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Kharasch-Type Cyclizations of 2-Substituted Indole Derivatives Surprisingly Lead to Spiroindoles

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Starting from 1*H*-indole-2-carboxylic acid, a series of spiro[2-oxoindole-pyrrolidines] could be synthesized in a straightforward manner. The key reaction is a Kharasch radical cyclization reaction of trichloroacetylated precursors. The identity of the tricyclic final products that were formed could be determined as spiro[2-oxoindole-pyrrolidines] by using a combination of different analytical techniques (^{1}H NMR, ^{13}C NMR, gHMBC, HRMS) and additional reactions. The produced skeletons are interesting from a medicinal point of view.

Introduction

Heterocyclic spiro compounds have raised a lot of interest because of their biological properties (such as anticancer activity, complexing agents, etc.)[1] as well as their synthetic use. From a synthetic point of view, in many cases the spiro carbon atom is difficult to construct and causes strain in the molecule. Often facile rearrangements opening perspectives for new pathways result.[2] Spirooxindoles belong to this class of spiro heterocycles and have been intensively investigated.[3] Their presence in several natural products and medicinal compounds have learned that these structures are interesting targets for synthetic programmes. The spiro[oxindole-3,3′-pyrrolidine] ring system in particular is a structural part in a number of bioactive compounds.[4] For example, pseudoindoxyl alkaloids (**1**, Figure 1) have an important antiviral activity and have raised attention in the area of cancer research.[5] Two other oxindole alkaloids used as antitumor compounds are horsfiline (**2**)[6] and coerusceline (**3**).[7] Recently a few spiro[oxindole-pyrrolidine] alkaloids were isolated as secondary metabolites from a.o. *Aspergillus fumigatus*, with as major function the disturbance of the animal cell cycle. The most important metabolites are spirotryprostatine A (**4**) and spirotryprostatine B (**5**).[8]

Some work has been performed on the synthesis of indole derivatives substituted at the C-3 position, since these can be synthesized more easily than 2-substituted ones.

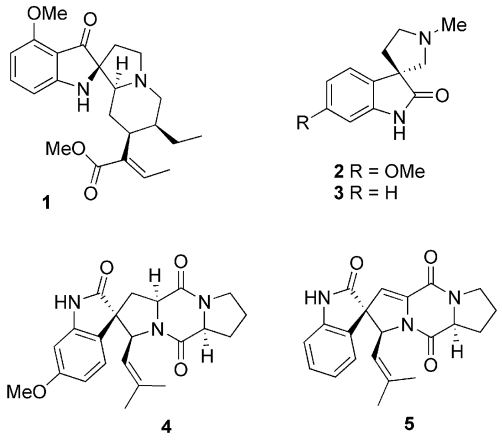

Figure 1. A few examples of biologically active spirooxindoles.

These examples mostly concern spirooxindole systems, having a C-3 spiro carbon atom. In earlier work, the HATRC (Halogen Atom Transfer Radical Cyclization) reaction and a domino radical cyclization route have been evaluated on highly functionalized 3-substituted indoles.[9] Related cyclizations of other substituted benzenes were also performed via radical reactions.[10] In this article, a straightforward synthetic route is presented towards spiroindoles having a spiro center at the C-2 position. The key step in this synthesis is a Kharasch-type ring closure resulting in the envisaged end products.

Results and Discussion

The synthesis of 1*H*-indole-2-carbaldehyde (**8**) has already been reported several times[11] and most of the procedures start with the reduction of the carboxylic acid **6** to indole-2-methanol (**7**), followed by oxidation to the alde-

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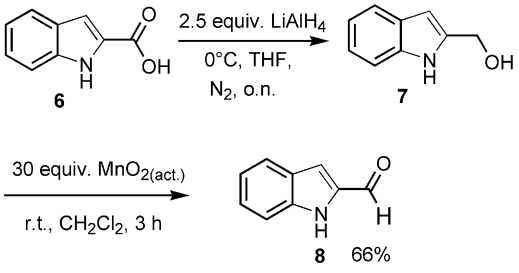
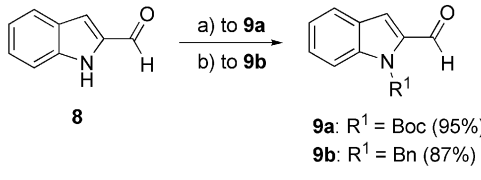
hyde **8**. Several procedures were evaluated: reduction of the carboxylic acid **6** with $LiAlH_4$ followed by oxidation with MnO_2 in one step,[11a] reduction of the corresponding ester with DIBAH again followed by oxidation,[11b] Rosenmund reduction of the corresponding acid chloride[12] and variations on these methods. However, the yields published by the authors (yields ranging from 64[11d] to 91[11a] and 95%[11f]) could not be repeated. The best results were obtained by reduction of indole-2-carboxylic acid (**6**) with $LiAlH_4$ in THF at 0 °C. After completion of the reaction, the mixture was quenched with saturated aqueous Na/K tartrate solution and filtered through Celite®. The tartrate enables the formed LiAl salts to dissolve again, releasing the indole-2-methanol **7** and making it again available for oxidation or isolation. The water layer and organic layer were then separated and the solvent was evaporated to give **7** as an intermediate. This alcohol was oxidized in CH_2Cl_2 with activated MnO_2 to give aldehyde **8**. The combined yield of this two-step synthesis was 66% (Scheme 1).



Scheme 1. Synthesis of starting compound 1*H*-indole-2-carbaldehyde (**8**).

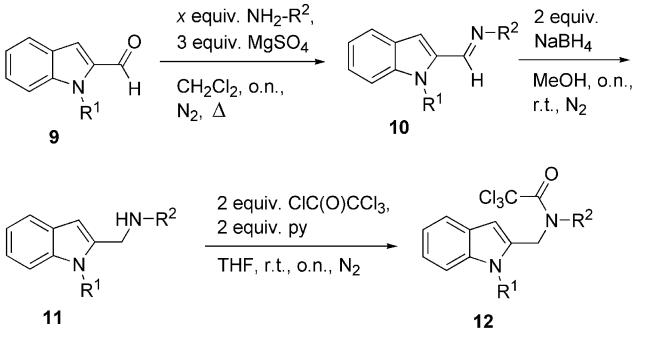
The carbaldehyde **8** was then first protected on the indole nitrogen to avoid the formation of byproducts in the following steps. Two protective groups were evaluated: a Boc group and a benzyl group. A literature procedure (reported yield 96%) was evaluated for the Boc protection, Boc anhydride (Boc_2O) and 4-(dimethylamino)pyridine in acetonitrile gave a complete conversion.[13] The protected carbaldehyde **9a** could be isolated in 95% yield after filtration through silica (Scheme 2). The benzyl group enlarges the electron density in the indole ring and thus promotes radical reactions with electrophilic radicals. The synthesis of this benzylated compound **9b** was also described several times in literature with a maximum yield of 94%.[14] Standard reaction conditions in one organic phase were evaluated (BnBr in dry acetone with K_2CO_3), but resulted in bad yields. Therefore, a benzylation procedure with 1 equiv. of



Scheme 2. *N*-protection of 1*H*-indole-2-carbaldehyde (**8**). Reaction conditions Scheme 2: a) 1.22 equiv. Boc_2O, 0.1 equiv. DMAP, CH_3CN, o.n., room temp.; b) 1 equiv. BnBr, 1.5 mol-% TBAB, *m*-THF/$NaOH_{(25\%)}$ (2:1), 2.5 h, reflux.

benzyl bromide in a mixture of methyl-THF and 25% $NaOH_{aq}$ (1:2) in the presence of TBAB as phase-transfer catalyst[15] was evaluated and resulted in the benzyl-protected indole-2-carbaldehyde **9b** in good yield (80%) (Scheme 2).

Having the protected aldehydes **9a**,**b** in hand, several imines were prepared thereof. For each protecting group, four different amines were used: isopropylamine, benzylamine, *p*-MeO-benzylamine and tritylamine. These amines were randomly picked, except for tritylamine. The trityl group was introduced to increase the molecular weight of the compounds in an attempt to prepare crystalline derivatives. A standard imination method was evaluated: the aldehyde together with 1 equiv. of amine (3 equiv. in the case of the volatile isopropylamine) and 3 equiv. of $MgSO_4$ were refluxed overnight, which led to good results in most of the cases (Scheme 3, Table 1). The imination of **9b** with isopropylamine, however, resulted in an incomplete conversion. With tritylamine, even no conversion was detected. Therefore, imines **10d**,**e**,**h** were prepared in the presence of 0.6 equiv. of the Lewis acid $TiCl_4$ and with an extra amount of amine (3.4 equiv. of isopropylamine or 1 equiv. of tritylamine + 2.4 equiv. of triethylamine) in dry diethyl ether. After work-up the imines could be recrystallized from methanol in fairly good yields: 57% for **10d**, 75% for **10e** and 61% for **10h**.



Scheme 3. Synthetic pathway from protected indole-2-carbaldehydes **9** to precursors for the ring-closure reaction of **12**.

Table 1. Reaction conditions for Scheme 3, towards the precursors for the ring closure of **12**.

Entry	R^1	R^2	Imine **10** yield (%)	Amine **11** yield (%)	Acetylated amine **12** yield (%)
a	Boc	*i*Pr	95	82	94
b	Boc	Bn	79	80	24
c	Boc	*p*-MeO-Bn	84	83	44
d	Boc	trityl	57[a]	–	–
e	Bn	*i*Pr	75[a]	98	74
f	Bn	Bn	81	83	53
g	Bn	*p*-MeO-Bn	83	82	62
h	Bn	trityl	61[a]	–	–

[a] Prepared with $TiCl_4$ instead of $MgSO_4$.

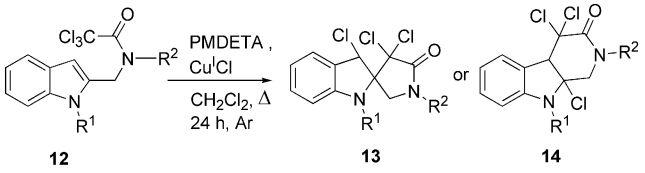
Subsequent reduction of these imines was accomplished with $NaBH_4$ in methanol while overnight stirring. This long reaction time was needed due to the poor solubility of the starting imines in methanol, but gave complete conversion and good yields in most of the cases (Table 1). However, no

reduction occurred in entry d and h with the tritylimines **10d** and **10h**. Another reduction method with $LiAlH_4$ in dry THF was evaluated on these imines, but this reaction resulted in degradation. Therefore, the reaction sequence was continued with the other derivatives.

Since the key ring-closing step in this synthesis is a Kharasch reaction, the precursors have to bear a halogen substituent to enable this radical reaction. Therefore, a trichloroacetyl group was introduced on the nitrogen atom using trichloroacetyl chloride. Pyridine was added as a base and the reaction was completed overnight. The resulting precursors **12** could be prepared in good yields (Table 1), however, exclusion of light was necessary (during work-up and afterwards) due to their light-sensitive character. Splitting of the signals in ^{1}H-NMR- and ^{13}C-NMR spectra was observed for the acetylated products **12b** and **12c**. This is due to the presence of rotamers caused by hindered rotation of the amide function in the proximity of the bulky Boc group, the trichloroacetyl group and the benzyl group. In the case of smaller side chains, no rotamers were observed.

The final key step in this synthetic route is the Kharasch cyclization. This radical reaction was performed under argon atmosphere in the presence of Cu^ICl and with PMDETA (*N*,*N*,*N*′,*N*′,*N*′′-pentamethyldiethylenetriamine) as a ligand. After 24 h of stirring in refluxing dichloromethane, the starting products were completely conversed into the new ring-closed products. These ring-closed products could be isolated after work-up in 81–85% crude yield. In most of the cases, several byproducts (ca. 20%) were formed and were difficult to remove. After a combination of chromatographic steps and recrystallizations, the compounds **13a**,**c**,**e**,**f**,**g** were obtained as powders in more than 95% purity. Unfortunately, this resulted in loss of product, which could not be avoided. In the case of **13b**, however, the impurities could not be removed and no spectroscopic data of this compound were included due to insufficient purity.

Although the AB-systems that appear in the ^{1}H-NMR spectra prove that the newly formed products are certainly cyclized molecules, two structures (**13** and **14**, same mass, functionalities and very similar spectra) were possible, resulting from two different ways of ring closing (Scheme 4). The spiro five-membered ring **13** results from a 5-*exo*-*trig* cyclization, while the annulated six-membered ring **14** would be formed by a 6-*endo*-*trig* cyclization. Many efforts were made to grow crystals from the obtained powders. This would enable X-ray crystallography on the resulting ring-closed compounds as a method for the unambiguous identification of the structure. Unfortunately, these efforts failed and no suitable crystals could be obtained. To determine which of the two possible compounds was formed, the spectroscopic data were thoroughly analyzed and a series of additional reactions were performed on the products (Table 2).



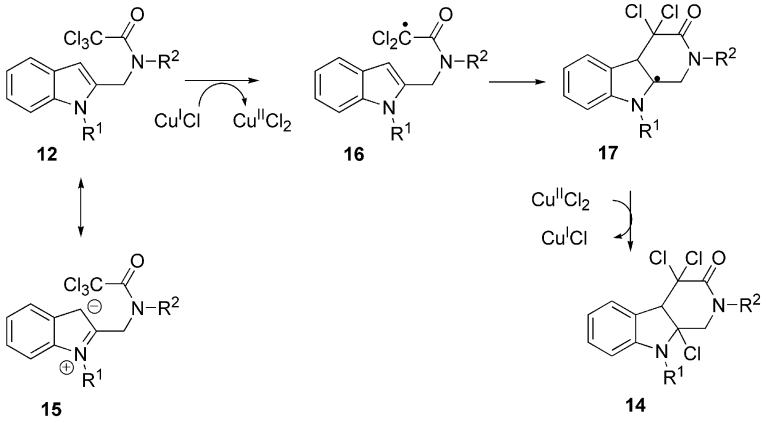
Scheme 4. Radical ring-closing reaction via HATRC.

Table 2. Conditions for the radical ring-closing reaction.

Entry	R^1	R^2	Product	Crude yield[a] (%)	Pure yield[b] (%)
1	Boc	*i*Pr	**13a** or **14a**	84	84[c]
2	Boc	Bn	**13b** or **14b**	85	–
3	Boc	*p*-MeO-Bn	**13c** or **14c**	83	20
4	Bn	*i*Pr	**13e** or **14e**	85	14
5	Bn	Bn	**13f** or **14f**	83	37
6	Bn	*p*-MeO-Bn	**13g** or **14g**	81	22

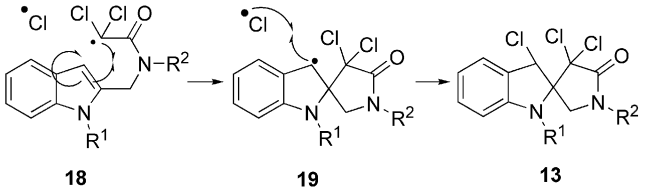
[a] Yield after work-up, without purification. [b] Yield after purification. [c] No purification necessary.

In theory, the radical formed with Cu^ICl on the trichloroacetamide function should attack the double bond at the most electron-rich position, which is C-3. When the radical reacts on this position, it would result in intermediate compound **17**. Termination of the reaction would occur when this radical reacts with a chlorine radical from $Cu^{II}Cl_2$, resulting in the annulated six-membered ring **14** (Scheme 5).



Scheme 5. Reaction mechanism towards the six-membered annulated ring **14**.

From the ^{1}H-NMR spectrum can be concluded that the compound is a ring closed product, since the signal from the CH_2 in the side chain is no longer a singlet, but an AB-system. The signal from the 3-H, however, has an abnormal high chemical shift: 6.02 ppm. This led to the consideration of another possible structure for this ring closed product, being a spiropyrrolidin-2-one-indole **13**. In this case, ring closing of the compound occurs at C-2 instead of C-3, resulting in the presence of a chlorine atom on the 3-position (Scheme 6). This could explain the upfield shift of the 3-H signal and the other signals could also be assigned to protons in the spiro structure.



Scheme 6. Reaction mechanism towards the five-membered spiro compound **13**.

HRMS (High Resolution Mass Spectrometry) confirmed that the exact mass of the investigated product was 433.7 g/mol, so corresponding to the compound containing all three chlorine atoms. This matches both of the proposed ring-closed products, but structure **14** would probably show more tendency to expel a chlorine atom, assisted by the nitrogen lone pair. In addition to the standard NMR analyses (^{1}H NMR, ^{13}C NMR, HSQC, DEPT), also a gHMBC (gradient-selected Heteronuclear Multiple Bond Correlation) spectrum was taken from **13a**. Some relevant long-range ^{1}H-^{13}C cross-couplings were observed and the most important ones are summarized in Table 3 and depicted in Figure 2.

Table 3. Most important long-range ^{1}H-^{13}C cross-couplings for **13a**.

	C-2 76.2	C-3 64.7	C-4 125.0	C-5 124.1	C-6 131.1	C-7 116.4	C-1′ 88.8	C-2′ 164.5	C-4′ 45.9
H-3 6.00							+		
H-4 7.39		+							
H-5 7.11									
H-6 7.35									
H-7 7.60									
Ha-4′ 4.13	+						+	+	
Hb-4′ 4.25	+						+	+	

Some conclusions could be made from these findings. The coupling of the protons at δ = 4.25 and 4.13 ppm with the carbon at δ = 88.8 ppm indicate that these atoms are three bonds apart, which is only possible on a five-membered structure. Hence it can be presumed that the ring-closed products are spirocyclic derivatives. These compounds possess two stereocenters, but only one diastereomer was isolated after ring-closure for each of the derivatives. This indicates the diastereoselectivity of the reaction towards only one of the diastereomers. However, since it was impossible to create single crystals of these

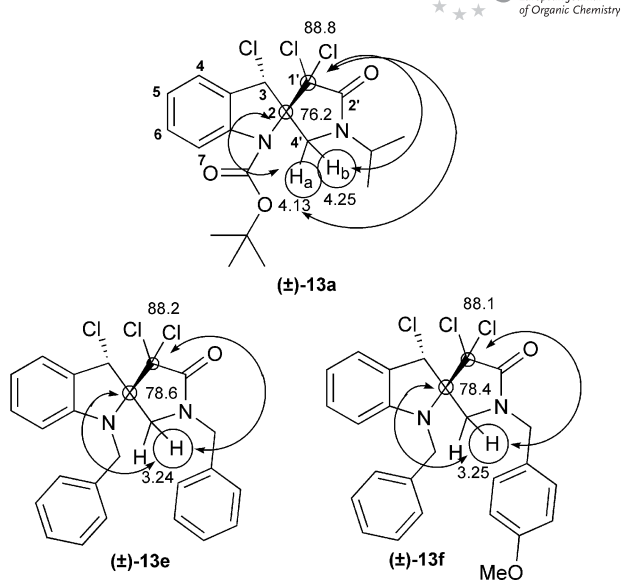


Figure 2. Important long-range ^{1}H-^{13}C cross-couplings for **13a**,**e**,**f**.

compounds, no X-ray analysis could be performed. From the NMR spectra, it was clear that the carbon signal at δ = 64.7 ppm is connected to a chlorine, which can be *syn* or *anti* to 88.8. The absence of a cross-peak between 6.00 ppm and 45.9 ppm in the gHMBC spectrum of **13a** indicated a small coupling constant and the presence of a cross-coupling of 6.00 ppm with 88.8 ppm indicated a larger coupling with this carbon. This is in agreement with an *anti* geometry of the chlorine at δ = 64.7 ppm and the carbon at δ = 88.8 ppm, relative to the five-membered ring of the indole moiety. Therefore, the *anti* diastereoisomer of the spiropyrrolidin-indol-2-one is suggested as the isolated compound.

Cyclic derivative **13f**, possessing a benzyl substituent on the indole nitrogen and a *p*-methoxy-benzyl substituent on the other nitrogen atom was also analyzed via HMBC spectroscopy. In this case, a clear cross-coupling was visible between one of the protons of the AB-system (at δ = 3.25 ppm) and the carbon containing two chlorine atoms (at δ = 88.13 ppm). Identical cross-couplings were visible in the HMBC spectrum of derivative **13e**. These findings confirm that the cyclic compounds are indeed spiro[indole-2,3′-pyrrolidines].

To get additional proof of the structure, a series of reactions were performed on one of the cyclic products, **13a**. In an aqueous solution, the compound remains stable, even after addition of NaOH. If the product would be an annulated six-membered ring **14a**, the chlorine atom on C-2 would probably be expelled under influence of the indole nitrogen, followed by the addition of OH^-. This does not occur which gives an indication that the structure is the spiropyrrolidin-2-one-indole **13a**. Attempts to remove the protective Boc group (to create a more electron-rich nitrogen atom, thus speeding up the expelling of the chlorine) failed under several reaction conditions, and therefore did not provide any additional information.

If a compound such as **14a** were treated with a base, a deprotonation of C-3 would be expected, followed by expulsion of the chlorine atom and thus restoring the aromatic system. In the case of a spiro compound **13a**, the addition of a base would have no result, since elimination of HCl is impossible from this structure. Upon treatment of the compound with the strong base KO*t*Bu, no reaction occurred and the compound remained completely intact. This is again indicative of the five-membered spiro-ring in **13a**. Repeating the reaction with K-HMDS resulted in complete decomposition, concluding that these reaction conditions were too harsh for the compound.

Removal of the chlorine atoms would result in different coupling patterns in the ^{1}H-NMR spectrum for the two possible structures. This hydrogenation was evaluated with zinc in acetic acid,[16] with H_2 and palladium on carbon and with L-Selectride. However, these reactions resulted in complex mixtures without identifiable products.

Conclusions

A straightforward synthesis of unexpected spiroindoles with a C-2 spiro atom is presented, starting from the commercial indole-2-carboxylic acid. The key ring closing step is a Kharasch reaction resulting in a tricyclic compound. Instead of the expected six-membered annulated indole derivative a five-membered spiro compound was formed. The identification of the structure as a spiro[indole-2,3′-pyrrolidine] could be concluded from a series of analytical results combined with synthetic reactions. The most decisive arguments are: 1) the coupling between the carbon bearing two chlorine atoms and the H-atoms from the AB-system in the side chain is clearly visible in the HMBC spectra, which is impossible in the case of a six-membered ring; 2) the recovery of the intact compound after treatment with base, so no deprotonation on C-3 followed by expelling of a chloride occurred, restoring the aromatic system (this deprotonation would be expected in the case of a six-membered ring) and 3) the stability of the compound in an aqueous solution, proving that nitrogen does not provide neighbouring group assistance to expel the chloride, followed by addition of OH^-.

Experimental Section

General: High-resolution ^{1}H NMR (300 MHz), ^{13}C NMR (75 MHz) and ^{31}P NMR (121 MHz) spectra were run on a Jeol Eclipse FT 300 NMR spectrometer. Peak assignments were obtained with the aid of DEPT, HSQC, DQFCOSY and HMBC spectra. The compounds were diluted in deuterated solvents and the used solvent is indicated for each compound. As internal standard, tetramethylsilane (TMS) was used. Multiplicities are described by the following symbols: s for singlet, d for doublet, t for triplet, q for quadruplet, p for pentuplet, m for multiplet; br.: broad, ps: pseudo. Low-resolution mass spectra of pure compounds were recorded via direct injection on an Agilent 1100 Series LC/MSD type SL mass spectrometer with Electron Spray Ionisation geometry (ESI 70 eV) and using a Mass Selective Detector (quadrupole). High resolution mass spectra were recorded on a Finnigan MAT 95 XP-API-GC-Trap tandem mass spectrometer system. IR spectra were obtained from a Perkin–Elmer Spectrum BX FT-IR System Spectrometer. Spectra for all of the compounds, liquid as well as crystalline were collected on a ZnSe-crystal in ATR mode. Only selected absorbances ($\tilde{\nu}_{max}$ /cm^{-1}) were reported. Melting points of crystalline compounds were measured with a Büchi B-540 apparatus. Elemental analyses were obtained by means of a Perkin–Elmer 2400 Series II apparatus.

Synthesis of Indole-2-methyleneamines 10a–h: As a representative example, the synthesis of [1-(*tert*-butoxycarbonyl)indole-2-methylene]isopropylamine (**10a**) is described here. To a solution of *tert*-butyl 2-formylindole-1-carboxylate (**9a**) (1.5 g; 6.12 mmol) in CH_2Cl_2 was added isopropylamine (1.09 g; 18.36 mmol) and $MgSO_4$ (2.21 g; 18.36 mmol). After stirring overnight at reflux temperature, the $MgSO_4$ was filtered off and the solvent was evaporated under vacuum. The product **10a** (1.66 g; 5.81 mmol; 95% yield) was obtained as a brown solid. The compound was too hygroscopic and sticky to take a reproducible melting point.

***tert*-Butyl 2-[(*E*)-(Isopropylimino)methyl]-1*H*-indole-1-carboxylate (10a):** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 [d, J = 6.4 Hz, 6 H, $CH(CH_3)_2$], 1.69 [s, 9 H, $C(CH_3)_3$], 3.59 [sept, J = 6.4 Hz, 1 H, $CH(CH_3)_2$], 7.16 (s, 1 H, 3-H), 7.22 (dd, J = 7.6, J = 7.6 Hz, 1 H, 5-H or 6-H), 7.33 (ddd, J = 8.0, J = 7.6, J = 1.1 Hz, 1 H, 5-H or 6-H), 7.55 (J = 7.6 Hz, 1 H, d, 4-H or 7-H), 8.11 (d, J = 8.0 Hz, 1 H, 4-H or 7-H), 8.79 (s, 1 H, C*H*=N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.11 [$CH(CH_3)_2$], 28.88 [$C(CH_3)_3$], 61.81 [$CH(CH_3)_2$], 84.55 [$C(CH_3)_3$], 110.82 (C-3), 115.75 (C-4 or C-7), 121.49 (C-4 or C-7), 123.21 (C-5 or C-6), 125.38 (C-5 or C-6), 128.89 (C_q), 137.06 (C_q), 137.29 (C_q), 150.27 (O=*C*–O), 152.24 (*C*H=N) ppm. IR: $\tilde{\nu}$ = 1731 ($\nu_{O=C-O}$) 1628 ($\nu_{C=N}$) cm^{-1}. MS (ESI, POS): *m*/*z* (%) = 287.3 (100) [M + H$^+$].

***tert*-Butyl 2-[(*E*)-(Benzylimino)methyl]-1*H*-indole-1-carboxylate (10b):** Compound **10b** was prepared from **9a** (2.2 g; 8.97 mmol) by the procedure described for **10a**. In this case, 1 equiv. of benzylamine was added. The product **10b** was obtained as a brown oil (2.37 g; 7.09 mmol; 79% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69 [s, 9 H, $C(CH_3)_3$], 4.85 (s, 2 H, CH_2-Ph), 7.24–7.36 (m, 8 H, 8× C*H*$_{ar}$), 7.57 (d, J = 7.7 Hz, 1 H, 4-H or 7-H), 8.11 (d, J = 8.8 Hz, 1 H, 4-H or 7-H), 8.96 (s, 1 H, C*H*=N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.45 [$C(CH_3)_3$], 65.40 (CH_2-Ph), 84.79 [$C(CH_3)_3$], 111.29 (*C*H$_{ar}$), 115.81 (C-4 or C-7), 121.70 (C-4 or C-7), 123.31 (*C*H$_{ar}$), 125.64 (*C*H$_{ar}$), 127.05 (*C*H$_{ar}$), 128.09 (2× *C*H$_{ar}$), 128.54 (*C*H$_{ar}$), 128.64 (C_q), 128.80 (C_q), 137.06 (C_q), 139.20 (C_q), 150.35 (*C*=O), 155.81 (*C*H=N) ppm. IR: $\tilde{\nu}$ = 1730 ($\nu_{C=O}$) 1631 ($\nu_{C=N}$) cm^{-1}. MS (ESI, POS): *m*/*z* (%) = 335.2 (100) [M + H$^+$].

***tert*-Butyl 2-[(*E*)-(4-Methoxybenzylimino)methyl]-1*H*-indole-1-carboxylate (10c):** Compound **10c** was prepared from **9a** (2.0 g; 8.15 mmol) by the procedure described for **10a**. In this case, 1 equiv. of *p*-methoxybenzylamine was added. The product **10c** was obtained as a brown oil (2.50 g; 6.85 mmol; 84% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69 [s, 9 H, $C(CH_3)_3$], 3.81 (s, 3 H, O-*C*H$_3$), 4.78 (s, 2 H, CH_2-Ph), 6.89 (d, J = 8.3 Hz, 2 H, 2× C*H*$_{ar}$), 7.21–7.37 (m, 5 H, 5× C*H*$_{ar}$), 7.56 (d, J = 7.7 Hz, 1 H, 4-H or 7-H), 8.11 (d, J = 8.8 Hz, 1 H, 4-H or 7-H), 8.93 (s, 1 H, C*H*=N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.29 [$C(CH_3)_3$], 55.33 (O-*C*H$_3$), 64.86 (CH_2-Ph), 84.75 [$C(CH_3)_3$], 111.21 (*C*H$_{ar}$), 113.95 (2× *C*H$_{ar}$), 115.81 (C-4 or C-7), 121.67 (C-4 or C-7), 123.29 (*C*H$_{ar}$), 125.61 (*C*H$_{ar}$), 128.80 (C_q), 129.29 (2× *C*H$_{ar}$), 131.31 (C_q), 137.06 (C_q), 137.11 (C_q), 150.35 (C_q), 155.42 (*C*H=N), 158.73 (C_q) ppm. IR: $\tilde{\nu}$ = 1730 ($\nu_{C=O}$) 1627 ($\nu_{C=N}$) cm^{-1}. MS (ESI, POS): *m*/*z* (%) = 365.2 (100) [M + H$^+$].

***tert*-Butyl 2-[(*E*)-(Tritylimino)methyl]-1*H*-indole-1-carboxylate (10d):** To a solution of 1-benzylindole-2-carbaldehyde **9a** (0.75 g; 3.06 mmol) in dry diethyl ether (40 mL) was added dropwise $TiCl_4$ (0.35 g; 0.6 equiv.; 1.84 mmol) in dry petroleum ether (20 mL) at 0 °C under a nitrogen atmosphere. After following dropwise addition of tritylamine (0.79 g; 3.06 mmol) and triethylamine (0.74 g; 7.34 mmol) in dry diethyl ether (20 mL), the mixture was stirred overnight at room temperature under nitrogen. The reaction mixture was then poured into an aqueous 2 N NaOH solution (40 mL) and extracted with diethyl ether (2 × 40 mL). The organic phase is dried with $MgSO_4$ and K_2CO_3, filtered and the solvents evaporated in vacuo. Recrystallization from methanol resulted in the product **10d** (0.85 g; 1.74 mmol; 57% yield) as a yellow glass-like powder; recrystallization from MeOH. No reproducible melting point could be determined due to the high hygroscopicity and stickyness of the product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.43 [s, 9 H, C(CH_3)$_3$], 7.21–7.36 (m, 17 H, 17 × CH_{ar}), 7.44 (s, 1 H, 3-H), 7.61 (d, J = 7.7 Hz, 1 H, 4-H or 7-H), 8.14 (d, J = 8.3 Hz, 1 H, 4-H or 7-H), 8.42 (s, 1 H, CH=N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.10 [C(CH_3)$_3$], 79.03 (CPh$_3$), 84.62 [C(CH$_3$)$_3$], 111.12 (CH$_{ar}$), 115.67 (CH$_{ar}$), 121.58 (CH$_{ar}$), 123.26 (CH$_{ar}$), 125.58 (CH$_{ar}$), 126.89 (3 × CH$_{ar}$), 127.83 (6 × CH$_{ar}$), 128.76 (C$_q$), 129.84 (C$_q$), 129.99 (6 × CH$_{ar}$), 137.63 (C$_q$), 145.66 (3 × C$_q$), 150.05 (C=O), 153.87 (CH=N) ppm. IR: $\tilde{\nu}$ = 1732 ($\nu_{C=O}$) 1629 ($\nu_{C=N}$) cm^{-1}. MS (ESI, POS): m/z (%) = 300.3 (100), 305.2 (80), 487.3 (60) [M + H$^+$].

***N*-[(*E*)-(1-Benzyl-1*H*-Indol-2-yl)methylidene]isopropylamine (10e):** Compound **10e** was prepared from **9b** (0.76 g; 3.23 mmol) by the procedure described for **10d**. In this case, 3.5 equiv. of isopropylamine (0.67 g; 11.31 mmol) was added (instead of tritylamine and triethylamine). The product **10e** was obtained as yellow-brown crystals (0.51 g; 1.84 mmol; 75% yield), m.p. 85.2–87.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 [d, J = 6.4 Hz, 6 H, CH-(CH_3)$_2$], 3.39 [sept, J = 6.4 Hz, 1 H, CH(CH$_3$)$_2$], 5.99 (s, 2 H, CH_2-Ph), 6.83 (s, 1 H, 3-H), 7.07–7.26 (m, 7 H, 7 × CH_{ar}), 7.33 (~d, J = 8.3 Hz, 1 H, 4-H or 7-H), 7.64 (d, J = 8.3 Hz, 1 H, 4-H or 7-H), 8.36 (s, 1 H, CH=N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.36 [CH(CH_3)$_2$], 47.95 (CH_2-Ph), 62.44 [CH(CH$_3$)$_2$], 109.59 (CH$_{ar}$), 110.40 (CH$_{ar}$), 120.20 (CH$_{ar}$), 121.68 (C-4 or C-7), 123.92 (CH$_{ar}$), 126.90 (3 × CH$_{ar}$), 127.33 (C$_q$), 128.37 (2 × CH$_{ar}$), 135.25 (C$_q$), 138.98 (C$_q$), 139.68 (C$_q$), 150.54 (C=N) ppm. IR: $\tilde{\nu}$ = 1638 ($\nu_{C=N}$) cm^{-1}. MS (ESI, POS): m/z (%) = 277.2 (100) [M + H$^+$].

***N*-[(*E*)-(1-Benzyl-1*H*-indol-2-yl)methylidene]-1-phenylmethanamine (10f):** Compound **10f** was prepared from **9b** (3.20 g; 13.60 mmol) by the procedure described for **10a**. In this case, 1 equiv. of benzylamine was added. After recrystallization from methanol, product **10f** was obtained as yellow crystals (3.57 g; 11.02 mmol; 81% yield), m.p. 87.9–89.3 °C. Recrystallization (MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.73 (s, 2 H, =N-CH_2-Ph), 6.01 (s, 2 H, Ph-CH_2-N$_{ind}$), 6.90 (s, 1 H, 3-H), 6.99–7.02 (m, 2 H, 2 × CH_{ar}), 7.09–7.28 (m, 10 H, 10 × CH_{ar}), 7.31 [ps (d), 1 H, CH_{ar}], 7.66 (d, J = 7.7 Hz, 1 H, 4-H or 7-H), 8.45 (s, 1 H, CH=N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.06 (CH$_2$-N$_{ind}$), 65.63 (=N-CH$_2$-Ph), 110.50 (CH$_{ar}$), 110.76 (CH$_{ar}$), 120.40 (CH$_{ar}$), 121.87 (C-4 or C-7), 124.38 (CH$_{ar}$), 126.63 (CH$_{ar}$), 126.83 (2 × CH$_{ar}$), 126.95 (CH$_{ar}$), 127.30 (C$_q$), 127.68 (2 × CH$_{ar}$), 128.46 (2 × CH$_{ar}$), 128.52 (2 × CH$_{ar}$), 135.03 (C$_q$), 138.84 (C$_q$), 139.73 (C$_q$), 139.88 (C$_q$), 154.46 (CH=N) ppm. IR: $\tilde{\nu}$ = 1629 ($\nu_{C=N}$) cm^{-1}. MS (ESI, POS): m/z (%) = 325.2 (100) [M + H$^+$]. $C_{23}H_{20}N_2$ (324.42): calcd. C 85.16, H 6.21, N 8.63; found C 84.86, H 6.43, N 8.57.

***N*-[(*E*)-(1-Benzyl-1*H*-indol-2-yl)methylidene]-1-(4-methoxyphenyl)-methanamine (10g):** Compound **10g** was prepared from **9b** (2.90 g; 12.33 mmol) by the procedure described for **10a**. In this case, 1 equiv. of *p*-methoxybenzylamine was added. After recrystallization from methanol, product **10g** was obtained as pale yellow crystals (3.63 g; 10.23 mmol; 83% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OCH_3), 4.66 (s, 2 H, =N-CH_2-Ph), 5.98 (s, 2 H, Ph-CH_2-N$_{ind}$), 6.78 [ps (d), J = 8.8 Hz, 2 H, 2 × CH_{ar}], 6.88 (s, 1 H, 3-H), 6.98–7.24 (m, 9 H, 9 × CH_{ar}), 7.30 (d, J = 8.3 Hz, 1 H, CH_{ar}), 7.65 (d, J = 7.7 Hz, 1 H, 4-H of 7-H), 8.41 (s, 1 H, CH=N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.03 (CH$_2$-N$_{ind}$), 55.37 (O-CH$_3$), 65.07 (=N-CH$_2$-Ph), 110.49 (2 × CH$_{ar}$), 110.61 (CH$_{ar}$), 113.85 (2 × CH$_{ar}$), 120.41 (CH$_{ar}$), 121.85 (C-4 of C-7), 124.31 (CH$_{ar}$), 126.64 (CH$_{ar}$), 126.93 (CH$_{ar}$), 127.32 (C$_q$), 128.51 (2 × CH$_{ar}$), 128.89 (2 × CH$_{ar}$), 131.81 (C$_q$), 135.07 (C$_q$), 138.87 (C$_q$), 139.84 (C$_q$), 154.10 (CH=N), 158.55 (C$_q$-OMe) ppm. IR: $\tilde{\nu}$ = 1632 ($\nu_{C=N}$) cm^{-1}. MS (ESI, POS): m/z = 355.2 (M + H$^+$, 100), m.p. 117.4–119.2 °C.

***N*-[(*E*)-(1-Benzyl-1*H*-indol-2-yl)methylidene]tritylamine (10h):** Compound **10h** was prepared from **9b** (0.61 g; 2.58 mmol) by the procedure described for **10d**. In this case, tritylamine (0.67 g; 2.58 mmol) and triethylamine (0.63 g; 2.4 equiv.; 6.2 mmol) in dry diethyl ether (20 mL) were added. The product **10h** was obtained as a white glass-like powder (0.75 g; 1.58 mmol; 61% yield) and was again too hygroscopic to take a reproducible melting point. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.16 (s, 2 H, CH_2-Ph), 6.77 (s, 1 H, 3-H), 6.96–7.00 (m, 2 H, 2 × CH$_{ar}$), 7.06–7.35 (m, 21 H, 21 × CH_{ar}), 7.61 (d, J = 7.7 Hz, 1 H, 4-H or 7-H), 7.92 (s, 1 H, CH=N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.41 (CH$_2$-Ph), 79.46 (CPh$_3$), 110.54 (CH$_{ar}$), 111.83 (C-3), 120.54 (CH$_{ar}$), 121.96 (C-4 or C-7), 124.63 (CH$_{ar}$), 126.35 (2 × CH$_{ar}$), 126.89 (3 × CH$_{ar}$), 127.04 (CH$_{ar}$), 127.36 (C$_q$), 127.89 (6 × CH$_{ar}$), 128.67 (3 × CH$_{ar}$), 129.97 (6 × CH$_{ar}$), 135.56 (C$_q$), 138.82 (C$_q$), 140.17 (C$_q$), 145.68 (3 × C$_q$), 153.38 (CH=N) ppm. IR: $\tilde{\nu}$ = 1633 ($\nu_{C=N}$) cm^{-1}. MS (ESI, POS): m/z (%) = 261.2 (100), 305.2 (80), 300.3 (60), 243.3 (60).

Synthesis of Indole-2-methylamines 11a,b,c,e,f,g: As a representative example, the synthesis of **11a** is described here. To a solution of [1-(*tert*-butoxycarbonyl)indole-2-methylene]isopropylamine (**10a**) (3.31 g; 11.56 mmol) in MeOH (150 mL), $NaBH_4$ (0.875 g; 23.12 mmol) was added stepwise at 0 °C under a nitrogen atmosphere. After stirring the mixture overnight at room temperature, 50 mL of NaOH (2 N) was added and again stirred for 10 min. The solution was poured into CH_2Cl_2 and the organic phase washed with NaOH (3 × 25 mL) and dried with $MgSO_4$. This was filtered through a fresh layer of $MgSO_4$ and after evaporation of the solvent, the product **11a** (2.73 g; 9.48 mmol; 82% yield) was obtained as a brown solid. No reproducible melting point could be determined due to the high hygroscopicity and stickyness of the product.

***tert*-Butyl 2-[(Isopropylamino)methyl]-1*H*-indole-1-carboxylate (11a):** Brown solid; yield 82%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 [d, J = 6.1 Hz, 6 H, CH(CH_3)$_2$], 1.70 [s, 9 H, C(CH_3)$_3$], 2.83 [sept, J = 6.1 Hz, 1 H, CH(CH$_3$)$_2$], 4.11 (s, 2 H, NH-CH_2), 7.19 (ddd, J = 7.6, J = 7.2, J = 1.7 Hz, 1 H, 5-H or 6-H), 7.25 (ddd, J = 8.0, J = 7.6, J = 1.8 Hz, 1 H, 5-H or 6-H), 7.48 (dd, J = 7.2, J = 1.8 Hz, 1 H, 4-H or 7-H), 8.06 (d, J = 8.0 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75.6 MHz, $CDCl_3$): δ = 22.95 [CH(CH_3)$_2$], 28.26 [C(CH_3)$_3$], 45.58 (CH_2-NH), 46.81 [CH(CH$_3$)$_2$], 84.11 [C(CH$_3$)$_3$], 108.91 (C-3), 115.67 (C-4 or C-7), 120.19 (C-4 or C-7), 122.76 (C-5 or C-6), 123.72 (C-5 or C-6), 129.11 (C$_q$), 136.63 (C$_q$), 139.95 (C$_q$), 150.56 (O=C–O) ppm. IR: $\tilde{\nu}$ = 1726 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): m/z (%) = 289.2 (100) [M + H$^+$].

***tert*-Butyl 2-[(Benzylamino)methyl]-1*H*-indole-1-carboxylate (11b):** Compound **11b** was prepared from **10b** (2.30 g; 6.88 mmol) by the procedure described for **11a**. The product **11b** was obtained as a pale brown oil (1.85 g; 5.50 mmol; 80% yield). ^{1}H NMR

(300 MHz, $CDCl_3$): δ = 1.68 [s, 9 H, C(CH_3)$_3$], 2.17 (br. s, 1 H, NH): 3.83 [s, 2 H, (Ph)-CH_2], 4.13 (s, 2 H, NH-CH_2), 6.54 (s, 1 H, 3-H), 7.18–7.38 (m, 7 H, 5-H, 6-H and 5× CH_{ar}), 7.50 (dd, J = 6.3, J = 1.4 Hz, 1 H, 4-H), 8.06 (d, J = 8.3 Hz, 1 H, 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.25 [3× C(CH_3)$_3$], 47.47 (NH-CH_2), 52.40 [(Ph)-CH_2], 84.20 [C(CH$_3$)$_3$], 109.32 (C-3), 115.66 (C-7), 120.25 (C-4), 122.79 (C-6), 123.79 (C-5), 126.91 (CH_{ar}), 12819 (2× CH_{ar}), 128.37 (2× CH_{ar}), 129.05 (C-7a), 136.63 (C-3a), 139.47 (C-2), 140.30 (C_q), 150.57 (C=O) ppm. IR: $\tilde{\nu}$ = 3346 (ν_{NH}) 1726 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): m/z (%) = 337.2 (100) [M + H$^+$].

***tert*-Butyl 2-[1-(4-Methoxybenzylamino)methyl]-1*H*-indole-1-carboxylate (11c):** Compound **11c** was prepared from **10c** (2.40 g; 6.59 mmol) by the procedure described for **11a**. After purification via preparative TLC (PE/EtOAc: 4:1; 4 runs, R_f = 0.14), The product **11b** was obtained as a dark yellow oil (2.00 g; 5.47 mmol; 83% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.68 [s, 9 H, OC(CH_3)$_3$], 2.16 (br. s, 1 H, NH), 3.76 (2 H, s. CH_2-NH), 3.9 (s, 3 H, OCH_3), 4.11 (s, 2 H, CH_2-NH), 6.52 (s, 1 H, 3-H), 6.84–6.88 (m, 2 H, 2× CH_{ar}), 718–7.28 (m, 4 H, 4× CH_{ar}), 7.49 (dd, J = 6.9, J = 1.4 Hz, 1 H, 4-H or 7-H), 8.07 (d, J = 8.3 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.23 [OC(CH_3)$_3$], 47.39 (CH_2-NH), 51.82 (Ph-CH_2-NH), 55.23 (OCH_3), 84.13 [C(CH$_3$)$_3$], 109.20 (C-3), 113.72 (2× CH_{ar}), 115.64 (C-4 or C-7), 120.21 (C-4 or C-7), 122.74 (CH_{ar}), 123.75 (CH_{ar}), 129.06 (C_q), 129.32 (2× CH_{ar}), 132.47 (C_q), 136.63 (C_q), 139.61 (C_q), 150.57 (C=O), 158.56 (C_q-OMe) ppm. IR: $\tilde{\nu}$ = 1726 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): m/z (%) = 367.2 (100) [M + H$^+$].

***N*-[(1-Benzyl-1*H*-indol-2-yl)methyl]propan-2-amine (11e):** Compound **11e** was prepared from **10e** (0.50 g; 1.81 mmol) by the procedure described for **11a**. The product **11e** was obtained as orange crystals (0.42 g; 1.52 mmol; 98% yield), m.p. 77.7–79.1 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 [d, J = 6.4 Hz, 6 H, CH(CH_3)$_2$], 2.79 [sept, J = 6.4 Hz, 1 H, CH(CH$_3$)$_2$], 3.84 [s, 2 H, (Ind)-CH_2-NH], 5.48 (s, 2 H, Ph-CH_2), 6.46 (s, 1 H, 3-H), 6.96–6.98 (m, 2 H, 2× CH_{ar}), 7.19–7.31 (m, 4 H, 4× CHar), 7.57–7.60 (m, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.77 [CH(CH_3)$_2$], 43.58 [(Ind)-CH_2-NH], 46.55 (Ph-CH_2), 47.99 [CH(CH$_3$)$_2$], 101.35 (C-3), 109.41 (C-4 or C-7), 119.53 (C-5 or C-6), 120.30 (C-4 or C-7), 121.43 (C-5 or C-6), 125.93 (2× CH_{ar}), 127.18 (CH_{ar}), 127.67 (C_q), 128.73 (2× CH_{ar}), 137.72 (C_q), 138.28 (C_q), 138.83 (C_q) ppm. IR: $\tilde{\nu}$ = 3316 (ν_{NH}) cm^{-1}. MS (ESI, POS): m/z (%) = 220 (100) [(M – NH – iPr)$^+$], 279 (70) [M + H$^+$]. $C_{19}H_{22}N_2$ (278.39): calcd. C 81.97, H 7.97, N 10.06; found C 81.48, H 8.46, N 9.81.

***N*-Benzyl-1-(1-benzyl-1*H*-indol-2-yl)methanamine (11f):** Compound **11f** was prepared from **10f** (3.50 g; 10.79 mmol) by the procedure described for **11a**. The product **11f** was obtained as yellow crystals (2.92 g; 8.95 mmol; 83% yield), m.p. 81.4–83.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (s, 1 H, NH), 3.77 (s, 2 H, N-CH_2), 3.85 (s, 2 H, N-CH_2), 5.47 (s, 2 H, Ph-CH_2-N$_{ind}$), 6.48 (s, 1 H, 3-H), 6.95 (dd, J = 8.0, J = 1.9 Hz, 2 H, 2× CH_{ar}), 7.06–7.16 (m, 2 H, 2× CH_{ar}), 7,18–7.33 (m, 9 H, 9× CH_{ar}), 7.60 (dd, J = 6.9, J = 1.9 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.25 (CH_2-NH), 46.61 (CH_2-N$_{ind}$), 53.12 (NH-CH_2), 101.87 (CH_{ar}), 109.52 (CH_{ar}), 119.56 (CH_{ar}), 120.34 (CH_{ar}), 121.52 (CH_{ar}), 125.98 (2× CH_{ar}), 126.97 (CH_{ar}), 127.11 (CH_{ar}), 127.64 (C_q), 128.16 (2× CH_{ar}), 128.36 (2× CH_{ar}), 128.66 (2× CH_{ar}), 137.76 (C_q), 138.22 (C_q), 138.27 (C_q), 140.02 (C_q) ppm. IR: $\tilde{\nu}$ = 1454 cm^{-1}. MS (ESI, POS): m/z (%) = 220.2 (100), 327.2 (60) [M + H$^+$]. $C_{23}H_{22}N_2$ (326.43): calcd. C 84.63, H 6.79, N 8.58; found C 84.43, H 6.64, N 8.65.

***N*-4-Methoxybenzyl-1-(1-benzyl-1*H*-indol-2-yl)methanamine (11g):** Compound **11g** was prepared from **10g** (3.50 g; 9.87 mmol) by the procedure described for **11a**. The product **11g** was obtained as a yellow oil (2.89 g; 8.10 mmol; 82% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (br. s, 1 H, NH), 3.70 (s, 2 H, N-CH_2), 3.77 (s, 3 H, OCH_3), 3.82 (s, 2 H, NH-CH_2), 5.44 (s, 2 H, Ph-CH_2-N$_{ind}$), 6.47 (s, 1 H, 3-H), 6.82 [ps (d), J = 8.8 Hz, 2 H, 2× CH_{ar}], 6.91–6.94 (m, 2 H, 2× CH_{ar}), 7.06–7.24 (m, 8 H, 8× CH_{ar}), 7.59 (dd, J = 6.6, J = 1.7 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.22 (CH_2-N), 46.71 (CH_2-N$_{ind}$), 52.62 (NH-CH_2), 55.36 (O-CH_3), 101.88 (C-3), 109.62 (CH_{ar}), 113.83 (2× CH_{ar}), 119.65 (CH_{ar}), 120.43 (C-4 or C-7), 121.59 (CH_{ar}), 126.09 (2× CH_{ar}), 127.21 (CH_{ar}), 1127.76 (C_q), 128.76 (2× CH_{ar}), 129.45 (2× CH_{ar}), 132.26 (C_q), 137.83 (C_q), 138.37 (C_q), 138.46 (C_q), 158.72 (C_q-OMe) ppm. IR: $\tilde{\nu}$ = 3336 (ν_{NH}) cm^{-1}. MS (ESI, POS): m/z (%) = 357.2 (100) [M + H$^+$].

Trichloroacetyl Derivatives 12a,b,c,e,f,g: As a representative example, the synthesis of 2,2,2-trichloro-*N*-[1-(*tert*-butoxycarbonyl)indole-2-methyl]-*N*-isopropylacetamide (**12a**) is described here. To a dry 100 mL bulb with a solution of **11a** (2.00 g; 6.95 mmol) in dry THF (60 mL) was added pyridine (1.10 g; 13.90 mmol) with a dry syringe. Then followed by dropwise addition (with a dry syringe) of a solution of tricholoroacetylchloride (2.53 g; 13.90 mmol) in dry THF (15 mL) at 0 °C and under a nitrogen atmosphere. The reaction mixture was shielded from the light and reacted for 15 min at 0 °C and was then warmed up to room temperature during the overnight reaction. Afterwards, the mixture was poured into a saturated $NaHCO_3$ solution (45 mL) and extracted with CH_2Cl_2 (3×40 mL). The organic layer was washed with 1 N HCl (3×40 mL) and then dried with $MgSO_4$. After filtration through a fresh layer of $MgSO_4$ and evaporation, the product **12a** (2.83 g; 6.52 mmol; 94% yield) was obtained as a red oil.

***tert*-Butyl 2-{[Isopropyl(trichloroacetyl)amino]methyl}-1*H*-indole-1-carboxylate (12a):** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 [d, J = 6.6 Hz, 6 H, CH(CH_3)$_2$], 1.71 [s, 9 H, C(CH_3)$_3$], 4.90 (s, 2 H, N-CH_2), 5.00 [sept, J = 6.6 Hz, 1 H, CH(CH$_3$)$_2$], 6.34 (s, 1 H, 3-H), 7.15–7.25 (m, 2 H, 5-H or 6-H), 7.45 (d, J = 6.6 Hz, 1 H, 4-H or 7-H), 8.04 (d, J = 8.3 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.24 [CH(CH_3)$_2$], 28.26 [C(CH_3)$_3$], 43.15 (N-CH_2), 51.07 [CH(CH$_3$)$_2$], 84.37 [C(CH$_3$)$_3$], 93.59 (CCl_3), 106.42 (C-3), 115.46 (C-4 or C-7), 120.27 (C-4 or C-7), 122.77 (C-5 or C-6), 123.66 (C-5 or C-6), 129.00 (C_q), 136.46 (C_q), 136.83 (C_q), 150.60 (O-C=O), 160.03 (CCl_3-C=O) ppm. IR: $\tilde{\nu}$ = 1729 ($\nu_{C=O}$) 1676 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): m/z (%) = 420.2 (100) [M + H$^+$], 289.2 (65) [M + H$^+$ – COCCl_3].

***tert*-Butyl 2-{[Benzyl(trichloroacetyl)amino]methyl}-1*H*-indole-1-carboxylate (12b):** Compound **12b** was prepared from **11b** (1.80 g; 5.35 mmol) by the procedure described for **12a**. After purification via preparative TLC (PE/EtOAc: 15:1, 6 runs), the product **12b** was obtained as a brown oil (2.37 g; 4.92 mmol; 24% yield). The signals of two rotamers were observed in the spectroscopic data of this compound (A and B; each 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.54 and 1.61 [s, 9 H, C(CH_3)$_3$], 4.84 and 4.91 [s, 2 H, (Ind)-CH_2], 5.14 and 5.26 (s, 2 H, Ph-CH_2), 6.45 and 6.57 (s, 1 H, 3-H), 7.19–7.40 (m, 7 H, 5× CH_{ar}, 5-H, 6-H), 7.49 and 7.55 (d, J = 7.2 Hz, 1 H, 4-H or 7-H), 8.09 (d, J = 7.7 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.20 and 28.27 [C(CH_3)$_3$], 47.40 and 52.29 [(Ind)-CH_2], 49.23 and 53.37 [(Ph)-CH_2], 84.57 and 84.93 [C(CH$_3$)$_3$], 92.98 and 93.12 (CCl_3), 106.37 and 108.12 (C-3), 115.65 (CH_{ar}), 120.38 and 120.52 (C-4 or C-7), 123.07 and 123.30 (CH_{ar}), 124.12 and 124.32 (CH_{ar}), 127.00 (CH_{ar}), 127.77 (CH_{ar}), 128.03 (CH_{ar}), 128.93 (C_q), 129.01 (2× CH_{ar}), 135.00 and 135.39 (C_q), 135.82 and 135.94 (C_q), 136.64 and 136.86 (C_q), 150.17 and 150.29 (O-C=O), 161.06 and 161.50 (CCl_3-C=O) ppm. IR: $\tilde{\nu}$ =

1731 ($\nu_{O-C=O}$) 1679 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): *m/z* (%) = 174.0 (100), 181.1 (75), [539.1 (25), 541.1 (30), 543.1 (10), 545.1 (1), Cl isotopes].

***tert*-Butyl 2-{[1-(4-Methoxybenzyl)(trichloroacetyl)amino]methyl}-1*H*-indole-1-carboxylate (12c):** Compound **12c** was prepared from **11c** (1.90 g; 5.18 mmol) by the procedure described for **12a**. After purification via preparative TLC (PE/EtOAc: 8:1; 4 runs), The product **12c** was obtained as a pale yellow oil (2.20 g; 4.30 mmol; 44% yield). Again signals of two rotamers were observed in the spectroscopic data of this compound (A and B; each 50%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.55 and 1.62 [s, 9 H, C(CH_3)$_3$], 3.79 (s, 3 H, OCH_3), 4.76 and 4.89 (s, 2 H, CH_2-N), 5.07 and 5.23 (s, 2 H, CH_2-N), 6.43 and 6.55 (s, 1 H, 3-H), 6.88 (dd, J = 8.3, J_2 = 8.3 Hz, 2 H, 2× CH_{ar}), 7.16–7.33 (m, 4 H, 4× CH_{ar}), 7.49 and 7.54 (d, J = 7.2 Hz, 1 H, 4-H or 7-H), 8.07–8.11 (m, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.27 [OC(*C*H$_3$)$_3$], 47.02 and 51.78 (N-*C*H$_2$), 48.85 and 52.85 (N-*C*H$_2$), 55.46 (O*C*H$_3$), 84.55 and 84.92 [*C*(CH$_3$)$_3$], 93.08 and 93.22 (*C*Cl$_3$), 106.40 and 108.17 (C-3), 114.37 (2× *C*H$_{ar}$), 115.65 (C-4 or C-7), 120.40 and 120.52 (C-4 or C-7), 123.06 and 123.29 (*C*H$_{ar}$), 124.09 and 124.31 (*C*H$_{ar}$), 127.18 and 127.87 (C$_q$), 128.42 (*C*H$_{ar}$), 128.96 (C$_q$), 129.48 (*C*H$_{ar}$), 135.13 and 136.00 (C$_q$), 136.64 and 136.83 (C$_q$), 150.23 and 150.31 (O-*C*=O), 158.56 (C$_q$-OMe), 160.97 and 161.41 (Cl$_3$C-*C*=O) ppm. IR: $\tilde{\nu}$ = 1731 ($\nu_{C=O}$) 1679 ($\nu_{C=O}$) cm^{-1}. MS: *m/z* (%) = 294.1 (100).

***N*-[(1-Benzyl-1*H*-indol-2-yl)methyl]-2,2,2-trichloro-*N*-isopropylacetamide (12e):** Compound **12e** was prepared from **11e** (0.40 g; 1.44 mmol) by the procedure described for **12a**. After recrystallization from methanol, the product **12e** was obtained as brown crystals (0.45 g; 1.06 mmol; 74% yield), m.p. 133.5–134.6 °C; recrystallization from MeOH. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 [d, J = 6.6 Hz, 6 H, CH(CH_3)$_2$], 4.50 (s, 2 H, N-CH_2), 4.91 [m, 1 H, C*H*(CH$_3$)$_2$], 5.41 (s, 2 H, CH_2-N), 6.35 (s, 1 H, 3-H), 7.03 (d, J = 7.2 Hz, 2 H, 2× CH_{ar}), 7.07–7.17 (m, 2 H, 2× CH_{ar}), 7.21–7.32 (m, 4 H, 4× CH_{ar}), 7.57 (d, J = 7.2 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.42 [CH(*C*H$_3$)$_2$], 40.13 (N-*C*H$_2$), 46.87 (N-*C*H$_2$), 51.13 [*C*H(CH$_3$)$_2$], 93.59 (*C*Cl$_3$), 100.31 (C-3), 109.27 (*C*H$_{ar}$), 119.91 (*C*H$_{ar}$), 120.52 (C-4 or C-7), 121.65 (*C*H$_{ar}$), 126.17 (2× *C*H$_{ar}$), 127.68 (*C*H$_{ar}$), 127.77 (C$_q$), 129.06 (2× *C*H$_{ar}$), 135.79 (C$_q$), 137.59 (C$_q$), 137.64 (C$_q$), 160.32 (*C*=O) ppm. IR: $\tilde{\nu}$ = 1673 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): *m/z* (%) = [423.0 (100), 425.0 (75), 427.0 (25), 429.0 (5), M + H$^+$, Cl isotopes]. $C_{21}H_{21}Cl_3N_2O$ (423.76): calcd. C 59.52, H 4.99, N 6.61; found C 59.33, H 4.86, N 6.37.

***N*-[(1-Benzyl-1*H*-indol-2-yl)methyl]-2,2,2-trichloro-*N*-benzylacetamide (12f):** Compound **12f** was prepared from **11f** (2.90 g; 8.88 mmol) by the procedure described for **12a**. The product **12f** was obtained as yellow-brown crystals (3.44 g; 7.28 mmol; 53% yield), m.p. 49.1–51.3 °C. Signals of two rotamers (A and B) were observed in the spectroscopic data of this compound [for *A* (printed in *italics*, 70%) and for B (underlined, 30%)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = *4.72* and 4.85 (br. s, 2 H, N-CH_2), *4.72* and 4.93 (br. s, 2 H, N-CH_2), 5.13 and *5.28* (br. s, 2 H, Ph-CH_2-N$_{ind}$), *6.35* and 6.52 (br. s, 1 H, 3-H), 6.84–6.86 (m, 2 H, 2× CH_{ar}), 7.01–7.36 (m, 11 H, 11× CH_{ar}), 7.59 (d, J = 7.7 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.20 and *45.86* (N-*C*H$_2$), 46.64 (N-*C*H$_2$), 51.22 and *54.45* (N-*C*H$_2$), 92.89 (*C*Cl$_3$), 102.13 and *103.40* (C-3), 109.27 and *109.99* (*C*H$_{ar}$), 119.99 (*C*H$_{ar}$), 120.76 (C-4 or C-7), 122.19 (*C*H$_{ar}$), 125.78 (2× *C*H$_{ar}$), 127.09 (*C*H$_{ar}$), 127.26 (C$_q$), 127.35 (*C*H$_{ar}$), 127.89 (2× *C*H$_{ar}$), 128.71 (2× *C*H$_{ar}$), 128.86 (2× *C*H$_{ar}$), 133.11 en *133.58* (C$_q$), *134.60* and 135.49 (C$_q$), 136.79 and *137.34* (C$_q$), 137.75 (C$_q$), 160.90 (*C*=O) ppm. IR: $\tilde{\nu}$ = 1674 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): *m/z* (%) = [471.0 (100), 473.1 (95), 475.0 (35), 477.0 (5), M + H$^+$, Cl isotopes]. $C_{25}H_{21}Cl_3N_2O$ (471.81): calcd. C 63.64, H 4.49, N 5.94; found C 62.96, H 4.34, N 6.12.

***N*-[(1-Benzyl-1*H*-indol-2-yl)methyl]-2,2,2-trichloro-*N*-(4-methoxybenzyl)acetamide (12g):** Compound **12g** was prepared from **11g** (2.80 g; 7.86 mmol) by the procedure described for **12a**. The product **12g** was obtained as a pale yellow powder (2.45 g; 4.87 mmol; 62% yield), m.p. 61.0 °C–63.1 °C. Signals of two rotamers were observed in the spectroscopic data of this compound [*A* (70%) and B (30%)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (br. s, 3 H, O-CH_3), *4.71* and 4.83 (br. s, 2 H, CH_2-N), 4.66 and *4.87* (br. s, 2 H, CH_2-N), 5.18 and *5.31* (br. s, 2 H, N$_{ind}$-CH_2-Ph), *6.36* and 6.53 (br. s, 1 H, 3-H), 6.75–6.92 (m, 4 H, 4× CH_{ar}), 7.13–7.23 (m, 8 H, 8× CH_{ar}), 7.61 (d, J = 7.2 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = *41.97* and 45.58 (N-*C*H$_2$), 46.71 (N$_{ind}$-*C*H$_2$-Ph), 50.77 and *51.01* (N-*C*H$_2$), 55.27 (O-*C*H$_3$), 93.00 (*C*Cl$_3$), 102.16 and *103.64* (C-3), 109.30 and *110.02* (*C*H$_{ar}$), 114.28 (2× *C*H$_{ar}$), 120.02 (*C*H$_{ar}$), 120.59 (C-4 or C-7), 122.18 (*C*H$_{ar}$), 125.84 (2× *C*H$_{ar}$), 126.42 (C$_q$), 127.31 (*C*H$_{ar}$), 127.41 (*C*H$_{ar}$), 127.64 (*C*H$_{ar}$), 128.53 (*C*H$_{ar}$), 128.75 (*C*H$_{ar}$), 129.66 (C$_q$), *133.29* and 133.70 (C$_q$), 136.92 and *137.40* (C$_q$), 137.80 (C$_q$), 159.28 (C$_q$-OMe), 160.86 (*C*=O) ppm. IR: $\tilde{\nu}$ = 1674 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): *m/z* (%) = [501.0 (100), 503.0 (95), 505.0 (40), 507.0 (5), M + H$^+$, Cl isotopes]. $C_{26}H_{23}Cl_3N_2O$ (501.83): calcd. C 62.23, H 4.62, N 5.58; found C 61.97, H 4.38, N 5.48.

Spiropyrrolidin-indol-2-ones 13a,c,e,f,g: As a representative example, the synthesis of **13a** is described here. To a dry 100 mL bulb with a solution of *N*-isopropyl-*N*-[1-(*tert*-butoxycarbonyl)indole-2-methyl]-2,2,2-trichloroacetamide (**12a**) (2.00 g; 4.61 mmol) in dry CH_2Cl_2 (75 mL) under argon was added PMDETA (0.641 g; 3.7 mmol; 0.77 mL) with a dry syringe. This mixture was stirred at room temperature for 15 min, followed by addition of Cu^{I}Cl (0.182 g; 1.84 mmol). The reaction mixture was heated up to reflux temperature and stirred at this temperature and under an argon atmosphere for 24 h. The reaction was stopped by pouring the mixture into H_2O (50 mL) and extracting this aqueous phase again with CH_2Cl_2 (50 mL). The combined organic phases were washed with H_2O (3× 50 mL) until the blue color disappeared and dried with $MgSO_4$. After filtration through a fresh layer of $MgSO_4$ and evaporation, the product **13a** (1.68 g; 3.87 mmol; 84% yield) was obtained as a pale brown powder.

***tert*-Butyl 3,4′,4′-Trichloro-5′-oxo-1′-(propan-2-yl)spiro[indole-2,3′-pyrrolidine]-1(3*H*)-carboxylate (13a):** M.p. 75.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 [d, J = 6.7 Hz, 3 H, CH(CH_3)], 1.29 [d, J = 6.7 Hz, 3 H, CH(CH_3)], 1.59 [s, 9 H, C(CH_3)$_3$], 4.13 (d, J = 11.6 Hz, 1 H, CONCH_AH$_B$), 4.25 (d, J = 11.6 Hz, 1 H, CONCH$_A$$H_B$), 4.43 [sept, J = 6.7 Hz, 1 H, C*H*(CH$_3$)$_2$], 6.00 (s, 1 H, 3-H), 7.11 (dd, J = 7.7, J = 7.6 Hz, 1 H, 5-H), 7.35 (dd, J = 8.1, J = 7.7 Hz, 1 H, 6-H), 7.39 (d, J = 7.6 Hz, 1 H, 4-H), 7.60 (d, J = 8.1 Hz, 1 H, 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.60 [CH(*C*H$_3$)], 19.72 [CH(*C*H$_3$)], 28.23 [C(*C*H$_3$)$_3$], 44.82 [*C*H(CH$_3$)$_2$], 45.89 (N-*C*H$_A$H$_B$), 64.72 (ClH*C*-3), 76.19 (C-2), 83.73 [*C*(CH$_3$)$_3$], 88.81 (*C*Cl$_2$), 116.41 (C-7), 124.11 (C-5), 125.00 (C-4), 127.62 (C$_q$), 131.10 (C-6), 142.76 (C$_q$), 151.63 (O-*C*=O), 164.52 (*C*=O) ppm. IR: $\tilde{\nu}$ = 1715 (2× $\nu_{C=O}$) cm^{-1}. MS (ESI, POS): *m/z* (%) = [415.3 (100), 417.0 (90), 419.0 (20), M – Cl + OH$_2^+$, Cl isotopes].

13c: Compound **13c** was prepared from **12c** (2.00 g; 3.91 mmol) by the procedure described for **13a**. After column chromatography (CH_2Cl_2/MeOH, 40:1, R_f = 0.32), the product **13c** was obtained as a brown powder (0.40 g; 0.78 mmol; 20% yield). The compound was too hygroscopic to take a reproducible melting point. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.55 [s, 9 H, C(CH_3)$_3$], 3.25 (s, 3 H, OCH_3),

3.87 (d, J = 12.1 Hz, 1 H, CONCH_AH_B), 4.08 (d, J = 12.1 Hz, 1 H, CONCH$_A$$H_B$), 4.23 (d, J = 16.0 Hz, 1 H, Ph-CH_AH_B), 4.98 (d, J = 16.0 Hz, 1 H, Ph-CH$_A$$H_B$), 5.01 (s, 1 H, 3-H), 7.07 (dd, J = 7.4, J = 7.4 Hz, 2 H, 5-H or 6-H), 7.17–7.36 (m, 5 H, 5× CH_{ar}), 7.69 (d, J = 8.8 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.27 [C(CH_3)$_3$], 47.54 (CONCH$_A$$H_B$), 48.05 (Ph-CH$_A$$H_B$), 55.74 (OCH$_3$), 76.23 (C-2), 81.91 (ClHC-3), 83.33 [C(CH$_3$)$_3$], 88.07 (CCl_2), 116.40 (C-4 or C-7), 122.97 (C-5 or C-6), 125.31; 126.27 (C_q), 127.92; 128.47 (2× CH_{ar}), 128.76 (2× CH_{ar}), 130.54; 134.94 (C_q), 143.46 (C_q), 151.73 (O-C=O), 166.07 (CCl_2C=O) ppm. IR: $\tilde{\nu}$ = 1726 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): m/z (%) = 289.2 (100).

13e: Compound **13e** was prepared from **12e** (0.4 g; 0.94 mmol) by the procedure described for **13a**. After column chromatography (CH_2Cl_2/MeOH, 40:1, R_f = 0.26) and recrystallization from diethyl ether, the product **13e** was obtained as a brown powder (0.06 g; 0.13 mmol; 14% yield). The compound was again too hygroscopic to take a reproducible melting point. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 [d, J = 6.8 Hz, 3 H, CH(CH_3)], 1.13 [d, J = 6.8 Hz, 3 H, CH(CH_3)], 3.49 (d, J = 11.3 Hz, 1 H, CONCH_AH_B), 4.11 (d, J = 11.3 Hz, 1 H, CONCH$_A$$H_B$), 4.32 [sept, J = 6.8 Hz, 1 H, CH-(CH$_3$)$_2$], 4.33 (d, J = 17.6 Hz, 1 H, Ph-CH_AH_B), 4.56 (d, J = 17.6 Hz, 1 H, Ph-CH$_A$$H_B$), 5.67 (s, 1 H, 3-H), 6.26 (d, J = 7.7 Hz, 1 H, 4-H or 7-H), 6.79 (dd, J = 7.6, J = 7.3 Hz, 1 H, 5-H or 6-H), 7.14 (ddd, J = 7.7, J = 7.6, J = 1.1 Hz, 1 H, 5-H or 6-H), 7.22–7.34 (m, 5 H, 5× CH_{ar}), 7.38 (d, J = 7.3 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.67 [CH(CH_3)], 18.99 [CH(CH_3)], 43.38 (CONCH$_2$), 44.66 [CH(CH$_3$)$_2$], 47.61 (CH_2-Ph), 74.89 (ClHC-3), 78.13 (C-2), 88.53 (CCl_2), 107.21 (C-4 or C-7), 118.74 (C-5 or C-6), 124.83 (C-4 or C-7), 125.96 (2× CH_{ar}), 126.79 (C_q), 127.21 (CH_{ar}), 128.83 (2× CH_{ar}), 130.94 (C-5 or C-6), 137.84 (C_q), 149.87 (C_q), 165.43 (C=O) ppm. IR: $\tilde{\nu}$ = 1708 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): m/z (%) = {405.2 (100), 407.0 (55), [M – Cl + OH$_2$]$^+$, Cl isotopes}.

13f: Compound **13f** was prepared from **12f** by the procedure described for **13a**. After preparative TLC as a purification step [PE/EtOAc (8:1), 3 runs, R_f = 0.17], the product **13f** was obtained as a yellow liquid (37% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.24 (d, J = 11.5 Hz, 1 H, CONCH_AH_B), 3.74 (d, J = 14.3 Hz, 1 H, Ph-CH_AH_B), 3.97 (d, J = 11.5 Hz, 1 H, CONCH$_A$$H_B$), 4.08 (d, J = 17.3 Hz, 1 H, N$_{ind}$-CH_AH_B), 4.55 (d, J = 17.3 Hz, 1 H, N$_{ind}$-CH$_A$$H_B$), 4.68 (d, J = 14.3 Hz, 1 H, Ph-CH$_A$$H_B$), 5.62 (s, 1 H, 3-H), 6.31 (d, J = 7.7 Hz, 1 H, CH_{ar}), 6.78 (dd, J = 7.4, J = 7.4 Hz, 1 H, CH_{ar}), 7.09–7.35 (m, 12 H, 12× CH_{ar}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.60 (Ph-CH$_A$$H_B$), 47.69 (N$_{ind}$-CH$_A$$H_B$), 47.91 (CONCH$_A$$H_B$), 74.79 (ClHC-3), 78.63 (C-2), 88.17 (CCl_2), 107.10 (CH_{ar}), 118.83 (CH_{ar}), 125.04 (CH_{ar}), 126.45 (2× CH_{ar}), 126.71 (C_q), 127.45 (CH_{ar}), 128.38 (CH_{ar}), 128.57 (2× CH_{ar}), 128.86 (2× CH_{ar}), 129.03 (2× CH_{ar}), 131.01 (CH_{ar}), 134.14 (C_q), 137.97 (C_q), 149.96 (C_q), 166.13 (C=O) ppm. IR: $\tilde{\nu}$ = 1708 ($\nu_{C=O}$) cm^{-1}. MS (ESI, POS): m/z (%) = {453.1 (100), 455.1 (75), 457.1 (15), [M – Cl + OH$_2$]$^+$, Cl isotopes}.

13g: Compound **13g** was prepared from **12g** by the procedure described for **13a**. After preparative TLC as a purification step (CH_2Cl_2/MeOH, 95:5, R_f = 0.50), the product **13g** was obtained as a yellow liquid (22% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.25 (d, J = 11.8 Hz, 1 H, CONCH_AH_B), 3.72 (s, 3 H, OCH_3), 3.84 (d, J = 14.3 Hz, 1 H, Ph-CH_AH_B), 3.97 (d, J = 11.8 Hz, 1 H, CON-CH$_A$$H_B$), 4.05 (d, J = 17.3 Hz, 1 H, N$_{ind}$-CH_AH_B), 4.50 (d, J = 17.3 Hz, 1 H, N$_{ind}$-CH$_A$$H_B$), 4.53 (d, J = 14.3 Hz, 1 H, Ph-CH$_A$$H_B$), 5.62 (s, 1 H, 3-H), 6.27 (d, J = 7.7 Hz, 1 H, CH_{ar}), 6.65–6.79 (m, 3 H, 3× CH_{ar}), 7.01–7.06 (m, 2 H, 2× CH_{ar}), 7.10–7.14 (m, 3 H, 3× CH_{ar}), 7.19–7.30 (m, 3 H, 3× CH_{ar}), 7.34 (d, J = 7.2 Hz, 1 H, 4-H or 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.19 (p-MeO-Ph-CH$_A$$H_B$), 47.38 (N$_{ind}$-CH$_A$$H_B$· CONCH$_A$$H_B$), 55.15 (OCH$_3$), 74.65 (ClHC-3), 78.42 (C-2), 88.13 (CCl_2), 107.01 (CH_{ar}), 114.19 (2× CH_{ar}), 118.66 (CH_{ar}), 124.88 (C-4 or C-7), 125.92 (C_q), 126.25 (2× CH_{ar}), 127.21 (CH_{ar}), 128.65 (2× CH_{ar}), 129.76 (C_q), 129.87 (2× CH_{ar}), 130.86 (CH_{ar}), 137.81 (C_q), 149.78 (C_q), 159.43 (C_q-OMe), 165.81 (C=O) ppm. IR: $\tilde{\nu}$ = 1705 ($\nu_{C=O}$) cm^{-1}. MS (ESI, NEG): m/z (%) = {517.0 (90), 519.0 (100), 521.0 (35), 523.0 (5), [M + OH]$^-$, Cl isotopes}.

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