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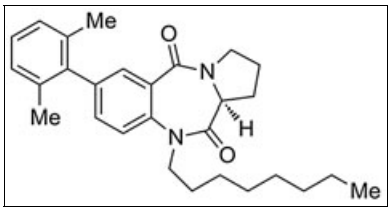

Pyrrolo[2,1-*c*][1,4]benzodiazepine-5,11-dione and its 7-bromo derivative were alkylated at the N10 atom applying various methods. The resulting products were subjected to Suzuki–Miyaura reactions using a catalyst system consisting of $Pd(Cl)_2(PPh_3)_2$ and sodium *tert*-butanolate in toluene. Results of an X-ray single crystal analysis are presented.

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INTRODUCTION

The 1,4-benzodiazepine ring system is the partial structure of diverse chemical compounds that display a variety of biological activities [1]. From those, four types of pharmacophores have been identified, the 1,4-benzodiazepine-2-ones, 1,4-benzodiazepine-2,5-diones, the dibenzodiazepinones, and the pyrrolobenzodiazepines **1** (PBDs) [1]. Some PBDs are minor groove sequence-specific DNA alkylating agents with considerable anticancer activities [2]. This class of compounds is quite widespread in nature. Since the discovery of anthramycin **2** in 1963 [3], other PBDs such as tomaymycin [4], neothramycin A and B [5], abbeymycin [6], chicamycin A [7], and sibiromycin [8] produced by micrococci and streptomyces have been isolated and characterized, some of which possess antimicrobial activities [9]. In addition, numerous synthetically produced PBDs have been reported that supplement the degrees and types of substitutions of naturally occurring compounds (Scheme 1).

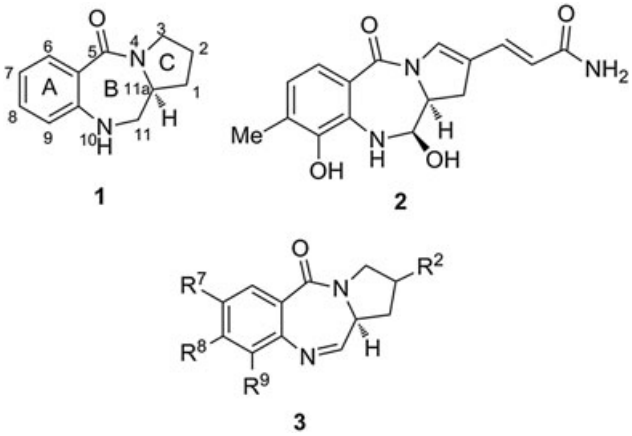
The (*S*)-configuration of C11a seemingly is *conditio sine qua non* for biological activity. The substituents R^2 of the PDB ring system **3** often are saturated or unsaturated groups in biologically active compounds, and a variety of electron-donating substituents R^7–R^9 are described to improve activity. Meanwhile, 10 pentacyclic PBDs, members of the class of circumdatines, have been identified from terrestrial and marine *Aspergillus* species [10]. Pyrrolo[2,1-*c*][1,4]benzodiazepine-5,11-dione **4** has been isolated from *Isatis indigotica* [11]. It is the parent compound of a family of substances that are important precursors in the synthesis [12], for example, of peptidomimetic agents [13], anxiolytic drugs [14], anticonvulsants [15], herbicides [16], APT1 inhibitors [17], and nonpeptidal inhibitors of platelet aggregation [18]. Substitution patterns at the A, B, and C rings as well as at N10 have been varied. The methoxy-substituted PBD-dione **5** was isolated in 2009, in addition to 2-hydroxycircumdatine C, as a new member of this interesting class of compounds [19]. Recently, a solid-phase synthesis of a library of related compounds as potential antitubercular substances has been developed [20] (Scheme 2).

In continuation of our interest in pyrrolobenzodiazepines [21], natural product derivatives [22], heterocyclic chemistry [23], *N*-heterocyclic carbenes [24], and their applications in palladium-catalyzed reactions [25], we report here the substitutions of the N10-position of PBD-diones and Suzuki–Miyaura reactions of 7-bromopyrrolobenzodiazepinediones.

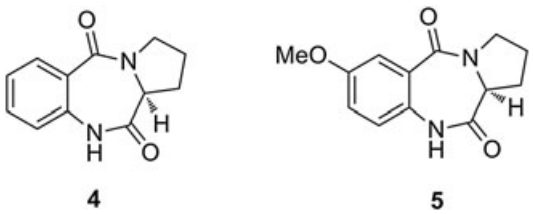
RESULTS AND DISCUSSION

We first studied the alkylations of the PBD ring system at N10. Methylation of **4a** to **6a**, which is known to exhibit anxiolytic activity [14], was achieved with methyliodide in DMSO in the presence of potassium hydroxide (Scheme 3, Table 1, entry 1). This method has been mentioned previously in the literature [26] for the syntheses of a series N10-alkylated PBDs, among them **6a**, **6b**, and **6c** [27]. Application of the alkylation agent in THF in the presence of potassium-*tert*-butanolate is advantageous with respect to a simpler work-up procedure. We used this method for the preparation of **6b–6g** and **6i,j** (Table 1, entries 2–8). Ethyl iodide (entry 2) and diethylsulfate (entry 3) gave almost identical yields. The use of *n*-propyl bromide (entry 4) resulted in considerably better yields in comparison to *n*-propyl iodide (33%). The benzyl derivative **6e** was

Scheme 1. Pyrrolobenzodiazepines.



Scheme 2. Pyrrolobenzodiazepinediones of natural origin.



Scheme 3. Alkylation of N10.

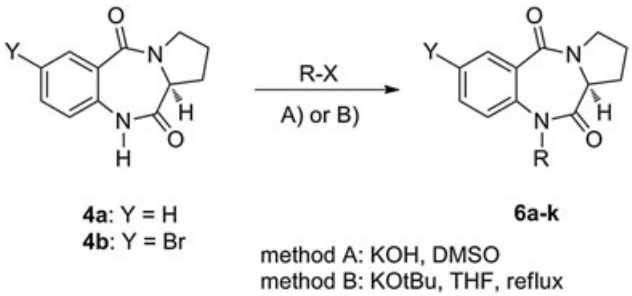


Table 1

Reaction conditions for the alkylation of N10.

Entry	Educt	Reagent	R	Y	Product	Yield (%)
1	**4a**	MeI	Me	H	**6a**	83
2	**4a**	EtI	Et	H	**6b**	94
3	**4a**	Et_2SO_4	Et	H	**6b**	96
4	**4a**	*n*-PrBr	*n*-Pr	H	**6c**	84
5	**4a**	*n*-BuBr	*n*-Bu	H	**6d**	75
6	**4a**	$PhCH_2Br$	Bz	H	**6e**	75
7	**4a**	4-NO_2-$PhCH_2Br$	4-NO_2Bz	H	**6f**	96
8	**4a**	*n*-octylbromide	*n*-octyl	H	**6g**	93
9	**4b**	MeI	Me	Br	**6h**	75
10	**4b**	$PhCH_2Br$	Bz	Br	**6i**	81
11	**4b**	*n*-octylbromide	*n*-octyl	Br	**6j**	97

prepared before by coupling of 1-(2-halobenzoyl)pyrrolidine-2-carboxylates with benzylamine and subsequent cyclizations using copper catalysts [28]. The 7-bromopyrrolobenzodiazepinedione **4b** was prepared according to modified literature procedures [26] and then alkylated at N10 (entries 9–11).

Single crystals of **6e** were obtained by slow evaporation of a concentrated solution in petroleum ether/EtOAc. The molecular drawing (Figure 1) shows the characteristic twisted configuration. Some selected bond lengths and dihedral angles are listed in Table 2.

Bromination of **6a** and **6e** at position 7 of the A ring was accomplished with bromine in concentrated acetic acid in the presence of sodium acetate (Scheme 4).

We first optimized the reaction conditions for Suzuki–Miyaura cross-couplings and began our studies with Pd $(OAc)_2$, sodium *tert*-butanolate, and phenylboronic acid in toluene that gave only unsatisfactory yields even under prolonged reaction times. Best results for the coupling were achieved using the reaction conditions as shown in Scheme 5, that is, $PdCl_2(PPh_3)_2$, aromatic boronic acids, and sodium *tert*-butanolate in toluene at 60–70°C over a period of 3 h (method A). Chromatographic work-up gave the C7-substituted PBDs **7a–j** in good yields (Table 3, entries 1–10). PBD **6i** did not react under these conditions. Using $Pd(PPh_3)_4$ in toluene in the presence of potassium phosphate (method B), however, resulted in the formation of the expected product **7k** in 76% yield (entry 11). These reaction conditions have also been applied to the formation of **7l–n** starting from **6j** (entries 12–14). Suzuki–Miyaura reactions at C-2 of the PBD ring system have been performed before starting from 2-triflates of unsaturated PDB's using $Pd(PPh_3)_4$ and Na_2CO_3 in aqueous ethanol and toluene [29] or benzene [30]. C-7 of 11-hydroxy-7-iodo-pyrrolobenzo-diazepine has been arylated before via Pro-N-TROC protection and subsequent Suzuki–Miyaura reaction employing $Pd(PPh_3)_4$ and Na_2CO_3 in the same solvent mixtures [31].

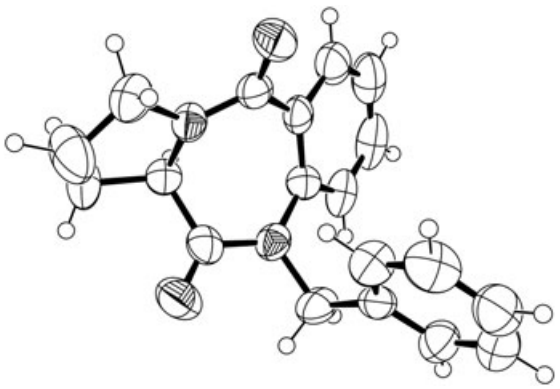


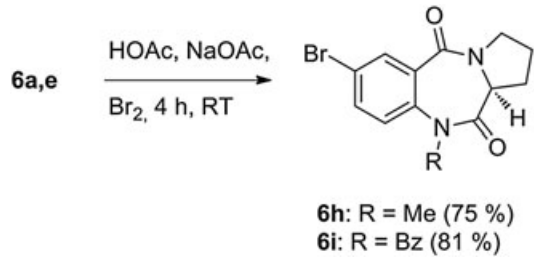
Figure 1. Molecular drawing of **6e**.

Table 2

Selected bond lengths and dihedral angles of **6e** (for numbering, cf. Scheme 1).

N4-C5	134.27(1) pm	C9-C9a-N10-C11	−136.886(7)°
N10-C11	136.61(1) pm	N10-C11-C11a-N4	−71.812(7)°
C11-C11a	151.97(1) pm	N10-C11-C11a-C1	174.093(6)°
N4-C11a	147.46(2) pm	C11-C11a-C1-C2	95.297(6)°
C1-C2-C3-N4	−25.919(7)°	C11-N10-CH_2-Ph	−109.021(7)°
C3-N4-C5-C5a	−172.636(6)°	C9-C9a-N10-CH_2	42.642(9)°

Scheme 4. Bromination of N10-alkylated pyrrolobenzodiazepines.



Scheme 5. Suzuki–Miyaura reactions.

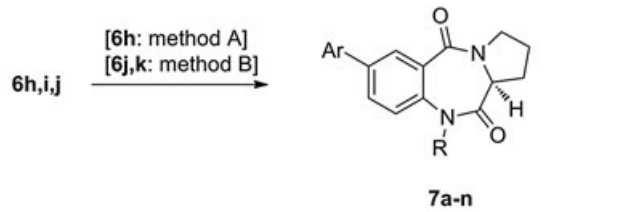


Table 3

Yields of the Suzuki–Miyaura reaction.

Entry	Educt	Ar	R	Product	Yield (%)
1	**6h**	Ph	Me	**7a**	88
2	**6h**	2-MePh	Me	**7b**	60
3	**6h**	2-EtPh	Me	**7c**	62
4	**6h**	2,6-Me_2Ph	Me	**7d**	51
5	**6h**	2,4,6-Me_3Ph	Me	**7e**	40
6	**6h**	3-F_3CPh	Me	**7f**	35
7	**6h**	2-MeOPh	Me	**7g**	86
8	**6h**	4-F_3COPh	Me	**7h**	68
9	**6h**	4-MeSPh	Me	**7i**	54
10	**6h**	1-naphthyl	Me	**7j**	70
11	**6i**	Ph	Bz	**7k**	76
12	**6j**	Ph	*n*-Octyl	**7l**	55
13	**6j**	4-MePh	*n*-Octyl	**7m**	53
14	**6j**	2,6-Me_2Ph	*n*-Ocytl	**7n**	55

In summary, we describe the reliable syntheses of novel N10-alkylated and 7-arylated PBDs that might be of interest as biologically active compounds.

EXPERIMENTAL

General. All boronic acids were purchased and used without further purification. The solvents were dried over sodium according to standard procedures. Flash-chromatography was performed with silica gel 60 (0.040–0.063 mm). NMR spectra were obtained with Bruker Avance 400 and Bruker Avance III 600 MHz spectrometers (Bruker, Ettlingen, Germany). ^{1}H NMR spectra were recorded at 400 or 600 MHz and ^{13}C NMR spectra at 100 or 150 MHz, with the solvent peak or tetramethylsilane used as the internal reference. Multiplicities are described by using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; and m, multiplet. FTIR spectra were obtained on a Bruker Vektor 22 (Bruker Vector, Bruker Optics, Bremen, Germany) in the range of 400 to 4000 cm^{-1}. Solids were measured as pellets (2.5%) in KBr, and oils were measured as films in NaCl plates. The mass spectra were measured with a Varian 320 MS Triple Quad GC/MS/MS with a Varian 450-GC (Varian Deutschland GmbH Instrumentelle Analytik, Darmstadt, Germany). Melting points are uncorrected and were determined in an apparatus according to Dr Tottoli (Büchi). The CHN analyses were performed in the Institute of Technical Chemistry of the Clausthal University of Technology. Whenever partial racemization during the reaction occurred, the optical rotation is not given. All yields refer to amounts of isolated compounds.

X-ray diffraction analysis. X-ray structure analysis for $C_{19}H_{18}N_2O_2$, $M = 306.35\ g\ mol^{-1}$: a suitable single crystal of the title compound was selected under a polarization microscope and mounted in a glass capillary ($d = 0.3$ mm). The crystal structure was determined by X-ray diffraction analysis using graphite monochromated Mo-K_α radiation (0.71073 Å) [$T = 223(2)$ K], whereas the scattering intensities were collected with a single crystal diffractometer (STOE IPDS II). The crystal structure was solved by direct methods using SHELXS-97 and refined using alternating cycles of least squares refinements against F2 (SHELXL-97) [32]. All non-H atoms were located in difference Fourier maps and were refined with anisotropic displacement parameters. The H positions were determined by a final difference Fourier synthesis.

$C_{19}H_{18}N_2O_2$ (**6e**) crystallized in the orthorhombic space group $P2_12_12_1$ (no. 19), lattice parameters $a = 8.7305(9)$ Å, $b = 11.402(2)$ Å, $c = 15.561(2)$ Å, $V = 1548.9(3)$ Å^3, $Z = 4$, $d_{calc} = 1.314\ g\ cm^{-3}$, $F(000) = 648$ using 2735 independent reflections and 270 parameters. $R^1 = 0.0497$, $wR^2 = 0.1126$ [$I > 2\sigma(I)$], goodness of fit on $F^2 = 1.105$, residual electron density = 0.170 and −0.181 e Å^{-3}.

Further details of the crystal structure investigations have been deposited with the Cambridge Crystallographic Data Center, CCDC 834712. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44(1223)-336 033; e-mail: fileserv@ccdc.ac.uk or http://www.ccdc.cam.ac.uk).

(11a*S*)-7-Bromo-2,3-dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]-diazepine-5,11-(10*H*,11a*H*)-dione (4b). A sample of 1.08 g (5.00 mmol) of 2,3-dihydro-1*H*-benzo[*e*]pyrrolo-[1,2-*a*][1,4] diazepine-5,11-(10*H*,11a*H*)-dione (**4a**) was dissolved in 10 mL of glacial acetic acid. After addition of 0.41 g (5.00 mmol) of sodium acetate, a solution of 0.25 mL (5.00 mmol, 0.8 g) of bromine in 10 mL of glacial acetic acid was added slowly. After the complete addition, the reaction mixture was stirred overnight at room temperature, diluted with water, and extracted with dichloromethane. The organic layer was washed twice with water and dried over sodium sulfate. The solvent was then distilled off and the residue was chromatographed (silica gel/CH_2Cl_2 : acetone = 20:1). Yield: 1.03 g (70%), mp 218–220°C. $[\alpha]_D^{20} = +420.0$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.97–2.07 (m, 3H, 1-H, 2-H), 2.71–2.78 (m, 1H, 1-H), 3.57–3.64 (m, 1H, 3-H), 3.79–3.84 (m, 1H, 3-H), 4.07 (d, *J* = 7.6 Hz, 1H, 11a-H), 6.94 (d, *J* = 8.8 Hz, 1H, 9-H), 7.57 (dd, *J* = 2.4, 8.8 Hz, 1H, 8-H), 8.12 (d, *J* = 2.4 Hz, 1H, 6-H), 9.65 (s, 1H, 10-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.5 (C-2), 26.2 (C-1), 47.6 (C-3), 56.7 (C-11a), 118.4 (C-7), 122.9 (C-9), 128.5, (C-5a) 133.8 (C-6), 134.3 (C-9a), 135.5 (C-8), 164.2 (C═O), 176.9 (C═O) ppm; ms: *m*/*z* (%) = 294/296 [M^+] (100/98); ir (KBr): 3226, 3161, 2972, 2941, 2872, 1703, 1615, 1478, 1448, 1370, 1264, 940, 825, 772 cm^{-1}. HRESIMS Calcd for $C_{12}H_{12}BrN_2O_2$: 295.0082. Found: 295.0081.

(11a*S*)-10-Methyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4] benzodiazepine-5,11(10*H*,11a*H*)-dione (6a). According to a modified literature procedure [33], a solution of 0.112 g (20.00 mmol) of potassium hydroxide in 10 mL of dimethylsulfoxide was stirred for 10 min. After the addition of 1.08 g (5.00 mmol) of PBD **4a** and 0.63 mL (10.00 mmol, 1.42 g) of methyl iodide, stirring was continued for 3 h. The reaction mixture was then diluted with water and extracted twice with dichloromethane. The combined organic layers were washed three times with water, dried over sodium sulfate, and evaporated. Yield: 0.950 g (83%), mp 108–110°C; $[\alpha]_D^{20} = +281.2$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.95–2.15 (m, 3H, 1-H, 2-H), 2.71–2.77 (m, 1H, 1-H), 3.41 (s, 3H, CH_3), 3.52–3.60 (m, 1H, 3-H), 3.78–3.84 (m, 1H, 3-H), 4.05–4.06 (m, 1H, 11a-H), 7.23 (dd, *J* = 0.8, 8.2 Hz, 1H, 9-H), 7.28–7.32 (m, 1H, 7-H), 7.51–7.55 (m, 1H, 8-H), 7.92 (dd, *J* = 1.7, 7.8 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.8 (C-2), 26.7 (C-1), 36.0 (Me), 46.7 (C-3), 57.2 (C-11a), 121.8 (C-9), 125.5 (C-7), 129.9 (C-5a), 130.2 (C-8), 132.0 (C-6), 140.6 (C-9a), 165.2 (C═O), 169.9 (C═O) ppm; ms: *m*/*z* (%) = 230 [M^+] (60), 201 (15), 174 (15), 161 (95), 146 (30), 133 (100), 104 (100); ir (KBr): 3010, 2952, 2881, 1679, 1635, 1599, 1463, 1424, 1377, 1252, 1185, 1151, 1126, 762, 680 cm^{-1}; HRESIMS Calcd for $C_{13}H_{15}N_2O_2$: 231.1134; Found: 231.1135.

(11a*S*)-10-Ethyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4] benzodiazepine-5,11-(10*H*,11a*H*)-dione (6b). Method A. A sample of 0.216 g (1.00 mmol) PBD **4a** and 0.112 g (1.00 mmol) of KOtBu was suspended in 10 mL of anhyd THF. After the addition of 0.16 mL (0.312 g, 2.0 mmol) of iodoethane, the mixture was heated for 3 h at reflux temperature. After evaporation, the residue was chromatographed (petroleum ether/EtOAc = 1/1), yield 0.229 g (94%). Method B. A sample of 0.229 g (1.10 mmol) PBD **4a** and 0.119 g (1.10 mmol) KOtBu was suspended in 10 mL of anhyd THF and stirred for 10 min. After the addition of 0.338 g (2.20 mmol) of diethyl sulfate, the mixture was heated at reflux temperature for 4 h. After evaporation, the resulting solid was chromatographed (petroleum ether/EtOAc = 1/1), yield 0.247 g (96%), mp 126–128°C; $[\alpha]_D^{20} = +381.5$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.20 (t, *J* = 6.8 Hz, 3H, 13-H), 1.95–2.05 (m, 2H, 1-H, 2-H), 2.09–2.21 (m, 1H, 2-H), 2.69–2.76 (m, 1H, 1-H), 3.52–3.59 (m, 1H, 3-H), 3.75–3.84 (m, 2H, 3-H, 12-H), 4.02–4.04 (m, 1H, 11a-H), 4.11–4.20 (m, 1H, 12-H), 7.29–7.33 (m, 2H, 7-H, 9-H), 7.50–7.55 (m, 1H, 8-H), 7.92 (dd, *J* = 1.6, 8.0 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 13.6 (C-13), 23.9 (C-2), 26.6 (C-1), 43.8 (C-12), 46.6 (C-3), 57.3 (C-11a), 122.3 (C-9), 125.8 (C-7), 130.3 (C-6), 130.9 (C-5a), 132.0 (C-8), 139.5 (C-9a) , 165.1 (C═O), 168.9 (C═O) ppm; ms: *m*/*z* (%) = 244 [M^+] (30), 175 (50), 147 (10), 119 (35), 84 (100); ir (KBr): 2970, 2875, 1672, 1650, 1599, 1459, 1413, 1291, 1245, 1112, 1090, 848, 791, 760, 707 cm^{-1}; HRESIMS Calcd for $C_{14}H_{17}N_2O_2$: 245.1290. Found: 245.1287.

(11a*S*)-10-*n*-Propyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4] benzodiazepine-5,11-(10*H*,11a*H*)-dione (6c). The synthesis was accomplished in analogy to the preparation of **6b** (method A). A 0.19 mL (0.340 g, 2.00 mmol) of iodopropane was used. The residue was chromatographed with petroleum ether/EtOAc = 1/2. Yield: 0.20 g (84%), mp 90–92°C; $[\alpha]_D^{20} = +412.4$ (c = 0.5 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 0.82 (t, *J* = 7.2 Hz, 3H, 14-H), 1.42–1.52 (m, 1H, 13-H), 1.53–1.66 (m, 1H, 13-H), 1.98–2.06 (m, 2H, 1-H, 2-H), 2.10–2.17 (m, 1H, 2-H), 2.70–2.76 (m, 1H, 1-H), 3.53–3.65 (m, 2H, 3-H, 12-H), 3.76–3.83 (m, 1H, 3-H), 4.03–4.05 (m, 1H, 11a-H), 4.16–4.24 (m, 1H, 12-H), 7.27–7.33 (m, 2H, 7-H, 9-H), 7.49–7.54 (m, 1H, 8-H), 7.92 (dd, *J* = 1.4, 7.6 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ = 11.1 (C-14), 21.2 (C-13), 23.9 (C-2), 26.7 (C-1), 46.5 (C-3), 49.8 (C-12), 57.4 (C-11a), 122.6 (C-9), 125.8 (C-7), 130.2 (C-6), 131.1 (C-5a), 132.0 (C-8), 139.4 (C-9a), 165.1 (C═O), 169.3 (C═O) ppm; ms: *m*/*z* (%) = 258 [M^+] (25), 189 (100), 146 (15), 132 (60), 104 (23); ir (KBr) 2963, 2876, 1679, 1648, 1601, 1462, 1411, 1247, 1226, 1136, 766, 710 cm^{-1}; HRESIMS Calcd for $C_{15}H_{19}N_2O_2$: 259.1447. Found: 259.1445.

(11a*S*)-10-*n*-Butyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4] benzodiazepine-5,11-(10*H*,11a*H*)-dione (6d). Synthesis in analogy to **6b** (method A). A 0.22 mL (0.274 g, 2.00 mmol) of bromobutane was used. The residue was chromatographed with petroleum ether/EtOAc = 1/1. Yield: 0.205 g (0.75 mmol, 75%); mp: 127°C; $[\alpha]_D^{20} = +455.2$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 0.86 (t, *J* = 7.2 Hz, 3H, 15-H), 1.20–1.30 (m, 2H, 14-H), 1.40–1.51 (m, 1H, 13-H), 1.51–1.61 (m, 1H, 13-H), 1.94–2.05 (m, 2H, 1-H, 2-H), 2.08–2.21 (m, 1H, 2-H), 2.62–2.77 (m, 1H, 1-H), 3.53–3.67 (m, 2H, 3-H, 12-H), 3.78–3.84 (m, 1H, 3-H), 4.02–4.05 (m, 1H, 11a-H), 4.20–4.28 (m, 1H, 12-H), 7.28–7.33 (m, 2H, 7-H, 9-H), 7.50–7.54 (m, 1H, 8-H), 7.92 (dd, *J* = 1.6, 8.0 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 13.7 (C-15), 19.9 (C-14), 23.9 (C-2), 26.7 (C-1), 30.0 (C-13), 46.5 (C-3), 48.1 (C-12), 57.4 (C-11a), 122.6 (C-9), 125.8 (C-7), 130.2 (C-6), 131.1 (C-5a), 131.9 (C-8), 139.5 (C-9a), 165.1 (C═O), 169.2 (C═O) ppm; ms: *m*/*z* (%) = 272 [M^+] (80), 203 (100), 175 (72), 161 (35), 146 (42), 132 (100), 119 (50), 90 (20); ir (KBr) 2952, 2927, 2877, 1667, 1640, 1598, 1465, 1416, 1401, 1250, 1207, 792, 767, 715 cm^{-1}; HRESIMS Calcd for $C_{16}H_{21}N_2O_2$: 273.1603. Found: 273.1603.

(11a*S*)-10-Benzyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4] benzodiazepine-5,11-(10*H*,11a*H*)-dione (6e). Preparation in analogy to **6b** (method A). A 0.24 mL (0.342 g, 2.0 mmol) of benzyl bromide was used. The residue was chromatographed with petroleum ether/EtOAc = 1/1.

Yield: 0.228 g (0.744 mmol, 75%), mp 206–208°C; $[\alpha]_D^{20}$ = +413.3 (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform) δ 1.96–2.22 (m, 3H, 1-H, 2-H), 2.72–2.81 (m, 1H, 1-H), 3.56–3.63 (m, 1H, 3-H), 3.80–3.68 (m, 1H, 3-H), 4.18 (d, *J* = 5.6 Hz, 1H, 11a-H), 5.01 (d, *J* = 16 Hz, 1H, 12-H), 5.17 (d, *J* = 16 Hz, 1H, 12-H), 7.14–7.31 (m, 7H, H_{arom}), 7.28–7.42 (m, 1H, 8-H), 7.90 (dd, *J* = 1.6, 7.6 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.9 (C-2), 26.8 (C-1), 46.7 (C-3), 52.5 (C-12), 57.3 (C-11a), 122.3 (C-9), 126.0 (C-7), 126.8 (C-15), 127.4 (C-16), 128.8 (C-14), 130.3 (C-6), 130.5 (C-5a), 132.0 (C-8), 137.0 (C-13), 139.9 (C-9a), 165.2 (C═O), 169.5 (C═O) ppm; ms: *m/z* (%) = 306 [M^+] (45), 237 (75), 180 (35), 146 (100), 91 (45); ir (KBr): 3066, 3032, 2982, 2956, 2890, 1666, 1637, 1598, 1463, 1412, 1366, 1300, 1250, 1209, 978, 789, 763, 730 cm^{-1}; HRESIMS Calcd for $C_{19}H_{19}N_2O_2$: 307.1447; Found: 307.1440.

(11a*S*)-10-(4-Nitrobenzyl)-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4] benzodiazepine-5,11-(10*H*,11a*H*)-dione (6f). Preparation in analogy to **6b** (method A). A 0.432 g (2.00 mmol) of 4-nitrobenzyl bromide was used. The residue was chromatographed with petroleum ether/EtOAc = 2/1. Yield: 0.335 g (96%); mp 126–128°C; $[\alpha]_D^{20}$ = +331.0 (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 2.01–2.21 (m, 3H, 1-H, 2-H), 2.72–2.80 (m, 1H, 1-H), 3.57–3.64 (m, 1H, 3-H), 3.80–3.86 (m, 1H, 3-H), 4.22 (d, *J* = 7.6 Hz, 1H, 11a-H), 5.18 (d, *J* = 4.0 Hz, 2H, 12-H), 7.14 (d, *J* = 8.4 Hz, 1H, 9-H), 7.28–7.34 (m, 3H, 7-H, 14-H), 7.43–7.47 (m, 1H, 8-H), 7.93 (dd, *J* = 1.6, 7.6 Hz, 1H, 6-H), 8.15 (d, *J* = 8.8 Hz, 2H, 15-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.8 (C-2), 26.8 (C-1), 46.8 (C-3), 52.0 (C-12), 57.2 (C-11a), 121.9 (C-9), 124.1 (C-15), 126.5 (C-7), 127.6 (C-14), 130.5 (C-5a), 130.6 (C-6), 132.3 (C-8), 139.3 (C-9a), 144.5 (C-13), 147.3 (C-16), 164.9 (C═O), 169.7 (C═O) ppm; ms: *m/z* (%) 351 [M^+] (45), 282 (100), 254 (20), 226 (45), 179 (48), 146 (97), 106 (10), 90 (48); ir (KBr): 2945, 2882, 1678, 1639, 1600, 1531, 1457, 1414, 1350, 1244, 1201, 841, 793, 768, 737, 715 cm^{-1}; HRESIMS Calcd for $C_{19}H_{18}N_3O_4$: 352.1297. Found: 352.1294.

(11a*S*)-10-Octyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4] benzodiazepine-5,11(10*H*,11a*H*)-dione (6g). A sample of 0.230 g (1.10 mmol) PBD **4a** and 0.119 g (1.10 mmol) of KOtBu was suspended in 15 mL of anhyd THF and stirred for 10 min. After the addition of 0.511 g (2.10 mmol) of octyl iodide, the mixture was heated at reflux temperature over a period of 12 h. After evaporation to dryness, the residue was chromatographed (petroleum ether/EtOAc = 1:1). The product was obtained as an oil. Yield: 0.326 g (93%); ^{1}H NMR (deuteriochloroform): δ 0.78 (t, *J* = 6.9 Hz, 3H, 19-H), 1.08–1.22 (m, 10H, 14-H, 15-H, 16-H, 17-H, 18-H), 1.38 (m, 1H, 13-H), 1.45 (m, 1H, 13-H), 1.85–1.99 (m, 2H, 2-H), 1.99–2.13 (m, 2H, 1-H), 3.45–3.60 (m, 2H, 3-H), 3.73 (m, 1H, 12-H), 3.95 (m, 1H, 12-H), 4.14 (m, 1H, 11a-H), 7.19–7.26 (m, 2H, 7-H, 9-H), 7.44 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H, 8-H), 7.85 (dd, *J* = 7.8, 1.7 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 14.1, 22.6, 23.9, 26.7, 27.9, 29.0, 29.2, 31.7, 46.5, 48.3, 57.4, 122.6, 125.8, 130.2, 131.1, 131.9, 139.5, 165.1, 169.2 ppm; ms: *m/z* (%) 328 [M^+] (35), 97 (75); ir (KBr): 3485, 2926, 2856, 2360, 2332, 1682, 1461, 1246, 1166, 764, 663 cm^{-1}. *Anal*. Calcd for $C_{20}H_{28}N_2O_2 * 0.25\ H_2O$: C, 72.15; H, 8.63; N, 8.41. Found: C, 72.08; H, 7.97; N, 8.73.

(11a*S*)-7-Bromo-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo [1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (6h). A sample of 0.448 g (8.00 mmol) of potassium hydroxide was dissolved in 10 mL of DMSO and stirred for 10 min. After the addition of 0.432 g (2.00 mmol) of PBD **4b** and 0.252 mL (4.00 mmol, 0.568 g) of iodomethane, the reaction was stirred for 1 h at room temperature. Then, the solution was diluted with water and extracted twice with dichloromethane. The combined organic layers were washed with water and dried over sodium sulfate. Yield: 0.460 g (75%), mp: 150°C. $[\alpha]_D^{20}$ = +197.5 (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.79–2.11 (m, 3H, 1-H, 2-H), 2.70–2.78 (m, 1H, 1-H), 3.38 (s, 3H, CH_3), 3.52–3.58 (m, 1H, 3-H), 3.76–3.83 (m, 1H, 3-H), 4.04–4.07 (m, 1H, 11a-H), 7.01 (d, *J* = 8.6 Hz, 1H, 9-H), 7.62 (dd, *J* = 2.4, 8.6 Hz, 1H, 8-H), 8.04 (d, *J* = 2.4 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.7 (C-2), 26.8 (C-1), 36.0 (Me), 46.9 (C-3), 57.2 (C-11a), 118.8 (C-7), 123.5 (C-9), 131.4 (C-5a), 132.9 (C-6), 135.0 (C-8), 139.6 (C-9a), 163.8 (C═O), 169.5 (C═O) ppm; ms: *m/z* (%) = 308 [M^+] (55), 240 (100); ir (KBr): 2950, 2874, 1679, 1640 cm^{-1}. HRESIMS Calcd for $C_{13}H_{14}BrN_2O_2$: 309.0237. Found: 309.0239.

(11a*S*)-7-Brom-10-benzyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*] [1,4]benzodiazepine-5,11(10*H*,11a*H*)-dione (6i). A sample of 0.616 g (2.10 mmol) of PBD **4b** and 0.260 g (2.30 mmol) of KOtBu was suspended in 10 mL of anhyd THF and stirred for 10 min. After the addition of 0.714 g (4.20 mmol) of benzyl bromide, the solution was refluxed for 12 h. After evaporation to dryness, the resulting residue was chromatographed (petroleum ether/EtOAC = 1/1). Yield: 0.65 g (81%); mp 189–193°C; ^{1}H NMR (deuteriochloroform): δ 1.98–2.21 (m, 4H, 1-H, 2-H), 3.59 (m, 1H, 3-H), 3.82 (m, 1H, 3-H), 4.17 (m, 1H, 11a-H), 5.00 (d, *J* = 15.8 Hz, 1H, 12-H), 5.13 (d, *J* = 15.8 Hz, 1H, 12-H), 7.07 (d, *J* = 8.8 Hz, 1H, 9-H), 7.13 (d, *J* = 7.0 Hz, 1H, 16-H), 7.21–7.33 (m, 4H, 14-H, 15-H), 7.49 (dd, *J* = 8.8, 2.5 Hz, 1H, 8-H), 8.02 (d, *J* = 2.5 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.8, 26.9, 46.9, 52.3, 57.3, 119.3, 124.0, 126.8, 127.6, 128.9, 132.1, 133.1, 134.9, 136.6, 138.8, 163.7, 169.2 ppm; ms: *m/z* (%) = 384/386 [M^+] (17/16), 91 (100); ir (KBr): 3332, 3266, 3035, 2978, 2958, 2877, 1849, 1783, 1675, 1443, 1238, 1213, 832, 730, 692 cm^{-1}; *Anal*. Calcd for $C_{19}H_{17}BrN_2O_2 \cdot 0.1\ H_2O$: C, 58.95; H, 4.74; N, 7.23. Found: C, 58.56; H, 4.26; N, 7.48.

(11a*S*)-7-Brom-10-octyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4] benzodiazepine-5,11(10*H*,11a*H*)-dione (6j). A suspension of 0.250 g (0.85 mmol) of PBD **4b** and 0.095 g (0.85 mmol) KOtBu in 15 mL of anhyd THF was stirred for 10 min. After the addition of 0.528 g (2.20 mmol) benzyl bromide, the mixture was refluxed for 12 h. Evaporation to dryness gave a residue that was chromatographed (petroleum ether/EtOAC = 1/1). The compound **6j** was obtained as an oil. Yield: 0.335 g (97%); ^{1}H NMR (deuteriochloroform): δ 0.79 (t, *J* = 7.0 Hz, 3H, 19-H), 1.06–1.25 (m, 10H, 14-H, 15-H, 16-H, 17-H, 18-H), 1.37 (m, 1H, 13-H), 1.49 (m, 1H, 13-H), 1.87–2.00 (m, 2H, 2-H), 2.07 (m, 1H, 1-H), 2.65 (m, 1H, 1-H), 3.42–3.56 (m, 2H, 3-H), 3.72 (m, 1H, 12-H), 3.95 (m, 1H, 12-H), 4.13 (m, 1H, 11a-H), 7.09 (d, *J* = 8.6 Hz, 1H, 9-H), 7.54 (dd, *J* = 8.6, 2.5 Hz, 1H, 8-H), 7.97 (d, *J* = 2.5 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 14.1, 22.6, 23.8, 26.6, 26.7, 27.9, 29.0, 29.2, 31.7, 46.7, 48.3, 57.4, 119.1, 124.3, 132.7, 133.0, 134.9, 138.4, 163.7, 168.9 ppm; ms: *m/z* (%) = 406/408 [M^+] (29/28), 97 (100); ir (KBr): 3483, 3349, 3277, 2927, 1690, 1590, 1561, 1291, 1240, 1091, 715, 614, 571 cm^{-1}. *Anal*. Calcd for $C_{20}H_{27}BrN_2O_2 \cdot 0.1\ H_2O$: C, 58.70; H, 6.62; N, 6.85. Found: C, 58.36; H, 6.11; N, 7.42.

General procedure for the Suzuki–Miyaura reactions. A sample of 0.152 g (0.50 mmol) of **6h**, 0.112 g (1.00 mmol) of sodium *tert*-butanolate, 36 mg (10 mol%, 0.05 mmol) of $PdCl_2(PPh_3)_2$, and 0.75 mmol of the boronic acid was suspended in 10 mL of anhyd toluene and heated at reflux temperature for 3 h. After cooling, the solvent was distilled off, and the residue was chromatographed. Unless otherwise noted, a mixture of petroleum ether/ethyl acetate (2:1) was used as eluent.

(11a*S*)-7-Phenyl-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo [1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7a). A sample of 92 mg of phenylboronic acid was used. Yield: 0.134 g (88%), mp 162–163°C. $[\alpha]_D^{20} = +464.8$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.97–2.06 (m, 2H, 1-H, 2-H), 2.08–2.16 (m, 1H, 2-H), 2.73–2.80 (m, 1H, 1-H), 3.45 (s, 3H, CH_3), 3.56–3.63 (m, 1H, 3-H), 3.81–3.87 (m, 1H, 3-H), 4.10–4.14 (m, 1H, 11a-H), 7.29 (d, *J* = 8.4 Hz, 1H, 9-H), 7.35–7.40 (m, 1H, 4′-H), 7.44–7.48 (m, 2H, 3′-H), 7.62–7.64 (m, 2H, 2′-H), 7.75 (dd, *J* = 2.4, 8.4 Hz, 1H, 8-H), 8.16 (d, *J* = 2.4 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.8 (C-2), 26.8 (C-1), 36.0 (Me), 46.8 (C-3), 57.3 (C-11a), 122.3 (C-9), 127.0 (C-3_{arom}), 127.9 (C-4_{arom}), 128.6 (C-8), 129.0 (C-2_{arom}), 130.2 (C-5a), 130.5 (C-6), 138.4 (C-1_{arom}), 139.0 (C-7), 139.7 (C-9a), 165.2 (C═O), 169.7 (C═O) ppm; ms: *m*/*z* (%) = 306 [M^+] (25), 84 (100); ir (KBr): 2974, 1678, 1638, 1606, 1457, 1439, 1370, 1320, 1242, 1114, 837, 765, 703 cm^{-1}. HRESIMS Calcd for $C_{19}H_{19}N_2O_2$: 307.1447. Found: 307.1447. *Anal.* Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.14. Found: C, 73.92; H, 5.33; N, 8.73.

(11a*S*)-7-(2-Methylphenyl)-10-methyl-2,3-dihydro-1*H*-benzo [*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7b). A 0.102 g of 2-methylphenylboronic acid was used. Yield: 0.097 g (60%), mp 229°C. ^{1}H NMR (deuteriochloroform): δ 1.97–2.09 (m, 2H, 1-H, 2-H), 2.10–2.17 (m, 1H, 2-H), 2.31 (s, 3H, 7′-H), 2.73–2.79 (m, 1H, 1-H), 3.45 (s, 3H, CH_3), 3.54–3.63 (m, 1H, 3-H), 3.80–3.85 (m, 1H, 3-H), 4.15 (d, *J* = 7.2 Hz, 1H, 11a-H), 7.22–7.29 (m, 5H, 3′-H, 4′-H, 5′-H, 6′-H, 9-H), 7.49 (dd, *J* = 2.2, 8.4 Hz, 1H, 8-H), 7.90 (d, *J* = 2.2 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 20.5 (Me), 23.8 (C-2), 26.8 (C-1), 36.0 (Me), 46.8 (C-3), 57.3 (C-11a) , 121.5 (C-9), 126.0 (C-5_{arom}), 127.8 (C-6_{arom}), 129.6 (C-5a), 129.8 (C-3_{arom}), 130.6 (C-4_{arom}), 130.7 (C-6), 132.9 (C-8), 135.3 (C-2_{arom}), 139.3 (C-1_{arom} + C-7), 139.8 (C-9a), 165.1 (C═O), 170.0 (C═O) ppm; ms: *m*/*z* (%) = 320 [M^+] (95), 251 (100); ir (KBr): 2972, 2924, 1682, 1640, 1608, 1445, 1368, 1112, 835, 776 cm^{-1}. HRESIMS Calcd for $C_{20}H_{21}N_2O_2$: 321.1603. Found: 321.1607.

(11a*S*)-7-(2-Ethylphenyl)-10-methyl-2,3-dihydro-1*H*-benzo [*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7c). A 0.113 g of 2-ethylphenylboronic acid was used. Yield: 0.105 g (62%), mp: 163–164°C. $[\alpha]_D^{20} = +298.1$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.15 (t, *J* = 7.7 Hz, 3H, 8′-H), 2-01–2.08 (m, 2H, 1-H, 2-H), 2.10–2.16 (m, 1H, 2-H), 2.63 (q, *J* = 7.7 Hz, 2H, 7′-H), 2.74–2.80 (m, 1H, 1-H), 3.46 (s, 3H, CH_3) 3.55–3.62 (m, 1H, 3-H), 3.81–3.85 (m, 1H, 3-H), 4.16 (d, *J* = 5.4 Hz, 1H, 11a-H), 7.20–7.22 (m, 1H, 4′-H), 7.24–7.26 (m, 1H, 5′-H), 7.28–7.29 (m, 1H, 9-H), 7.33–7.35 (m, 2H, 3′-H, 6′-H), 7.49 (dd, *J* = 1.8, 7.8 Hz, 1H, 8-H), 7.90 (d, *J* = 1.8 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 15.6 (Et), 23.8 (C-2), 26.1 (Et), 26.8 (C-1), 36.0 (Me), 46.8 (C-3), 57.3 (C-11a), 121.5 (C-9), 125.8 (C-5_{arom}), 128.0 (C-6_{arom}), 128.7 (C-3_{arom}), 129.6 (C-5a), 130.0 (C-4_{arom}), 130.7 (C-6), 132.9 (C-8), 139.4 (C-1_{arom} + C-7), 139.6 (C-2_{arom}), 141.6 (C-9a), 165.1 (C═O), 170.0 (C═O) ppm; ms: *m*/*z* (%) = 334 [M^+] (100); ir (KBr): 2968, 2874, 1681, 1643, 1562, 1502, 1478, 1438, 1368, 1318, 1241, 1158, 1111, 837, 760 cm^{-1}. HRESIMS Calcd for $C_{21}H_{23}N_2O_2$: 335.1760. Found: 335.1760.

(11a*S*)-7-(2,6-Dimethylphenyl)-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7d). A 0.113 g of 2,6-dimethylphenylboronic acid was used. Yield: 0.086 g (51%), mp. 193°C (dec.). $[\alpha]_D^{20} = +129.4$ (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.99–2.16 (m, 9H, 1-H, 2-H, 7′-H), 2.73–2.80 (m, 1H, 1-H), 3.46 (s, 3H, CH_3), 3.53–3.60 (m, 1H, 3-H), 3.74–3.82 (m, 1H, 3-H), 4.19–4.16 (m, 1H, 11a-H), 7.10–7.13 (m, 2H, 3′-H, 5′-H), 7.17 (d, *J* = 7.8 Hz, 1H, 9-H), 7.27–7.34 (m, 2H, 4′-H, 8-H), 7.74 (d, *J* = 1.6 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 21.0 (Me), 21.1 (Me), 23.8 (C-2), 26.8 (C-1), 36.1 (Me), 46.8 (C-3), 57.3 (C-11a), 121.9 (C-9), 127.4 (C-4_{arom}), 127.6 (C-3_{arom} + C-5_{arom}), 129.9 (C-5a), 130.8 (C-6), 133.0 (C-8), 135.8 (C-2_{arom}), 136.2 (C-6_{arom}), 138.5 (C-1_{arom}), 139.3 (C-7), 139.8 (C-9a), 165.1 (C═O), 170.0 (C═O) ppm; ms: *m*/*z* (%) 334 [M^+] (75), 84 (100); ir (KBr): 3383, 2975, 2952, 1682, 1642, 1563, 1448, 1368, 1319, 1240, 1116, 773, 752 cm^{-1}. HRESIMS Calcd for $C_{21}H_{23}N_2O_2$: 335.1760. Found: 335.1758.

(11a*S*)-7-(2,4,6-Trimethylphenyl)-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7e). A 0.123 g of 2,4,6-trimethylphenylboronic acid was used. Yield: 0.069 g (40%), mp. 186°C (dec.). ^{1}H NMR (deuteriochloroform): δ 2.00–2.07 (m, 8H, 1-H, 2-H, 5′-H), 2.10–2.17 (m, 1H, 2-H), 2.33 (s, 3H, 6′-H), 2.75–2.79 (m, 1H, 1-H), 3.46 (s, 3H, CH_3), 3.55–3.60 (m, 1H, 3-H), 3.80–3.84 (m, 1H, 3-H), 4.14 (d, *J* = 6.0 Hz, 1H, 11a-H), 6.94 (s, 1H, 3′-H), 6.96 (s, 1H, 3′-H), 7.27 (d, *J* = 8.0 Hz, 1H, 9-H), 7.32 (dd, *J* = 8.0, 1.8 Hz, 1H, 8-H), 7.73 (d, *J* = 1.8 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 20.8 (Me), 20.9 (Me), 21.1 (Me), 23.8 (C-2), 26.8 (C-1), 36.1 (Me), 46.8 (C-3), 57.3 (C-11a), 121.8 (C-9), 128.2 (C-3_{arom}), 128.4 (C-3_{arom}), 129.8 (C-5a), 131.1 (C-6), 133.3 (C-8), 135.7 (C-2_{arom}), 136.1 (C-2_{arom}), 137.0 (C-1_{arom}), 137.2 (C-4_{arom}), 138.6 (C-7), 139.2 (C-9a), 165.2 (C═O), 170.0 (C═O) ppm; ms: *m*/*z* (%) = 348 [M^+] (100), 279 (95), 251 (55), 222 (10), 165 (10), 84 (90); ir (KBr): 3448, 2921, 1682, 1642, 1449, 1367, 1319, 1240, 1112, 850, 751 cm^{-1}. HRESIMS Calcd for $C_{22}H_{25}N_2O_2$: 349.1916. Found: 349.1910.

(11a*S*)-7-(3-Trifluoromethylphenyl)-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7f). A 0.142 g of 3-trifluoromethylphenylboronic acid was used. Column chromatography was performed with petroleum ether/ethyl acetate = 3:1. Yield: 0.065 g (35%). ^{1}H NMR (deuteriochloroform): δ 1.99–2.07 (m, 2H, 1-H, 2-H), 2-08–2.16 (m, 1H, 2-H), 2.72–2.79 (m, 1H, 1-H), 3.45 (s, 3H, CH_3), 3.58–3.62 (m, 1H, 3-H), 3.82–3.86 (m, 1H, 3-H), 4.11 (d,*J* = 6.8 Hz, 1H, 11a-H), 7.33 (d, *J* = 8.4 Hz, 1H, 9-H), 7.61–7.64 (m, 1H, 5′-H), 7.61–7.64 (m, 1H, 4′-H), 7.76 (dd, *J* =2.4, 8.4 Hz, 1H, 8-H), 7.81 (d, *J* = 7.8 Hz, 1H, 6′-H), 7.87 (s, 1H, 2′-H), 8.17 (d, *J* = 2.4 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.8 (C-2), 26.8 (C-1), 36.0 (Me), 46.9 (C-3), 57.3 (C-11a), 122.5 (C-9), 123.7 (q, *J* = 3.6 Hz; C2$_{arom}$), 124.0 (q, *J* = 270.8 Hz; CF_3), 124.5 (q, *J* = 3.6 Hz; C-4_{arom}), 128.8 (C-6), 129.5 (C-5_{arom}), 130.2 (C-6_{arom}), 130.3 (C-5a), 130.4 (C-8), 131.4 (q, *J* = 32.0 Hz; C-3_{arom}), 136.8 (C-7), 139.8 (C-1_{arom}), 140.4 (C-9a), 165.0 (C═O), 169.7 (C═O) ppm; ms: *m*/*z* (%) = 374 [M^+] (30), 305 (55), 277 (30), 248 (15), 84 (100); ir (KBr): 2925, 2880, 1684, 1642, 1607, 1449, 1371, 1337, 1265, 1164, 1119, 1076, 802 cm^{-1}. HRESIMS Calcd for $C_{20}H_{18}F_3N_2O_2$: 375.1320. Found: 375.1320.

(11a*S*)-7-(2-Methoxyphenyl)-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7g). A 0.114 g of 2-methoxyphenylboronic acid was used. Column chromatography was performed with petroleum ether/ethyl acetate = 1/2. Yield: 0.144 g (86%), mp. 148–180°C. $[\alpha]_D^{20}$ = +187.8 (c = 0.5 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.96–2.05 (m, 2H, 1-H, 2-H), 2.08–2.15 (m, 1H, 2-H), 2.73–2.78 (m, 1H, 1-H), 3.44 (s, 3H, N-CH_3), 3.54–3.61 (m, 1H, 3-H), 3.78–3.85 (m, 4H, 3-H, O-CH_3), 4.14–4.17 (m, 1H, 11a-H), 6.98–7.06 (m, 2H, 3′-H, 5′-H), 7.23 (d, *J* = 8.5 Hz, 1H, 9-H), 7.32–7.37 (m, 2H, 4′-H, 6′-H), 7.72 (dd, *J* = 2.2, 8.5 Hz, 1H, 8-H), 8.09 (d, *J* = 2.2 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.8 (C-2), 26.8 (C-1), 36.0 (Me), 46.7 (C-3), 55.6 (OMe), 57.2 (C-11a), 111.2 (C-3_{arom}), 121.0 (C-5_{arom}), 121.4 (C-9), 128.5 (C-1_{arom}), 129.3 (C-6_{arom}), 129.5 (C-5a), 130.7 (C-4), 131.0 (C-6), 133.2 (C-8), 136.0 (C-7), 139.3 (C-9a), 156.5 (C-2_{arom}), 165.3 (C═O), 170.0 (C═O) ppm; ms: *m*/*z* (%) = 336 [M^+] (80), 267 (100); ir (KBr): 2980, 1677, 1643, 1606, 1478, 1442, 1372, 1245, 1113, 1026, 828, 762 cm^{-1}. HRESIMS Calcd for $C_{20}H_{21}N_2O_3$: 337.1552. Found: 337.1551.

(11a*S*)-7-(4-Trifluoromethoxyphenyl)-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7h). A 0.155 g of 4-(trifluoromethoxy)phenylboronic acid was used. Column chromatography was performed with petroleum ether/ethyl acetate = 1/2. Yield: 0.132 g (68%), mp 175°C (dec.), ^{1}H NMR (deuteriochloroform): δ 1.99–2.08 (m, 2H, 1-H, 2-H), 2.09–2.16 (m, 1H, 2-H), 2.71–2.80 (m, 1H, 1-H), 3.45 (s, 3H, CH_3), 3.56–3.63 (m, 1H, 3-H), 3.80–3.87 (m, 1H, 3-H), 4.09–4.14 (m, 1H, 11a-H), 7.30 (d, *J* = 8.4 Hz, 3H, 3′-H, 9-H overlapped), 7.64 (d, *J* = 8.4 Hz, 2H, 2′-H), 7.71 (dd, *J* = 8.4, 2.2 Hz, 1H, 8-H), 8.13 (d, *J* = 2.2 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.8 (C-2), 26.8 (C-1), 36.0 (Me), 46.9 (C-3), 57.3 (C-11a), 120.5 (q, *J* = 256.0 Hz; CF_3), 121.4 (C-3_{arom}), 122.4 (C-9), 128.3 (C2$_{arom}$), 128.6 (C-6), 130.3 (C-5a), 130.4 (C-8), 137.0 (C-1_{arom}), 137.8 (C-7), 140.1 (C-9a), 149.1 (C-4_{arom}), 165.0 (C═O), 169.8 (C═O) ppm; ms: *m*/*z* (%) = 390 [M^+] (75), 321 (100); ir (KBr): 2957, 1677, 1645, 1489, 1456, 1256, 1205, 1158, 1114, 839, 757 cm^{-1}. HRESIMS Calcd for $C_{20}H_{17}F_3N_2O_3$: 391.1270. Found: 391.1264.

(11a*S*)-7-(4-Methylthiophenyl)-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7i). A 0.126 g of 4-(methylthio)phenylboronic acid was used. Column chromatography was performed with petroleum ether/ethyl acetate = 1:2. Yield: 0.095 (54%), mp 184°C. ^{1}H NMR (deuteriochloroform): δ 1.97–2.06 (m, 2H, 1-H, 2-H), 2.07–2.16 (m, 1H, 2-H), 2.53 (s, 3H, S-CH_3), 2.73–2.78 (m, 1H, 1-H), 3.44 (m, 3H, N-CH_3), 3.55–3.62 (m, 1H, 3-H), 3.81–3.87 (m, 1H, 3-H), 4.09–4.14 (m, 1H, 11a-H), 7.27 (d, *J* = 8.4 Hz, 1H, 9-H), 7.32 (d, *J* = 8.4 Hz, 2H, 3′-H), 7.55 (d, *J* = 8.4 Hz, 2H, 2′-H), 7.72 (dd, *J* = 2.4, 8.4 Hz, 1H, 8-H), 8.13 (d, *J* = 2.4 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 15.7 (Me), 23.8 (C-2), 26.8 (C-1), 36.0 (Me), 46.8 (C-3), 57.3 (C-11a), 122.3 (C-9), 126.8 (C-2_{arom}), 127.2 (C-3_{arom}), 128.2 (C-6), 130.1 (C-8), 130.2 (C-5a), 135.6 (C-4_{arom}), 137.7 (C-1_{arom}), 138.6 (C-7), 139.6 (C-9a), 165.2 (C═O), 169.8 (C═O) ppm; ms: *m*/*z* (%) = 352 [M^+] (100), 283 (85), 255 (70), 227 (20), 180 (15), 152 (20); ir (KBr): 2952, 2864, 1676, 1634, 1483, 1448, 1368, 1241, 1117, 812 cm^{-1}. HRESIMS Calcd for $C_{20}H_{21}N_2O_2S$: 353.1324. Found: 353.1324.

(11a*S*)-7-(1-Naphthyl)-10-methyl-2,3-dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-5,11-(10*H*,11a*H*)-dione (7j). A 0.129 g of naphthyl-1-boronic acid was used. Column chromatography was performed with petroleum ether/ethyl acetate = 1/1. Yield: 0.126 g (70%). $[\alpha]_D^{20}$ = +307.1 (c = 1.0 in $CHCl_3$); ^{1}H NMR (deuteriochloroform): δ 1.98–2.11 (m, 2H, 1-H, 2-H), 2.17–2.19 (m, 1H, 2-H), 2.78–2.83 (m, 1H, 1-H), 3.50 (m, CH_3), 3.58–3.63 (m, 1H, 3-H), 3.83–3.88 (m, 1H, 3-H), 4.22 (d, *J* = 6.0 Hz, 1H, 11a-H), 7.34 (d, *J* = 8.4 Hz, 1H, 9-H), 7.43–7.49 (m 2H, $H_{Naphthyl}$), 7.51–7.56 (m 2H, $H_{Naphthyl}$), 7.67 (dd, *J* = 2.4, 8.4 Hz, 1H, 8-H), 7.89–7.91 (m 2H, $H_{Naphthyl}$), 7.93–7.94 (m 1H, $H_{Naphthyl}$), 8.09 (d, *J* = 2.4 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 23.8, 26.8, 36.1, 46.9, 57.3, 121.7, 125.4, 125.5, 126.0, 126.4, 127.2, 128.3, 128.5, 129.9, 131.3, 131.5, 133.7, 133.8, 138.1, 138.2, 139.7, 165.1, 170.0 ppm; ms: *m*/*z* (%) = 356 [M^+] (100); ir (KBr): 2978, 2925, 2877, 1680, 1641, 1606, 1563, 1447, 1395, 1369, 1317, 1158, 1106, 927, 838, 803, 751 cm^{-1}. HRESIMS Calcd for $C_{23}H_{21}N_2O_2$: 357.1603. Found: 357.1599.

(11a*S*)-10-Benzyl-7-phenyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5,11(10*H*,11a*H*)-dione (7k). A mixture of 0.093 g (0.24 mmol) of PDB **6i** and 0.012 g (5.00 mol%, 0.01 mmol) of $Pd(PPh_3)_4$ in 5 mL of anhyd toluene was stirred for 30 min. After the addition of 0.032 g (0.26 mmol) of phenylboronic acid and 0.200 g (0.94 mmol) of K_3PO_4, the mixture was stirred for additional 10 min. Then, 0.2 mL of degassed water was added. After 24 h at reflux temperature, the mixture was filtered, treated with 10 mL of dichloromethane, and washed three times with 10 mL portions of water. After evaporation to dryness, the resulting residue was chromatographed (petroleum ether/EtOAc = 5/1). Yield: 0.070 g (76%), mp 146–149°C. ^{1}H NMR (deuteriochloroform): δ 1.98–2.11 (m, 2H, 2-H), 2.17 (m, 1H, 1-H), 2.80 (m, 1H, 1-H), 3.64 (m, 1H, 3-H), 3.86 (m, 1H, 3-H), 4.25 (m, 1H, 11a-H), 5.04 (d, *J* = 15.6 Hz, 1H, 12-H), 5.22 (d, *J* = 15.6 Hz, 1H, 12-H), 7.07 (d, *J* = 8.4 Hz, 1H, H_{arom}), 7.17–7.21 (m, 2H, H_{arom}), 7.21–7.38 (m, 4H, H_{arom}), 7.41–7.46 (m, 2H, H_{arom}), 7.57–7.61 (m, 2H, H_{arom}), 7.60 (dd, *J* = 8.4, 2.4 Hz, 1H, H_{arom}), 8.14 (d, *J* = 2.4 Hz, 1H, H_{arom}) ppm; ^{13}C NMR (deuteriochloroform): δ 23.9, 26.9, 46.8, 52.5, 57.3, 122.7, 126.8, 126.9, 127.4, 127.9, 128.6, 128.9, 129.0, 130.4, 130.8, 137.0, 138.7, 138.9 (2C), 165.2, 169.5 ppm; ms: *m*/*z* (%) = 382 [M^+] (27), 97 (100); ir (KBr): 3266, 3062, 2871, 2638, 2357, 1640, 1457, 1243, 765, 724, 573 cm^{-1}. *Anal.* Calcd for $C_{25}H_{22}N_2O_2$: C, 78.51; H, 5.80; N, 7.32. Found: C, 78.03; H, 5.79; N, 7.91.

(11a*S*)-10-Octyl-7-phenyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5,11(10*H*,11a*H*)-dione (7l). A suspension of 0.100 g (0.25 mmol) of PBD **6i** and 0.015 g (5.00 mol%, 0.01 mmol) of $Pd(PPh_3)_4$ in 5 mL anhyd toluene was stirred for 30 min. Then, 0.032 g (0.26 mmol) of phenylboronic acid and 0.200 g (0.94 mmol) of K_3PO_4 were added and stirring was continued for 10 min. After the addition of 0.2 mL of degassed water, the mixture was heated at reflux temperature for 24 h. After filtration, the mixture was treated with 10 mL of dichloromethane and washed three times with 10 mL portions of water. After evaporation to dryness, the residue was chromatographed (petroleum ether/EtOAc = 7/1). The compound was obtained as an oil. Yield: 0.055 g (55%); ^{1}H NMR (deuteriochloroform): δ 0.79 (t, *J* = 6.8 Hz, 3H, 19-H), 1.11–1.23 (m, 10H, 14-H, 15-H, 16-H, 17-H, 18-H), 1.45 (m, 1H, 13-H), 1.54 (m, 1H, 13-H), 1.91–2.01 (m, 2H, 2-H), 2.08 (m, 1H, 1-H), 2.67 (m, 1H, 1-H), 3.47–3.63 (m, 2H, 3-H), 3.74 (m, 1H, 12-H), 4.02 (m, 1H, 12-H), 4.17 (m, 1H, 11a-H), 7.28 (d, *J* = 8.6 Hz, 1H, 9-H), 7.29–7.33 (m, 1H, H_{arom}), 7.36–7.41 (m, 4H, H_{arom}), 7.67 (dd, *J* = 8.6, 2.3 Hz, 1H, 8-H), 8.09 (d, *J* = 2.3 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 14.1, 22.6,

23.9, 26.7 (2C), 28.0, 29.1, 29.2, 31.7, 46.6, 48.3, 57.4, 123.0, 127.0, 127.9, 128.6, 129.0, 130.4, 131.4, 138.5, 138.6, 139.0, 165.1, 169.2 ppm; ms: *m/z* (%) = 404 [M^+] (73), 335 (77), 208 (75), 97 (100); ir (KBr): 3061, 3035, 2925, 2346, 1680, 1563, 1456, 1240, 764, 732 cm^{-1}. HRESIMS Calcd for $C_{26}H_{34}N_2O_2$: 406.2620. Found: 406.2623.

(11a*S*)-10-Octyl-7-(*p*-tolyl)-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5,11(10*H*,11a*H*)-dione (7m). Preparation in analogy to **7l**. 0.133 g (0.33 mmol) of **6i**, 0.03 g (8 mol%, 0.03 mmol) of $Pd(PPh_3)_4$, 0.050 g (0.36 mmol) of *p*-tolylboronic acid, and 0.270 g (1.26 mmol) K_3PO_4 in 10 mL of anhyd toluene were used. Column chromatography was performed with petroleum ether/EtOAC = 7/1. The compound was obtained as an oil. Yield: 0.081 g (53%); ^{1}H NMR (deuteriochloroform): δ 0.85 (t, *J* = 6.7 Hz, 3H, 19-H), 1.19–1.28 (m, 10H, 14-H, 15-H, 16-H, 17-H, 18-H), 1.50 (m, 1H, 13-H), 1.60 (m, 1H, 13-H), 1.96–2.06 (m, 2H, 2-H), 2.15 (m, 1H, 1-H), 2.39 (s, 3H, 7′-H), 2.73 (m, 1H, 1-H), 3.54–3.69 (m, 2H, 3-H), 3.82 (m, 1H, 12-H), 4.08 (m, 1H, 12-H), 4.24 (m, 1H, 11a-H), 7.26–7.31 (m, 2H, H_{arom}), 7.33 (d, *J* = 8.6 Hz, 1H, H_{arom}), 7.53–7.56 (m, 2H, H_{arom}), 7.72 (dd, *J* = 8.6, 2.5 Hz, 1H, H_{arom}), 8.13 (d, *J* = 2.3 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 14.1, 21.2, 22.6, 23.9, 26.7, 28.0, 29.1, 29.2, 31.7, 46.6, 48.3, 57.4, 123.0, 126.8, 128.3, 129.0, 129.7, 130.1, 131.3, 136.1, 137.8, 138.2, 138.6, 165.2, 169.2 ppm; ms: *m/z* (%) = 418 [M^+] (20), 97 (100); ir (KBr): 3342, 3028, 2926, 2855, 2359, 2340, 1908, 1680, 1645, 1445, 813 cm^{-1}. HRESIMS Calcd for $C_{27}H_{36}N_2O_2$: 420.2777. Found: 420.2775.

(11a*S*)-7-(2′,6′-Dimethylphenyl)-10-octyl-2,3-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-5,11(10*H*,11a*H*)-dione (7n). Preparation in analogy to **7l**. 0.144 g (0.35 mmol) of PBD **6i**, 0.03 g (7 mol%, 0.03 mmol) of $Pd(PPh_3)_4$, 0.060 g (0.39 mmol) of 2,6-dimethylphenylboronic acid, and 0.299 g (1.4 mmol) of K_3PO_4 in 10 mL of anhyd toluene were used. Chromatography was performed with petroleum ether/EtOAC = 7/1. Yield: 0.085 g (55%); ^{1}H NMR (deuteriochloroform): δ 0.86 (t, *J* = 6.7 Hz, 3H, 19-H), 1.19–1.32 (m, 10H, 14-H, 15-H, 16-H, 17-H, 18-H), 1.54 (m, 1H, 13-H), 1.66 (m, 1H, 13-H), 2.00–2.06 (m, 3H, 2-H, H_{aliph}), 2.07–2.10 (m, 3H, H_{aliph}) 2.16 (m, 1H, 1-H), 2.75 (m, 1H, 1-H), 3.56 (m, 1H, 3-H), 3.70 (m, 1H, 3-H), 3.82 (m, 1H, 12-H), 4.11 (m, 1H, 12-H), 4.20 (m, 1H, 11a-H), 7.08–7.14 (m, 4H, H_{arom}), 7.16–7.20 (m, 1H, H_{arom}), 7.22 (d, 1H, *J* = 2.3 Hz, H_{arom}), 7.30 (m, 1H, H_{arom}), 7.74 (d, *J* = 2.0 Hz, 1H, 6-H) ppm; ^{13}C NMR (deuteriochloroform): δ 14.1, 20.9, 21.0, 22.6, 23.9, 26.8, 28.1, 29.1, 29.2, 31.8, 46.7, 48.6, 57.5, 122.6, 127.4, 127.6, 130.8, 132.9, 135.8, 136.2, 138.3, 138.7, 139.8, 165.0, 169.2 ppm; ms: *m/z* (%) = 432 [M^+] (70); ir (KBr): 3343, 2926, 2855, 1928, 1680, 1648, 1440, 1237, 771 cm^{-1}. HRESIMS Calcd for $C_{28}H_{38}N_2O_2$: 434.2933. Found: 434.2933.

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