Synthesis of Substituted 1,2,3,4-Tetrahydro-1-thiacarbazole and Spiro[pyrrolidinone-3,3′-indolinones] through a Common Intermediate Obtained by Condensation of Indolin-2-one, (Aryl)aldehydes, and Meldrum's Acid

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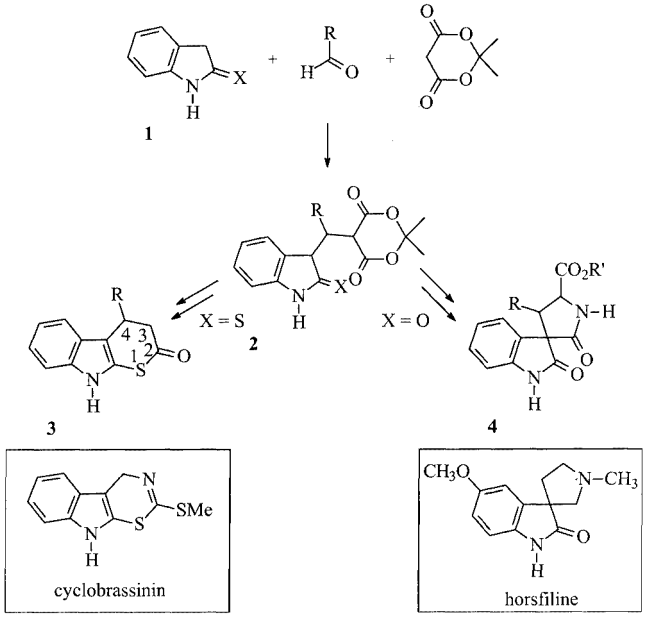
Trimolecular adducts resulting from condensation between indolin-2-one (or indoline-2-thione), (aryl)aldehydes, and Meldrum's acid are useful intermediates for the synthesis of either 1,2,3,4-tetrahydro-1-thiacarbazoles or spiro[pyrrolidino-3,3′-oxindoles] related to the natural product horsfiline. These latter compounds were obtained in a three-step procedure characterized by acyl azide formation, Curtius rearrangement, and subsequent thermal spiro cyclization. The relative stereochemistry of the spiro derivatives was determined by comparison of NOESY data and calculated conformational analyses.

Introduction

We recently reported a simple synthesis of β-substituted tryptophans based on a trimolecular condensation involving indole, aldehydes, and Meldrum's acid as the key step.[1] In view of the close pk_{HA} values of indoline-2-thione[2] and indole, it was speculated that replacement of the latter by **1** (X = S) (Scheme 1) might afford trimolecular adduct of type **2** (X = S), a possible intermediate for the preparation of thiacarbazoles **3**. Although 3- and 4-substituted thiacarbazoles have been prepared as analgesics and inflammation inhibitors,[3] no attention had been paid to their 2-functionalized derivatives, accessible from **2**.

The related indolo-1,3-thiazine skeleton is present in cyclobrassinin, a frequently isolated metabolite from the *Cruciferae* family.[4] Cyclobrassinin has been reported to possess cancer-preventing properties in the in vitro development of mice carcinogen-induced mammary lesions.[5]

A similar trimolecular approach with indolin-2-one (oxindole) **1** (X = O) as nucleophile should give the analogous trimolecular adduct **2** (X = O), from which it might be possible to prepare the functionalized spiro[pyrrolidinone-3,3′-indolone] derivatives **4**, related to the simple oxindole alkaloid horsfiline.[6]



Scheme 1

Here we report a convergent pathway that allows the preparation of both thiopyranoindole **3** and spirooxindoles **4** by simple functional group transformations (Scheme 1).

Results and Discussion

Initially, indoline-2-thione **1** (X = S) was treated with benzaldehyde and Meldrum's acid according to our previ-

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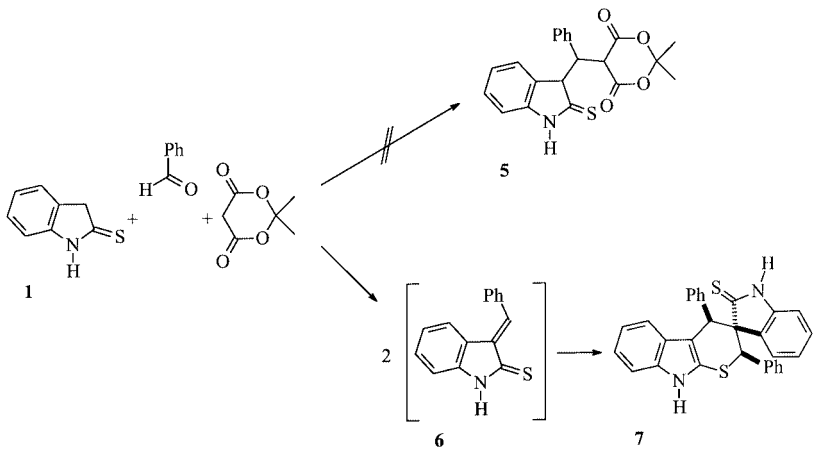
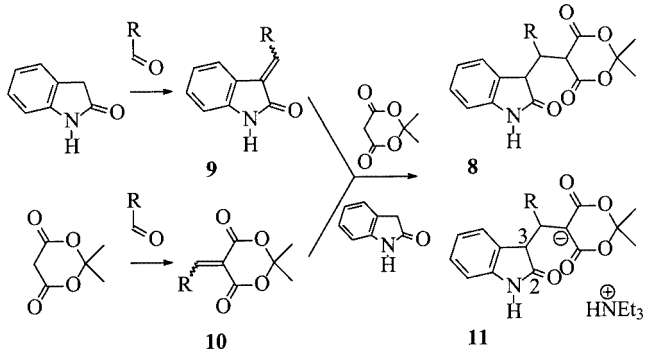


Scheme 2

ous findings.[1] Contrary to expectations, the only isolated compound was cycloadduct **7**, resulting from the [4+2]-cycloaddition of two Knoevenagel adducts **6** (Scheme 2). Such a reaction has already been described in the literature when indoline-2-thione is treated with benzaldehyde.[7]

As 3-arylidene-2-indolinones are less prone to self-condensation,[8] we examined reactions between oxindole, Meldrum's acid, and aldehydes, postponing the introduction of a sulfur atom at position 2 to a later stage of the synthesis.

Under Yonemitsu's conditions[9] (CH_3CN, DL-proline; Conditions A), trimolecular condensation with oxindole gave a much more complex reaction mixture than in the case of indole (Scheme 3, Table 1). It appeared that the reversibility of the process prevented the isolation of the formed trimolecular adduct **8** by conventional chromatography on silica gel: in addition to recovered starting materials, the Knoevenagel intermediate **10**, the 'double-condensed' product **12**, or the ring-cleaved diacid **13** could be isolated, depending on the used aldehyde (Scheme 4). It must be noticed that, in some occassions, Knoevenagel's derivative **9**, another postulated intermediate, can be isolated in minute amounts.



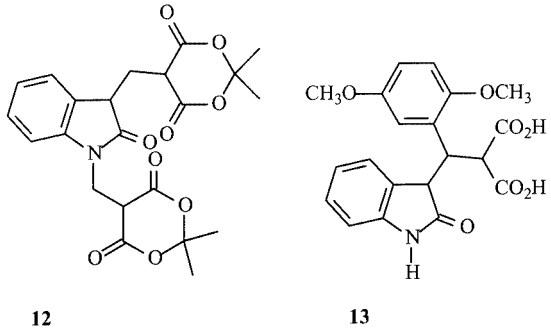
a R = H
b R = Ph
c R = (2,5-OMe)Ph
d R = (2-NO_2)Ph
e R = (4-F)Ph

Scheme 3

Table 1. Yields and ratios of **8** and **11**, depending on the experimental conditions

Entry	R	Conditions	Yield **8** (%)	Yield **11** (%)	Other products (%)
1	**a**: H	A	–	–	**12** (2)
		B	29	–	–
		C	38	–	–
2	**b**: Ph	A	56 (100:0)[a]	–	–
		B	–	66 (92:8)[a]	–
3	**c**: (2,5-OMe)Ph	A	–	–	**10c**[b] (31) + **13**[c] (35)
		B	–	59 (60:40)[a]	–
4	**d**: (2-NO_2)Ph	A	trace	–	–
		B	36 (100:0)[a]	–	–
5	**e**: (4-F)Ph	B	51 (100:0)[a]	–	–

[a] Diastereomer ratio. [b] Two isomers, 60:40. [c] One diastereomer.



Scheme 4

When R = Ph, however, the equilibrium was pushed towards the trimolecular adduct **8b** (one diastereomer) by its spontaneous crystallization (56%) from the reaction mixture (Scheme 3).

Since this target adduct was removed from the reaction mixture by crystallization, we turned our attention to our recently described procedure for 2-substituted indoles,[10] in which the corresponding adducts were isolated as stable triethylamine salts.

Indeed, condensation of oxindole with Meldrum's acid and benzaldehyde or 2,5-dimethoxybenzaldehyde in dry acetonitrile in the presence of one equivalent of triethylamine (Conditions B) smoothly gave the corresponding crystalline adduct triethylamine salts **11b** and **11c** (Scheme 3).

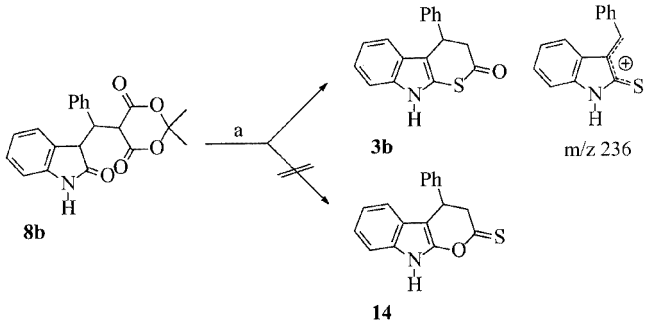
The disappearance of the malonic proton (δ = 4.61 ppm in **8b**) and a strongly deshielded (δ = 75.7 ppm vis-a-vis δ = 49.3 ppm in **8b**) quaternary carbon in **11b** attested to the location of a negative charge on the malonic carbon and not on the indolic C(3) one. Indeed, in **11b**, the two coupled protons [doublets (J = 11.0 Hz) at δ = 3.83 ppm and δ = 4.74 ppm] are linked to the carbons at δ = 44.9 and 46.7 ppm, respectively. These latter have been shown, by HMQC and HMBC correlation spectrums, to be the benzylic carbon and the indole C(3) carbon, respectively. Similar measurements were carried out on adduct salt **11c**.

Although no salt precipitation was observed in the remainder of the series [R = H, (2-NO_2)-Ph, (4-F)-Ph], the presence of triethylamine proved to be essential for the formation and stabilization of trimolecular adducts **8a**, **8d**, and **8e**. These could be isolated in neutral form after acid workup followed by rapid purification by column chromatography (Scheme 3).

With formaldehyde (R = H) under Conditions B or C[11] (microwave oven irradiation), the yield of the reaction did not exceed that of the two-step procedure recently described by Rajeswaran et al.[12]

It is important to note that only one racemic diastereomer was obtained in each case for derivatives **8**, whereas mixtures (each with one isomer as major compound) were isolated for salts **11** (Scheme 3).

With the trimolecular adducts to hand, the phenyl-substituted **8b** was chosen for thionation. Treatment of **8b** with Lawesson's reagent[13] (2.2 equivalents) at 80 °C afforded the target thiopyranoindole **3b**, the result of a thionation/ring closure/decarboxylation process (Scheme 5).



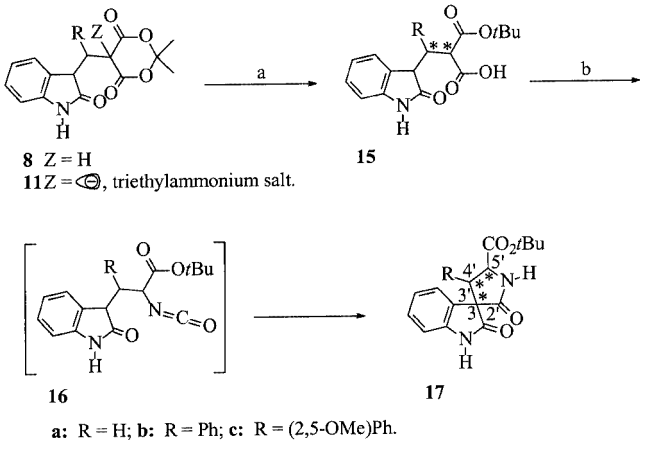
Scheme 5. (a) Lawesson's reagent, dry toluene, 80 °C, 3 days

The alternative structure **14** can be discounted on the basis of the chemical shift of C(3) methylene (δ = 48.3 ppm), which precluded the presence of any thiocarbonyl function. Moreover, the base peak in the EI mass spectrum, at m/z = 236, corresponded to **3b**, with the sulfur atom attached to the indole 2-position.

A few years ago we published a short synthesis, starting from 2-hydroxy-5-methoxytryptamine and formaldehyde, for the preparation of simple oxindole alkaloid horsfiline.[14] Since that time, a number of chemical approaches toward these spiranic oxindoles have been reported, either to explore new synthetic methods[15] or to obtain derivatives of biological interests.[16]

We have recently reported a simple synthesis for the preparation of some spiro[pyrrolidinone-3,3′-indole] derivatives starting from 2-substituted indoles, aldehydes, and Meldrum's acid.[10] Continuing our activity in the field of functionalized spirooxindoles, related to horsfiline, we wondered if a similar approach, starting from oxindole-type trimolecular adducts **8** or **11**, could be used for these purposes.

Ring opening of the 1,3-dioxane-4,6-dione appendages of trimolecular adducts **8a**, **8b**, **11b**, and **11c** in boiling *tert*-butyl alcohol smoothly gave the ester-acids **15a**, **15b**, and **15c** as mixtures of diastereomers. Treatment of these with diphenylphosphoryl azide (DPPA) in the presence of triethylamine afforded the corresponding acyl azides, which were subjected, without isolation, to thermal Curtius rearrangement to afford isocyanates **16a**, **16b**, and **16c**. These spontaneously cyclized to the spirooxindole derivatives **17a**, **17b**, and **17c** in 50−74% overall yields, as a mixture of two diastereomers in the case of **17a** and as mixtures of three diastereomers (of the four possible) for **17b** and **17c**, named **I**, **II**, **III** in descending order of importance (Scheme 6) (Table 2).



Scheme 6. (a) *t*BuOH, reflux; (b) DPPA, Et_3N, CH_3CN, 50 °C

Their separation could not be achieved by chromatography. Fortunately, in the case of **17b**, the minor component **III** (M.p. 188−189 °C) could be isolated by crystallization from diethyl ether, which allowed measurement of NMR spectroscopic data.

In the mother liquor, it was easily possible to distinguish the NMR signals of the major isomer **I** from those of the remaining minor isomer **II**.

Table 2. Yields and ratios of spiro derivatives **17**

Entry	Starting material	R	Yield **15** (%)	Yield **17** (%)	**17** Isomer ratio
1	**8a**	H	79[a]	70	[a]
2	**8b**	Ph	90[b]	74	47:33:20[c]
3	**11b**	Ph	45[b]	74	47:33:20[c]
4	**11c**	(2,5-MeO)Ph	45[c]	50	53:34:13[c]

[a] Isomer ratio 50:50. [b] Mixture of four isomers. [c] Mixture of three isomers.

In order to determine the relative configurations of carbon atoms 3, 4′, and 5′, we used correlation measurements (HMQC, HMBC) to assign every ^{1}H NMR signal for each isomer of **17b** (pure **III**, 80:20 mixture of **I/II**).

As it is well known that stereochemical relationships of hydrogens attached to a five-membered ring cannot confidently be assigned by coupling constant values and/or NOE measurements,[18] we decided to use comparison of quantitative NOE data (NOESY)[19] with conformational analyses obtained by calculation.

In this study, the configuration of the spiranic 3,3′ carbon was arbitrary set as *R**.

The distances between the oxindole proton H(4) and the pyrrolidinone protons H(4′) and H(5′) are representative of their forward or backward location, respectively, on the pyrrolidinone plane, whereas the H(4′)−H(5′) distance indicates their *cis* or *trans* relationship. These NOESY calculated distances are collected in Table 3.

Table 3. Calculated distances (nm) between H(4), H(4′), and H(5′) by NOESY for isomers **I**, **II**, **III** of **17b**

Isomer **17b**	*d*(4-4′)	*d*(4-5′)	*d*(4′-5′)
I	0.24	[a]	[b]
II	[a]	[a]	0.23
III	[a]	0.26	0.31

[a] No visible NOE cross peak: $d > 0.4$ nm. [b] No measurement was possible.

After that, we calculated the average of the above-mentioned distances for all conformations, for each of the four isomers, by two different methods. The first is based on a Monte-Carlo selection[20] and the second on a molecular dynamics method.[21]

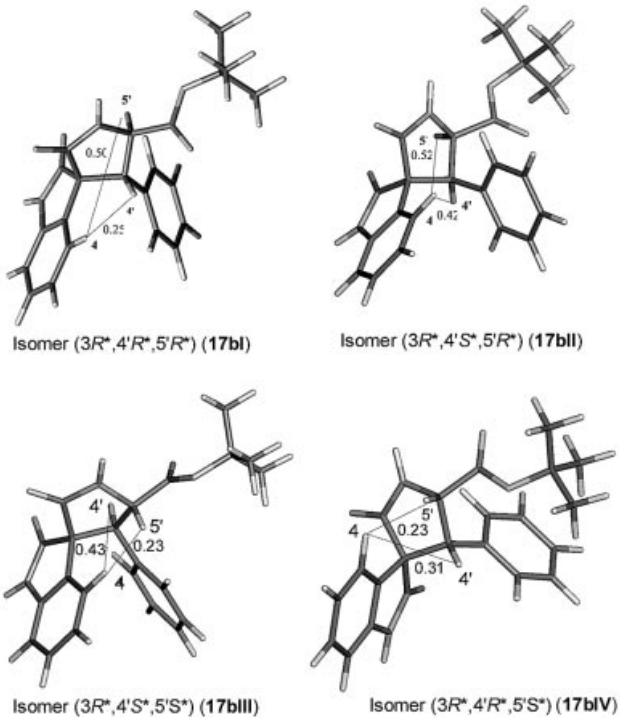
Whatever the chosen method, the calculated distances are almost identical, and are reported on Table 4.

Table 4. Calculated distances (nm) between H(4), H(4′), and H(5′) by molecular dynamic (and by the Monte-Carlo method, if different) for the four possible isomers (racemates) **17b**

Isomer **17b**	*d*(4-4′)	*d*(4-5′)	*d*(4′-5′)	Inferred **17b** isomer
(3*R**,4′*R**,5′*R**)	0.25 (0.26)	0.50 (0.54)	0.30 (0.31)	**I**
(3*R**,4′*S**,5′*R**)	0.42	0.52 (0.54)	0.23 (0.24)	**II**
(3*R**,4′*S**,5′*S**)	0.43	0.23 (0.24)	0.30 (0.31)	**III**
(3*R**,4′*R**,5′*S**)	0.31	0.23	0.23	–

The data in Table 4 unambiguously show that the (3*R**,4′*R**,5′*S**) isomer, in which all distances are less than 0.31 nm, is not present in the isomer mixture. For the others, the correlation is particularly satisfying; this could be due to the high degree of rigidity of these molecules.

The shielding ($\delta = 6.0$ ppm) of the H(4) oxindole proton in isomer **II** is the result of its proximity to the symmetry axis of the C(4′)-attached phenyl ring. This effect is severely diminished for isomer **III** ($\delta = 6.9$ ppm) and no longer exists for isomer **I** ($\delta = 7.4$ ppm) (Scheme 7).



Scheme 7

In summary, a short route to 1-thiacarbazol-2-one and 3-spiranic oxindole derivatives through a common intermediate has been described. This method provides sufficient flexibility to permit the incorporation of various substituents into this spirocyclic system.

Experimental Section

General Remarks: Melting points were determined on a Reichert Thermovar hot-stage apparatus and are uncorrected. IR (film or KBr) spectra were measured with a Bomem FTIR instrument. UV spectra were obtained with a UNICAM 8700 UV/Vis spectrophotometer in MeOH. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were acquired on a Bruker AC 300 spectrometer in $CDCl_3$, with TMS as internal standard, or in [D_6]DMSO. Mass spectra were recorded with a VG Autospec apparatus. Elemental analyses were carried out by the Microanalysis Service of the University of Reims. All solvents were purified by standard literature methods. Diphenylphosphoryl azide was purchased from Aldrich. Chromatography was performed on 60 silica gel (Merck) with hexane/CH_2Cl_2, cyclohexane/ethyl acetate, CH_2Cl_2, and CH_2Cl_2/MeOH as

eluents. Reactions were monitored by TLC with Merck TLC aluminium sheets (Kieselgel 60F_{254}). Microwave irradiation was carried out in a Normalab Analis Normatron 112 oven. The stereochemical study of isomers **17bI**, **II**, and **III** was carried out at 500 MHz on a DRX 500 Bruker NMR spectrometer (HMBC, delay: 40 ms). Build-up curves of NOE effects were drawn from data collected by using the noesyst standard acquisition program and six mixing times ranging from 50 to 700 ms.[19] The minimum energy conformations were determined by Monte-Carlo searches with the MacroModel® software.[20] For the molecular dynamic studies, all molecules plots were drawn with Insight II® version 98.0 from molecular simulations, Inc. (MSI). Conformational searches were performed with MSI's Discover® version 2.98 module.[21] Energy calculations were made with the consistent forcefield (CFF91). All calculations were performed on Silicon Graphics Octane.

Spiro Compound 7: Meldrum's acid (0.482 g, 3.35 mmol), benzaldehyde (0.337 mL, 3.35 mmol), and triethylamine (0.466 mL, 3.35 mmol) were stirred at room temperature in dry acetonitrile (7 mL) for 1 h. A solution of indoline-2-thione (0.500 g, 3.35 mmol) in dry acetonitrile (10 mL) was added dropwise to the reaction mixture and the mixture was stirred at room temperature for 12 h. The crude orange solid was purified twice by column chromatography on silica gel (eluent: cyclohexane/ethyl acetate, 90:10) and crystallized (CH_3OH) to afford **7** as a beige powder. Yield: 0.527 g (40%). M.p. 215−216 °C (ref.[7] M.p. 216.5−218 °C).

General Procedures for the Preparation of Compounds 8 and 11. General Procedure A (GPA): Meldrum's acid and the aldehyde were suspended under nitrogen atmosphere in dry acetonitrile at room temperature (room temp.) for 10 min. A solution of oxindole and DL-proline in dry acetonitrile was then added, and the mixture was stirred under nitrogen atmosphere at room temperature. The reaction was stopped when TLC monitoring showed no further conversion of oxindole. Two workups of the reaction mixture were used: filtration, when the product precipitated, or concentration under reduced pressure followed either by column chromatography on silica gel (eluent: CH_2Cl_2/CH_3OH, 94:6) or by crystallization (diethyl ether or hexane/CH_2Cl_2). When R = (2,5-OMe)Ph, the Knoevenagel adduct **10c** was obtained after the purification of the diacid's **13** mother liquor by column chromatography on silica gel (eluent: CH_2Cl_2).

General Procedure B (GPB): The aldehyde and triethylamine were successively added to a solution of Meldrum's acid in dry acetonitrile. The reaction mixture was stirred under nitrogen atmosphere either at room temperature or at 50 °C. Oxindole was then added, and the reaction mixture was stirred at room temperature under nitrogen atmosphere until no further conversion of oxindole was observed (TLC). Two workups of the reaction mixture were used: either filtration under reduced pressure when the trimolecular adduct precipitated in its salt form **11**, or extraction followed by column chromatography on silica gel, when the adduct was obtained as its neutral form **8**. When the reaction mixture was extracted to remove the excess of triethylamine, it was first diluted in diethyl ether, and then washed with a 5% aqueous solution of citric acid. The aqueous layer was washed several times with diethyl ether. The combined organic layers were dried with anhydrous $MgSO_4$ and filtered. The product could then be isolated either by concentration of the acetonitrile filtrate under reduced pressure until it started to crystallize, or by column chromatography on silica gel (eluents: CH_2Cl_2 and CH_2Cl_2/CH_3OH).

General Procedure C (GPC): The molar ratio of oxindole, Meldrum's acid, and aldehyde was as described by Nemes and Laronze.[11]

A solution of oxindole, Meldrum's acid, aldehyde, and triethylamine in dry acetonitrile was irradiated in a 250-Watt microwave oven until TLC monitoring showed no further conversion of oxindole. The colored solution was diluted with diethyl ether and extracted with a 5% aqueous solution of citric acid. The aqueous layer was washed several times with diethyl ether. The combined organic layers were dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (eluent: CH_2Cl_2/CH_3OH).

5-[(2′,3′-Dihydro-2′-oxo-1*H*-indol-3′-yl)methyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (8a): This compound was synthesized from paraformaldehyde according to GPB, with extraction: paraformaldehyde (0.174 g, 5.26 mmol) and triethylamine (0.733 mL, 5.26 mmol) were added to Meldrum's acid (0.757 g, 5.26 mmol) in acetonitrile (6 mL). The mixture was stirred for 2 h at 50 °C. Oxindole (0.700 g, 5.26 mmol) was then added successively to the yellow solution, which was stirred for 2 days. The solution was diluted with diethyl ether (4 mL) and extracted with citric acid solution (5%, 8 mL). The aqueous layer was washed with diethyl ether (2 × 7 mL), the combined organic layers were dried, filtered, and concentrated, and the crude solid was purified by column chromatography to obtain **8a** as a yellow powder (eluent: CH_2Cl_2/CH_3OH, 92:8). Yield: 0.440 g (29%). M.p. 135−137 °C (ref.[12] m.p. 148−149 °C).

The compound was also synthesized from paraformaldehyde according to GPC: oxindole (0.400 g, 3 mmol), Meldrum's acid (0.476 g, 3.3 mmol), paraformaldehyde (0.180 g, 4.5 mmol), and triethylamine (1.68 mL, 12 mmol) in acetonitrile (50 mL) were heated under reflux for 2 h 40 min. The green solution was diluted with diethyl ether (10 mL) and extracted with citric acid solution (5%, 40 mL). The aqueous layer was washed with diethyl ether (2 × 35 mL). The combined organic layers were dried, filtered, and concentrated, and the crude green solid (1.072 g) was purified by column chromatography to afford **8a** (eluent: CH_2Cl_2/CH_3OH, 92:8). Yield: 0.333 g (38%).

5-[(2′,3′-Dihydro-2′-oxo-1*H*-indol-3′-yl)(phenyl)methyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (8b): This compound was synthesized from benzaldehyde according to GPA, with filtration: Meldrum's acid (1.080 g, 7.51 mmol) and benzaldehyde (0.823 mL, 8.26 mmol) were stirred in acetonitrile (18 mL). Oxindole (1.0 g, 7.51 mmol) and DL-proline (0.043 g, 0.38 mmol) in acetonitrile (12 mL) were then added to the orange mixture and stirring was continued for 15 h. The yellow precipitate was filtered under reduced pressure, washed with cold acetonitrile (2 × 9 mL), and dried under reduced pressure to afford **8b** as a pale yellow powder (one diastereomer). Yield: 1.537 g (56%). M.p. 171 °C. IR (film): $\tilde{\nu}$ = 3177 cm^{-1} (br), 3079 (br), 3034 (br), 2949, 2897, 2864, 1778 (s, CO), 1746 (s, CO), 1703 (s, CO), 1620, 1472, 1341, 1306 (s), 1206 (s), 1067, 1013, 752. UV: λ_{max} = 212 nm, 253, 272. ^{1}H NMR ([D$_6$]DMSO): δ = 1.70 [s, 3 H, C(C*H*$_3$)$_2$], 1.80 [s, 3 H, C(C*H*$_3$)$_2$], 3.85 (dl, *J* = 11.9 Hz, 1 H, C*H*-Ph), 4.42 (d, *J* = 11.9 Hz, 1 H, 3′-H), 4.61 (sl, 1 H, 5-H), 5.94 (d, *J* = 7.7 Hz, 1 H, 4′-H), 6.68 (t, *J* = 7.7 Hz, 1 H, 5′-H), 6.88 (d, *J* = 7.7 Hz, 1 H, 7′-H), 7.15 (t, *J* = 7.7 Hz, 1 H, 6′-H), 7.35−7.50 (m, 3 H, 3′′-H, 4′′-H, 5′′-H), 7.69 (d, *J* = 7.2 Hz, 2 H, 2′′-H, 6′′-H), 10.6 (s, 1 H, N*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 26.5 [C(*C*H$_3$)$_2$], 28.3 [C(*C*H$_3$)$_2$], 42.9 (C-3′), 43.9 (*C*HPh), 49.3 (C-5), 105.0 [*C*(CH$_3$)$_2$], 109.7 (C-7′), 121.1 (C-5′), 124.3 (C-4′), 127.1 (C-4′′), 128.1 (C-6′), 128.6, 129.3 (C-3′a), 130.3, 140.9, 142.5 (C-7′a), 164.4 (*C*O), 164.5 (*C*O), 178.0 (NH*C*O) ppm. MS (EI): *m*/*z* (%) = 365 (2) [M$^+$], 307 (38), 263 (25), 221 (100), 193 (25), 174 (25), 144 (25), 133 (56), 131 (68). $C_{21}H_{19}NO_5$ (365.4): calcd. C 69.03, H 5.24, N 3.83; found C 68.87, H 4.86, N 3.84.

5-[(2′,3′-Dihydro-2′-oxo-1*H*-indol-3′-yl)(2′′-nitrophenyl)methyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (8d): This compound was synthesized from 2-nitrobenzaldehyde according to GPB, with extraction followed by chromatography: 2-nitrobenzaldehyde (1.135 g, 7.52 mmol) and triethylamine (1.057 mL, 7.52 mmol) were added successively to Meldrum's acid (1.084 g, 7.52 mmol) in acetonitrile (1.5 mL). The mixture was stirred for 1 h at room temp. Oxindole (1.0 g, 7.52 mmol) was then added to the orange solution, which was stirred for 42 h. The brown solution was diluted with diethyl ether (2 mL) and extracted with citric acid solution (5%, 2 mL). The aqueous layer was washed with diethyl ether (2 × 3 mL). The combined organic layers were dried, filtered and concentrated, and the crude solid was purified by column chromatography to afford **8d** (one diastereomer) as a beige powder (eluent: CH_2Cl_2/CH_3OH, 95:5). Yield: 1.110 g (36%). M.p. 162−163 °C. IR (KBr): $\tilde{\nu}$ = 3205 cm^{-1} (br), 3073, 2881, 1773 (CO), 1738 (s, CO), 1698 (s, CO), 1527 (s), 1346, 1336, 1310 (s), 1200, 752. UV: λ_{max} = 253 nm, 261, 274. ^{1}H NMR ([D$_6$]DMSO): δ = 1.75 [s, 3 H, C(C*H*$_3$)$_2$], 1.82 [s, 3 H, C(C*H*$_3$)$_2$], 4.32 [d, *J* = 11.9 Hz, 1 H, C*H*-(2′′-NO$_2$-Ph)], 4.55 (dd, *J* = 11.9 Hz, 1 H, 3′-H), 4.79 (sl, 1 H, 5-H), 5.81 (d, *J* = 7.5 Hz, 1 H, 4′-H), 6.70 (t, *J* = 7.5 Hz, 1 H, 5′-H), 6.87 (d, *J* = 7.5 Hz, 1 H, 7′-H), 7.16 (t, *J* = 7.5 Hz, 1 H, 6′-H), 7.70 (t, *J* = 8.0 Hz, 1 H, 4′′-H), 7.95 (t, *J* = 8.0 Hz, 1 H, 5′′-H), 8.03 (d, *J* = 8.0 Hz, 1 H, 3′′-H), 8.59 (d, *J* = 8.0 Hz, 1 H, 6′′-H), 10.67 (s, 1 H, N*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 26.4 [C(*C*H$_3$)$_2$], 28.4 [C(*C*H$_3$)$_2$], 37.7 [*C*H-(2′′-NO$_2$-Ph)], 42.7 (C-3′), 48.1 (C-5), 105.1 [*C*(CH$_3$)$_2$], 109.9 (C-7′), 121.5 (C-5′), 123.3 (C-4′), 124.6 (C-3′′), 128.4 (C-6′), 128.8 (C-3′a), 129.2 (C-4′′), 132.4 (C-6′′), 133.4 (C-5′′), 134.4 (C-1′′), 142.4 (C-7′a), 150.7 (C-2′′), 164.5 (*C*O), 165.0 (*C*O), 177.4 (NH*C*O) ppm. MS (EI): *m*/*z* (%) = 411 (1) [M$^+$ + 1], 281 (28), 239 (100), 220 (66), 219 (43), 218 (35), 211 (32), 133 (80), 119 (74). $C_{21}H_{18}N_2O_7$ (410.4): calcd. C 61.46, H 4.42, N 6.82; found C 61.27, H 4.35, N 6.73.

5-[(2′,3′-Dihydro-2′-oxo-1*H*-indol-3′-yl)(4′′-fluorophenyl)methyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (8e): This compound was synthesized from 4-fluorobenzaldehyde according to GPB, with extraction followed by crystallization: 4-fluorobenzaldehyde (0.81 mL, 7.52 mmol) and triethylamine (1.057 mL, 7.52 mmol) were added successively to Meldrum's acid (1.084 g, 7.52 mmol) in acetonitrile (2 mL). The mixture was stirred for 1 h at room temp. Oxindole (1.0 g, 7.52 mmol) was then added to the yellow solution, which was stirred for 45 h. The dark yellow solution was diluted with diethyl ether (2 mL) and extracted with citric acid solution (5%, 2 mL). The aqueous layer was washed with diethyl ether (2 × 3 mL). The combined organic layers were dried and filtered, and the solution was concentrated until **8e** started to crystallize. After filtration and washing (2 × 4 mL of acetonitrile), **8e** (one diastereomer) was obtained as a white crystalline powder. Yield: 1.456 g (51%). M.p. 159 °C. IR (KBr): $\tilde{\nu}$ = 3175 cm^{-1} (br), 3073 (s), 2942, 2861, 1779 (CO), 1743 (s, CO), 1703 (s, CO), 1617, 1507, 1472, 1336, 1311 (s), 1225, 1205 (s), 1064, 1019, 833, 752. UV: λ_{max} = 251 nm, 261, 271, 279. ^{1}H NMR ([D$_6$]DMSO): δ = 1.72 [s, 3 H, C(C*H*$_3$)$_2$], 1.79 [s, 3 H, C(C*H*$_3$)$_2$], 3.86 [d, *J* = 11.9 Hz, 1 H, C*H*-(4′′-F-Ph)], 4.38 (d, *J* = 11.9 Hz, 1 H, 3′-H), 4.62 (s, 1 H, 5-H), 5.97 (d, *J* = 6.5 Hz, 1 H, 4′-H), 6.72 (t, *J* = 6.5 Hz, 1 H, 5′-H), 6.88 (d, *J* = 6.5 Hz, 1 H, 7′-H), 7.18 (t, *J* = 6.5 Hz, 1 H, 6′-H), 7.28 (d, *J* = 8.8 Hz, 1 H, 3′′-H), 7.29 (d, *J* = 8.8 Hz, 1 H, 5′′-H), 7.71 (d, *J* = 8.8 Hz, 1 H), 7.73 (d, *J* = 8.8 Hz, 1 H), 10.6 (s, 1 H, N*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 26.5 [C(*C*H$_3$)$_2$], 28.3 [C(*C*H$_3$)$_2$], 43.0, 43.1, 49.2 (C-5), 105.0 [*C*(CH$_3$)$_2$], 109.7 (C-7′), 115.2 (C-3′′), 115.4 (C-5′′), 121.2 (C-5′), 124.2 (C-4′), 128.1 (C-6′), 129.2 (C-3′a), 132.2, 132.3, 137.0 (C-1′′), 142.5 (C-7′a), 161.6 (d, *J* = 244.4 Hz, C-F, C-4′′), 164.5 (*C*O), 165.7 (*C*O), 177.8 (NH*C*O). MS (EI): *m*/*z* (%) = 281 (51) [M$^+$ − CO$_2$CO(CH$_3$)$_2$], 239 (100), 211 (39), 133 (51). MS (FAB): *m*/*z* (%) = 384 (1) [M$^+$ + H], 326 (20), 282 (10), 193 (41), 149 (100), 133 (34). $C_{21}H_{18}FNO_5$ (383.4): calcd. C 65.79, H 4.73, N 3.65; found C 65.20, H 4.50, N 3.59.

Triethylammonium Salt 11b: This compound was synthesized from benzaldehyde according to GPB, with filtration: benzaldehyde (0.764 mL, 7.52 mmol) and triethylamine (1.057 mL, 7.52 mmol) were added successively to Meldrum's acid (1.084 g, 7.52 mmol) in acetonitrile (4 mL). The mixture was stirred for 1 h at room temp. Oxindole (1.0 g, 7.52 mmol) was then added to the yellow solution. After 119 h stirring, the vivid yellow suspension was filtered and washed with acetonitrile (2 × 4 mL) to obtain **11b** (mixture of two inseparable diastereomers in a ratio of 92:8) as a white powder. Yield: 2.328 g (66%). M.p. 165−167 °C. IR (KBr): $\tilde{\nu}$ = 3140 cm^{-1} (br), 3079, 3001, 1709 (s, CO), 1580 (s), 1566 (s), 1472, 1389, 1204, 1115, 745. UV: λ_{max} = 263 nm, 274. The relative proportions of the two isomers were determined by ^{1}H NMR spectroscopy. For ^{1}H and ^{13}C NMR analyses, only the major isomer could be ascribed: ^{1}H NMR ([D$_6$]DMSO): δ = 1.18 (t, *J* = 7.2 Hz, 9 H, N(CH$_2$C*H*$_3$)$_3$], 1.53 [s, 6 H, C(C*H*$_3$)$_2$], 3.07 [q, *J* = 7.2 Hz, 6 H, N(C*H*$_2$CH$_3$)$_3$], 3.83 (d, *J* = 11.0 Hz, 1 H, C*H*-Ph), 4.74 (d, *J* = 11.0 Hz, 1 H, 3′-H), 5.95 (d, *J* = 7.5 Hz, 1 H, 4′-H), 6.48 (t, *J* = 7.5 Hz, 1 H, 5′-H), 6.73 (d, *J* = 7.5 Hz, 1 H, 7′-H), 6.98 (t, *J* = 7.5 Hz, 1 H, 6′-H), 7.07−7.20 (m, 3 H, 3′′-H, 4′′-H, 5′′-H), 7.42 (d, *J* = 7.3 Hz, 2 H, 2′′-H, 6′′-H), 10.0 (s, 1 H, N*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 8.8 [N(CH$_2$*C*H$_3$)$_3$], 26.3 [C(*C*H$_3$)$_2$], 44.9 (*C*HPh), 45.9 [N(*C*H$_2$CH$_3$)$_3$], 46.7 (C-3′), 75.5 (C-5), 99.7 [*C*(CH$_3$)$_2$], 108.5 (C-7′), 119.8 (C-5′), 125.2 (C-4′), 126.6 (C-4′′), 127.2 (C-3′′, C-5′′), 128.4 (C-6′), 128.9 (C-2′′, C-6′′), 130.7 (C-3′a), 142.8 (C-1′′), 146.5 (C-7′a), 165.1 (*C*O), 165.2 (*C*O), 178.1 (NH*C*O) ppm. MS (EI): *m*/*z* (%) = 263 (10) [M$^+$ − CO$_2$CO(CH$_3$)$_2$], 222 (93), 221 (100), 193 (41), 165 (37), 144 (46). $C_{27}H_{34}N_2O_5$ (466.6): calcd. C 69.50, H 7.34, N 6.00; found C 69.69, H 7.28, N 5.81.

Triethylammonium Salt 11c: This compound was synthesized from 2,5-dimethoxybenzaldehyde according to GPB, with filtration: 2,5-dimethoxybenzaldehyde (1.249 g, 7.52 mmol) and triethylamine (1.057 mL, 7.52 mmol) were added successively to Meldrum's acid (1.084 g, 7.52 mmol) in acetonitrile (4 mL). The mixture was stirred for 1 h at room temp. Oxindole (1.0 g, 7.52 mmol) was then added to the orange solution. After 118 h stirring, the vivid orange suspension was filtered and washed with acetonitrile (2 × 4 mL) to obtain **11c** (mixture of two inseparable diastereomers in a ratio, 60:40) as a pale orange powder. Yield: 2.338 g (59%). M.p. 133−135 °C. IR (KBr): $\tilde{\nu}$ = 3165 cm^{-1} (br), 2992, 2931, 2830, 1713 (s, CO), 1557 (s), 1497, 1461, 1386, 1210 (s), 1044, 747. UV: λ_{max} = 253 nm, 267, 283, 301. The relative proportion of the two isomers (M for major, m for minor) was determined by ^{1}H NMR spectroscopy: ^{1}H NMR ([D$_6$]DMSO): δ = 1.23^{M+m} [t, *J* = 7.3 Hz, 18 H, 2 × N(CH$_2$C*H*$_3$)$_3$], 1.48^M [s, 6 H, C(C*H*$_3$)$_2$], 1.54^m [s, 6 H, C(C*H*$_3$)$_2$], 3.05^{M+m} [q, *J* = 7.3 Hz, 12 H, 2 × N(C*H*$_2$CH$_3$)$_3$], 3.19^m (s, 3 H, OC*H*$_3$), 3.60^M (s, 3 H, OC*H*$_3$), 3.68^M (s, 3 H, OC*H*$_3$), 3.76^m (s, 3 H, OC*H*$_3$), 4.30^m (d, *J* = 6.9 Hz, 1 H, 3′-H), 4.34^M [d, *J* = 11.1 Hz, 1 H, C*H*-(2′′,5′′-diOMe-Ph)], 4.61^m [d, *J* = 6.9 Hz, 1 H, C*H*-(2′′,5′′-diOMe-Ph)], 4.62^M (d, *J* = 11.1 Hz, 1 H, 3′-H), 6.26^m (d, *J* = 7.4 Hz, 1 H, 4′-H), 6.47^m (t, *J* = 7.4 Hz, 1 H, 5′-H), 6.49^m (d, *J* = 8.8 Hz, 1 H, 3′′-H), 6.57^m (dd, *J* = 3.1, 8.8 Hz, 1 H, 4′′-H), 6.60^M (dd, *J* = 3.0, 8.8 Hz, 1 H, 4′′-H), 6.67^M (d, *J* = 8.8 Hz, 1 H, 3′′-H), 6.68^m (d, *J* = 7.4 Hz, 1 H, 7′-H), 6.75^M (d, *J* = 7.5 Hz, 1 H, 7′-H), 6.80^M (t, *J* = 7.5 Hz, 1 H, 5′-H), 6.92^m (t, *J* = 7.4 Hz, 1 H, 6′-H), 7.07^M (t, *J* = 7.5 Hz, 1 H, 6′-H), 7.08^M (d, *J* = 7.5 Hz,

1 H, 4′-H), 7.30[m] (d, J = 3.1 Hz, 1 H, 6′′-H), 7.42[M] (d, J = 3.0 Hz, 1 H, 6′′-H), 9.90[M+m] (s, 2 H, 2 × N*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 8.8[M+m] [2 × N(CH$_2$*C*H$_3$)$_3$], 26.2[m] [C(*C*H$_3$)$_2$], 26.3[M] [C(*C*H$_3$)$_2$], 35.6[m] [*C*H-(2′′,5′′-diOMe-Ph)], 36.3[M] [*C*H-(2′′,5′′-diOMe-Ph)], 45.8[M+m] [2 × N(*C*H$_2$CH$_3$)$_3$], 47.0[M] (C-3′), 47.8[m] (C-3′), 55.1[M] (O*C*H$_3$), 55.3[m] (O*C*H$_3$), 55.7[m] (O*C*H$_3$), 56.2[M] (O*C*H$_3$), 75.4[M] (C-5), 75.6[m] (C-5), 99.2[m] [*C*(CH$_3$)$_2$], 99.4[M] [*C*(CH$_3$)$_2$], 107.8[m] (C-7′), 108.1[M] (C-7′), 109.9[M] (C-4′′), 110.0[m] (C-4′′), 110.7[m] (C-3′′), 111.1[M] (C-3′′), 116.0[M] (C-6′′), 116.4[m] (C-6′′), 117.1[m] (C-5′), 119.5[M] (C-5′), 125.3[m] (C-4′), 125.4[M] (C-4′), 126.1[m] (C-6′), 126.6[M] (C-6′), 130.6[m] (C-3′a), 131.6[M] (C-3′a), 135.8[m] (C-1′′), 136.3[M] (C-1′′), 142.8[M] (C-7′a), 142.9[m] (C-7′a), 151.4[m] (C-2′′), 151.9[M] (C-2′′), 152.9[m] (C-5′′), 153.1[M] (C-5′′), 165.8[m] (2 × *C*O), 165.9[M] (2 × *C*O), 178.3[M] (NH*C*O), 179.8[m] (NH*C*O) ppm. MS (EI): *m*/*z* (%) = 281 (36) [M$^+$ − CH$_2$(CO$_2$)$_2$C(CH$_3$)$_2$], 250 (100). C$_{29}$H$_{38}$N$_2$O$_7$ (526.6): calcd. C 66.14, H 7.27, N 5.32; found C 66.38, H 7.02, N 5.20.

5-[(2′,5′-Dimethoxybenzylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (10c) and 2-[(2′,3′-Dihydro-2′-oxo-1*H*-indol-3′-yl)(2′′,5′′-dimethoxyphenyl)methyl]malonic Acid (13): This compound was synthesized from 2,5-dimethoxybenzaldehyde according to GPA, with concentration followed by crystallization: Meldrum's acid (0.108 g, 0.75 mmol) and 2,5-dimethoxybenzaldehyde (0.137 g, 0.83 mmol) were stirred in acetonitrile (4 mL). Oxindole (0.100 g, 0.75 mmol) and DL-proline (0.004 g, 0.04 mmol) in acetonitrile (2 mL) were then added to the yellow solution, which was stirred for 50 h. After concentration, the crude yellow solid (0.381 g) was crystallized (hexane/CH$_2$Cl$_2$, 70:30) to obtain **13** (one diastereomer) as a vivid yellow powder. Yield: 0.102 g (35%). M.p. 157 °C. IR (film): $\tilde{\nu}$ = 3250 cm^{-1} (br), 3181, 2994, 2947, 2830, 1694 (s, CO), 1591 (s), 1215, 1046, 750. UV: λ_{max} = 261 nm, 294. ^{1}H NMR (CDCl$_3$): δ = 3.55 (s, 6 H, 2 × OC*H*$_3$), 3.79 (d, J = 12.5 Hz, 1 H), 3.87 (d, J = 12.5 Hz, 1 H), 5.31 (s, 1 H, 2-H), 6.87 (d, J = 8.0 Hz, 1 H), 7.02 (t, J = 8.0 Hz, 1 H), 7.21 (t, J = 8.0 Hz, 1 H), 7.24 (d, J = 8.0 Hz, 1 H), 8.13 (s, 1 H, N*H*) ppm. ^{13}C NMR (CDCl$_3$): δ = 35.5, 48.9, 55.1, 55.2, 55.3, 108.5 (C-7′), 109.6, 110.8, 115.5 (C-6′′), 121.0, 125.2, 126.4, 130.0 (C-3′a), 132.9 (C-1′′), 141.1 (C-7′a), 151.2, 153.0, 167.8 (*C*O), 168.0 (*C*O), 183.1 (NH*C*O) ppm. MS (EI): *m*/*z* (%) = 385 (39) [M$^+$], 384 (100), 320 (27), 293 (48). HRMS: calcd. 385.1161; found 385.1130. From the mother liquor of **13**, Knoevenagel adduct **10c** (two isomers, 60:40) was isolated after a column chromatography (eluent: CH$_2$Cl$_2$). Yield: 0.069 g (31%). M.p. 119 °C (ref [17] M.p. 120−121 °C).

1,3-Bis[(2′,2′-dimethyl-4′,6′-dioxo-1,3-dioxan-5′-yl)methyl]-2,3-dihydro-2-oxo-1*H*-indole (12): This compound was synthesized from paraformaldehyde according to GPA, with concentration followed by chromatography: Meldrum's acid (1.080 g, 7.51 mmol) and paraformaldehyde (0.248 g, 8.26 mmol) were stirred in acetonitrile (18 mL). Oxindole (1.0 g, 7.51 mmol) and DL-proline (0.043 g, 0.38 mmol) in acetonitrile (12 mL) were then added to the beige mixture, which was stirred for 17 h 30 min. After concentration, the crude brown solid was purified by column chromatography to obtain **12** as a pale yellow powder (eluent: CH$_2$Cl$_2$/CH$_3$OH, 94:6). Yield: 0.078 g (2%). M.p. > 350 °C. IR (film): $\tilde{\nu}$ = 3111 cm^{-1}, 2994, 2922, 1771 (br, CO), 1703 (CO), 1701 (s, CO), 1557 (s), 1470, 1416, 1206, 1128, 760. UV: λ_{max} = 258 nm, 263. ^{1}H NMR (CDCl$_3$): δ = 1.60−1.80 (4s, 12 H, 2 × C(C*H*$_3$)$_2$], 2.50−5.30 (m, 7 H, 2 × C*H*$_2$, 3-H, , 2 × 5′-H), 6.90 (d, J = 8.0 Hz, 1 H, 4-H), 7.05 (t, J = 8.0 Hz, 1 H, 5-H), 7.21 (d, J = 8.0 Hz, 1 H, 7-H), 7.26 (t, J = 8.0 Hz, 1 H, 6-H) ppm. ^{13}C NMR (CDCl$_3$): δ = 26.4 [C(*C*H$_3$)$_2$], 26.5 [C(*C*H$_3$)$_2$], 28.4 [C(*C*H$_3$)$_2$], 28.5 [C(*C*H$_3$)$_2$], 41.1 (2 × C-5′), 41.4 (C-3), 49.5 (*C*H$_2$), 49.8 (*C*H$_2$), 105.3 [*C*(CH$_3$)$_2$], 105.6 [*C*(CH$_3$)$_2$], 109.9 (C-7), 122.6 (C-5), 123.8 (C-4), 128.1 (C-6), 129.2 (C-3a), 141.0 (C-7a), 165.3 (*C*O), 165.4 (*C*O), 165.8 (2 × *C*O), 180.2 (NH*C*O) ppm. C$_{22}$H$_{23}$NO$_9$. MS (EI): *m*/*z* (%) = 446 (98) [M$^+$ + 1], 187 (40), 145 (100), 117 (52).

1,2,3,4-Tetrahydro-4-phenyl-1-thiacarbazol-2-one (3b): A solution of **8b** (0.300 g, 0.82 mmol) and Lawesson's reagent (0.400 g, 0.98 mmol) in dry toluene was heated and stirred at 80 °C under nitrogen atmosphere for 3 days. After concentration under reduced pressure, the crude product was diluted with CH$_2$Cl$_2$ to obtain an orange suspension, which was filtered. The mother liquor was purified by column chromatography on silica gel (eluent: CH$_2$Cl$_2$) to afford **3b** as a pale yellow foam. Yield: 0.086 g (31%). IR (film): $\tilde{\nu}$ = 3418 cm^{-1} (br), 1645 (s, CO), 1404, 1017, 951. UV: λ_{max} = 224 nm, 284, 326. ^{1}H NMR ([D$_6$]DMSO): δ = 3.22 (dd, J = 5.0, 16.7 Hz, 1 H, C*H*$_2$), 3.39 (dd, J = 5.0, 16.7 Hz, 1 H, C*H*$_2$), 4.78 (t, J = 5.0 Hz, 1 H, C*H*-Ph), 6.96 (tl, J = 7.7 Hz, 1 H, 5′-H), 7.04−7.18 (m, 2H indole), 7.19− 7.34 (m, 5 H aromatic), 7.39 (dl, J = 8.6 Hz, 2 H, 2′′-H, 6′′-H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 36.2 (*C*HPh), 48.3 (*C*H$_2$), 108.6 (C-3′), 111.3 (C-7), 117.5, 119.6, 121.3, 124.3, 126.2, 127.0 (C-4′′), 127.4, 128.6, 137.2 (C-7′a), 142.3, 197.0 (CO) ppm. C$_{17}$H$_{13}$NOS. MS (EI): *m*/*z* (%) = 279 (48) [M$^+$], 236 (100). HRMS (*m*/*z* = 279, C$_{17}$H$_{13}$NOS) calcd. 279.0707; found 279.0718. HRMS (*m*/*z* = 237, C$_{15}$H$_{11}$NS) calcd. 237.0616; found 237.0612. HRMS (*m*/*z* = 236, C$_{15}$H$_{10}$NS calcd. 236.0575; found 236.0534. C$_{17}$H$_{13}$NOS (279.4): calcd. C 73.09, H 4.69, N 5.01; found C 72.92, H 4.61, N 4.69.

General Procedure for the Preparation of Compounds 15 from 8 or 11: A pale suspension of **8** or **11** in dry *tert*-butyl alcohol was heated under reflux under nitrogen atmosphere, during which it became progressively colored and dissolved. The stirring was continued until no further conversion of the starting material **8** or **11** was observed (TLC). After concentration under reduced pressure, the crude mixture was purified by column chromatography on silica gel (eluent: CH$_2$Cl$_2$/CH$_3$OH) to obtain **15** as a mixture of inseparable diastereomers.

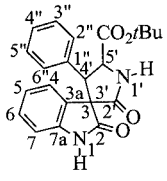
2-*tert*-Butoxycarbonyl-3-(2′,3′-dihydro-2′-oxo-1*H*-indol-3′-yl)-propionic Acid (15a): This compound was synthesized from **8a**, according to the above GP. A white suspension of **8a** (0.265 g, 0.92 mmol) in *tert*-butyl alcohol (20 mL) was heated under reflux for 1 h 30 min, during which it progressively became a pale yellow solution. The crude beige solid (0.334 g) was purified by column chromatography to obtain **15a** (two inseparable diastereomers, ratio, 50:50) as a yellow, amorphous solid (eluent: CH$_2$Cl$_2$/CH$_3$OH, 92:8). Yield: 0.221 g (79%). M.p. 57−59 °C (mixture). IR (film): $\tilde{\nu}$ = 3310 cm^{-1} (br), 3261, 2980, 2933, 1732 (s, CO), 1716 (s, CO), 1707 (s, CO), 1622, 1472, 1369, 1298, 1255, 1227, 1147, 742. UV: λ_{max} = 250 nm, 284. The relative proportions of the two isomers (*A*:*B*, ratio 50:50) were determined by ^{1}H NMR spectroscopy: ^{1}H NMR (CDCl$_3$): δ = 1.43[B] [s, 9 H, C(C*H*$_3$)$_3$], 1.47[A] [s, 9 H, C(C*H*$_3$)$_3$], 2.30−2.60[A+B] (m, 4 H, 2 × C*H*$_2$), 3.49−3.61[A+B] (m, 2 H, 2 × 3′-H), 3.78[B] (t, J = 7.5 Hz, 1 H, 2-H), 3.88[A] (t, J = 7.4 Hz, 1 H, 2-H), 6.90−7.10[A+B] (m, 4 H), 7.12−7.31[A+B] (m, 4 H), 9.69[B] (s, 1 H, N*H*), 9.76[A] (s, 1 H, N*H*), 10.67[A+B] (sl, 2 H, 2 × CO$_2$ *H*) ppm. ^{13}C NMR (CDCl$_3$): δ = 27.7[A+B] [2 × C(*C*H$_3$)$_3$], 29.2[B] (*C*H$_2$), 29.4[A] (*C*H$_2$), 43.5[B] (C-3′), 43.6[A] (C-3′), 49.3[B] (C-2), 49.6[A] (C-2), 82.4[B] [*C*(CH$_3$)$_3$], 82.5[A] [*C*(CH$_3$)$_3$], 110.3[B] (C-7′), 110.5[A] (C-7′), 122.6[B] (C-5′), 122.7[A] (C-5′), 124.2[B] (C-4′), 124.3[A] (C-4′), 128.2[A+B] (2 × C-6′), 128.3[B] (C-3′a), 128.5[A] (C-3′a), 141.1[B] (C-7′a), 141.2[A] (C-7′a), 167.9[B] [*C*O$_2$C(CH$_3$)$_3$], 168.0[A] [*C*O$_2$C(CH$_3$)$_3$], 173.5[B] (*C*O$_2$ H), 173.7[A] (*C*O$_2$H), 181.1[A+B] (2 × NH*C*O) ppm. MS (EI): *m*/*z* (%) = 305 (1) [M$^+$], 187 (27), 145 (100). C$_{16}$H$_{19}$NO$_5$·1/2H$_2$O

(314.3): calcd. C 61.13, H 6.11, N 4.45; found C 61.52, H 6.00, N 4.52.

2-*tert*-Butoxycarbonyl-3-[(2′,3′-dihydro-2′-oxo-1*H*-indol-3′-yl)]-hydrocinnamic Acid (15b): This compound was synthesized from **8b**, according to the above GP. A pale yellow suspension of **8b** (1.0 g, 2.74 mmol) in *tert*-butyl alcohol (48 mL) was heated under reflux for 2 h 30 min, during which it progressively became a vivid yellow solution. The crude yellow solid was purified by column chromatography to obtain **15b** (four inseparable diastereomers, ratio, 40:40:10:10) as a pale yellow amorphous solid (eluent: CH_2Cl_2/CH_3OH, 80:20). Yield: 0.939 g (90%). It was also synthesized from **11b** by the above GP: A white suspension of **11b** (1.9 g, 4.08 mmol) in *tert*-butyl alcohol (60 mL) was heated under reflux for 2 h 20, during which it progressively became a vivid yellow solution. The crude yellow oil (2.017 g) was purified by column chromatography to obtain **15b** (four inseparable diastereomers, ratio, 40:40:10:10) as a pale yellow, amorphous solid (eluent: CH_2Cl_2/CH_3OH, 80:20). Yield: 0.693 g (45%). M.p. 144 °C (mixture). IR (film): $\tilde{\nu}$ = 3408 cm^{-1} (br), 3217 (br), 3063, 3032, 2980, 2933, 1721 (s, CO), 1703 (s, CO), 1694 (s, CO), 1622 (s), 1603, 1472, 1393, 1369 (s), 1337, 1302, 1252, 1152 (s), 750, 700. UV: λ_{max} = 250 nm, 284. The relative proportions of the four isomers {(A):[B], ratio, (40:40):[10:10]} were determined by ^{1}H NMR spectroscopy: ^{1}H NMR ([D$_6$]DMSO): δ = 0.99^A [s, 9 H, C(CH_3)$_3$], 1.03^A [s, 9 H, C(CH_3)$_3$], 1.47^B [s, 9 H, C(CH_3)$_3$], 1.49^B [s, 9 H, C(CH_3)$_3$], 3.89−4.18^{A+B} (m, 11 H), 4.68^A (d, J = 12.0 Hz, 1 H), 6.50−6.62^{A+B} (m, 4 H, 4 × 4′-H), 6.70−6.85^A (m, 1 H), 6.90−7.19^{A+B} (m, 28 H), 7.41^A (d, J = 7.0 Hz, 1 H, 7′-H), 7.48^B (d, J = 6.9 Hz, 1 H, 7′-H), 7.66^A (d, J = 7.0 Hz, 1 H, 7′-H), 9.99^A (s, 1 H, N*H*), 10.09^B (s, 1 H, N*H*), 10.21^A (s, 1 H, N*H*), 10.24^B (s, 1 H, N*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 27.2 [C(*C*H$_3$)$_3$], 27.4 [C(*C*H$_3$)$_3$], 27.8 [C(*C*H$_3$)$_3$], 27.9 [C(*C*H$_3$)$_3$], 45.6, 46.1, 46.5, 46.6, 48.0, 48.8, 49.9, 50.2, 54.7 (C-2), 54.8 (C-2), 58.4 (C-2), 79.7 [*C*(CH$_3$)$_3$], 79.9 [*C*(CH$_3$)$_3$], 81.3 [*C*(CH$_3$)$_3$], 81.5 [*C*(CH$_3$)$_3$], 109.0 (2 × C-7′), 109.1 (C-7′), 109.2 (C-7′), 121.1 (C-5′), 121.2 (C-5′), 121.3 (C-5′), 121.4 (C-5′), 124.1, 126.0, 126.7, 126.9 (C-3′a), 127.2, 127.4, 127.45 (C-3′a), 129.0 (2 × CH), 129.4, 137.5 (C-1′′), 137.6 (C-1′′), 138.0 (C-1′′), 142.3 (C-7′a), 142.4 (C-7′a), 143.2 (C-7′a), 143.3 (C-7′a), 168.2 (*C*O$_2$C(CH$_3$)$_3$], 168.5 (*C*O$_2$C(CH$_3$)$_3$], 171.0 (*C*O$_2$ H), 171.2 (*C*O$_2$ H), 176.9 (NH*C*O), 177.5 (NH*C*O), 177.6 (NH*C*O), 178.1 (NH*C*O) ppm. $C_{22}H_{23}NO_5$. MS (EI): *m*/*z* (%) = 382 (1) [M$^+$], 281 (30), 222 (62), 221 (100), 133 (53). $C_{22}H_{23}NO_5$·H_2O (399.4): calcd. C 66.15, H 6.31, N 3.50; found C 66.05, H 5.76, N 3.48.

2-*tert*-Butoxycarbonyl-3-(2′,3′-dihydro-2′-oxo-1*H*-indol-3′-yl)-3-(2′′,5′′-dimethoxyphenyl)propionic Acid (15c): This compound was synthesized from **11c**, according to the above GP: a yellow suspension of **11c** (1.5 g, 2.85 mmol) in *tert*-butyl alcohol (50 mL) was heated under reflux for 2 h 30 min, during which it progressively became a orange solution. The crude amorphous orange solid (1.479 g) was purified by column chromatography to obtain **15c** (four inseparable diastereomers, ratio, 66:22:9:3) as an orange, amorphous solid (eluent: CH_2Cl_2/CH_3OH, 85:15). Yield: 0.676 g (45%). M.p. 144−145 °C (mixture). IR (KBr): $\tilde{\nu}$ = 3266 cm^{-1} (br), 2984, 2940, 1721 (s, CO), 1717 (s, CO), 1709 (s, CO), 1622, 1601, 1503, 1472, 1368, 1308, 1225 (s), 1150 (s), 1047, 750. UV: λ_{max} = 253 nm, 294. The relative proportions of the four isomers (*A*:*B*:*C*:*D*, ratio, 66:22:9:3) were determined by ^{1}H NMR spectroscopy: ^{1}H NMR ([D$_6$]DMSO): δ = 0.97^A [s, 9 H, C(CH_3)$_3$], 1.02^C [s, 9 H, C(CH_3)$_3$], 1.39^B [s, 9 H, C(CH_3)$_3$], 1.41^D [s, 9 H, C(CH_3)$_3$], 3.03^B (s, 3 H, OCH_3), 3.31^B (s, 3 H, OCH_3), 3.45^A (s, 3 H, OCH$_3$), 4.07^B (d, J = 5.33 Hz, 1 H, 3′-H), 4.21^A (sl, 1 H, 3′-H), 4.41−4.69$^{A+B+C+D}$ (m, 4 H, 4 × 2-H), 6.49−6.61^{A+C+D} (m, 6 H), 6.62−6.79^{B+C} (m, 4 H), 6.80−6.92$^{A+B+C+D}$ (m, 5 H), 6.93−7.05$^{A+B+C+D}$ (m, 4 H), 7.06−7.19^{B+C+D} (m, 3 H), 7.19−7.36^{A+C+D} (m, 3 H), 7.50^B (d, J = 7.0 Hz, 1 H), 9.91^B (s, 1 H, N*H*), 10.10^D (s, 1 H, N*H*), 10.21^A (s, 1 H, N*H*), 10.28^C (s, 1 H, N*H*) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 27.4 [C(*C*H$_3$)$_3$], 27.5 [C(*C*H$_3$)$_3$], 28.0 [C(*C*H$_3$)$_3$], 28.1 [C(*C*H$_3$)$_3$], 48.3 (C-3′), 48.7 (C-3′), 55.1, 55.4, 55.5, 55.6, 55.9, 56.4, 56.5, 79.4 [*C*(CH$_3$)$_3$], 79.5 [*C*(CH$_3$)$_3$], 80.1 [*C*(CH$_3$)$_3$], 81.2 [*C*(CH$_3$)$_3$], 108.9 (C-7′), 109.4 (C-7′), 111.3, 112.0, 112.6, 112.9, 113.2, 115.5, 120.8 (C-5′), 121.0 (C-5′), 121.1 (C-5′), 125.1 (C-4′), 126.2 (C-4′), 127.5 (C-6′), 128.0 (C-6′), 128.1 (C-3′a), 128.4 (C-3′a), 128.7 (C-3′a), 128.8 (C-3′a), 142.2, 142.5, 143.6, 151.5, 151.6, 152.4, 152.5, 168.2, 168.9, 169.1, 169.4, 172.5, 177.8 (NH*C*O), 178.4 (NH*C*O), 179.1 (NH*C*O) ppm. MS (EI): *m*/*z* (%) = 281 (46) [M$^+$ − $CH_2CO_2HCO_2C(CH_3)_3$], 251 (55), 250 (100). $C_{24}H_{27}NO_7$·$2H_2O$ (477.5): calcd. C 60.36, H 6.54, N 2.93; found C 59.72, H 5.84, N 2.66.

General Procedure for the Preparation of Compounds 17 from 15: Diphenylphosphoryl azide (DPPA) and triethylamine were added successively to a suspension of the mixture of isomers **15** in dry acetonitrile. The suspension was then heated at 50 °C under nitrogen atmosphere, while it progressively became colored and dissolved. The stirring was continued until no further conversion of the starting material **15** was observed (TLC). The reaction mixture was diluted in diethyl ether and extracted with a 5% aqueous solution of citric acid. The aqueous layer was washed several times with diethyl ether. The combined organic layers were filtered, dried with anhydrous $MgSO_4$, and concentrated under reduced pressure. The crude product was then purified by column chromatography on silica gel (eluent: CH_2Cl_2/CH_3OH) to obtain **17** as a mixture of diastereomers.



17

Spiro Compound 17aI,II: This compound was synthesized according to the GP: DPPA (0.126 mL, 0.59 mmol) and triethylamine (0.083 mL, 0.59 mmol) were added successively to **15a** (0.163 g, 0.53 mmol) in acetonitrile (10 mL). The suspension was heated for 1 h 40 min until it had become a pale yellow solution. The mixture was diluted with diethyl ether (4 mL) and extracted with a 5% aqueous solution of citric acid (10 mL). The aqueous layer was washed with diethyl ether (2 × 10 mL). The combined organic layers were dried, filtered, and concentrated, and the crude product was purified by column chromatography. A mixture of two inseparable diastereomers **17aI**,**II** (ratio, 50:50) was obtained as a white crystalline powder (eluent: CH_2Cl_2/CH_3OH, 94:6). Yield: 0.114 g (70%). M.p. 174−176 °C (mixture). IR (film): $\tilde{\nu}$ = 3205 cm^{-1} (br), 2978, 2932, 1732 (s, CO), 1714 (s, CO), 1620, 1471, 1369, 1248, 1155. UV: λ_{max} = 253 nm, 289. The relative proportions of the two isomers (**I**/**II**, ratio, 50:50) were determined by ^{1}H NMR spectroscopy: ^{1}H NMR ($CDCl_3$): δ = 1.50^{I+II} [s, 18 H, 2 × C(CH_3)$_3$], 2.50^I (dd, J = 5.6, 13.7 Hz, 1 H, CH*H*), 2.72^{II} (dd, J = 8.6, 13.5 Hz, 1 H, CH*H*), 2.95^{II} (dd, J = 5.9, 13.5 Hz, 1 H, C*H*H), 3.09^I (dd, J = 5.6, 13.7 Hz, 1 H, C*H*H), 4.43^{II} (dd, J = 5.9, 8.6 Hz, 1 H, 5′-H), 4.53^I (dd, J = 5.6, 9.0 Hz, 1 H, 5′-H), 6.86^{II} (d, J = 7.4 Hz, 1 H, 4-H), 6.88^I (d, J = 7.6 Hz, 1 H, 4-H), 7.02^{I+II} (t, J = 7.6 Hz, 2 H, 2 × 5-H), 7.12−7.23^{I+II} (m, 4 H, 2 × C-6, 2 × C-7), 7.63^{II} (s, 1

H, 1′-H), 7.71[I] (s, 1 H, 1′-H), 9.52[II] (s, 1 H, 1-H), 9.59[I] (s, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.9[I+II] [C(CH_3)$_3$], 34.7[II] (CH_2), 35.0[I](CH_2), 53.9[II] (C-5′), 54.2[I] (C-5′), 57.8[II] (C-3), 57.9[I] (C-3), 82.9[I+II] [C(CH_3)$_3$], 110.5[II] (C-7), 110.7[I] (C-7), 122.7[II] (C-5), 122.8[I] (C-5), 122.9[II] (C-4), 123.5[I] (C-4), 129.1[II] (C-6), 129.2[I] (C-6), 129.3[II] (C-3a), 129.4[I] (C-3a), 141.8[I+II] (C-7a), 169.5[II] (C-2′), 170.1[I] (C-2′), 177.1[II] (C-2), 177.6[I] (C-2) ppm. $C_{16}H_{18}N_2O_4$. MS (EI): *m/z* (%) = 302 (× 40, 14) [M$^+$], 246 (11), 201 (20), 174 (28), 146 (100). $C_{16}H_{18}N_2O_4$·1/2H_2O (311.3): calcd. C 61.72, H 6.15, N 8.99; found C 62.21, H 5.95, N 8.90.

Spiro Compound 17bI,II and 17bIII: This compound was synthesized according to the GP: DPPA (0.093 mL, 0.43 mmol) and triethylamine (0.061 mL, 0.43 mmol) were added successively to **15b** (0.150 g, 0.39 mmol) in acetonitrile (10 mL). The suspension was heated for 2 h 30 min until it had become a yellow solution. The mixture was diluted with diethyl ether (4 mL) and extracted with a 5% aqueous solution of citric acid (9 mL). The aqueous layer was washed with diethyl ether (2 × 10 mL). The combined organic layers were dried, filtered, and concentrated, and the crude product (0.333 g) was purified by column chromatography. A mixture of three diastereomers **17bI**,**II**,**III** (ratio, 47:33:20), was obtained as a white crystalline powder (eluent: CH_2Cl_2/CH_3OH, 98:2). Yield: 0.111 g (74%). The relative proportions of the three isomers (**I/II/III**, ratio, 47:33:20) were determined by ^{1}H NMR spectroscopy. The minor component **(3*R**,4′*S**,5′*S**)-17bIII** was isolated by crystallization from diethyl ether. M.p. 188−189 °C. ^{1}H NMR ($CDCl_3$): δ = 1.35 [s, 9 H, C(CH_3)$_3$], 4.42 (d, *J* = 8.2 Hz, 1 H, 4′-H), 4.85 (d, *J* = 8.2 Hz, 1 H, 5′-H), 6.53 (s, 1 H, 1′-H), 6.72 (d, *J* = 7.8 Hz, 1 H, 7-H), 6.83−6.89 (m, 2 H, 4-H, 5-H), 7.11 (t, *J* = 7.8 Hz, 1 H, 6-H), 7.12−7.22 (m, 5 H, 2′′-H, 3′′-H, 4′′-H, 5′′-H, 6′′-H), 7.71 (s, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.8 [C(CH_3)$_3$], 52.7 (C-4′), 58.3 (C-5′), 63.9 (C-3), 83.2 [C(CH_3)$_3$], 110.2 (C-7), 122.5 (C-5), 125.0 (C-4), 125.6 (C-3a), 127.8 (C-4′′), 128.2, 128.3, 129.2 (C-6), 135.0 (C-1′′), 141.1 (C-7a), 168.5 (CO_2tBu), 171.5 (C-2′), 174.9 (C-2) ppm. $C_{22}H_{22}N_2O_4$ (378.4): calcd. C 69.83, H 5.86, N 7.40; found C 69.26, H 5.76, N 7.42. From the mother liquor of **17bIII**, **(3*R**,4′*R**,5′*R**)-17bI** and **(3*R**,4′*S**,5′*R**)-17bII** were isolated as a mixture. The relative proportions of the two isomers (**I/II**, ratio, 80:20) were determined by ^{1}H NMR spectroscopy. M.p. 127−129 °C (mixture). IR (film): $\tilde{\nu}$ = 3227 cm^{-1} (br), 3070, 1734 (s, CO), 1717 (s, CO), 1622, 1471, 1369, 1242, 1157, 746. UV: λ_{max} = 256 nm, 265, 289. ^{1}H NMR ($CDCl_3$): δ = 1.09[II] [s, 9 H, C(CH_3)$_3$], 1.28[I] [s, 9 H, C(CH_3)$_3$], 3.97[I] (d, *J* = 10.3 Hz, 1 H, 4′-H), 4.11[II] (d, *J* = 6.6 Hz, 1 H, 4′-H), 5.23[I] (d, *J* = 10.3 Hz, 1 H, 5′-H), 5.48[II] (d, *J* = 6.6 Hz, 1 H, 5′-H), 5.99[II] (d, *J* = 7.8 Hz, 1 H, 4-H), 6.63[II] (t, *J* = 7.8 Hz, 1 H, 5-H), 6.68[II] (s, 1 H, 1′-H), 6.69[I] (d, *J* = 7.8 Hz, 1 H, 7-H), 6.79[I] (s, 1 H, 1′-H), 6.80[II] (d, *J* = 7.8 Hz, 1 H, 7-H), 6.83−6.89[I+II] (m, 13 H), 7.40[I] (d, *J* = 7.8 Hz, 1 H, 4-H), 7.68[I] (s, 1 H, 1-H), 8.12[II] (s, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.4[II] [C(CH_3)$_3$], 27.6[II] [C(CH_3)$_3$], 52.3[II] (C-4′), 55.5[II] (C-4′), 57.1[I] (C-5′), 58.8[II] (C-5′), 64.0[II] (C-3), 64.8[I] (C-3), 82.5[II] [C(CH_3)$_3$], 82.7[I] [C(CH_3)$_3$], 109.8[II] (C-7), 110.2[I] (C-7), 122.6[II] (C-5), 123.0[I] (C-5), 123.9[I] (C-4), 124.6[II] (C-3a), 126.5[I] (C-3a), 126.8[II] (C-4), 127.9[I] (C-4′′), 128.1[I], 128.2[I+II], 128.3[II], 128.4[II], 129.1[II] (C-6), 129.3[I] (C-6), 133.1[I] (C-1′′), 136.6[II] (C-1′′), 141.6[II] (C-7a), 142.1[I] (C-7a), 168.2[II] (CO_2tBu), 169.3[I] (CO_2tBu), 171.6[I] (C-2′), 171.7[II] (C-2′), 174.5[I] (C-2), 175.9[II] (C-2) ppm. $C_{22}H_{22}N_2O_4$. MS (EI): *m/z* (%) = 378 (1) [M$^+$], 322 (17), 277 (16), 222 (100). $C_{22}H_{22}N_2O_4$·1/2H_2O (387.4): calcd. C 68.20, H 5.98, N 7.23; found C 68.08, H 5.83, N 7.17.

Spiro Compound 17cI,II,III: This compound was synthesized according to the GP: DPPA (0.154 mL, 0.72 mmol) and triethylamine (0.100 mL, 0.72 mmol) were added successively to **15c** (0.287 g, 0.65 mmol) in acetonitrile (10 mL). The yellow suspension was heated for 4 h until it had become a yellow solution. The mixture was diluted with diethyl ether (6 mL) and extracted with a 5% aqueous solution of citric acid (12 mL). The aqueous layer was washed with diethyl ether (2 × 12 mL). The combined organic layers were dried, filtered, and concentrated, and the crude product (0.612 g) was purified by column chromatography. A mixture of three inseparable diastereomers **17cI**,**II**,**III** (ratio, 53:34:13) was obtained as a white crystalline powder (eluent: CH_2Cl_2/CH_3OH, 92:8). Yield: 0.144 g (50%). M.p. 188−189 °C (mixture). IR (film): $\tilde{\nu}$ = 3215 cm^{-1} (br), 1734 (s, CO), 1716 (s, CO), 1622, 1502, 1471, 1226, 1159. UV: λ_{max} = 254 nm, 295. The relative proportions of the three isomers (**I/II/III**, ratio, 53:34:13) were determined by ^{1}H NMR spectroscopy: ^{1}H NMR ($CDCl_3$): δ = 1.13[II] [s, 9 H, C(CH_3)$_3$], 1.25[I] [s, 9 H, C(CH_3)$_3$], 1.44[III] [s, 9 H, C(CH_3)$_3$], 3.27[I] (s, 3 H, OCH_3), 3.29[II] (s, 3 H, OCH_3), 3.33[III] (s, 3 H, OCH_3), 3.64[I] (s, 3 H, OCH_3), 3.70[III] (s, 3 H, OCH_3), 3.72[II] (s, 3 H, OCH_3), 4.69[II] (d, *J* = 7.1 Hz, 1 H, 4′-H), 4.76[I] (d, *J* = 10.3 Hz, 1 H, 4′-H), 4.82[III] (d, *J* = 6.2 Hz, 1 H, 4′-H), 5.06[I] (d, *J* = 10.3 Hz, 1 H, 5′-H), 5.38[II] (d, *J* = 7.1 Hz, 1 H, 5′-H), 6.02[II] (d, *J* = 7.6 Hz, 1 H, 4-H), 6.40−6.69[I+II+III] (m, 9 H), 6.71−6.92[I+II+III] (m, 3 H), 6.98−7.11[I+II+III] (m, 6 H), 7.22−7.97[I+II+III] (m, 6 H), 9.12[I] (s, 1 H, 1-H), 9.65[II] (s, 1 H, 1-H), 9.69[III] (s, 1 H, 1-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.3[II] [C(CH_3)$_3$], 27.5[I] [C(CH_3)$_3$], 27.7[III] [C(CH_3)$_3$], 45.1[II] (C-4′), 45.8[I] (C-4′), 54.8[III] (OCH_3), 55.5[I] (OCH_3), 55.6[I] (OCH_3), 55.65[III] (OCH_3), 55.7[II] (OCH_3), 55.8[II] (OCH_3), 57.6[I] (C-5′), 57.8[III] (C-5′), 58.1[II] (C-5′), 62.6[III] (C-3), 63.6[II] (C-3), 64.4[I] (C-3), 82.0[II] [C(CH_3)$_3$], 82.1[I] [C(CH_3)$_3$], 82.2[III] [C(CH_3)$_3$], 109.9[I] (C-7), 110.7[II] (C-7), 111.5[I], 112.4[II], 112.7[II], 112.8[III], 113.7[I], 114.2[II] (C-6′′), 114.3[III] (C-6′′), 114.9[I] (C-6′′), 121.8[II+III] (2 × C-5), 122.2[I] (C-5), 123.3[I] (C-3a), 124.5[I] (C-4), 125.0[II] (C-3a), 125.7[II] (C-4), 126.0[II] (C-5′), 126.1[III] (C-5′), 126.9[I] (C-5′), 128.6[II+III] (2 × C-6), 128.7[I] (C-6), 141.9[I] (C-7a), 142.2[II] (C-7a), 151.7[II+III], 151.8[I], 153.0[III], 153.1[I], 153.2[II], 168.5[II] (CO_2C(CH_3)$_3$], 169.2[I] (CO_2C(CH_3)$_3$], 172.0[I] (C-2′), 172.7[II] (C-2′), 172.8[III] (C-2′), 175.2[I] (C-2), 177.0[II] (C-2) ppm. $C_{24}H_{26}N_2O_6$. MS (EI): *m/z* (%) = 438 (1) [M$^+$], 382 (7), 337 (19), 282 (100), 223 (33). HRMS: calcd. 438.1779; found 438.1791. $C_{24}H_{26}N_2O_6$ (438.5): calcd. C 65.74, H 5.98, N 6.39; found C 65.19, H 6.16, N 6.27.

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