotamers in 7:3 ratio. Spectrum of the main isomer: 7.49 (d, J=7.3 Hz, 1H), 7.29 (d, J=7.9 Hz, 1H), 7.23 (t, J=7.3 Hz, 1H), 7.11 (t, J=7.3 Hz, 1H), 6.63 (dd,

J_1=17.1 Hz, J_2=10.4 Hz, 1H), 6.44 (d, J=10.4 Hz, 1H), 6.30 (d, J=17.1 Hz, 1H), 5.76 (d, J=10.4 Hz, 1H), 4.78 (dt, J_1=10.4 Hz, J_2=3.3 Hz, 1H), 4.56 (dd, J_1=13.5 Hz, J_2=3.6 Hz, 1H), 4.26 (d, J=15.0 Hz, 1H), 3.95 (t, J=13.5 Hz, 1H), 3.51 (dt, J_1=15.0 Hz, J_2=8.5 Hz, 1H), 2.90–2.78 (m, 2H), 2.68–2.41 (m, 2H), 2.34–2.20 (m, 1H), 1.64–1.44 (m, 1H); Distinguished peaks from the spectrum of the minor rotamer: 6.76 (dd, J_1=16.4 Hz, J_2=10.4 Hz), 5.90 (d, J=10.4 Hz), 5.47 (br d, J=9.2 Hz), 4.98–4.78 (m, partially overlapping), 3.16–2.90 (m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.8, 136.1, 132.0, 129.2, 127.1, 125.8, 122.3, 119.5, 118.5, 109.3, 108.8, 86.9, 51.2, 43.3, 41.2, 32.4, 26.4, 22.1; Distinguished peaks from the spectrum of the minor rotamer: 130.1, 128.1, 127.6, 122.6, 118.7, 87.5, 55.5, 37.8, 33.1, 20.3; MS *m*/*z* 325 (M^+, 4), 278 (89), 277 (100). ESIHRMS calcd for $C_{18}H_{19}N_3O_3$+H (MH^+) 326.14992, found 326.14961.

4.4.2.2. (±)-1-[(3a*R*,4*R*)-4-Nitro-1,3a,4,5,6,7-hexahydro-3,7a-diazacyclohepta[*jk*]fluoren-3(2*H*)-yl]-2-propen-1-one (19b). Oil (0.028 g, 17%); IR (liquid film) cm^{-1} 1645, 1555, 1375, 1342; ^{1}H NMR ($CDCl_3$, 300 MHz) δ: Mixture of rotamers in 8:2 ratio. Spectrum of the main isomer: 7.50 (d, J=7.7 Hz, 1H), 7.34 (d, J=8.3 Hz, 1H), 7.25 (t, J=7.1 Hz, 1H), 7.11 (t, J=7.4 Hz, 1H), 6.71 (dd, J_1=16.7 Hz, J_2=10.6 Hz, 1H), 6.36 (d, J=16.7 Hz, 1H), 5.94 (br s, 1H), 5.82 (d, J=10.6 Hz, 1H), 5.39 (br s, 1H), 4.65 (dd, J_1=14.4 Hz, J_2=4.5 Hz, 1H), 4.24 (dd, J_1=12.5 Hz, J_2=3.8 Hz, 1H), 3.85 (t, J=12.5 Hz, 1H), 3.42 (dt, J_1=14.4 Hz, J_2=3.8 Hz, 1H), 2.90–2.72 (m, 2H), 2.72–2.54 (m, 1H), 2.40–2.20 (m, 1H), 2.18–2.00 (m, 1H), 1.78–1.51 (m, 1H); Distinguished peaks from the spectrum of the minor rotamer: 6.27 (d, J=15.3 Hz), 5.71 (br s), 5.63 (d, J=10.3 Hz), 4.40–4.28 (m, overlapping), 3.75–3.60 (m), 3.25 (t, J=6.4 Hz), 2.74–2.55 (m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.9, 136.8, 131.4, 128.9, 127.8, 126.6, 122.1, 119.3, 118.5, 109.4, 108.9, 85.6, 52.0, 44.3, 41.7, 31.7, 23.8, 21.7; Distinguished peaks from the spectrum of the minor rotamer: 130.7, 129.3, 128.8, 121.6, 120.5, 111.9, 52.9, 45.2, 40.9, 30.5, 24.9, 23.9; MS *m*/*z* (%) 325 (M^+, 6), 278 (100), 277 (19). ESIHRMS *m*/*z* calcd for $C_{18}H_{19}N_3O_3$+Na (MNa^+) 348.13186, found 348.13248.

4.4.3. Reaction of 9-(5-nitropentyl)-4,9-dihydro-3*H*-β-carboline (5c) with acryloyl chloride. The reaction was performed in the scale of 0.1 mmol (0.034 g) of **5c**. From the column there were obtained in order of elution.

4.4.3.1. (±)-1-[(3a*R*,4*S*)-4-Nitro-1,2,3a,4,5,6,7,8-octahydro-3*H*-3,8a-diazacycloocta[*jk*]fluoren-3-yl]-2-propen-1-one (18c). Oil (0.011 g, 32%); IR (liquid film) cm^{-1} 1652, 1613, 1558, 1542, 1373, 1345; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51 (d, J=7.0 Hz, 1H), 7.30 (d, J=7.0 Hz, 1H), 7.24 (t, J=7.3 Hz, 1H), 7.12 (t, J=7.0 Hz, 1H), 6.72–6.47 (m, 2H), 6.26 (d, J=16.5 Hz, 1H), 5.72 (d, J=10.4 Hz, 1H), 5.00–4.82 (m, 1H), 4.45 (d, J=14.6 Hz, 1H), 4.42–4.08 (m, 2H), 3.91–3.66 (m, 1H), 3.10–2.75 (m, 2H), 2.53–2.20 (m, 2H), 2.20–1.68 (m, 3H), 1.00–0.72 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.5, 135.9, 130.2, 129.3, 127.1, 126.3, 122.6, 119.7, 118.6, 109.1, 108.1, 89.9, 49.7, 40.1, 39.9, 28.3, 22.2, 19.2; MS *m*/*z* (%) 339 (M^+, 15), 293 (55), 277 (43), 263 (45), 239 (100). Anal. Calcd for $C_{19}H_{21}N_3O_3$: C, 67.24; H, 6.24; N, 12.38. Found: C, 67.17; H, 6.32; N, 12.19.

4.4.3.2. (±)-1-[(3a*R*,4*R*)-4-Nitro-1,2,3a,4,5,6,7,8-octahydro-3*H*-3,8a-diazacycloocta[*jk*]fluoren-3-yl]-2-propen-1-one (19c). Oil (0.003 g, 8%); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.54 (d, J=7.3 Hz, 1H), 7.42–7.24 (m, 2H), 7.16 (t, J=6.7 Hz, 1H), 6.68 (dd, J_1=17.1 Hz, J_2=10.7 Hz, 1H), 6.35 (d, J=15.3 Hz, 1H), 5.99 (d, J=4.9 Hz, 1H), 5.79 (d, J=10.7 Hz, 1H), 5.52–5.43 (m, 1H), 4.43 (br d, J=14.6 Hz, 1H), 4.16–3.75 (m, 2H), 3.75–3.42 (two overlapping m, 3H), 2.91 (m, 2H), 2.33–2.05 (m, 2H), 2.05–1.82 (m, 1H), 0.95–0.80 (m, 1H). MS *m*/*z* (%) 339 (M^+, 20), 293 (85), 292 (100). ESIHRMS *m*/*z* calcd for $C_{19}H_{21}N_3O_3$+H (MH^+) 340.16564, found 340.16589.

4.4.4. Reaction of 9-allyl-4,9-dihydro-3*H*-β-carboline (21) with acryloyl chloride. The reaction was carried out under the conditions described previously affording *N*-[2-(1-allyl-2-formyl-1*H*-indol-3-yl)ethyl]acrylamide (**23**) (0.100 g, 71%), oil; IR (liquid film) cm^{-1} 3303, 2921, 2720, 1657, 1626; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.07 (s, 1H), 7.77 (d, J=7.9 Hz, 1H), 7.50–7.30 (m, 2H), 7.17 (t, J=7.9 Hz, 1H), 6.25 (d, J=17.1 Hz, 1H), 6.19–5.90 (m, 3H), 5.61 (d, J=10.3 Hz, 1H), 5.22–5.14 (m, 2H), 5.11 (d, J=10.4 Hz, 1H), 4.91 (d, J=17.1 Hz, 1H), 3.76–3.60 (m, 2H), 3.36 (t, J=6.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 181.4, 165.8, 139.2, 133.5, 131.1, 130.7, 127.6, 127.3, 126.5, 126.4, 121.4, 120.9, 116.5, 110.7, 46.6, 41.2, 23.8; MS *m*/*z* (%) 282 (M^+, 25), 211 (100), 198 (24), 182 (23), 115 (7). Anal. Calcd for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.21; H, 6.75; N, 9.64.

4.5. Reaction of 9-(3-nitropropyl)-4,9-dihydro-3*H*-β-carboline (5a) with phenyl isocyanate

In a suspension of crude 9-(3-nitropropyl)-4,9-dihydro-3*H*-β-carboline (**5a**) (0.129 g, 0.5 mmol) and Et_3N (5 drops) in benzene (8 mL) phenyl isocyanate (0.179 g, 1.5 mmol) was added. After stirring for 2 h, benzene was removed in vacuo and the residue was subjected to column chromatography (silica gel, light petroleum ether–ethyl acetate 4:1 as eluant) affording in order of elution: (a) diphenylurea (0.145 g) and (b) 4-(3,4-dihydro-9*H*-β-carbolin-9-yl)-2-nitro-*N*-phenylbutanamide (**15**) (0.045 g, 24%), yellow crystals, mp 214–216 °C ($CHCl_3$); IR (nujol) cm^{-1} 3255, 1620, 1545, 1370; ^{1}H NMR ($CDCl_3$–DMSO-d_6, 300 MHz) δ 8.10 (s, 1H), 7.96 (br s, exchanges with D_2O, 1H), 7.73 (d, J=7.6 Hz, 1H), 7.41–7.28 (m, 4H), 7.22 (t, J=7.7 Hz, 2H), 7.12 (t, J=7.2 Hz, 1H), 6.93 (t, J=7.0 Hz, 1H), 5.92 (br s, exchanges with D_2O, 1H), 4.25 (t, J=6.9 Hz, 2H), 3.49 (m, 2H), 3.26 (t, J=6.9 Hz, 2H), 3.13 (t, J=6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$–DMSO-d_6, 75 MHz) δ 154.9, 141.8, 140.0, 138.2, 128.3, 128.2, 125.5, 121.4, 121.3, 121.27, 120.2, 119.9, 118.1, 109.2, 40.3, 39.4, 24.9, 23.1; MS *m*/*z* (%) 376 (M^+, 17), 359 (19), 332 (9), 257 (7), 240 (24), 227 (34), 211 (37), 180 (100), 169 (17), 119 (40). Anal. Calcd for $C_{21}H_{20}N_4O_3$: C, 67.01; H, 5.36; N, 14.88. Found: C, 66.84; H, 5.28; N, 14.71.

4.6. Acylation of diazacycloalkano[*jk*]fluorenes 13b and c with acryloyl chloride

To a solution of (±)-(3a*R*,4*S*)-4-nitro-1,2,3,3a,4,5,6,7-octahydro-3,7a-diazacyclohepta[*jk*]fluorene (**13b**) or (±)-(3a*R*,4*S*)-4-nitro-2,3,3a,4,5,6,7,8-octahydro-1*H*-3,8a-

diazacycloocta[*jk*]fluorene (**13c**) (0.5 mmol) in CH_2Cl_2 (10 mL), triethylamine (0.101 g, 1 mmol) was added followed by acryloyl chloride (0.068 g, 0.75 mmol) after 15 min. Following the procedure described previously (Section 4.4) (±)-1-[(3a*R*,4*S*)-4-nitro-1,3a,4,5,6,7-hexahydro-3,7a-diazacyclohepta[*jk*]fluoren-3(2*H*)-yl]-2-propen-1-one (**18b**) or 1-[(3a*R*,4*S*)-4-nitro-1,2,3a,4,5,6,7,8-octahydro-3*H*-3,8a-diazacycloocta[*jk*]fluoren-3-yl]-2-propen-1-one (**18c**), in all respects identical to the trans stereoisomers isolated from the reactions of the corresponding 9-(ω-nitroalkyl)-4,9-dihydro-3*H*-β-carbolines **5b** or **5c** with acryloyl chloride, were eluted, respectively from the column in 80 and 64% yields.

4.7. Acylation (±)-(3a*R*,4*S*)-4-nitro-1,3a,4,5,6,7-hexahydro-3,7a-diazacyclohepta[*jk*]fluorene (13b) with phenyl isocyanate

The reaction was carried out under the conditions described previously (Section 4.6) starting from **13b** (0.136 g, 0.5 mmol). (±)-(3a*R*,4*S*)-4-Nitro-*N*-phenyl-1,3a,4,5,6,7-hexahydro-3,7a-diazacyclohepta[*jk*]fluorene-3(2*H*)-carboxamide (**20**) (0.076 g, 39%) was eluted from the column. Yellow crystals, mp 213–216 °C ($CHCl_3$–Et_2O); IR (nujol) cm^{-1} 3320, 1625, 1535, 1370; ^1H NMR ($CDCl_3$–DMSO-d_6–D_2O, 300 MHz) δ 8.61 (br s, 1H), 7.49–7.41 (m, 3H), 7.35 (d, J=8.2 Hz, 1H), 7.27–7.13 (m, 3H), 7.04 (t, J=8.2 Hz, 1H), 6.97 (t, J=7.1 Hz, 1H), 6.13 (d, J=10.3 Hz, 1H), 4.95 (dt, J_1=10.3 Hz, J_2=3.6 Hz, 1H), 4.60 (dd, J_1=14.1 Hz, J_2=3.9 Hz, 1H), 4.51 (dd, J_1=14.4 Hz, J_2=4.1 Hz, 1H), 4.02 (t, J=14.1 Hz, 1H), 3.30 (dt, J_1=14.4 Hz, J_2=3.3 Hz, 1H), 2.87 (dt, J_1=13.7 Hz, J_2=4.2 Hz, 1H), 2.79–2.73 and 2.73–2.66 (two overlapping m, 3H), 2.35–2.20 (m, 1H), 1.62–1.42 (m, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 155.1, 139.9, 135.9, 131.1, 128.3, 125.5, 122.3, 121.6, 120.1, 118.8, 118.2, 109.4, 86.8, 52.2, 43.0, 39.6, 32.4, 26.0, 20.8; MS *m*/*z* (%) 390 (M^+, −), 343 (18), 341 (12), 271 (15), 224 (100), 196 (46), 169 (44), 119 (93), 91 (73), 77 (86). Anal. Calcd for $C_{22}H_{22}N_4O_3$: C, 67.68; H, 5.68; N, 14.35. Found: C, 67.44; H, 5.39; N, 14.20.

4.8. Reactions of annulated 1,2,3,4-tetrahydro-β-carbolines 18, 19 with sodium hydride

Sodium hydride (0.120 g, 5 mmol) was added to a solution of **18** or **19** (0.5 mmol) in dry THF (5 mL) and the mixture was stirred for 4 h at room temperature or until the starting material was consumed. Methanol (0.5 mL) was added to decompose the excess of NaH and then solvent was removed in vacuo. Dichloromethane (10 mL) was added to dissolve the residue and the solution was decanted to a separatory funnel and washed with water (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2×20 mL) and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Column chromatography of the residue (silica gel, light petroleum ether–ethyl acetate 3:1 as eluant) gave pentacyclic compounds **26a**,**b** or tetracyclic compound **27** from the reactions of **18a**,**b** or **18c**, respectively. Compound **26b** was isolated from the reaction of both diastereoisomers **18b** and **19b**, in 60 and 55% yields, respectively.

4.8.1. 1,2,5,6,12,13-Hexahydro-3*H*-indolo[3,2,1-*de*]pyrido[3,2,1-*ij*][1,5]naphthyridin-3-one (26a). White crystals (0.116 g, 88%), mp 140–143 °C (CH_2Cl_2–petroleum ether); IR (KBr) cm^{-1} 1652, 1632; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.49 (d, J=7.3 Hz, 1H), 7.38–7.06 (m, 3H), 4.19–3.97 (two overlapping t, 4H), 2.93 (t, J=6.0 Hz, 2H), 2.83–2.64 (m, 4H), 2.47 (t, J=6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.4, 138.1, 128.2, 127.3, 124.8, 122.2, 120.3, 119.7, 119.0, 109.3, 105.6, 40.0, 39.6, 31.6, 27.4, 24.2, 20.5; MS *m*/*z* (%) 264 (M^+, 100), 207 (19). EIHRMS *m*/*z* calcd for $C_{17}H_{16}N_2O$ (M^+) 264.12626, found 264.12696.

4.8.2. 1,2,5,10,11,12-Hexahydro-3*H*,4*H*-3a,9b-diazabenzo[*a*]naphtho[2,1,8-*cde*]azulen-3-one (26b). White crystals, mp 142–144 °C (CH_2Cl_2–petroleum ether); IR (KBr) cm^{-1} 1650, 1625; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.51 (d, J=7.4 Hz, 1H), 7.35–7.18 (m, 2H), 7.11 (t, J=7.0 Hz, 1H), 4.24 (t, J=4.9 Hz, 2H), 4.09 (t, J=6.2 Hz, 2H), 2.88 (t, J=6.2 Hz, 2H), 2.67 (t, J=4.9 Hz, 2H), 2.50 (t, J=6.2 Hz, 2H), 2.35 (t, J=6.2 Hz, 2H), 2.30–2.18 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.8, 137.7, 129.3, 126.2, 125.4, 122.8, 120.2, 119.5, 118.7, 112.2, 109.0, 28.1, 25.8, 21.4; MS *m*/*z* (%) 278 (M^+, 74), 221 (12), 86 (100). Anal. Calcd for $C_{17}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.43; H, 6.40; N, 9.84.

4.8.3. 3-Methoxy-1-(4-nitro-1,2,3a,4,5,6,7,8-octahydro-3*H*-3,8a-diazacycloocta[*jk*]fluoren-3-yl)-1-propanone (27). Oil (0.0612 g, 33%); IR (liquid film) cm^{-1} 1653, 1553, 1363, 1186; ^1H NMR ($CDCl_3$, 300 MHz) mixture of rotamers in ~7.5:2.5 ratio. Spectrum of the main rotamer: δ 7.50 (d, J=7.9 Hz, 1H), 7.36–7.20 (m, 2H), 7.12 (t, J=7.3 Hz, 1H), 6.49 (d, J=11.0 Hz, 1H), 4.89 (ddd, J_1=17.9 Hz, J_2=11.0 Hz, J_3=6.0 Hz, 1H), 4.44 (dd, J_1=14.9 Hz, J_2=4.6 Hz, 1H), 4.31–4.14 (m, 2H), 3.79–3.58 (m, 3H), 3.32 (s, 3H), 3.04–2.82 (m, 2H), 2.82–2.57 (m, 2H), 2.42–2.22 (m, 2H), 2.15–1.66 (m, 3H), 0.98–0.72 (m, 1H); Distinguished peaks from the spectrum of the minor rotamer: 5.67 (d, J=10.4 Hz), 4.99 (dt, J_1=10.4 Hz, J_2=4.6 Hz), 4.55–4.45 (m, overlapping), 4.15–4.02 (m, overlapping), 3.55–3.46 (m, overlapping), 3.09 (s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.3, 135.9, 130.4, 126.3, 122.5, 119.7, 118.6, 109.1, 108.9, 89.8, 68.5, 58.8, 49.2, 40.1, 39.6, 33.6, 28.3, 21.9, 19.1. Distinguished peaks from the spectrum of the minor rotamer: 171.6, 118.9, 108.1, 90.3, 69.2, 53.9, 35.9, 34.0, 28.9, 28.5, 20.3, 19.3; MS *m*/*z* (%) 371 (M^+, 73), 338 (10), 324 (48), 309 (45), 293 (26), 279 (25), 265 (57), 237 (100), 210 (95), 183 (96), 168 (73). ESIHRMS *m*/*z* calcd for $C_{20}H_{25}N_3O_4$+H (MH^+) 372.19178, found: 372.19206.

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