EurJOC
European Journal of Organic Chemistry

Full Paper
doi.org/10.1002/ejoc.202001226

Chemistry Europe
European Chemical Societies Publishing

Hexahydrocarbazoles

Preparation of Hexahydrocarbazole Derivatives by Reductive Indolization

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Abstract: The reductive indolization is a two-step protocol performed in one flask: First, the acid-mediated Fischer indolization of a cyclic ketone with phenylhydrazine forms an iminium ion which is subsequently reduced by a hydrido borate reagent to the indoline as the final product. We utilized this new strategy for the preparation of hexahydrocarbazole derivatives with a side chain in the quaternary C4a-position. Starting materials were several *N*1- and aryl-substituted phenylhydrazines and a cyclic ketone with propanoic ester moiety, which is the product of the conjugated addition of cyclohexanone to ethyl acrylate. Furthermore, benzannulated congeners as well as a pyrido[4,3-*b*]-indole derivative were accessed. The hexahydrocarbazole defines a molecular scaffold with two points of diversification. Therefore, several derivatives at N9 and at the C4a-side chain were prepared.

Introduction

The carbazoles,[1] as well as their tetrahydro[2] and hexahydro congeners,[3] are an important class of heterocyclic compounds and the core structural motif of numerous indole alkaloids.[4] Furthermore, several synthetic pharmaceuticals carry this heterocycle.[5] Figure 1 shows four naturally occurring and synthetic tetra- and hexahydrocarbazole derivatives. (+)-Aristotelin (**1**) can be isolated from several *Aristotelia* species (Elaeocarpaceae).[6] (+)-Aspidospermidine (**2**) is the archetypical member of the Aspidosperma alkaloids.[7] Cebranopadol (**3**), a 2-oxa-congener, is a novel opioid analgesic presently in clinical trials for the therapy of a variety of different acute and chronic pain states.[8] Compound **4** shows remarkable antibiotic activity against the multi-resistant MRSA and is therefore a valuable starting point for the development of new antibiotics.[9] In this compound, the five and six-membered rings are *cis*-annulated.

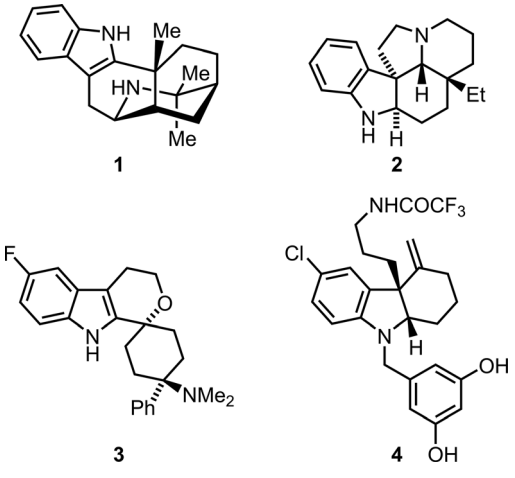
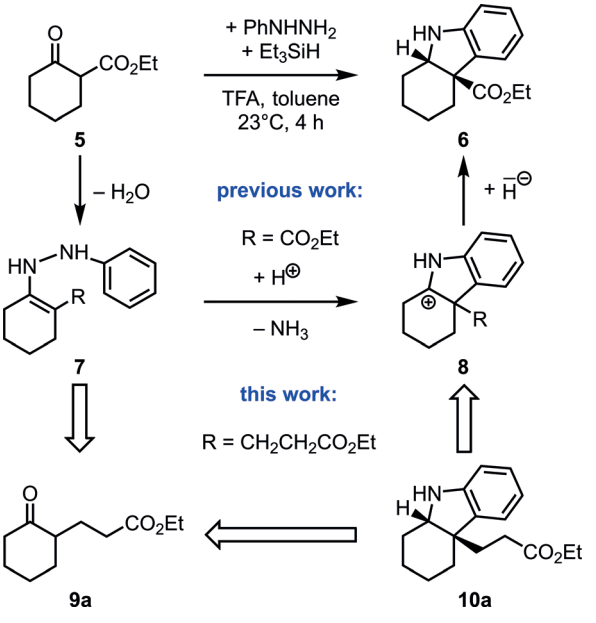


Figure 1. Four naturally occurring and synthetic tetra- and hexahydrocarbazole derivatives.

We have recently reported on a novel route to indolines called "reductive indolization", i.e. a Fischer indolization reaction under reductive conditions (Scheme 1).[10] Oxoester **5** was con-



Scheme 1. Reductive indolization of β-oxoester **5** (previous work) and δ-oxoester **9a** (this publication).

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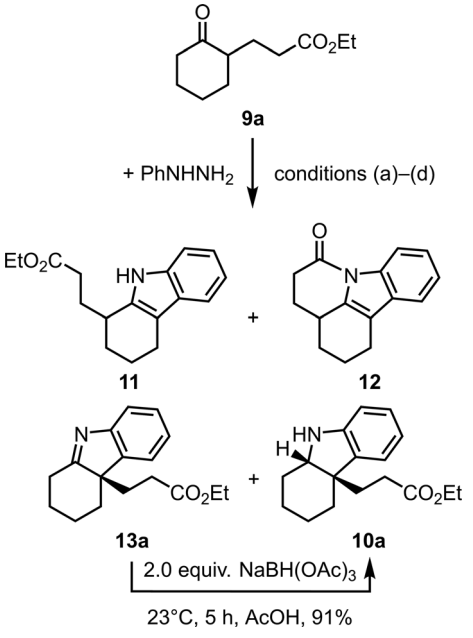
Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under https://doi.org/10.1002/ejoc.202001226.

Full Paper
doi.org/10.1002/ejoc.202001226

verted with phenylhydrazine under acidic conditions in the presence of Et_3SiH as reducing agent furnishing the racemic hexahydrocarbazole derivative **6** exclusively as the diastereoisomer with *cis*-annulated rings. After formation of the hydrazone and its tautomeric enamine **7**, the reaction proceeded along the known mechanistic pathway: protonation at nitrogen, [3,3]-sigmatropic rearrangement, nucleophilic addition of the aniline-NH_2 to the iminium ion at the alicyclic ring followed by elimination of ammonia furnishing the iminium ion **8**. Instead of being deprotonated (since R ≠ H) forming the aromatic tetrahydrocarbazole, the cation **8** was reduced by the silane forming the hexahydrocarbazole derivative **6**. The concept of "reductive indolization" has been applied in the past for the synthesis of dihydroindole derivatives,[11] and very recently for Aspidosperma alkaloids.[12] It can be regarded as the reductive case of an interrupted Fischer indolization, as introduced by Garg and co-workers.[13] We now report our efforts to extend the reductive indolization towards hexahydrocarbazole derivatives **10** with a C_3-side chain at the position 4a, thus, accessing the carbon skeleton of compound **4** (Figure 1). Consequently, we started our investigation with δ-oxoester **9a**, which resulted from the conjugated addition of cyclohexanone to ethyl acrylate.[14]

Results and Discussion

The hunt for suitable reaction conditions furnishing target structure **10a** started with our previously established protocol (Scheme 2). However, when converting δ-oxoester **9a** with phenylhydrazine in the presence of Et_3SiH according to conditions (a), a mixture of compounds **11**, **12** (together 61 % yield) and **13a** (23 %) were formed. While known compound **12**[15] is clearly a subsequent lactamization product of compound **11**, the latter is the resulting from the regioisomeric enamine. This enamine is the kinetic, trisubstituted isomer, while the correct enamine (leading to 3*H*-indol derivative **13a**) is the thermodynamic, tetrasubstituted isomer. Consequently, we raised the reaction temperature from 23 °C to 100 °C (together with a change of the solvent), and indeed, the correct regioisomer **13a** became the main product when applying conditions (b). Actually, the target compound **10a** (8 %) was only a minor component in this mixture. We then screened changes of the solvent, the temperature, and the stoichiometry and after some experimentation, we were able to maximize the correct regiochemistry. Applying conditions (c) gave compound **13a** (which is actually literature known)[16] now in 74 % yield together with 10 % of lactam **12**. Unfortunately, no traces of target compound **10a** were detectable. From this observation, we concluded that Et_3SiH is not the appropriate reducing reagent for compound **13a**. Therefore, we isolated compound **13a** and converted it with other reducing reagents. With $NaBH_4$, for example, only the ester moiety was reduced to the primary alcohol. With $NaBH(OAc)_3$,[17] however, we could successfully transform 3*H*-indole derivative **13a** to hexahydrocarbazole **10a** (91 % yield, Scheme 2, lower arrow). After further, tedious experimentation finally a two-step, one flask protocol was developed depicted as conditions (d) in Table 1, which gave the target structure **10a** in 85 % yield together with minor amounts of the unwanted regioisomers **11** and **12** (together 10 %), which could be separated by column chromatography.



Scheme 2. Searching for appropriate reaction conditions; for conditions and yields see Table 1.

Compound **10a** was obtained as a single diastereoisomer. It is furthermore a crystalline material suitable for single-crystal X-ray structure determination.[18] Figure 2 shows an ORTEP-representation of the molecular structure in the solid-state. The alicyclic A-ring is in chair-conformation with the C_3-side chain at C4a in the equatorial position. A- and B-ring are *cis*-annulated. The bond angle C8a–N9–C9a of 106.0° clearly indicated that this nitrogen atom is sp^3-hybridized.

After identification of suitable conditions, we went out to check the scope of the reaction concerning the phenylhydrazine derivative (Scheme 3 and Table 2). Respective bromo-, methoxy-, dimethyl- and fluoro-substituted phenylhydrazines were commercially available and gave products **10b**–**10e** in 51–71 % yields (Table 2, entries 2–5). Phenylhydrazines with an ad-

Table 1. Screening for suitable reaction conditions.

Conditions	Yield **11**	Yield **12**	Yield **13a**	Yield **10a**
(a) 1.1 equiv. $PhNHNH_2$, 1.1 equiv. Et_3SiH, TFA, toluene (1:3), 23 °C, 16 h	41 %[a]	20 %	23 %	–
(b) 1.1 equiv. $PhNHNH_2$, 1.5 equiv. Et_3SiH, TFA, AcOH (1:3), 100 °C, 16 h	–	34 %	41 %	8 %
(c) 1.1 equiv. $PhNHNH_2$, 2.0 equiv. Et_3SiH, AcOH, 100 °C, 16 h	–	10 %	74 %[b]	–
(d) 1. 1.1 equiv. $PhNHNH_2$, AcOH, 100 °C, 2.5 h; 2. 2.0 equiv. $NaBH(OAc)_3$, 23 °C, 1.5 h	6 %[a]	4 %	–	85 %[b]

[a] Not completely separable mixture with compound **12**. [b] Yield of isolated product.

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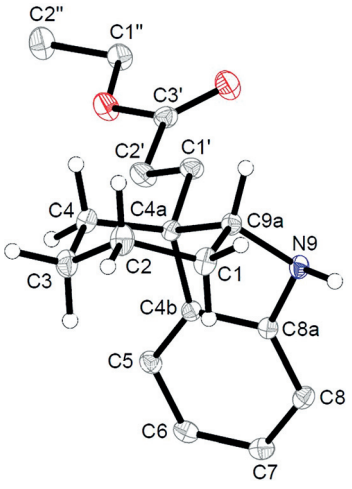
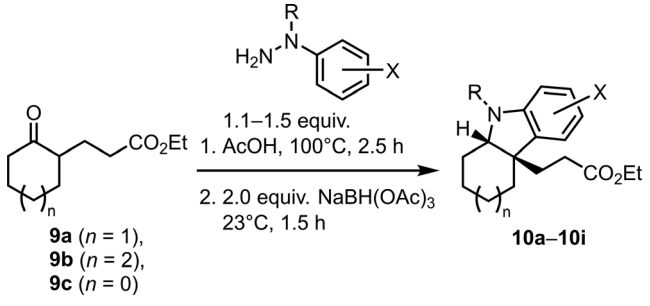


Figure 2. The ORTEP-representation of the molecular structure of compound **10a** in the solid-state proves the constitution and relative *cis*-configuration.

ditional benzyl[19] or allyl[20] residue at N1 could be prepared according to literature protocols. Conversion with δ-oxoester **9a** under standard conditions gave the respective *N*-substituted hexahydrocarbazoles **10f** and **10g** in 73 % and 78 % yields, respectively (entries 6 and 7). We then investigated the ring size of the δ-oxoesters and prepared the cycloheptanone (compound **9b**)[21] and cyclopentanone derivatives (compound **9c**)[22] according to literature protocols. Starting material **9b** gave product **10h** in moderate yield (37 %, entry 8) when applying longer reaction times. In contrast, the cyclopenta[*b*]-indole **10i** was only obtained in trace amounts and could not be fully purified when the cyclopentanone derivative **9c** was submitted to reaction with phenylhydrazine (entry 9).



Scheme 3. Investigating the scope of the reductive indolization, for ring size *n*, residues R and X and yields see Table 2.

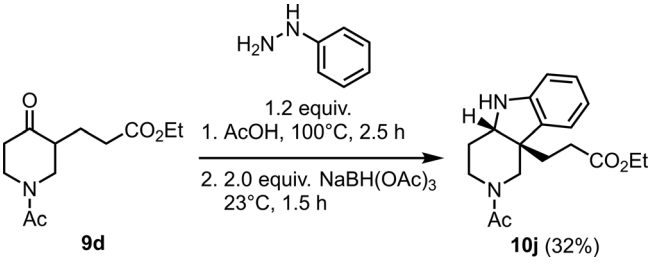
To pursue the preparation of a product with an additional nitrogen function, we prepared the δ-oxoester **9d** from *N*-acetylpiperidone and ethyl acrylate. It was submitted to our standard conditions for reductive indolization (Scheme 4). However, compound **10j** was only obtained in unsatisfactory yield (32 %). At ambient temperature, compounds **9d** and **10j** showed broad proton NMR spectra and partly doubled signal sets in the ^{13}C NMR spectra due to *E*/*Z*-isomerism along with the amide C-N bond. At 100 °C, the proton NMR spectra contained single signal sets.

Benzannulated δ-oxoesters, i.e. tetralone (**9e**) and indanone derivatives (**9f**), also underwent reductive indolization, though,

Table 2. Scope of the reductive indolization upon variation of the phenylhydrazine derivative and the ring size of the δ-oxoester.

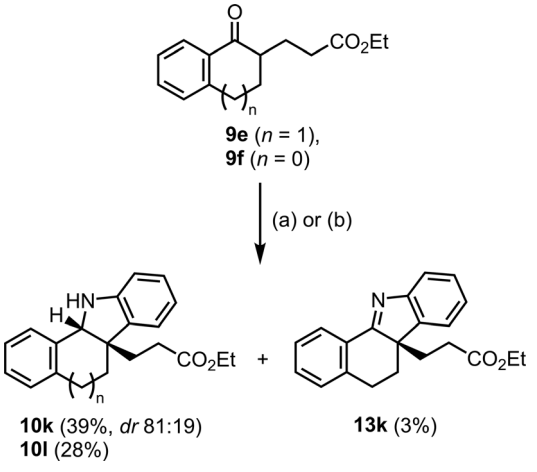
Entry	*n*	R	X[a]	Product	Yield[b]
1	1	H	H	**10a**	85 %
2	1	H	6-Br	**10b**	61 %
3	1	H	6-OMe	**10c**	51 %
4	1	H	5,7-Me_2	**10d**	68 %
5	1	H	6-F	**10e**	71 %
6	1	Bn	H	**10f**	73 %
7	1	allyl	H	**10g**	78 %
8	2	H	H	**10h**	37 %[c]
9	0	H	H	**10i**	0 %[d]

[a] Locants refer to compounds **10** (see Figure 2). [b] Isolated product. [c] Modified reaction times: 1. 5 h; 2. 16 h. [d] Product **10i** was formed in ca. 3 %, but could not be completely purified.



Scheme 4. Preparation of pyrido[4,3-*b*]indole derivative **10j** from piperidone **9d**.

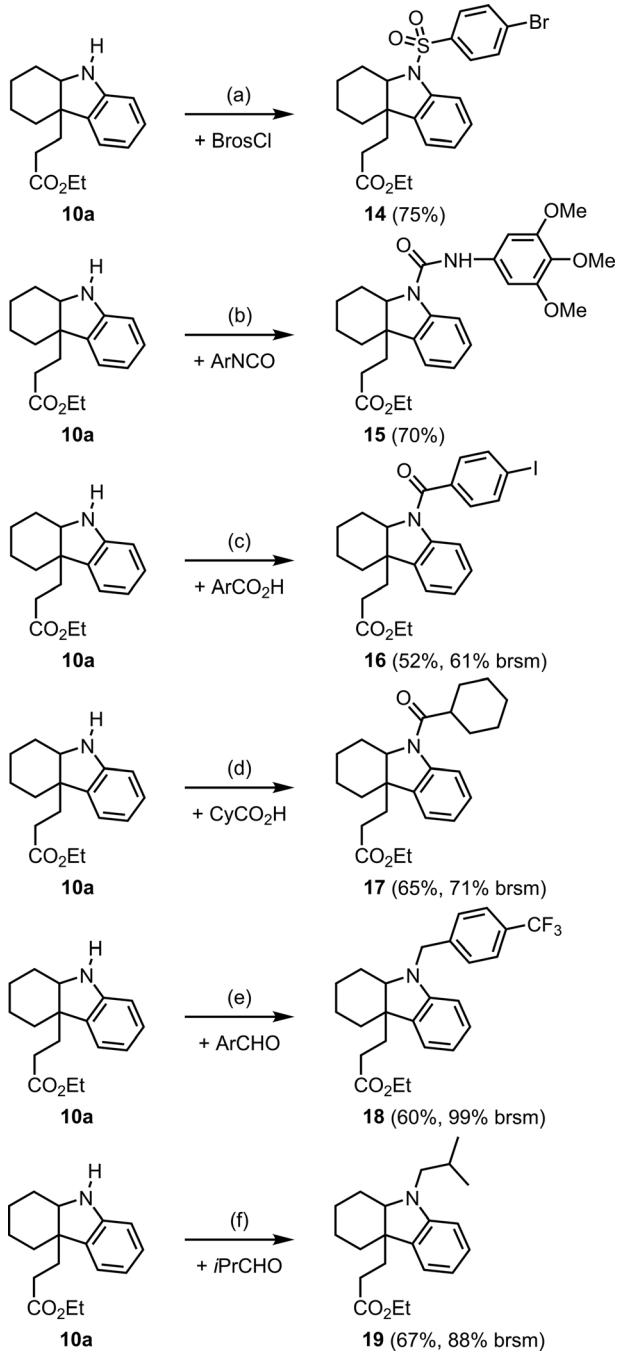
yields remained unsatisfactory (Scheme 5). Moreover, compound **10k** (39 % yield, 56 % based on recovered starting material) always contained a minor diastereoisomer. Upon attempts to separate these isomers by chromatography, always a small amount of 3*H*-indole derivative **13k** ("di-dehydro-**10k**") was formed, presumably by oxidation. It is unclear whether the main diastereoisomer of **10k** is *cis*- or *trans*-configured. The product **10l** with two five-membered rings is of course only the *cis*-isomer (yield 28 %).



Scheme 5. Conversion of benzannulated δ-oxoesters **9e** and **9f**; reagents and conditions: (a) for **9e**: 1. 1.5 equiv. $PhNHNH_2$, AcOH, 100 °C, 16 h; 2. 2.5 equiv. $NaBH(OAc)_3$, 23 °C, 3 h; (b) for **9f**: 1. 1.2 equiv. $PhNHNH_2$, AcOH, 100 °C, 2.5 h; 2. 2 equiv. $NaBH(OAc)_3$, 23 °C, 1.5 h.

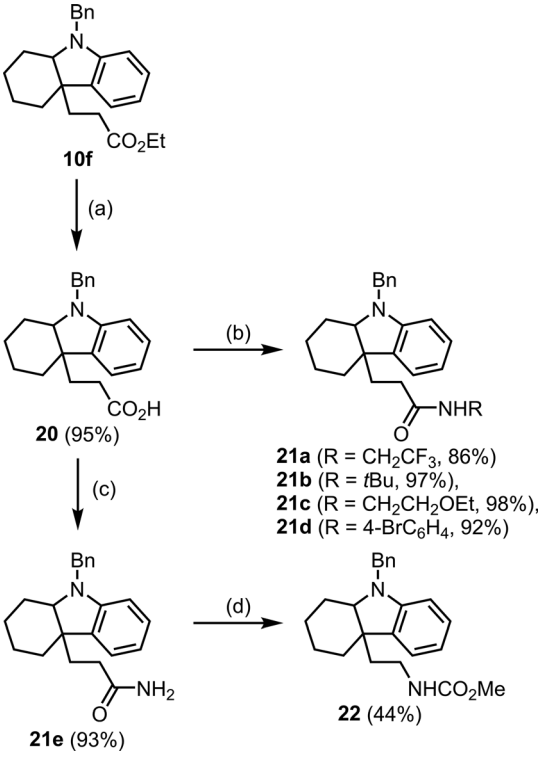
The heterocyclic compound **10a** defines a molecular scaffold holding two points for potential diversification: The nitrogen N-

9 and the carboxylic acid in the side chain. Therefore, standard transformations of the amino and carboxylate groups, which are often found in the field of Medicinal Chemistry, were exemplarily performed. Starting with the amino function of compound **10a** (Scheme 6), sulfonamide **14** was obtained in 75 % yield from BrosCl and pyridine. Conversion with a trimethoxyphenyl isocyanate in boiling toluene gave urea **15** in 70 % yield. Amidation of compound **10a** with an aromatic carboxylic acid utilized HATU-DIPEA[17,23] as coupling reagent and gave 52 % of product **16** [61 % based on recovered starting material (brsm)]. Coupling of the aliphatic cyclohexane carboxylic acid with HATU-DIPEA gave the amide **17** with superior result (65 % yield, 71 % brsm). And finally, reductive amination with trifluoromethylbenzaldehyde and isobutyraldehyde with $NaCNBH_3$ in an acidic milieu[24] gave the tertiary amines **18** (60 %, 99 % brsm) and **19** (67 %, 88 % brsm).



Scheme 6. Derivatization at nitrogen; reagents and conditions: (a) 1 equiv. BrosCl (Bros = 4-$BrC_6H_4SO_2$), pyridine/CH_2Cl_2, 23 °C, 3 h; (b) 1.2 equiv. 3,4,5-$(MeO)_3C_6H_2NCO$, toluene, 100 °C, 3 h; (c) 1.5 equiv. 4-$IC_6H_4CO_2H$, 1.5 equiv. HATU, 1.5 equiv. DIPEA, CH_2Cl_2, 23 °C, 17 h; (d) 1.1 equiv. $CyCO_2H$, 1.1 equiv. HATU, 1.1 equiv. DIPEA, CH_2Cl_2, 23 °C, 17 h; (e) 1 equiv. 4-$CF_3C_6H_4CHO$, 0.5 equiv. $ZnCl_2$, 1 equiv. $NaCNBH_3$, EtOH, 23 °C, 4 h. (f) 1 equiv. *i*PrCHO, 0.5 equiv. $ZnCl_2$, 1 equiv. $NaCNBH_3$, EtOH, 23 °C, 4 h. HATU = *O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate), DIPEA = ethyldiisopropylamine.

For the second diversifying strategy we first submitted compound **10f** to ester saponification with hydrochloric acid yielding compound **20** in 95 % yield (Scheme 7). It was then coupled with the HATU-DIPEA protocol with trifluoroethylamine to furnish compound **21a** with 86 % yield. With *tert*-butyl and ethoxyethylamine, the amides **21b** and **21c** were obtained in very good yield (97 % and 98 %, resp.). By application of 4-bromo aniline, the compound **21d** was formed also in good yield (92 %). Furthermore, we intended to prepare the 4a-(2-aminoethyl) derivative of the scaffold by Hofmann degradation of the carboxylate function in compound **20**. We relied on a literature procedure applying the hypervalent iodine reagent $PhI(OAc)_2$.[25] First of all, the parent unsubstituted amide **21e** was prepared in 93 % yield by activation of the acid **20** with Boc_2O and conversion of the mixed anhydride with hartshorn salt. The degradation proceeded with $PhI(OAc)_2$ and the inter-



Scheme 7. Derivatization at the carboxylate function; reagents and conditions: (a) HCl/H_2O (conc.), 100 °C, 2 h; (b) 1.1 equiv. HATU, 1.1 equiv. DIPEA, 1.5 equiv. RNH_2, CH_2Cl_2, 23 °C, 17 h; (c) 1.8 equiv. pyridine, 1.5 equiv. Boc_2O, 2.8 equiv. $(NH_4)_2CO_3$, 1,4-dioxane, 23 °C, 17 h; (d) 2.5 equiv. KOH, 1.0 equiv. $PhI(OAc)_2$, MeOH, 16 h.

Full Paper
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mediate isocyanate was solvolyzed with MeOH to furnish the carbamate **22**, however, the yield was moderate (44 %).

Conclusion

Hexahydrocarbazole derivatives **10a**–**10g** are accessed by reductive indolization, i.e. a two-step protocol performed consecutively in one flask consisting of acid-catalyzed 3*H*-indole formation with phenylhydrazine followed by reduction of the iminium-moiety with $NaBH(OAc)_3$. The starting material for this transformation is δ-oxoester **9a** resulting from the conjugated addition of cyclohexanone to ethyl acrylate via the enamine. Thus, the hexahydrocarbazoles **10a**–**10g** carry a 2-(ethoxycarbonyl)ethyl side chain at their quaternary C4a-position. The scope of the transformation was investigated by application of phenylhydrazine derivatives with substituents at the phenyl ring (Me, OMe, Br, F) as well as residues at the *N*1-position (allyl, benzyl). Yields of products **10a**–**10g** range between 85 % and 51 %. Furthermore, δ-oxoesters **9b** and **9c** with cycloheptanone and cyclopentanone ring were investigated, however, the yields of respective cyclohepta[*b*]indole **10h** (37 %) are unsatisfactory or in the case of cyclopenta[*b*]indole **10i** almost zero. Conversion of 4-piperidone derived δ-oxoester **9d** gave pyrido[4,3-*b*]indole derivative **10j** also with unsatisfactory yield (32 %). The same drawback was observed for products **10k** (39 %) and **10l** (28 %) obtained from tetralone- and indanone derived δ-oxoesters **9e** and **9f.** Since the hexahydrocarbazoles **10** define a molecular scaffold with two points for diversification, several derivatives at N9 (carboxamides, sulfonamides, ureas, and *N*-alkyl derivatives) were prepared. Also, the carboxylate function in the side chain was addressed by carboxamide formation (five examples). The *N*-unsubstituted amide **21e** at the C4a side chain was furthermore submitted to Hofmann degradation.

Experimental Section

General. Preparative column chromatography was carried out using Merck SiO_2 (35–70 μm, type 60 A) with hexanes (mixture of isomers, bp. 64–71 °C), *tert*-butyl methyl ether (MTBE), EtOAc, CH_2Cl_2, and MeOH as eluents. TLC was performed on aluminum plates coated with SiO_2 F_{254}. ^1H, ^{19}F, and ^{13}C NMR spectra were recorded on Bruker Avance DRX 500 and 300 instruments. Multiplicities of carbon signals were determined with DEPT experiments. HRMS spectra of products were obtained with Waters Q-TOF Premier (ESI, pos. mode) or Thermo Scientific DFS (EI) spectrometers. IR spectra were recorded on a Bruker Tensor 27 spectrometer equipped with a diamond ATR unit. 1-Benzyl-1-phenylhydrazine[19] and 1-Allyl-1-phenylhydrazine[20] are literature known and were prepared accordingly. δ-Oxoesters **9a**–**9c** and **9e** were literature known and prepared accordingly.[14,21,22] All other starting materials were commercially available.

1-Benzyl-1-phenylhydrazine.[19] Phenylhydrazine (541 mg, 5.00 mmol) and benzyl bromide (855 mg, 5.00 mmol) were added to a solution of $NaHCO_3$ (420 mg, 5.00 mmol) in H_2O (5 mL). The resulting mixture was stirred at 100 °C for 3 h, subsequently cooled to ambient temperature, and extracted with MTBE (3 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/MTBE, 3:1, R_f = 0.26) to yield the title compound (767 mg, 3.87 mmol, 77 %) as a pale yellow oil. ^1H-NMR (300 MHz, $CDCl_3$): δ = 3.40 (br s, 2H), 4.62 (s, 2H), 6.84 (t, *J* = 7.2 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.26–7.39 (m, 7H) ppm. All spectroscopic data are in accordance with the literature.[19] $C_{13}H_{14}N_2$ (198.27 g mol^{-1}).

1-Allyl-1-phenylhydrazine.[20] Phenylhydrazine (541 mg, 5.00 mmol) and allyl bromide (605 mg, 5.00 mmol) were added to a solution of $NaHCO_3$ (420 mg, 5.00 mmol) in H_2O (5 mL). The resulting mixture was stirred at 100 °C for 3 h, subsequently cooled to ambient temperature, and extracted with MTBE (3 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/MTBE, 2:1, R_f = 0.26) to yield the title compound (153 mg, 1.03 mmol, 21 %) as a pale yellow oil. ^1H-NMR (300 MHz, $CDCl_3$): δ = 3.61 (br s, 2H), 4.04 (d, *J* = 5.9 Hz, 2H), 5.25–5.31 (m, 2H), 5.89 (ddt, *J* = 17.5 Hz, *J* = 9.8 Hz, *J* = 5.9 Hz, 1H), 6.81 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 7.9 Hz, 2H), 7.24–7.29 (m, 2H) ppm. All spectroscopic data are in accordance with the literature.[20] $C_9H_{12}N_2$ (148.21 g mol^{-1}).

General procedure A (GPA) for the preparation of δ-oxoesters 9.[14,21,22] A solution of cyclic ketone (1.0 equiv.) and pyrrolidine (2.0 equiv.) in toluene (1.3 L mol^{-1}) was heated to reflux under water separation using a Dean–Stark trap for 3–5 h. Subsequently, all volatile materials were removed under reduced pressure and the crude enamine was dissolved in abs. THF (1.3 L mol^{-1}). Ethyl acrylate (1.3 equiv.) was added and the resulting mixture was heated to reflux for 16 h. Then H_2O (0.4 L mol^{-1}) was added and the mixture was further heated to reflux for 2 h. Subsequently, all volatile materials were removed under reduced pressure and the residue was diluted with H_2O (1 L mol^{-1}) and extracted with MTBE (3 × 1 L mol^{-1}). The combined organic layers were washed with hydrochloric acid (2 mol L^{-1}, 1 × 2 L mol^{-1}) and brine (1 × 2 L mol^{-1}), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography to furnish δ-oxoesters **9a–9f**.

Ethyl 3-(2-oxocyclohexyl)propanoate (9a).[14] According to GPA, cyclohexanone (1.50 g, 15.3 mmol) was converted with pyrrolidine (2.18 g, 30.6 mmol) and ethyl acrylate (1.99 g, 19.9 mmol) to yield the title compound **9a** (1.79 g, 9.03 mmol, 59 %) after chromatography (SiO_2, hexanes/MTBE, 2:1, R_f = 0.30) as a colorless liquid. ^1H-NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3H), 1.32–1.45 (m, 1H), 1.47–1.59 (m, 1H), 1.62–1.69 (m, 2H), 1.80–1.90 (m, 1H), 1.99–2.14 (m, 3H), 2.24–2.44 (m, 5H), 4.11 (q, *J* = 7.1 Hz, 2H) ppm. All spectroscopic data are in accordance with the literature.[14] $C_{11}H_{18}O_3$ (198.26 g mol^{-1}).

Ethyl 3-(2-oxocycloheptyl)propanoate (9b).[21] According to GPA, cycloheptanone (1.00 g, 8.92 mmol) was converted with pyrrolidine (1.27 g, 17.8 mmol) and ethyl acrylate (1.16 g, 11.6 mmol) to yield the title compound **9b** (1.07 g, 5.04 mmol, 57 %) after chromatography (SiO_2, hexanes/EtOAc, 2:1, R_f = 0.48) as a colorless liquid. ^1H-NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3H), 1.30–1.43 (m, 3H), 1.54–2.65 (m, 12H), 4.11 (q, *J* = 7.1 Hz, 2H) ppm. All spectroscopic data are in accordance with the literature.[21] $C_{12}H_{20}O_3$ (212.29 g mol^{-1}).

Ethyl 3-(2-oxocyclopentyl)propanoate (9c).[22] According to GPA, cyclopentanone (1.00 g, 11.9 mmol) was converted with pyrrolidine (1.69 g, 23.8 mmol) and ethyl acrylate (1.55 g, 15.5 mmol) to yield the title compound **9c** (1.39 g, 7.57 mmol, 64 %) after chromatography (SiO_2, hexanes/MTBE, 1:1, R_f = 0.39) as a colorless liquid. ^1H-

NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.2 Hz, 3H), 1.48–2.33 (m, 9H), 2.40 (t, *J* = 7.6 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H) ppm. All spectroscopic data are in accordance with the literature.[22] $C_{10}H_{16}O_3$ (184.24 g mol^{-1}).

Ethyl 3-(1-acetyl-4-oxopiperidin-3-yl)propanoate (9d). According to GPA, *N*-acetyl-4-piperidone (988 mg, 7.00 mmol) was converted with pyrrolidine (966 mg, 14.0 mmol) and ethyl acrylate (911 mg, 9.10 mmol) to yield the title compound **9d** (431 mg, 1.79 mmol, 26 %) after chromatography (SiO_2, EtOAc/MeOH, 10:1, R_f = 0.41) as a colorless liquid. NMR spectra showed partly doubled signal sets due to *E*/*Z*-isomers (ratio 1:0.9) at the amide C–N-bond. ^{1}H-NMR (500 MHz, $CDCl_3$), major isomer: δ = 1.11–1.15 (m, 3H), 1.44–1.51 (m, 2H), 1.90–2.00 (m, 2H), 2.07 (s, 3H), 2.21–2.43 (m, 1H), 2.85 (dd, *J* = 13.0 Hz, *J* = 10.4 Hz, 1H), 3.10 (dd, *J* = 13.4 Hz, *J* = 10.5 Hz, 1H), 3.44 (dt, *J* = 13.8 Hz, *J* = 7.1 Hz, 1H), 3.83–3.92 (m, 2H), 3.97–4.02 (m, 2H), 4.37 (ddd, *J* = 13.0 Hz, *J* = 5.8 Hz, *J* = 1.5 Hz, 1H) ppm; minor isomer: δ = 1.11–1.15 (m, 3H), 2.08 (s, 3H), 2.21–2.43 (m, 9H), 3.18 (ddd, *J* = 13.8 Hz, *J* = 9.1 Hz, *J* = 5.4 Hz, 1H), 3.97–4.02 (m, 2H), 4.32 (dtd, *J* = 13.0 Hz, *J* = 5.7 Hz, *J* = 1.8 Hz, 1H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$), major isomer: δ = 13.90 (CH_3), 21.0 (CH_3), 21.9 (CH_2), 22.1 (CH_2), 45.3 (CH_2), 45.4 (CH_2), 48.6 (CH), 50.1 (CH_2), 60.1 (CH_2), 168.9 (C), 172.59 (C), 207.7 (C) ppm; minor isomer: δ = 13.91 (CH_3), 21.0 (CH_3), 31.2 (2 CH_2), 40.2 (CH_2), 40.6 (CH_2), 41.0 (CH_2), 49.0 (CH), 60.3 (CH_2), 169.0 (C), 172.58 (C), 207.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2970 (w), 2937 (w), 2876 (w), 1724 (vs), 1644 (vs), 1424 (s), 1366 (m), 1312 (w), 1267 (m), 1234 (w), 1164 (m), 1139 (w), 1096 (w), 1029 (s), 854 (m), 600 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 241.1309 (for $C_{12}H_{19}NO_4^+$), found 241.1307 [M$^+$]. $C_{12}H_{19}NO_4$ (241.29 g mol^{-1}).

Ethyl 3-(1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)propanoate (9e).[21] A solution of 1-tetralone (1.02 g, 7.00 mmol), pyrrolidine (996 mg, 14.0 mmol), and *p*TosOH•H_2O (133 mg, 699 µmol) in toluene (9 mL) was heated to reflux under water separation using a Dean–Stark trap for 24 h. Subsequently, all volatile materials were removed under reduced pressure and the crude enamine was dissolved in abs. 1,4-dioxane (9 mL). Ethyl acrylate (911 mg, 9.10 mmol) was added and the resulting mixture was heated to reflux for 16 h. Then H_2O (3 mL) was added and the mixture was further refluxed for 2 h. Subsequently, all volatile materials were removed under reduced pressure and the residue was diluted with hydrochloric acid (2 mol L^{-1}, 10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (1 × 10 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2, R_f = 0.34) to yield the title compound **9e** (753 mg, 3.06 mmol, 44 %) as an orange oil. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3H), 1.78–1.96 (m, 2H), 2.18–2.31 (m, 2H), 2.45–2.58 (m, 3H), 2.99–3.03 (m, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.45 (td, *J* = 7.5 Hz, *J* = 1.4 Hz, 1H), 8.00 (dd, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H) ppm. All spectroscopic data are in accordance with the literature.[21] $C_{15}H_{18}O_3$ (246.31 g mol^{-1}).

Ethyl 3-(1-oxo-2,3-dihydro-1*H*-inden-2-yl)propanoate (9f).[26] According to GPA, 1-indanone (925 mg, 7.00 mmol) was converted with pyrrolidine (996 mg, 14.0 mmol) and ethyl acrylate (911 mg, 9.10 mmol) to yield the title compound **9f** (404 mg, 1.74 mmol, 25 %) after chromatography (SiO_2, CH_2Cl_2, R_f = 0.23) as a pale yellow liquid. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.1 Hz, 3H), 1.79 (dtd, *J* = 13.8 Hz, *J* = 8.5 Hz, *J* = 7.4 Hz, 1H), 2.16 (dtd, *J* = 13.8 Hz, *J* = 7.8 Hz, *J* = 5.8 Hz, 1H), 2.44 (t, *J* = 7.7 Hz, 2H), 2.63 (tdd, *J* = 8.2 Hz, *J* = 5.8 Hz, *J* = 4.1 Hz, 1H), 2.73 (dd, *J* = 17.1 Hz, *J* = 4.1 Hz, 1H), 3.29 (dd, *J* = 17.1 Hz, *J* = 7.9 Hz, 1H), 4.07 (q, *J* = 7.1 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.38 (dt, *J* = 7.7 Hz, *J* = 1.0 Hz, 1H), 7.51 (td, *J* = 7.5 Hz, *J* = 1.2 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 26.4 (CH_2), 31.8 (CH_2), 32.6 (CH_2), 46.2 (CH), 60.2 (CH_2), 123.7 (CH), 126.3 (CH), 127.2 (CH), 134.6 (CH), 136.4 (C), 153.1 (C), 172.8 (C), 207.6 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2980 (w), 2933 (w), 1729 (s), 1706 (vs), 1609 (m), 1589 (w), 1474 (w), 1464 (m), 1436 (w), 1376 (w), 1326 (w), 1296 (w), 1275 (w), 1206 (w), 1177 (w), 1146 (w), 1094 (w), 1069 (w), 1032 (w), 857 (w), 751 (m), 724 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 232.1094 (for $C_{14}H_{16}O_3^+$), found 232.1087 [M$^+$]. $C_{14}H_{16}O_3$ (232.28 g mol^{-1}). The compound was reported in literature, but insufficiently characterized.[26]

Conversion of δ-oxoester 9a with phenylhydrazine (Table 1, conditions c). Et_3SiH (163 mg, 1.40 mmol) was added to a solution of δ-oxoester **9a** (139 mg, 701 µmol) and phenylhydrazine (83 mg, 0.77 mmol) in glacial acetic acid (3 mL), and the resulting mixture was stirred at 100 °C for 16 h. Subsequently, the mixture was cooled to ambient temperature, diluted with H_2O (5 mL), and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ solution (1 × 5 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/EtOAc, 1:1) to yield in the first fraction the lactam **12** (16 mg, 71 µmol, 10 %, R_f = 0.57) as a light brown solid, mp. 120–123 °C; Lit.[15b] 126 °C. Secondly, the tetrahydrocarbazole **13a** (140 mg, 516 µmol, 74 %, R_f = 0.28) was obtained as a yellow resin in another fraction.

2,3,3a,4,5,6-Hexahydro-6*H*-pyrido[3,2,1-*jk*]carbazole-6-one (12).[15b] ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.33–1.41 (m, 1H), 1.62 (qd, *J* = 12.9 Hz, *J* = 4.5 Hz, 1H), 1.76–1.85 (m, 1H), 2.08–2.18 (m, 3H), 2.56 (dddt, *J* = 15.4 Hz, *J* = 9.4 Hz, *J* = 6.1 Hz, *J* = 3.5 Hz, 1H), 2.68–2.83 (m, 4H), 7.24–7.31 (m, 2H), 7.38–7.40 (m, 1H), 8.42–8.44 (m, 1H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 20.1 (CH_2), 22.5 (CH_2), 28.7 (CH_2), 29.5 (CH_2), 32.5 (CH), 34.5 (CH_2), 114.2 (C), 116.1 (CH), 117.8 (CH), 123.6 (CH), 123.9 (CH), 130.0 (C), 134.7 (C), 136.9 (C), 168.9 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2942 (m), 2837 (m), 1699 (vs), 1632 (m), 1456 (vs), 1440 (s), 1389 (vs), 1330 (m), 1310 (m), 1297 (m), 1246 (m), 1236 (m), 1176 (m), 1142 (m), 1129 (m), 1013 (m), 944 (m), 757 (vs), 682 (m), 582 (m), 567 (s), 560 (s) cm^{-1}. HR-MS (EI, 70 eV): calcd. 225.1148 (for $C_{15}H_{15}NO^+$), found 225.1145 [M$^+$]. $C_{15}H_{15}NO$ (225.29 g mol^{-1}). The compound was reported in literature, but insufficiently characterized.[15b]

Ethyl 3-(2,3,4,4a-tetrahydro-1*H*-carbazol-4a-yl)propanoate (13a).[16] ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.1 Hz, 3H), 1.15–1.25 (m, 1H), 1.42 (qt, *J* = 13.4 Hz, *J* = 4.4 Hz, 1H), 1.51–1.71 (m, 3H), 1.86 (qt, *J* = 13.6 Hz, *J* = 3.7 Hz, 1H), 2.10–2.24 (m, 2H), 2.31–2.47 (m, 2H), 2.55 (td, *J* = 13.2 Hz, *J* = 5.7 Hz, 1H), 2.86–2.90 (m, 1H), 3.91–4.07 (m, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.27 (d, *J* = 6.4 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 7.7 Hz, 1H) ppm. All spectroscopic data are in accordance with the literature.[16] $C_{17}H_{21}NO_2$ (271.36 g mol^{-1}).

General procedure B (GPB) for the preparation of hexahydrocarbazole derivatives 10: A solution of δ-oxoester **9** (1.0 equiv.) and arylhydrazine (1.1–1.2 equiv.) in glacial acetic acid (2 L mol^{-1} δ-oxoester) was stirred at 100 °C for 2.5 h and subsequently cooled to ambient temperature. Then $NaBH(OAc)_3$ (2.0 equiv.) was added and the resulting mixture was further stirred at ambient temperature for 1.5 h. The mixture was diluted with H_2O (5 L mol^{-1}) and extracted with CH_2Cl_2 (3 × 5 L mol^{-1}). The combined organic layers were washed with sat. aq. $NaHCO_3$ solution (1 × 5 L mol^{-1}), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography to furnish hexahydrocarbazole derivatives **10**.

Ethyl *cis*-3-(2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)propanoate (10a). According to GPB, δ-oxoester **9a** (198 mg, 1.00 mmol)

and phenylhydrazine (119 mg, 1.10 mmol) were converted with $NaBH(OAc)_3$ (424 mg, 2.00 mmol) in AcOH (2 mL) to yield the title compound **10a** (233 mg, 852 μmol, 85 %) after chromatography (SiO_2, hexanes/CH_2Cl_2/MeOH, 1:1:0.03, R_f = 0.09) as a light brown solid, mp. 60–62 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.21 (t, J = 7.1 Hz, 3H), 1.27–1.35 (m, 2H), 1.41–1.52 (m, 3H), 1.54–1.60 (m, 1H), 1.69–1.75 (m, 1H), 1.81–1.91 (m, 2H), 2.12 (ddd, J = 13.9 Hz, J = 10.5 Hz, J = 6.2 Hz, 1H), 2.20–2.31 (m, 2H), 3.44 (dd, J = 6.6 Hz, J = 5.2 Hz, 1H), 3.59 (br s, 1H), 4.07 (q, J = 7.1 Hz, 2H), 6.66 (d, J = 7.7 Hz, 1H), 6.74 (td, J = 7.4 Hz, J = 0.9 Hz, 1H), 6.98 (d, J = 7.3 Hz, 1H), 7.03 (td, J = 7.6 Hz, J = 1.3 Hz, 1H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 21.2 (CH_2), 21.4 (CH_2), 29.0 (CH_2), 30.0 (CH_2), 32.88 (CH_2), 32.93 (CH_2), 46.4 (C), 60.2 (CH_2), 63.4 (CH), 110.3 (CH), 118.6 (CH), 122.6 (CH), 127.3 (CH), 134.5 (C), 150.1 (C), 174.0 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3362 (w), 2927 (s), 2856 (m), 1729 (vs), 1607 (m), 1480 (m), 1462 (s), 1452 (m), 1373 (w), 1303 (w), 1247 (w), 1174 (m), 1152 (m), 1019 (m), 742 (vs), 677 (w), 603 (w), 554 (w), 534 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 273.1723 (for $C_{17}H_{23}NO_2^{+}$), found 273.1731 [M$^+$]. $C_{17}H_{23}NO_2$ (273.38 g mol^{-1}).

Reduction of tetrahydrocarbazole 13a with $NaBH(OAc)_3$. $NaBH(OAc)_3$ (158 mg, 745 μmol) was added to a solution of tetrahydrocarbazole **13a** (100 mg, 369 μmol) in glacial acetic acid (1 mL) and the resulting mixture was stirred at ambient temperature for 5 h. Subsequently, the mixture was diluted with H_2O (5 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ solution (1 × 5 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo to yield the title compound **10a** (92 mg, 0.34 mmol, 91 %) as a light brown solid, mp. 60–62 °C.

Ethyl *cis*-3-(6-bromo-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)propanoate (10b). According to GPB, δ-oxoester **9a** (198 mg, 1.00 mmol) and 4-bromophenylhydrazine (225 mg, 1.20 mmol) were converted with $NaBH(OAc)_3$ (424 mg, 2.00 mmol) in AcOH (2 mL) to yield the title compound **10b** (215 mg, 610 μmol, 61 %) after chromatography (SiO_2, hexanes/CH_2Cl_2/MeOH, 1:1:0.03, R_f = 0.31) as a pale yellow solid, mp. 116–118 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.1 Hz, 3H), 1.27–1.33 (m, 2H), 1.38–1.60 (m, 4H), 1.69–1.75 (m, 1H), 1.78–1.87 (m, 2H), 2.07–2.13 (m, 1H), 2.22–2.25 (m, 2H), 3.45 (dd, J = 6.6 Hz, J = 5.3 Hz, 1H), 3.60 (br s, 1H), 4.08 (q, J = 7.1 Hz, 2H), 6.51 (d, J = 8.2 Hz, 1H), 7.04 (d, J = 2.0 Hz, 1H), 7.11 (dd, J = 8.2 Hz, J = 2.0 Hz, 1H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 21.0 (CH_2), 21.3 (CH_2), 28.9 (CH_2), 29.9 (CH_2), 32.8 (CH_2), 32.9 (CH_2), 46.8 (C), 60.4 (CH_2), 63.8 (CH), 110.2 (C), 111.6 (CH), 125.7 (CH), 130.1 (CH), 136.9 (C), 149.1 (C), 173.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3346 (m), 2959 (w), 2925 (m), 2856 (w), 1729 (vs), 1596 (w), 1467 (m), 1447 (w), 1416 (w), 1376 (m), 1299 (w), 1209 (m), 1180 (m), 1147 (w), 1082 (w), 1047 (w), 1024 (w), 1013 (w), 996 (w), 876 (m), 860 (w), 834 (w), 824 (m), 773 (w), 739 (m), 706 (w), 629 (m), 599 (s), 547 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 351.0828 (for $C_{17}H_{22}BrNO_2^{+}$), found 351.0819 [M$^+$]. $C_{17}H_{22}BrNO_2$ (352.27 g mol^{-1}).

Ethyl *cis*-3-(6-methoxy-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)propanoate (10c). According to GPB, δ-oxoester **9a** (198 mg, 1.00 mmol) and 4-methoxyphenylhydrazine (170 mg, 1.23 mmol) were converted with $NaBH(OAc)_3$ (424 mg, 2.00 mmol) in AcOH (2 mL) to yield the title compound **10c** (156 mg, 514 μmol, 51 %) after chromatography (SiO_2, hexanes/MTBE, 1:1, R_f = 0.24) as a pale yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, J = 7.1 Hz, 3H), 1.25–1.33 (m, 2H), 1.40–1.50 (m, 3H), 1.54–1.59 (m, 1H), 1.66–1.72 (m, 1H), 1.79–1.87 (m, 2H), 2.07–2.13 (m, 1H), 2.23–2.27 (m, 2H), 3.29 (br s, 1H), 3.42 (dd, J = 6.7 Hz, J = 5.0 Hz, 1H), 3.74 (s, 3H), 4.06 (q, J = 7.1 Hz, 2H), 6.56–6.60 (m, 3H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.1 (CH_3), 21.3 (CH_2), 21.4 (CH_2), 28.8 (CH_2), 29.9 (CH_2), 32.7 (CH_2), 32.9 (CH_2), 46.8 (C), 55.8 (CH_3), 60.2 (CH_2), 63.7 (CH), 109.8 (CH), 110.8 (CH), 111.7 (CH), 136.4 (C), 143.8 (C), 153.4 (C), 173.9 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3353 (w), 2980 (w), 2927 (s), 2856 (m), 1727 (vs), 1597 (w), 1484 (s), 1447 (w), 1433 (m), 1373 (m), 1299 (w), 1251 (w), 1209 (m), 1174 (m), 1033 (s), 862 (w), 804 (m), 747 (w), 674 (w), 562 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 303.1829 (for $C_{18}H_{25}NO_3^{+}$), found 303.1822 [M$^+$]. $C_{18}H_{25}NO_3$ (303.40 g mol^{-1}).

Ethyl *cis*-3-(5,7-dimethyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)propanoate (10d). According to GPB, δ-oxoester **9a** (198 mg, 1.00 mmol) and 3,5-dimethylphenylhydrazine (163 mg, 1.20 mmol) were converted with $NaBH(OAc)_3$ (424 mg, 2.00 mmol) in AcOH (2 mL) to yield the title compound **10d** (205 mg, 680 μmol, 68 %) after chromatography (SiO_2, hexanes/CH_2Cl_2/MeOH, 1:1:0.02, R_f = 0.17) as a pale yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.22 (t, J = 7.1 Hz, 3H), 1.38–1.47 (m, 3H), 1.55–1.72 (m, 4H), 1.79 (ddd, J = 13.8 Hz, J = 9.5 Hz, J = 4.5 Hz, 1H), 2.07 (ddd, J = 14.2 Hz, J = 11.5 Hz, J = 4.9 Hz, 1H), 2.11–2.23 (m, 2H), 2.21 (s, 3H), 2.25 (s, 3H), 2.31 (ddd, J = 15.2 Hz, J = 11.5 Hz, J = 5.4 Hz, 1H), 3.45 (t, J = 4.5 Hz, 1H), 4.09 (q, J = 7.1 Hz, 2H), 6.32 (s, 1H), 6.34 (s, 1H) ppm; a signal for the NH proton was not observed. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 18.6 (CH_3), 20.57 (CH_2), 20.62 (CH_2), 21.2 (CH_3), 27.3 (CH_2), 30.9 (CH_2), 31.1 (CH_2), 33.3 (CH_2), 47.6 (C), 60.2 (CH_2), 61.5 (CH), 108.9 (CH), 122.6 (CH), 129.3 (C), 133.7 (C), 137.1 (C), 150.6 (C), 174.1 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3362 (w), 2927 (m), 2857 (m), 1727 (vs), 1614 (m), 1587 (m), 1447 (m), 1373 (m), 1297 (m), 1259 (m), 1174 (vs), 1160 (s), 1023 (m), 826 (s), 643 (m), 606 (m), 569 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 301.2036 (for $C_{19}H_{27}NO_2^{+}$), found 301.2034 [M$^+$]. $C_{19}H_{27}NO_2$ (301.43 g mol^{-1}).

Ethyl *cis*-3-(6-fluoro-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)propanoate (10e). According to GPB, δ-oxoester **9a** (198 mg, 1.00 mmol) and 4-fluorophenylhydrazine (151 mg, 1.20 mmol) were converted with $NaBH(OAc)_3$ (424 mg, 2.00 mmol) in AcOH (2 mL) to yield the title compound **10e** (208 mg, 714 μmol, 71 %) after chromatography (SiO_2, hexanes/CH_2Cl_2/MeOH, 1:1:0.03, R_f = 0.21) as a pale yellow solid, mp. 86–89 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.21 (t, J = 7.1 Hz, 3H), 1.25–1.33 (m, 2H), 1.39–1.50 (m, 3H), 1.53–1.59 (m, 1H), 1.67–1.73 (m, 1H), 1.78–1.84 (m, 2H), 2.07–2.14 (m, 1H), 2.22–2.25 (m, 2H), 3.41 (br s, 1H), 3.44 (dd, J = 6.7 Hz, J = 5.1 Hz, 1H), 4.06 (q, J = 7.1 Hz, 2H), 6.53 (dd, J = 8.2 Hz, J = 4.3 Hz, 1H), 6.67–6.72 (m, 2H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.1 (CH_3), 21.1 (CH_2), 21.3 (CH_2), 28.7 (CH_2), 29.9 (CH_2), 32.6 (CH_2), 32.9 (CH_2), 46.8 (C), 60.3 (CH_2), 63.8 (CH), 110.0 (d, ^2J = 23.6 Hz, CH), 110.4 (d, ^3J = 8.1 Hz, CH), 113.2 (d, ^2J = 23.2 Hz, CH), 136.4 (d, ^3J = 6.9 Hz, C), 145.9 (C), 157.0 (d, ^1J = 235.3 Hz, C), 173.7 (C) ppm. ^{19}F{^{1}H}-NMR (470 MHz, $CDCl_3$): δ = –126.00 ppm. IR (ATR): $\tilde{\nu}$ = 3353 (m), 2989 (w), 2932 (m), 2857 (w), 1724 (vs), 1604 (w), 1479 (s), 1450 (m), 1417 (w), 1376 (m), 1296 (m), 1250 (m), 1206 (s), 1180 (m), 1046 (m), 1029 (m), 1016 (m), 1001 (m), 904 (m), 876 (m), 861 (m), 823 (m), 810 (m), 744 (m), 663 (m), 562 (m), 504 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 291.1629 (for $C_{17}H_{22}FNO_2^{+}$), found 291.1627 [M$^+$]. $C_{17}H_{22}FNO_2$ (291.37 g mol^{-1}).

Ethyl *cis*-3-(9-benzyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)propanoate (10f). According to GPB, δ-oxoester **9a** (198 mg, 1.00 mmol) and 1-benzyl-1-phenylhydrazine[19] (238 mg, 1.20 mmol) were converted with $NaBH(OAc)_3$ (424 mg, 2.00 mmol) in AcOH (2 mL) to yield the title compound **10f** (266 mg, 732 μmol, 73 %) after chromatography (SiO_2, hexanes/MTBE, 9:1, R_f = 0.28) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3H), 1.29–1.41 (m, 2H), 1.46–1.60 (m, 3H), 1.61–1.72 (m, 2H), 1.82–1.87 (m, 1H), 1.94–1.99 (m, 1H), 2.12–2.35 (m, 3H), 3.28 (t, J = 5.0 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 4.15 (d, J = 15.7 Hz, 1H), 4.42 (d, J = 15.7 Hz, 1H), 6.43 (d, J = 7.8 Hz, 1H), 6.72 (t, J = 7.3 Hz, 1H), 6.99 (d, J =

7.2 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 7.1 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.40 (d, *J* = 7.4 Hz, 2H) ppm. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 21.0 (CH_2), 21.4 (CH_2), 24.0 (CH_2), 30.2 (CH_2), 31.4 (CH_2), 34.2 (CH_2), 45.7 (C), 50.2 (CH_2), 60.2 (CH_2), 67.3 (CH), 107.9 (CH), 117.6 (CH), 121.9 (CH), 126.8 (CH), 127.3 (2 CH), 127.4 (CH), 128.4 (2 CH), 135.2 (C), 139.0 (C), 151.2 (C), 173.9 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2929 (m), 2855 (w), 1730 (vs), 1603 (m), 1494 (w), 1479 (s), 1452 (m), 1374 (w), 1353 (w), 1300 (w), 1266 (w), 1174 (m), 1156 (w), 1026 (m), 734 (vs), 696 (s) cm^{-1}. HR-MS (EI, 70 eV): calcd. 363.2193 (for $C_{24}H_{29}NO_2^+$), found 363.2192 [M^+]. $C_{24}H_{29}NO_2$ (363.50 g mol^{-1}).

Ethyl *cis*-3-(9-allyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)-propanoate (10g). According to GPB, δ-oxoester **9a** (117 mg, 590 µmol) and 1-allyl-1-phenylhydrazine[20] (105 mg, 708 µmol) were converted with $NaBH(OAc)_3$ (250 mg, 1.18 mmol) in AcOH (1 mL) to yield the title compound **10g** (144 mg, 459 µmol, 78 %) after chromatography (SiO_2, hexanes/MTBE, 9:1, R_f = 0.30) as a colorless oil. ^1H-NMR (500 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.1 Hz, 3H), 1.34–1.39 (m, 2H), 1.42–1.56 (m, 3H), 1.62–1.65 (m, 2H), 1.69–1.74 (m, 1H), 1.93 (ddd, *J* = 13.7 Hz, *J* = 10.5 Hz, *J* = 5.6 Hz, 1H), 2.16–2.31 (m, 3H), 3.26 (t, *J* = 4.8 Hz, 1H), 3.59 (ddt, *J* = 16.1 Hz, *J* = 6.7 Hz, *J* = 1.5 Hz, 1H), 3.85 (ddt, *J* = 16.1 Hz, *J* = 4.8 Hz, *J* = 1.8 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 5.17 (dq, *J* = 10.3 Hz, *J* = 1.6 Hz, 1H), 5.28 (dq, *J* = 17.2 Hz, *J* = 1.6 Hz, 1H), 5.89 (dddd, *J* = 17.2 Hz, *J* = 10.3 Hz, *J* = 6.7 Hz, *J* = 4.8 Hz, 1H), 6.50 (d, *J* = 7.7 Hz, 1H), 6.68 (td, *J* = 7.4 Hz, *J* = 1.0 Hz, 1H), 6.94 (dd, *J* = 7.2 Hz, *J* = 1.3 Hz, 1H), 7.06 (td, *J* = 7.6 Hz, *J* = 1.4 Hz, 1H) ppm. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 20.7 (CH_2), 21.3 (CH_2), 23.7 (CH_2), 30.3 (CH_2), 31.0 (CH_2), 34.6 (CH_2), 45.5 (C), 48.2 (CH_2), 60.3 (CH_2), 66.4 (CH), 107.8 (CH), 116.7 (CH_2), 117.5 (CH), 121.8 (CH), 127.4 (CH), 134.3 (CH), 135.4 (C), 150.7 (C), 174.0 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3073 (w), 3049 (w), 2980 (w), 2929 (m), 2856 (w), 1732 (vs), 1604 (m), 1477 (s), 1460 (m), 1373 (w), 1302 (w), 1249 (w), 1176 (m), 1157 (m), 1024 (m), 917 (m), 754 (s), 739 (vs) cm^{-1}. HR-MS (EI, 70 eV): calcd. 313.2036 (for $C_{20}H_{27}NO_2^+$), found 313.2028 [M^+]. $C_{20}H_{27}NO_2$ (313.44 g mol^{-1}).

Ethyl *cis*-3-(5a,6,7,8,9,10-hexahydro-5*H*-cyclohepta[*b*]indol-10a-yl)propanoate (10h). A solution of δ-oxoester **9b** (213 mg, 1.00 mmol) and phenylhydrazine (162 mg, 1.50 mmol) in glacial acetic acid (2 mL) was stirred at 100 °C for 5 h and subsequently cooled to ambient temperature. Then $NaBH(OAc)_3$ (424 mg, 2.00 mmol) was added and the resulting mixture was further stirred at ambient temperature for 16 h. The mixture was diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ solution (10 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by column chromatography (SiO_2, hexanes/MTBE, 4:1 + 2 % NEt_3, R_f = 0.27) to yield the crude product together with some starting material **9b**. For further purification, this fraction was diluted with MTBE (10 mL) and washed with half-concentrated hydrochloric acid (10 mL). The aqueous layer was then neutralized with sat. aq. $NaHCO_3$ solution (50 mL) and extracted with MTBE (3 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo to yield the title compound **10h** (106 mg, 369 µmol, 37 %) as a pale yellow oil. ^1H-NMR (500 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.2 Hz, 3H), 1.35–1.44 (m, 2H), 1.48–1.59 (m, 4H), 1.69–1.80 (m, 3H), 1.86 (ddd, *J* = 13.6 Hz, *J* = 11.8 Hz, *J* = 4.9 Hz, 1H), 1.93–2.03 (m, 2H), 2.09 (ddd, *J* = 15.5 Hz, *J* = 11.6 Hz, *J* = 5.0 Hz, 1H), 2.32 (ddd, *J* = 15.5 Hz, *J* = 11.8 Hz, *J* = 4.6 Hz, 1H), 3.56 (dd, *J* = 8.9 Hz, *J* = 2.6 Hz, 1H), 3.66 (br s, 1H), 4.02–4.08 (m, 2H), 6.53 (d, *J* = 7.8 Hz, 1H), 6.67 (td, *J* = 7.4 Hz, *J* = 1.0 Hz, 1H), 6.89 (dd, *J* = 7.3 Hz, *J* = 1.2 Hz, 1H), 7.00 (td, *J* = 7.6 Hz, *J* = 1.3 Hz, 1H) ppm. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$): δ = 14.1 (CH_3), 24.5 (CH_2), 25.7 (CH_2), 29.6 (CH_2), 30.9 (CH_2), 33.9 (CH_2), 36.8 (CH_2), 37.2 (CH_2), 51.1 (C), 60.1 (CH_2), 68.5 (CH), 108.2 (CH), 117.7 (CH), 123.4 (CH), 127.5 (CH), 134.0 (C), 149.8 (C), 174.1 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3380 (w), 2980 (w), 2922 (m), 2853 (m), 1724 (s), 1606 (m), 1486 (m), 1464 (m), 1456 (m), 1374 (w), 1314 (w), 1297 (w), 1254 (w), 1162 (m), 1094 (w), 1020 (m), 910 (m), 860 (w), 730 (vs), 649 (w), 586 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 287.1880 (for $C_{18}H_{25}NO_2^+$), found 287.1875 [M^+]. $C_{18}H_{25}NO_2$ (287.40 g mol^{-1}).

Ethyl *cis*-3-(2-acetyl-2,3,4,4a,5,9b-hexahydro-1*H*-pyrido[4,3-*b*]-indol-9b-yl)propanoate (10j). According to GPB, δ-oxoester **9d** (241 mg, 1.00 mmol) and phenylhydrazine (130 mg, 1.20 mmol) were converted with $NaBH(OAc)_3$ (424 mg, 2.00 mmol) in AcOH (2 mL) to yield the title compound **10j** (100 mg, 316 µmol, 32 %) after chromatography (SiO_2, EtOAc/MeOH, 10:0.4, R_f = 0.22) as a pale yellow oil. At ambient temperature, NMR spectra showed partly doubled and broadened signal sets due to the amide moiety. At 373 K, the ^1H-NMR spectrum showed a single signal set. ^1H-NMR (500 MHz, [D_6]DMSO, 373 K): δ = 1.16 (t, *J* = 7.1 Hz, 3H), 1.68–1.72 (m, 1H), 1.82–1.98 (m, 7H), 2.08–2.14 (m, 1H), 2.25–2.32 (m, 1H), 3.40–3.65 (m, 5H), 4.02 (q, *J* = 7.1 Hz, 2H), 6.52 (d, *J* = 7.8 Hz, 1H), 6.56 (t, *J* = 7.3 Hz, 1H), 6.93–7.01 (m, 2H) ppm. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$): δ = 14.1 (2 CH_3), 21.2 (CH_3), 21.3 (CH_3), 26.4 (CH_2), 28.0 (CH_2), 29.55 (CH_2), 29.58 (CH_2), 30.3 (CH_2), 31.1 (CH_2), 37.5 (CH_2), 41.3 (CH_2), 45.7 (CH_2), 48.6 (C), 48.8 (C), 51.9 (CH_2), 59.9 (CH), 60.1 (CH), 60.3 (CH_2), 60.5 (CH_2), 109.4 (CH), 109.8 (CH), 118.8 (CH), 119.0 (CH), 122.6 (CH), 123.4 (CH), 128.2 (CH), 128.6 (CH), 130.4 (C), 131.3 (C), 150.1 (C), 150.5 (C), 169.4 (C), 169.7 (C), 173.2 (C), 173.4 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3312 (w), 2980 (w), 2927 (w), 2872 (w), 1727 (vs), 1629 (vs), 1607 (s), 1484 (m), 1466 (m), 1424 (m), 1367 (w), 1267 (w), 1179 (m), 1020 (m), 984 (w), 749 (s), 596 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 316.1781 (for $C_{18}H_{24}N_2O_3^+$), found 316.1776 [M^+]. $C_{18}H_{24}N_2O_3$ (316.40 g mol^{-1}).

Conversion of δ-oxoester 9e with phenylhydrazine and $NaBH(OAc)_3$: A solution of δ-oxoester **9e** (246 mg, 1.00 mmol) and phenylhydrazine (162 mg, 1.50 mmol) in glacial acetic acid (2 mL) was stirred at 100 °C for 16 h and subsequently cooled to ambient temperature. Then $NaBH(OAc)_3$ (530 mg, 2.50 mmol) was added and the resulting mixture was further stirred at ambient temperature for 3 h. The mixture was diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ solution (10 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by column chromatography (SiO_2, hexanes/MTBE, 3:1, R_f = 0.29) to yield in the first fraction the crude product **10k** together with some starting material **9e**. Secondly, dihydrobenzocarbazole **13k** (10 mg, 31 µmol, 3 %, R_f = 0.20) was obtained as a colorless oil in another fraction. For further purification, the crude product **10k** was diluted with MTBE (10 mL) and washed with half-concentrated hydrochloric acid (10 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent was removed in vacuo to recover the starting material **9e** (74 mg, 0.30 mmol, 30 %). The aqueous layer was then neutralized with sat. aq. $NaHCO_3$ solution (60 mL) and extracted with MTBE (3 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo to yield the title compound **10k** (126 mg, 392 µmol, 39 %) as a colorless oil. The product was isolated as a mixture of two diastereomers (*dr* = 81:19).

Ethyl 3-(6,6a,11,11a-tetrahydro-5*H*-benzo[*a*]carbazol-6a-yl)-propanoate (10k). ^1H-NMR (500 MHz, $CDCl_3$), major isomer: δ = 1.22 (t, *J* = 7.1 Hz, 3H), 1.79 (ddd, *J* = 13.3 Hz, *J* = 10.2 Hz, *J* = 5.4 Hz, 1H), 2.07–2.11 (m, 2H), 2.19–2.31 (m, 2H), 2.48 (ddd, *J* = 16.3 Hz, *J* = 10.0 Hz, *J* = 6.6 Hz, 1H), 2.59–2.64 (m, 2H), 4.05–4.12 (m, 2H), 4.60 (s, 1H), 6.54 (d, *J* = 7.7 Hz, 1H), 6.77 (t, *J* = 7.4 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.12–

7.30 (m, 3H) ppm; minor isomer: δ = 1.13 (t, J = 7.1 Hz, 3H), 1.27–1.30 (m, 2H), 1.52–1.59 (m, 1H), 2.13–2.15 (m, 2H), 2.19–2.31 (m, 1H), 3.03–3.06 (m, 2H), 3.92–3.96 (m, 2H), 4.58 (s, 1H), 6.86 (t, J = 7.4 Hz, 1H), 6.89 (d, J = 7.7 Hz, 1H), 7.12–7.49 (m, 6H) ppm; signals for the NH protons were not observed. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$), major isomer: δ = 14.2 (CH_3), 27.0 (CH_2), 29.8 (CH_2), 33.2 (CH_2), 36.0 (CH_2), 48.1 (C), 60.3 (CH_2), 65.3 (CH), 109.6 (CH), 118.8 (CH), 123.2 (CH), 126.7 (CH), 127.1 (CH), 127.8 (CH), 128.58 (CH), 128.62 (CH), 132.7 (C), 138.0 (C), 138.1 (C), 150.5 (C), 173.80 (C) ppm; minor isomer: δ = 14.1 (CH_3), 25.87 (CH_2), 25.92 (CH_2), 28.0 (CH_2), 29.3 (CH_2), 47.2 (C), 60.1 (CH_2), 70.4 (CH), 111.5 (CH), 119.6 (CH), 123.4 (CH), 123.6 (CH), 125.8 (CH), 126.5 (CH), 127.6 (CH), 128.3 (CH), 136.0 (C), 136.2 (C), 136.6 (C), 151.2 (C), 173.82 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3369 (w), 2980 (w), 2926 (w), 2852 (w), 1724 (vs), 1607 (m), 1484 (s), 1463 (m), 1393 (w), 1374 (w), 1306 (w), 1252 (w), 1177 (m), 1156 (m), 1122 (w), 1093 (w), 1023 (m) 944 (w), 909 (m), 864 (w), 742 (vs), 670 (w), 647 (w), 607 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 321.1723 (for $C_{21}H_{23}NO_2^+$), found 321.1714 [M$^+$]. $C_{21}H_{23}NO_2$ (321.42 g mol^{-1}).

Ethyl 3-(6,6a-dihydro-5*H*-benzo[*a*]carbazol-6a-yl)propanoate (13k). ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.11 (t, J = 7.1 Hz, 3H), 1.63–1.70 (m, 1H), 1.75–1.83 (m, 2H), 2.17–2.20 (m, 2H), 2.51 (dd, J = 13.6 Hz, J = 5.0 Hz, 1H), 3.01 (dd, J = 17.8 Hz, J = 6.0 Hz, 1H), 3.36 (ddd, J = 18.1 Hz, J = 12.6 Hz, J = 5.8 Hz, 1H), 3.88–3.98 (m, 2H), 7.24 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 7.33–7.36 (m, 2H), 7.38 (td, J = 7.6 Hz, J = 1.1 Hz, 1H), 7.42 (td, J = 7.5 Hz, J = 1.3 Hz, 1H), 7.70 (d, J = 7.7 Hz, 1H), 8.12 (d, J = 7.5 Hz, 1H) ppm. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$): δ = 14.0 (CH_3), 25.8 (CH_2), 27.9 (CH_2), 28.8 (CH_2), 31.4 (CH_2), 54.9 (C), 60.4 (CH_2), 120.9 (CH), 122.1 (CH), 125.4 (CH), 126.1 (CH), 126.9 (CH), 128.4 (CH), 129.0 (CH), 129.8 (C), 131.3 (CH), 139.7 (C), 142.4 (C), 156.1 (C), 172.9 (C), 182.5 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3057 (w), 2980 (w), 2926 (w), 2857 (w), 1729 (s), 1574 (w), 1552 (m), 1453 (m), 1376 (w), 1352 (w), 1182 (w), 1157 (w), 1020 (w), 907 (m), 772 (m), 750 (s), 730 (s), 646 (w), 582 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 319.1567 (for $C_{21}H_{21}NO_2^+$), found 319.1571 [M$^+$]. $C_{21}H_{21}NO_2$ (319.40 g mol^{-1}).

Ethyl *cis*-3-(4b,5,9b,10-tetrahydroindeno[1,2-*b*]indol-9b-yl)propanoate (10l). According to GPB, δ-oxoester **9f** (220 mg, 947 μmol) and phenylhydrazine (123 mg, 1.14 mmol) were converted with $NaBH(OAc)_3$ (401 mg, 1.89 mmol) in AcOH (2 mL) to yield the title compound **10l** (82 mg, 0.27 mmol, 28 %) after chromatography (SiO_2, CH_2Cl_2/MeOH, 10:0.1, R_f = 0.45) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.22 (t, J = 7.1 Hz, 3H), 2.17–2.29 (m, 3H), 2.43–2.50 (m, 1H), 3.25 (d, J = 16.2 Hz, 1H), 3.39 (d, J = 16.2 Hz, 1H), 4.05–4.11 (m, 2H), 4.88 (s, 1H), 6.59 (d, J = 7.8 Hz, 1H), 6.75 (td, J = 7.4 Hz, J = 0.8 Hz, 1H), 7.01 (td, J = 7.7 Hz, J = 1.2 Hz, 1H), 7.13–7.22 (m, 4H), 7.29 (d, J = 7.0 Hz, 1H) ppm; a signal for the NH proton was not observed. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 30.3 (CH_2), 35.2 (CH_2), 45.5 (CH_2), 56.7 (C), 60.3 (CH_2), 72.2 (CH), 110.4 (CH), 119.3 (CH), 123.7 (CH), 123.8 (CH), 124.9 (CH), 127.1 (CH), 128.0 (CH), 128.2 (CH), 134.1 (C), 141.8 (C), 144.0 (C), 149.8 (C), 173.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3367 (w), 2980 (w), 2922 (w), 1724 (vs), 1607 (m), 1483 (s), 1464 (s), 1447 (w), 1392 (w), 1376 (m), 1297 (w), 1253 (w), 1163 (m), 1184 (m), 1100 (w), 1032 (m), 856 (w), 744 (vs), 582 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 307.1567 (for $C_{20}H_{21}NO_2^+$), found 307.1568 [M$^+$]. $C_{20}H_{21}NO_2$ (307.39 g mol^{-1}).

Ethyl *cis*-3-[9-(4-bromophenyl)sulfonyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl]propanoate (14). Brosyl chloride (102 mg, 399 μmol) was added to a solution of hexahydrocarbazole **10a** (109 mg, 399 μmol) in pyridine (0.4 mL) and CH_2Cl_2 (0.4 mL) and the resulting mixture was stirred at ambient temperature for 3 h. Subsequently, the mixture was diluted with CH_2Cl_2 (10 mL) and washed with brine (1 × 5 mL) and water (1 × 5 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/MTBE, 3:1, R_f = 0.29) to yield the title compound **14** (147 mg, 299 μmol, 75 %) as a colorless solid, mp. 116–118 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.04–1.14 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H), 1.20–1.28 (m, 2H), 1.36 (ddd, J = 13.8 Hz, J = 11.5 Hz, J = 5.2 Hz, 1H), 1.46–1.64 (m, 4H), 1.68 (ddd, J = 16.2 Hz, J = 11.4 Hz, J = 5.2 Hz, 1H), 1.85 (ddd, J = 16.2 Hz, J = 11.6 Hz, J = 5.1 Hz, 1H), 1.92–1.96 (m, 1H), 2.05–2.11 (m, 1H), 3.91 (dd, J = 8.1 Hz, J = 5.7 Hz, 1H), 4.00 (q, J = 7.1 Hz, 2H), 6.97 (d, J = 7.1 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1H), 7.22 (td, J = 7.8 Hz, J = 1.4 Hz, 1H), 7.57 (d, J = 8.6 Hz, 2H), 7.63 (d, J = 8.1 Hz, 1H), 7.71 (d, J = 8.6 Hz, 2H) ppm. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 19.9 (CH_2), 20.0 (CH_2), 28.6 (CH_2), 29.2 (CH_2), 29.8 (CH_2), 36.9 (CH_2), 46.5 (C), 60.4 (CH_2), 68.5 (CH), 115.3 (CH), 123.5 (CH), 123.8 (CH), 128.0 (C), 128.2 (2 CH), 128.3 (CH), 132.3 (2 CH), 136.0 (C), 137.9 (C), 140.4 (C), 172.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3086 (w), 2934 (m), 2855 (w), 1727 (s), 1603 (w), 1573 (m), 1473 (m), 1459 (s), 1392 (m), 1347 (s), 1302 (w), 1279 (w), 1247 (w), 1160 (s), 1097 (m), 1069 (m), 1009 (m), 979 (m), 846 (m), 833 (m), 760 (s), 733 (m), 712 (w), 701 (w), 616 (vs), 599 (s), 564 (vs), 550 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 491.0760 (for $C_{23}H_{26}BrNO_4S^+$), found 491.0770 [M$^+$]. $C_{23}H_{26}BrNO_4S$ (492.43 g mol^{-1}).

Ethyl *cis*-3-[9-(3,4,5-trimethoxyphenyl)carbamoyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl]propanoate (15). 3,4,5-Trimethoxyphenyl isocyanate (100 mg, 478 μmol) was added to a solution of hexahydrocarbazole **10a** (109 mg, 399 μmol) in abs. toluene (0.4 mL) and the resulting mixture was stirred at 100 °C for 3 h. Subsequently, the mixture was cooled to ambient temperature, diluted with CH_2Cl_2 (10 mL) and washed with hydrochloric acid (1 mol L^{-1}, 2 × 5 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/EtOAc, 1:1, R_f = 0.30) to yield the title compound **15** (136 mg, 282 μmol, 70 %) as a colorless solid, mp. 162–164 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.14–1.30 (m, 3H), 1.17 (t, J = 7.1 Hz, 3H), 1.50–1.63 (m, 3H), 1.71 (ddd, J = 13.8 Hz, J = 10.1 Hz, J = 5.8 Hz, 1H), 1.93 (ddd, J = 13.8 Hz, J = 10.3 Hz, J = 5.9 Hz, 1H), 2.03–2.10 (m, 1H), 2.19–2.25 (m, 3H), 3.81 (s, 3H), 3.86 (s, 6H), 3.97–4.04 (m, 2H), 4.07 (dd, J = 9.3 Hz, J = 6.2 Hz, 1H), 6.77–6.78 (m, 3H), 7.02 (t, J = 7.4 Hz, 1H), 7.09 (d, J = 7.0 Hz, 1H), 7.24 (td, J = 7.8 Hz, J = 1.6 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H) ppm. $^{13}C\{^1H\}$-NMR (125 MHz, $CDCl_3$): δ = 14.1 (CH_3), 21.4 (CH_2), 21.9 (CH_2), 28.5 (CH_2), 29.1 (CH_2), 30.1 (CH_2), 37.4 (CH_2), 46.1 (C), 56.1 (2 CH_3), 60.5 (CH_2), 60.9 (CH_3), 67.0 (CH), 97.5 (2 CH), 115.6 (CH), 122.7 (CH), 123.4 (CH), 128.2 (CH), 134.0 (C), 134.6 (C), 135.6 (C), 141.7 (C), 152.1 (C), 153.3 (2 C), 173.6 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3303 (w), 2929 (m), 2856 (w), 1732 (s), 1646 (vs), 1600 (vs), 1507 (vs), 1472 (s), 1447 (s), 1414 (s), 1370 (m), 1349 (m), 1317 (m), 1234 (m), 1124 (vs), 1014 (m), 823 (m), 752 (vs), 734 (s), 664 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 482.2411 (for $C_{27}H_{34}N_2O_6^+$), found 482.2412 [M$^+$]. $C_{27}H_{34}N_2O_6$ (482.58 g mol^{-1}).

Ethyl *cis*-3-[9-(4-iodobenzoyl)-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl]propanoate (16). 4-Iodobenzoic acid (149 mg, 600 μmol) was added to a solution of HATU (228 mg, 600 μmol) and DIPEA (78 mg, 0.60 mmol) in CH_2Cl_2 (2 mL) and the resulting mixture was stirred at ambient temperature for 1 h. Hexahydrocarbazole **10a** (109 mg, 399 μmol) was then added and the mixture was further stirred at ambient temperature for 16 h. Subsequently, the mixture was diluted with CH_2Cl_2 (5 mL) and washed with water (5 mL), sat. aq. $NaHCO_3$ solution (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/MTBE/CH_2Cl_2, 3:1:1) to yield in the first fraction the title compound **16** (105 mg, 209 μmol, 52 %, R_f = 0.39) as a

colorless oil. Secondly, starting material **10a** (15 mg, 55 μmol, 14 %, R_f = 0.31) was recovered in another fraction. ^{1}H-NMR (500 MHz, [D$_6$]DMSO, 373 K): δ = 0.99–1.13 (m, 3H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.41–1.45 (m, 1H), 1.50–1.57 (m, 2H), 1.79 (ddd, *J* = 14.0 Hz, *J* = 9.9 Hz, *J* = 6.0 Hz, 1H), 1.86–1.91 (m, 2H), 2.13 (ddd, *J* = 15.8 Hz, *J* = 9.9 Hz, *J* = 6.0 Hz, 1H), 2.18–2.26 (m, 2H), 4.01 (q, *J* = 7.1 Hz, 2H), 4.08 (t, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 7.3 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.33–7.34 (m, 1H), 7.88 (d, *J* = 8.2 Hz, 2H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, [D$_6$]DMSO, 373 K): δ = 13.3 (CH_3), 20.3 (CH_2), 22.6 (CH_2), 27.6 (CH_2), 28.39 (CH_2), 28.40 (CH_2), 35.9 (CH_2), 45.5 (C), 59.2 (CH_2), 66.4 (CH), 95.8 (C), 116.7 (CH), 122.7 (CH), 123.3 (CH), 126.8 (CH), 128.1 (2 CH), 135.8 (C), 136.5 (C), 137.0 (2 CH), 140.6 (C), 166.8 (C), 171.8 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2983 (w), 2936 (m), 2856 (w), 1716 (s), 1637 (s), 1584 (m), 1473 (s), 1459 (s), 1447 (m), 1393 (s), 1384 (vs), 1367 (m), 1272 (m), 1252 (m), 1032 (m), 1007 (s), 829 (s), 763 (m), 753 (vs), 746 (s), 687 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 503.0952 (for $C_{24}H_{26}INO_3^+$), found 503.0952 [M$^+$]. $C_{24}H_{26}INO_3$ (503.38 g mol^{-1}).

Ethyl *cis*-3-[9-(cyclohexylcarbonyl)-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl]propanoate (17). Cyclohexanecarboxylic acid (56 mg, 0.44 mmol) was added to a solution of HATU (167 mg, 439 μmol) and DIPEA (57 mg, 0.44 mmol) in CH_2Cl_2 (2 mL) and the resulting mixture was stirred at ambient temperature for 1 h. Hexahydrocarbazole **10a** (109 mg, 399 μmol) was then added and the mixture was further stirred at ambient temperature for 16 h. Subsequently, the mixture was diluted with CH_2Cl_2 (5 mL) and washed with water (5 mL), sat. aq. $NaHCO_3$ solution (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/MTBE/CH_2Cl_2, 3:1:1) to yield in the first fraction the title compound **17** (99 mg, 0.26 mmol, 65 %, R_f = 0.35) as a colorless oil. Secondly, starting material **10a** (10 mg, 38 μmol, 10 %, R_f = 0.30) was recovered in another fraction. ^{1}H-NMR (500 MHz, [D$_6$]DMSO, 323 K): δ = 0.95–1.03 (m, 2H), 1.11 (t, *J* = 7.1 Hz, 3H), 1.20–1.35 (m, 3H), 1.37–1.51 (m, 4H), 1.53–1.60 (m, 2H), 1.65–1.72 (m, 4H), 1.74–1.78 (m, 2H), 1.82–1.84 (m, 1H), 1.96–2.02 (m, 2H), 2.17–2.27 (m, 2H), 2.59 (br s, 1H), 3.95 (q, *J* = 7.1 Hz, 2H), 4.18–4.21 (m, 1H), 7.06 (td, *J* = 7.5 Hz, *J* = 0.9 Hz, 1H), 7.18–7.21 (m, 2H), 8.03 (br s, 1H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.1 (CH_3), 21.5 (CH_2), 22.5 (CH_2), 25.5 (CH_2), 25.7 (CH_2), 26.1 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 29.6 (CH_2), 29.9 (CH_2), 30.4 (CH_2), 37.3 (CH_2), 43.4 (CH), 46.1 (C), 60.4 (CH_2), 67.1 (CH), 119.0 (CH), 122.7 (CH), 123.5 (CH), 128.0 (CH), 135.3 (C), 141.6 (C), 173.4 (C), 174.7 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2926 (s), 2855 (m), 1732 (vs), 1652 (vs), 1597 (m), 1474 (s), 1460 (m), 1450 (m), 1403 (s), 1346 (m), 753 (vs), 737 (m) cm^{-1}. HR-MS (ESI, pos. mode): calcd. 384.2533 (for $C_{24}H_{34}NO_3^+$), found 384.2529 [M + H$^+$]. $C_{24}H_{33}NO_3$ (383.53 g mol^{-1}).

Ethyl *cis*-3-{9-[4-(trifluoromethyl)benzyl]-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl}propanoate (18). 4-(Trifluoromethyl)-benzaldehyde (70 mg, 0.40 mmol) was added to a solution of hexahydrocarbazole **10a** (109 mg, 399 μmol) in EtOH (0.8 mL) and the resulting mixture was stirred at 0 °C for 1 h. Then $ZnCl_2$ (27 mg, 0.20 mmol) and $NaCNBH_3$ (25 mg, 0.40 mmol) were added at 0 °C and the mixture was further stirred at ambient temperature for 3 h. Subsequently, the mixture was diluted with water (5 mL) and extracted with MTBE (3 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/MTBE, 2:1) to yield in the first fraction the title compound **18** (103 mg, 239 μmol, 60 %, R_f = 0.50) as a colorless solid, mp. 92–94 °C. Secondly, starting material **10a** (43 mg, 0.16 mmol, 40 %, R_f = 0.29) was recovered in another fraction. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.1 Hz, 3H), 1.31–1.41 (m, 2H), 1.47–1.55 (m, 3H), 1.57–1.63 (m, 1H), 1.65–1.72 (m, 1H), 1.81–1.86 (m, 1H), 1.94–2.00 (m, 1H), 2.20–2.35 (m, 3H), 3.27 (t, *J* = 5.0 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 4.20 (d, *J* = 16.2 Hz, 1H), 4.41 (d, *J* = 16.2 Hz, 1H), 6.35 (d, *J* = 7.8 Hz, 1H), 6.73 (td, *J* = 7.4 Hz, *J* = 1.0 Hz, 1H), 7.00 (dd, *J* = 7.3 Hz, *J* = 1.3 Hz, 1H), 7.03 (td, *J* = 7.7 Hz, *J* = 1.3 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3), 21.0 (CH_2), 21.4 (CH_2), 24.1 (CH_2), 30.2 (CH_2), 31.3 (CH_2), 34.2 (CH_2), 45.8 (C), 50.2 (CH_2), 60.3 (CH_2), 67.7 (CH), 108.0 (CH), 118.2 (CH), 122.1 (CH), 124.2 (q, *J* = 271.8 Hz, C), 125.4 (q, *J* = 3.7 Hz, 2 CH), 127.47 (CH), 127.49 (2 CH), 129.2 (q, *J* = 32.2 Hz, C), 135.3 (C), 143.4 (C), 150.9 (C), 173.9 (C) ppm. ^{19}F{^{1}H}-NMR (470 MHz, $CDCl_3$): δ = –62.40 ppm. IR (ATR): $\tilde{\nu}$ = 2993 (w), 2919 (m), 2850 (m), 1727 (vs), 1600 (m), 1476 (m), 1449 (m), 1323 (vs), 1313 (s), 1202 (m), 1126 (m), 1106 (m), 1066 (s), 1017 (m), 856 (m), 843 (s), 829 (m), 764 (vs), 756 (s), 749 (s), 604 (m) cm^{-1}. HR-MS (ESI, pos. mode): calcd. 454.1964 (for $C_{25}H_{28}F_3NNaO_2^+$), found 454.1972 [M + Na$^+$]. $C_{25}H_{28}F_3NO_2$ (431.50 g mol^{-1}).

Ethyl *cis*-3-(9-isobutyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)propanoate (19). Isobutyraldehyde (29 mg, 0.40 mmol) was added to a solution of hexahydrocarbazole **10a** (109 mg, 399 μmol) in EtOH (0.8 mL) and the resulting mixture was stirred at 0 °C for 1 h. Then $ZnCl_2$ (27 mg, 0.20 mmol) and $NaCNBH_3$ (25 mg, 0.40 mmol) were added at 0 °C and the mixture was further stirred at ambient temperature for 3 h. Subsequently, the mixture was diluted with water (5 mL) and extracted with MTBE (3 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, hexanes/MTBE, 5:1) to yield in the first fraction the title compound **19** (88 mg, 0.27 mmol, 67 %, R_f = 0.47) as a colorless oil. Secondly, starting material **10a** (26 mg, 95 μmol, 24 %, R_f = 0.06) was recovered in another fraction. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.98 (d, *J* = 6.6 Hz, 3H), 1.00 (d, *J* = 6.6 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.28–1.32 (m, 2H), 1.43–1.58 (m, 4H), 1.70–1.76 (m, 1H), 1.82–1.91 (m, 2H), 1.93–2.01 (m, 1H), 2.14–2.23 (m, 3H), 2.78–2.85 (m, 2H), 3.22 (dd, *J* = 6.4 Hz, *J* = 4.8 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 6.45 (d, *J* = 7.8 Hz, 1H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.93 (dd, *J* = 7.2 Hz, *J* = 0.8 Hz, 1H), 7.07 (td, *J* = 7.7 Hz, *J* = 1.2 Hz, 1H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 14.1 (CH_3), 20.7 (CH_3), 20.9 (CH_3), 21.2 (CH_2), 21.6 (CH_2), 24.5 (CH_2), 28.1 (CH), 30.1 (CH_2), 32.2 (CH_2), 33.3 (CH_2), 45.7 (C), 54.3 (CH_2), 60.2 (CH_2), 68.3 (CH), 107.1 (CH), 116.7 (CH), 122.0 (CH), 127.4 (CH), 134.4 (C), 151.5 (C), 174.0 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2927 (m), 2856 (w), 1732 (vs), 1604 (m), 1479 (s), 1460 (m), 1450 (m), 1174 (m), 1157 (m), 1024 (m), 737 (vs) cm^{-1}. HR-MS (EI, 70 eV): calcd. 329.2349 (for $C_{21}H_{31}NO_2^+$), found 329.2348 [M$^+$]. $C_{21}H_{31}NO_2$ (329.48 g mol^{-1}).

***cis*-3-(9-Benzyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)-propanoic acid (20).** A solution of hexahydrocarbazole **10f** (449 mg, 1.24 mmol) in conc. hydrochloric acid (4 mL) was heated to reflux for 2 h. Subsequently, the mixture was diluted with ice-water (15 mL) and extracted with MTBE (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo to yield the title compound **20** (394 mg, 1.17 mmol, 95 %) as a colorless solid, mp. 100–104 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.26–1.39 (m, 2H), 1.44–1.69 (m, 6H), 1.81–1.86 (m, 1H), 1.93 (ddd, *J* = 13.9 Hz, *J* = 10.8 Hz, *J* = 5.3 Hz, 1H), 2.17–2.24 (m, 1H), 2.26–2.37 (m, 2H), 3.24 (t, *J* = 5.1 Hz, 1H), 4.12 (d, *J* = 15.7 Hz, 1H), 4.40 (d, *J* = 15.7 Hz, 1H), 6.41 (d, *J* = 7.8 Hz, 1H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.96 (d, *J* = 7.2 Hz, 1H), 7.03 (td, *J* = 7.7 Hz, *J* = 1.0 Hz, 1H), 7.24–7.27 (m, 1H), 7.31–7.38 (m, 4H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 21.0 (CH_2), 21.4 (CH_2), 24.1 (CH_2), 29.9 (CH_2), 31.3 (CH_2), 34.1 (CH_2), 45.6 (C), 50.2 (CH_2), 67.3 (CH), 108.1 (CH), 117.7 (CH), 121.9 (CH), 126.9 (CH), 127.4 (2 CH), 127.5 (CH), 128.5 (2 CH), 134.9 (C), 138.9 (C), 151.2 (C), 179.8 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3023

(w), 2925 (m), 2850 (m), 1699 (vs), 1603 (m), 1476 (s), 1452 (m), 1433 (m), 1307 (m), 767 (m), 757 (m), 746 (s), 729 (vs), 696 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 335.1880 (for $C_{22}H_{25}NO_2^+$), found 335.1876 [M^+]. $C_{22}H_{25}NO_2$ (335.45 g mol^{-1}).

General procedure C (GPC) for the amide coupling of hexahydrocarbazole derivative 20. Hexahydrocarbazole carboxylic acid **20** (1.0 equiv.) was added to a solution of HATU (1.1 equiv.) and DIPEA (1.1 equiv.) in CH_2Cl_2 (5 L mol^{-1}) and the resulting mixture was stirred at ambient temperature for 1 h. Then the primary amine (1.5 equiv.) was added and the mixture was further stirred at ambient temperature for 16 h. Subsequently, the mixture was washed with water (1 × 5 L mol^{-1}), sat. aq. $NaHCO_3$ solution (1 × 5 L mol^{-1}) and brine (1 × 5 L mol^{-1}). The organic layer was dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography to yield hexahydrocarbazole carboxamides **21a–21d**.

***cis*-3-(9-Benzyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)-*N*-(2,2,2-trifluoroethyl)propanamide (21a).** According to GPC, hexahydrocarbazole carboxylic acid **20** (168 mg, 500 μmol) and 2,2,2-trifluoroethylamine (74 mg, 0.75 mmol) were converted with HATU (209 mg, 550 μmol) and DIPEA (71 mg, 0.55 mmol) in CH_2Cl_2 (2.5 mL) to yield the title compound **21a** (178 mg, 427 μmol, 86 %) after chromatography (SiO_2, hexanes/MTBE/CH_2Cl_2, 3:1:1, R_f = 0.34) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.28–1.38 (m, 2H), 1.47–1.56 (m, 3H), 1.57–1.63 (m, 1H), 1.65–1.71 (m, 1H), 1.81–1.86 (m, 1H), 1.91–1.97 (m, 1H), 2.08–2.14 (m, 1H), 2.17–2.28 (m, 2H), 3.24 (t, J = 5.0 Hz, 1H), 3.77–3.88 (m, 2H), 4.12 (d, J = 15.6 Hz, 1H), 4.41 (d, J = 15.6 Hz, 1H), 5.77 (br s, 1H), 6.44 (d, J = 7.8 Hz, 1H), 6.70 (t, J = 7.4 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H), 7.04 (td, J = 7.7 Hz, J = 1.2 Hz, 1H), 7.25–7.29 (m, 1H), 7.32–7.39 (m, 4 H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 20.8 (CH_2), 21.2 (CH_2), 24.0 (CH_2), 31.9 (CH_2), 32.0 (CH_2), 34.2 (CH_2), 40.5 (q, ^2J = 34.6 Hz, CH_2), 45.8 (C), 50.0 (CH_2), 67.3 (CH), 108.0 (CH), 117.6 (CH), 121.9 (CH), 124.0 (q, ^1J = 278.4 Hz, C), 126.9 (CH), 127.4 (2 CH), 127.5 (CH), 128.4 (2 CH), 135.0 (C), 138.9 (C), 151.2 (C), 173.4 (C) ppm. ^{19}F{^{1}H}-NMR (470 MHz, $CDCl_3$): δ = –72.45 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3300 (w), 3063 (w), 3029 (w), 2932 (m), 2856 (w), 1663 (m), 1603 (m), 1549 (m), 1494 (m), 1479 (m), 1460 (m), 1453 (m), 1396 (w), 1354 (w), 1266 (m), 1153 (vs), 1116 (m), 1027 (m), 991 (m), 953 (w), 906 (w), 873 (w), 833 (m), 733 (vs), 697 (s), 669 (m), 550 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 416.2070 (for $C_{24}H_{27}F_3N_2O^+$), found 416.2072 [M^+]. $C_{24}H_{27}F_3N_2O$ (416.49 g mol^{-1}).

***cis*-3-(9-Benzyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)-*N*-(*tert*-butyl)propanamide (21b)**. According to GPC, hexahydrocarbazole carboxylic acid **20** (168 mg, 500 μmol) and *tert*-butylamine (55 mg, 0.75 mmol) were converted with HATU (209 mg, 550 μmol) and DIPEA (71 mg, 0.55 mmol) in CH_2Cl_2 (2.5 mL) to yield the title compound **21b** (190 mg, 486 μmol, 97 %) after chromatography (SiO_2, hexanes/MTBE, 2:1, R_f = 0.32) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.30 (s, 9H), 1.32–1.40 (m, 2H), 1.47–1.56 (m, 3H), 1.60–1.71 (m, 2H), 1.76–1.81 (m, 1H), 1.89–2.00 (m, 2H), 2.03–2.09 (m, 1H), 2.20–2.26 (m, 1H), 3.26 (t, J = 4.8 Hz, 1H), 4.13 (d, J = 15.8 Hz, 1H), 4.40 (d, J = 15.8 Hz, 1H), 5.14 (s, 1H), 6.42 (d, J = 7.8 Hz, 1H), 6.70 (td, J = 7.4 Hz, J = 0.9 Hz, 1H), 6.97 (dd, J = 7.2 Hz, J = 1.0 Hz, 1H), 7.03 (td, J = 7.7 Hz, J = 1.3 Hz, 1H), 7.25 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 7.5 Hz, 2H), 7.38 (d, J = 7.5 Hz, 2H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 20.8 (CH_2), 21.3 (CH_2), 23.9 (CH_2), 28.7 (3 CH_3), 31.6 (CH_2), 33.1 (CH_2), 34.6 (CH_2), 45.8 (C), 50.2 (CH_2), 51.0 (C), 67.2 (CH), 107.9 (CH), 117.6 (CH), 121.9 (CH), 126.8 (CH), 127.3 (CH), 127.4 (2 CH), 128.4 (2 CH), 135.7 (C), 139.0 (C), 151.3 (C), 172.3 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3317 (w), 3050 (w), 3029 (w), 2966 (w), 2930 (m), 2857 (w), 1647 (m), 1603 (m), 1544 (m), 1510 (m), 1494 (m), 1479 (s), 1452 (s), 1392 (w), 1364 (m), 1317 (w), 1264 (m), 1224 (m), 1143 (w), 1027 (m), 731 (vs), 697 (s) cm^{-1}. HR-MS (EI, 70 eV): calcd. 390.2666 (for $C_{26}H_{34}N_2O^+$), found 390.2666 [M^+]. $C_{26}H_{34}N_2O$ (390.57 g mol^{-1}).

***cis*-3-(9-Benzyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)-*N*-(2-ethoxyethyl)propanamide (21c).** According to GPC, hexahydrocarbazole carboxylic acid **20** (168 mg, 500 μmol) and 2-ethoxyethylamine (67 mg, 0.75 mmol) were converted with HATU (209 mg, 550 μmol) and DIPEA (71 mg, 0.55 mmol) in CH_2Cl_2 (2.5 mL) to yield the title compound **21c** (199 mg, 489 μmol, 98 %) after chromatography (SiO_2, hexanes/MTBE, 1:4, R_f = 0.30) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.19 (t, J = 7.0 Hz, 3H), 1.26–1.37 (m, 2H), 1.45–1.55 (m, 3H), 1.59–1.69 (m, 2H), 1.77–1.82 (m, 1H), 1.94 (ddd, J = 13.4 Hz, J = 11.1 Hz, J = 4.9 Hz, 1H), 2.05 (ddd, J = 14.4 Hz, J = 11.0 Hz, J = 5.4 Hz, 1H), 2.13 (ddd, J = 14.4 Hz, J = 11.0 Hz, J = 4.9 Hz, 1H), 2.23 (ddd, J = 13.4 Hz, J = 11.1 Hz, J = 5.4 Hz, 1H), 3.26 (t, J = 4.9 Hz, 1H), 3.37–3.40 (m, 2H), 3.44–3.50 (m, 4H), 4.12 (d, J = 15.7 Hz, 1H), 4.40 (d, J = 15.7 Hz, 1H), 5.72 (br s, 1H), 6.43 (d, J = 7.8 Hz, 1H), 6.70 (t, J = 7.3 Hz, 1H), 6.97 (d, J = 7.1 Hz, 1H), 7.03 (td, J = 7.7 Hz, J = 0.9 Hz, 1H), 7.25 (t, J = 7.2 Hz, 1H), 7.32 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.4 Hz, 2H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 15.1 (CH_3), 20.9 (CH_2), 21.3 (CH_2), 23.9 (CH_2), 31.9 (CH_2), 32.3 (CH_2), 34.4 (CH_2), 39.3 (CH_2), 45.8 (C), 50.3 (CH_2), 66.3 (CH_2), 67.2 (CH), 69.0 (CH_2), 108.2 (CH), 117.8 (CH), 122.0 (CH), 126.9 (CH), 127.4 (CH), 127.5 (2 CH), 128.4 (2 CH), 135.5 (C), 138.8 (C), 151.1 (C), 173.0 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3440 (w), 3312 (w), 3050 (w), 2929 (m), 2856 (m), 1649 (m), 1603 (m), 1549 (m), 1522 (m), 1494 (m), 1479 (s), 1460 (m), 1452 (m), 1377 (m), 1352 (m), 1264 (m), 1113 (s), 1027 (m), 731 (vs), 697 (s) cm^{-1}. HR-MS (EI, 70 eV): calcd. 406.2615 (for $C_{26}H_{34}N_2O_2^+$), found 406.2612 [M^+]. $C_{26}H_{34}N_2O_2$ (406.57 g mol^{-1}).

***cis*-3-(9-Benzyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)-*N*-(4-bromophenyl)propanamide (21d).** According to GPC, hexahydrocarbazole carboxylic acid **20** (168 mg, 500 μmol) and 4-bromoaniline (129 mg, 0750 μmol) were converted with HATU (209 mg, 550 μmol) and DIPEA (71 mg, 0.55 mmol) in CH_2Cl_2 (2.5 mL) to yield the title compound **21d** (225 mg, 460 μmol, 92 %) after chromatography (SiO_2, hexanes/MTBE, 2:1, R_f = 0.35) as a colorless solid, mp. 72–79 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.27–1.38 (m, 2H), 1.49–1.55 (m, 3H), 1.56–1.62 (m, 1H), 1.66–1.72 (m, 1H), 1.82–1.88 (m, 1H), 1.95–2.01 (m, 1H), 2.17–2.24 (m, 1H), 2.25–2.34 (m, 2H), 3.26 (t, J = 5.0 Hz, 1H), 4.11 (d, J = 15.6 Hz, 1H), 4.40 (d, J = 15.6 Hz, 1H), 6.44 (d, J = 7.8 Hz, 1H), 6.70 (t, J = 7.3 Hz, 1H), 6.97 (d, J = 7.1 Hz, 1H), 7.02 (br s, 1H), 7.05 (t, J = 7.7 Hz, 1H), 7.23–7.27 (m, 1H), 7.30–7.40 (m, 8H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 20.9 (CH_2), 21.3 (CH_2), 24.0 (CH_2), 32.0 (CH_2), 33.4 (CH_2), 34.2 (CH_2), 45.8 (C), 50.0 (CH_2), 67.4 (CH), 108.0 (CH), 116.6 (C), 117.6 (CH), 121.2 (2 CH), 122.0 (CH), 127.0 (CH), 127.5 (2 CH), 127.6 (CH), 128.5 (2 CH), 131.9 (2 CH), 135.0 (C), 137.0 (C), 138.8 (C), 151.3 (C), 171.4 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3292 (w), 3180 (w), 3112 (w), 3053 (w), 3027 (w), 2927 (m), 2853 (m), 1659 (s), 1602 (s), 1590 (s), 1534 (s), 1487 (s), 1478 (s), 1452 (m), 1394 (s), 1351 (w), 1313 (m), 1243 (m), 1176 (w), 1144 (w), 1112 (w), 1072 (m), 1026 (m), 1009 (m), 953 (w), 876 (w), 823 (s), 737 (vs), 696 (s), 536 (w), 506 (m) cm^{-1}. HR-MS (EI, 70 eV): calcd. 488.1458 (for $C_{28}H_{29}BrN_2O^+$), found 488.1463 [M^+]. $C_{28}H_{29}BrN_2O$ (489.46 g mol^{-1}).

***cis*-3-(9-Benzyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)-propanamide (21e).** Pyridine (214 mg, 2.70 mmol) and Boc_2O (491 mg, 2.25 mmol) were added to a solution of carboxylic acid **20** (503 mg, 1.50 mmol) in 1,4-dioxane (3 mL) and the resulting mixture was stirred at ambient temperature for 30 min. Then $(NH_4)_2CO_3$ (404 mg, 4.20 mmol) was added and the resulting mixture was stirred at ambient temperature for 16 h. Subsequently, the mixture was diluted with H_2O (7 mL) and extracted with MTBE (3 ×

7 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, EtOAc, R_f = 0.35) to yield the title compound **21e** (464 mg, 1.39 mmol, 93 %) as a colorless solid, mp. 44–52 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.32–1.41 (m, 2H), 1.48–1.59 (m, 3H), 1.61–1.72 (m, 2H), 1.81–1.86 (m, 1H), 1.95 (ddd, *J* = 12.9 Hz, *J* = 11.1 Hz, *J* = 4.7 Hz, 1H), 2.05–2.17 (m, 2H), 2.19–2.28 (m, 1H), 3.28 (t, *J* = 4.9 Hz, 1H), 4.14 (d, *J* = 15.7 Hz, 1H), 4.42 (d, *J* = 15.7 Hz, 1H), 5.54 (br s, 1H), 6.11 (br s, 1H), 6.45 (d, *J* = 7.8 Hz, 1H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 7.0 Hz, 1H), 7.05 (td, *J* = 7.7 Hz, *J* = 1.1 Hz, 1H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 7.4 Hz, 2H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 20.8 (CH_2), 21.2 (CH_2), 23.8 (CH_2), 31.4 (CH_2), 31.7 (CH_2), 34.2 (CH_2), 45.6 (C), 50.0 (CH_2), 67.1 (CH), 107.9 (CH), 117.5 (CH), 121.8 (CH), 126.8 (CH), 127.28 (2 CH), 127.31 (CH), 128.3 (2 CH), 135.2 (C), 138.8 (C), 151.1 (C), 176.1 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3447 (w), 3329 (w), 3186 (w), 3026 (w), 2926 (m), 2854 (m), 1660 (vs), 1602 (s), 1494 (m), 1477 (s), 1452 (m), 1399 (w), 1350 (w), 1314 (w), 1262 (w), 1182 (w), 1143 (w), 1113 (w), 1070 (w), 1026 (m), 950 (w), 874 (w), 734 (s), 696 (s), 569 (w) cm^{-1}. HR-MS (EI, 70 eV): calcd. 334.2040 (for $C_{22}H_{26}N_2O^+$), found 334.2035 [M$^+$]. $C_{22}H_{26}N_2O$ (334.46 g mol^{-1}).

Methyl *cis*-[2-(9-benzyl-2,3,4,4a,9,9a-hexahydro-1*H*-carbazol-4a-yl)ethyl]carbamate (22). A solution of KOH (139 mg, 2.48 mmol) in MeOH (2 mL) was added at 0 °C to a solution of amide **21e** (330 mg, 987 μmol) and $PhI(OAc)_2$ (319 mg, 990 μmol) in CH_2Cl_2 (2 mL). The resulting mixture was stirred at 0 °C for 15 min and for further 16 h at ambient temperature. Subsequently, the reaction mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2 hexanes/MTBE, 1:1, R_f = 0.39) to yield the title compound **22** (157 mg, 431 μmol, 44 %) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.27–1.38 (m, 2H), 1.45–1.63 (m, 4H), 1.65–1.71 (m, 1H), 1.78–1.88 (m, 2H), 2.04–2.10 (m, 1H), 3.09–3.23 (m, 2H), 3.30 (br t, *J* = 4.5 Hz, 1H), 3.64 (s, 3H), 4.13 (d, *J* = 15.7 Hz, 1H), 4.40 (d, *J* = 15.7 Hz, 1H), 4.60 (br s, 1H), 6.42 (d, *J* = 7.8 Hz, 1H), 6.72 (t, *J* = 7.3 Hz, 1H), 7.01–7.05 (m, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 7.3 Hz, 2H) ppm. ^{13}C{^{1}H}-NMR (125 MHz, $CDCl_3$): δ = 21.0 (CH_2), 21.4 (CH_2), 24.1 (CH_2), 34.2 (CH_2), 37.0 (CH_2), 37.6 (CH_2), 45.1 (C), 50.2 (CH_2), 51.9 (CH_3), 67.6 (CH), 108.1 (CH), 117.7 (CH), 121.9 (CH), 126.9 (CH), 127.3 (2 CH), 127.5 (CH), 128.4 (2 CH), 135.3 (C), 139.0 (C), 151.0 (C), 156.9 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3420 (w), 3339 (w), 3062 (w), 3026 (w), 2926 (m), 2854 (w), 1700 (s), 1603 (m), 1520 (m), 1494 (w), 1477 (s), 1452 (s), 1379 (w), 1354 (m), 1253 (s), 1190 (w), 1140 (m), 1113 (w), 1026 (m), 1001 (w), 946 (w), 777 (m), 733 (vs), 697 (s) cm^{-1}. HR-MS (EI, 70 eV): calcd. 364.2145 (for $C_{23}H_{28}N_2O_2^+$), found 364.2140 [M$^+$]. $C_{23}H_{28}N_2O_2$ (364.49 g mol^{-1}).

Acknowledgments

MTBE was obtained as a generous gift from Evonik Industries, Marl, Germany.

Keywords: Cyclization · Nitrogen heterocycles · Reductive indolization · Synthetic methods

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Received: September 10, 2020