Microwave-Assisted Solvent-Free Synthesis of Hexahydrochromeno-[4,3-*b*]pyrroles

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Dedicated to Professor Branko Stanovnik on the occasion of the 65th birthday

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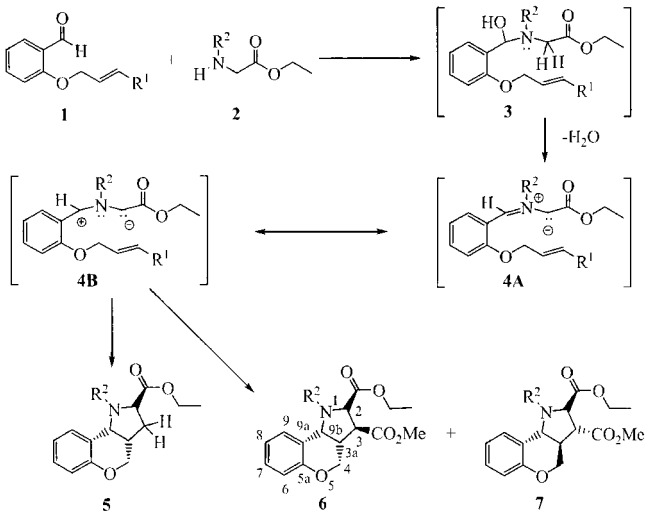
We report the microwave-assisted solvent-free synthesis of hexahydrochromeno[4,3-*b*]pyrroles. Intramolecular 1,3-dipolar cycloadditions proceed under these conditions within 15 min in 80% yields. Moreover, we have observed pronounced steric requirements of alkyl substituents toward the 1,3-dipolar cycloadditions.

Introduction

The synthesis of complex organic structures in a single step under mild conditions is a dream of every chemist. Nowadays, ecological aspects enter into the considerations of every chemist when a new compound is the target of a synthesis. With this situation in mind, we have realized the one-pot synthesis of fused heterocycles by intramolecular 1,3-dipolar cycloaddition in solvent-free conditions[1] under microwave initiation. To the best of our knowledge, this type of reaction has never been studied before under these reaction conditions.

A number of methods for azomethine ylide-mediated cycloadditions are present in the literature.[2,3] Many of these reactions, however, require catalysis either by Lewis or protic acids. Additionally, cycloadditions of azomethine ylides generated from condensations of simple aldehydes and α-amino acid esters are present in the literature.[4−6] This type of reaction usually requires a long time (2−48 h) and high temperature (the reactions are usually carried out in boiling toluene) for it to take place. Moreover, decomposition of the intermediates and products is observed under these reaction conditions.

Our study of intramolecular 1,3-dipolar cycloadditions focused on the synthesis of compounds containing hexahydrochromeno[4,3-*b*]pyrrolidine skeletons (**5**−**7**) by the reaction of an aldehyde **1** and an α-amino acid ester **2** (Scheme 1). Previously, this type of the reaction has been studied[4−6] under classical reaction conditions, but such reactions, as mentioned above, require long reaction times or afforded products in low yields and with low selectivity.



Compound **1**	R^1
a	H
b	CO_2Me

Compound **2**, **5**-**7**	R^2
a	benzyl
b	ethyl
c	*n*-butyl
d	isopropyl
e	adamantyl
f	*tert*-butyl
g	phenyl

Scheme 1

Compounds containing this structural motif are known to be noncompetive antagonists of the muscular nicotin receptor.[7] Moreover, similar structures are contained in some natural compounds, such as martinelline[8] and sceletium alkaloid A-4.[4]

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Results and Discussion

We report here the development of a simple, rapid, one-pot, solvent-free synthesis of compounds containing hexahydrochromeno[4,3-*b*]pyrrolidine skeletons (**5**−**7**) by the intramolecular 1,3-dipolar cycloaddition of azomethine ylides. Azomethine ylide was generated by the reaction of aromatic aldehyde **1** with ethyl *N*-substituted glycinate **2**. A dipolarophile required for subsequent cycloaddition of the generated 1,3 dipole in situ is present in the molecular structure of aldehyde **1**.

At first, the reaction between *O*-allylsalicylaldehyde (**1a**) and ethyl *N*-benzylglycinate (**2a**) was attempted in the "classical" way, which means that the reaction was carried out in a preheated oil bath (150 °C) by simply mixing 1.0 equiv. of both aldehyde **1a** and amine **2a**. In this case, however, the reaction proceeded in only 16% yield after 1 h of heating (Figure 1; the reaction was followed by HPLC). Also significant decomposition of the intermediate or cycloadduct **5a** was observed during the reaction.

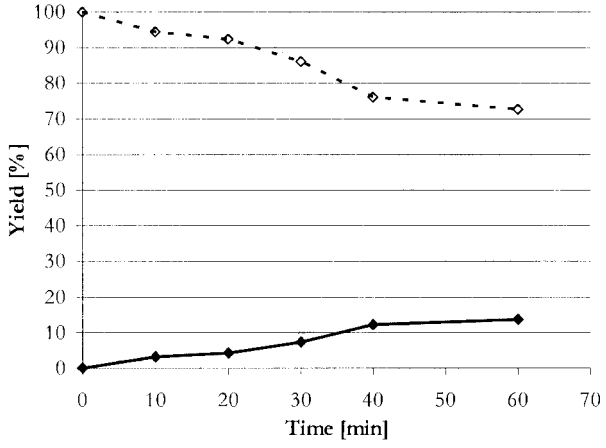


Figure 1. Thermal reaction carried out at 150 °C. Conversion of aldehyde **1a** and amine **2a**; solid diamond: product; open diamond: aldehyde

Therefore, we decided to use microwave irradiation as a source of heating.[9] It is known that microwave irradiation generates heating directly inside the sample: the so-called microwave dielectric heating effect.[10] Moreover, the existence of hot-spots (places in the sample where the temperature is much higher than the measured average temperature of the sample) in the irradiated samples has been postulated.[11]

The reaction between the aldehyde **1a** and the amine **2a** was carried out at different temperatures under microwave irradiation. Our first attempt was carried out at 150 °C. The reaction under these conditions proceeded within 1 h in 79% conversion of the aldehyde **1a**, but the isolated yield of cyclic product was only 60% (Figure 2). Therefore, we sought better conditions and found that the best temperature was 200 °C. At this temperature the reaction proceeds in > 99% conversion of **1a** within 15 min (Figure 2) and the isolated yield of the cycloadduct **5a** was 83%. At first we were afraid that at higher temperatures might cause a significant increase in the degree of decomposition of the intermediate and product, which would be accompanied by a decrease in yield. We found, however, that the cycloadduct **5a** is thermally stable under the reaction conditions (Table 1, Entries 1−4). Thus, we assume that it must be either intermediate **3** or the generated azomethine ylide **4** that undergoes decomposition and decreases the yield of the reaction. This effect is more pronounced under "classical" conditions where the formation of the final adduct does not correspond to the conversion of starting material (see Figure 1).

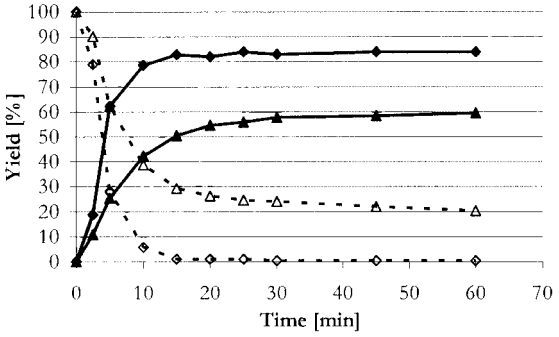


Figure 2. Microwave-assisted reactions carried out at 150 and 200 °C. Conversion of aldehyde **1a** and amine **2a;** Reaction carried out at 200 °C: solid diamond: product; open diamond: aldehyde. Reaction carried out at 150 °C: black triangle: product; open triangle: aldehyde

Table 1. Optimising conditions for the reaction between aldehyde **1a** and amine **2a**

Entry	Reaction time [min]	Base	Equiv. of the base	Isolated yield [%]
1	15	**2a**	1.0	83
2	20	**2a**	1.0	82
3	25	**2a**	1.0	84
4	30	**2a**	1.0	83
5	15	**2a**	1.1	85
6	15	**2a**	1.2	84
7	15	**2a**	1.5	80
8	15	Et_3N	1.0	81

To increase the yields of **5a**, we modified the procedure by adding a base in an attempt to aid the formation of the azomethine ylide from intermediate **3** (Table 1, Entries 5−8). We expected that the base could help in the proton transfer that occurs during the formation of dipole **4**. The yields of the reactions, however, were nearly the same either way.

After we had found the optimal reaction conditions (200 °C, 15 min), we focused on evaluating the effect of alkyl substituent R^2 of the dipole **4** on the reactivity of the dipole. When we carried out the cycloaddition between the aldehyde **1a** and the amines **2b**−**c** containing small substituents, ethyl and *n*-butyl groups, respectively, the yields were similar than the reaction with amine **2a** (Table 2, Entries 3 and 4).

Table 2. Reaction of aldehyde **1a** with amines **2a−g**

Entry	Amine	Reaction time [min]	Temperature [°C]	Cyclo-adduct	Isolated yield [%]
1	**2a**	30	150	**3a**	60
2	**2a**	15	200	**3a**	83
3	**2b**	15	200	**3b**	81
4	**2c**	15	200	**3c**	80
5	**2d**	30	200	**3d**	79
6	**2e**	60	200	–	–
7	**2f**	60	200	–	–
8	**2g**	60	200	–	–

When the sterically larger isopropyl group was present (amine **2d**), the reaction required twice the time to reach comparable yields. Moreover, we detected no products during the reaction of amines **2e,f** (R^2 = adamantyl and *tert*-butyl, respectively; Table 2, Entries 6 and 7). The same situation was observed in a case when R^2 was a phenyl group (amine **2g**, Table 2, Entry 8).

We assume that the unreactivity in the case R^2 = phenyl (amine **2g**) is caused probably by electronic reasons that arise because of conjugation with the π-electron system of the neighboring phenyl ring. The intermediate **3** is probably not formed in this case.

In the case of substituents such as adamantyl or *tert*-butyl (amines **2e** and **2f**), however, one would not expect any electronic influence on the formation of the intermediate **3** and dipole **4**. It is probable that they might change the reactivity of the generated dipole **4** as a result of changing its HOMO/LUMO energies. To test this hypothesis, we carried out quantum calculations of the HOMO (dipole)/LUMO (dipolarophile) energies, and their differences, by the semi-empirical AM1 method (Table 3).[12] We see from the calculations that the energy differences between the HOMOs and LUMOs of dipoles generated from aldehyde **1a** and amines **2a−f** are very similar.

Based on this knowledge, we conclude that the lower reactivity or unreactivity of the dipoles having R^2 = isopropyl, adamantyl, or *tert*-butyl groups is result of the steric requirements of these groups. These bulky groups probably have a significant effect in shielding the approach of the dipolarophile toward the dipole (Scheme 2).

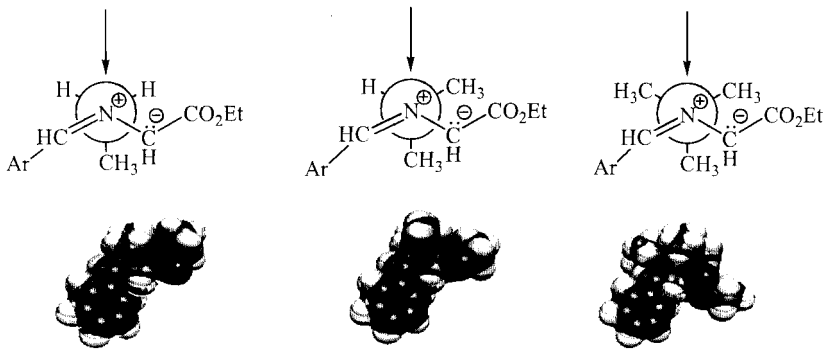
Our further investigations focused on the 1,3-dipolar cycloaddition of azomethine ylides with 1,2-disubstituted dipolarophiles. For these experiments, again we used the amines **2a−g** and methyl *trans*-4-(2-formylphenyloxy)crotonate **1b** as the aldehyde.

We observed the same influence of the substituent R^2 upon the reactivity as in the previous cases (Table 4). In this reaction, however, we observed the formation of two diastereoisomeric cycloadducts, **6** and **7**, in a 4:1 (R^2 = benzyl, ethyl, and *n*-butyl) or 2.8:1 (R^2 = isopropyl) ratio. The formation of products **6** and **7** must proceed via two different transition states (Scheme 3).

The decreased *endo*/*exo* selectivity in a case of the isopropyl-substituted 1,3-dipole might be caused by the relatively high steric requirements of the isopropyl group. Surprisingly, Kanemasa et al.,[5] who carried out the reaction

Table 3. Quantum calculations of HOMO (dipole)/LUMO (dipolarophile) for the reaction between aldehyde **1a** and amines **2a−f**

Entry	R^2	HOMO (dipole) [eV]	LUMO (dipolarophile) [eV]	Energy difference (absolute value) [kJ/mol]
1	benzyl	−7.5250	1.3735	858.60
2	ethyl	−7.7827	0.9886	846.43
3	*n*-butyl	−7.8272	0.9978	851.51
4	isopropyl	−7.4633	1.2116	837.03
5	adamantyl	−7.6003	1.3795	866.44
6	*tert*-butyl	−7.5327	1.3488	856.97

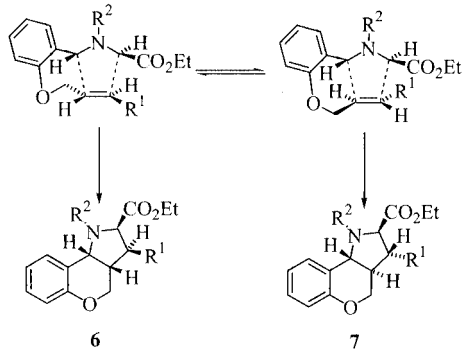


Scheme 2. Newman projections of azomethine ylides **4** substituted on the central nitrogen atom by ethyl, isopropyl, and *tert*-butyl groups, respectively, showing the increasingly restricted access to the dipole (the dipolarophile placed at the Ar part of the molecule is not depicted)

Table 4. Reaction of aldehyde **1b** with amines **2a−g**

Entry	Amine	Reaction time [min]	Temperature [°C]	Cycloadducts	Isolated yield [%][a]	Product ratio[b]
1	**2a**	15	200	**6a + 7a**	79	3.8:1
2	**2b**	15	200	**6b + 7b**	82	3.8:1
3	**2c**	15	200	**6c + 7c**	81	4.0:1
4	**2d**	30	200	**6d + 7d**	82	2.8:1
5	**2e**	60	200	–	–	–
6	**2f**	60	200	–	–	–
7	**2g**	60	200	–	–	–

[a] Overall yield. [b] Detected by GS-MS.



6 **7**

Scheme 3

classically in toluene under heating, observed no *endo*/*exo* selectivity in the case of **6b** and **7b**. An explanation for our observed selectivity is now in progress.

Conclusion

We have developed the first solvent-free microwave-assisted intramolecular 1,3-dipolar cycloaddition of azomethine ylides. We found that the conditions we have developed for the reactions aldehydes **1** and amines **2** afford their cyclic products **5−7** of intramolecular 1,3-dipolar cycloaddition within a short reaction time and in high yields. Moreover, a substantial steric influence of the R^2 substituent on the nitrogen atom of the azomethine ylide was observed on the yields of 1,3-dipolar cycloaddition.

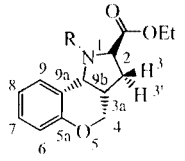
Experimental Section

General Remarks: Melting points were measured with a Kofler VEB Wagetechnik Rapido 79/2106 hot stage. IR spectra were recorded with a FTIR ATI MATTSON spectrophotometer using NaCl cells or KBr tablets. Microwave irradiation was carried out in PROLABO 402 Synthewave oven (power = 300 W, frequency = 2450 MHz). NMR spectra were recorded with an Avance 300 Varian apparatus at a working frequency of 300 MHz for ^{1}H and 75 MHz for ^{13}C in $CDCl_3$ using TMS as the internal standard. Chemical shifts are given in ppm, coupling constants (*J*) in Hz. Mass spectra were recorded with a Fisons Instruments TRIO 1000 spectrometer in the positive-ion mode using EI. Gas chromatography was carried out with a SPIRA KI 8 column (30 m, 5% diphenyldimethylsiloxane) using a Fisons Instruments TRIO 1000 spectrometer as a detector. HPLC was carried out with a Shimadzu LC-20AD using an RP-HPLC glass column SGC C-18 (7 μm; 3 × 150 nm). A Shimadzu SPD-10A was used as a UV detector. Flash column chromatography was carried out with Merck silica gel 63−100 μm using petroleum ether/ethyl acetate as the mobile phase (for the precise ratios, consult the data below).

Structure determination was carried out with a help of 2D-COSY, HSQC, HMBS, and 2D-NOESY NMR spectroscopy experiments.

Aldehydes **1**[13] and amines **2**[14] were synthesized according to published procedures.

General Method for Preparation of Hexahydrochromeno[4,3-*b*]pyrroles (5−7): A mixture of the aldehyde **1** (2.5 mmol) and the amine **2** (2.5 mmol) was irradiated whilst stirring for 15 min (amines **2a−c**) or 30 min (amines **2d**). The temperature of the reaction mixture was maintained to 200 °C. The reaction mixture was cooled to room temp. and separated by column chromatography.



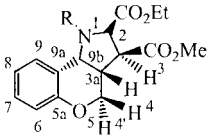
Ethyl (2*R,3a*S**,9b*R**)-1-Benzyl-1,2,3,3a,4,9b-hexahydrochromeno-[4,3-*b*]pyrrole-2-carboxylate (5a):** Flash chromatography (0:100) gave **5a** as a yellowish crystals (700 mg, 83%). M.p. (166−168) °C. IR (KBr): $\tilde{\nu}$ = 3068 (m), 3021 (m), 2945 (s), 2876 (s), 1721 (s, C=O), 1608 (m), 1580 (s), 1490 (m), 1451 (m), 1225 (w), 1193 (w), 1048 (w), 760(w) cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.20 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 1.89 (ddd, $^2J_{3',3}$ = 13.6, $^3J_{3',2}$ = 8.9, $^3J_{3',3a}$ = 3.6 Hz, 1 H, H-3′), 2.10 (ddd, $^2J_{3,3'}$ = 13.6, $^3J_{3,3a}$ = 8.3, $^3J_{3,2}$ = 3.6 Hz, 1 H, H-3), 2.58 (m, 1 H, H-3a), 3.49 (dd, $^3J_{2,3'}$ = 8.9, $^3J_{2,3}$ = 3.6, 1 H, H-2), 3.78 (d, ^2J = 13.2 Hz, 1 H, one of NCH_2Ph), 4.01 (d, $^3J_{4,3a}$ = 7.3 Hz, 2 H, H-4), 4.08 (dq, ^3J = 7.3, ^2J = 3.0 Hz, 2 H, OCH_2CH_3), 4.18 (d, ^2J = 13.2 Hz, 1 H, the other of NCH_2Ph), 4.28 (d, $^3J_{9b,3a}$ = 5.9 Hz, 1 H, H-9b), 6.80−7.12 (m, 9 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 14.5 (OCH_2CH_3), 30.5 (C-3), 35.0 (C-3a), 51.3 (NCH_2Ph), 58.0 (C-2), 59.5 (C-9b), 60.3 (OCH_2CH_3), 68.0 (C-4), 117.3−155.3 (arom. CH and C_q), 174.5 (C=O) ppm. EI-MS: *m*/*z* (%) = 338.2 (1) [M$^+$ + H], 337.1 (1) [M$^+$], 266.4 (2), 265.4 (15), 264.3 (95), 174.2 (2), 173.1 (14), 172.1 (15), 131.0 (13), 92.1 (8), 90.9 (100), 64.8 (18). $C_{21}H_{23}NO_3$ (337.4): calcd. C 74.75, H 6.87, N 4.15; found C 74.68, H 6.81, N 4.11.

Ethyl (2*R,3a*S**,9b*R**)-1-Ethyl-1,2,3,3a,4,9b-hexahydrochromeno-[4,3-*b*]pyrrolo-2-carboxylate (5b):** Flash chromatography (7:1) gave

5b as a yellowish oil (560 mg, 81%). IR (film): $\tilde{\nu}$ = 3022 (m), 2944 (s), 2882 (s), 1722 (s, C=O), 1609 (m), 1580 (m), 1490 (m), 1451 (m), 1230 (w), 1195 (m), 1048 (w), 761 (w) cm^{-1}. ^1H NMR (300 MHz): δ = 1.03 (t, ^3J = 7.3 Hz, 3 H, NCH_2CH_3), 1.32 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 1.99 (ddd, $^2J_{3',3}$ = 13.5, $^3J_{3',2}$ = 8.6, $^3J_{3',3a}$ = 4.0 Hz, 1 H, H-3′), 2.19 (ddd, $^2J_{3,3'}$ = 13.5, $^3J_{3,3a}$ = 8.5, $^3J_{3,2}$ = 3.0 Hz, 1 H, H-3), 2.58 (m, 1 H, H-3a), 2.73 (m, 2 H, one of NCH_2CH_3), 2.92 (m, 2 H, the other of NCH_2CH_3), 3.87 (dd, $^3J_{2,3'}$ = 8.6, $^3J_{2,3}$ = 3.0 Hz, 1 H, H-2), 3.96 (dd, $^2J_{4,4}$ = 11.7, $^3J_{4,3a}$ = 4.6 Hz, 1 H, one of H-4), 3.99 (dd, $^2J_{4,4}$ = 11.7, $^3J_{4,3a}$ = 2.0 Hz, 1 H, the other of H-4), 4.11 (d, $^3J_{9b,3a}$ = 6.3 Hz, 1 H, H-9b), 4.18 (dq, ^3J = 7.3, ^2J = 2.3 Hz, 2 H, OCH_2CH_3), 6.81−7.23 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 13.8 (NCH_2CH_3), 14.6 (OCH_2CH_3), 30.4 (C-3), 35.2 (C-3a), 41.7 (NCH_2CH_3), 58.3 (C-2), 60.0, 60.3 (OCH_2CH_3), 68.3 (C-4), 117.3−156.0 (arom. CH and C_q), 174.5 (C=O) ppm. EI-MS: *m*/*z* (%) = 276.3 (39) [M^+ + H], 274.3 (9), 203.7 (7), 202.3 (100), 173.2 (15), 159.0 (21), 144.7 (22), 131.0 (58), 115.0 (12), 107.1 (13), 55.9 (13). $C_{16}H_{21}NO_3$ (275.3): calcd. C 69.79, H 7.69, N 5.09; found C 69.65, H 7.61, N 4.98.

Ethyl (2*R,3a*S**,9b*R**)-1-Butyl-1,2,3,3a,4,9b-hexahydrochromeno-[4,3-*b*]pyrrolo-2-carboxylate (5c):** Flash chromatography (5:1) gave **5c** as a yellowish oil (610 mg, 80%). IR (film): $\tilde{\nu}$ = 3022 (m), 2942 (s), 2882 (s), 1722 (s, C=O), 1610 (m), 1508 (m), 1490 (m), 1451 (m), 1226 (w), 1145 (w), 1048 (w), 759 (w) cm^{-1}. ^1H NMR (300 MHz): δ = 0.79 (t, ^3J = 7.3 Hz, 3 H, $NCH_2(CH_2)_2CH_3$), 1.28 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 1.32 (m, 4 H, $NCH_2(CH_2)_2CH_3$),1.92 (ddd, $^2J_{3',3}$ = 13.6, $^3J_{3,2}$ = 8.9, $^3J_{3,3a}$ = 4.0 Hz, 1 H, H-3′), 2.18 (ddd, $^2J_{3,3'}$ = 13.6, $^3J_{3,3a}$ = 8.3, $^3J_{3,2}$ = 4.0 Hz, 1 H, H-3), 2.62 (m, 1 H, H-3a), 2.67 (m, 1 H, one of $NCH_2(CH_2)_2CH_3$), 2.89 (m, 1 H, the other of $NCH_2(CH_2)_2CH_3$), 3.89 (dd, $^3J_{2,3'}$ = 8.9, $^3J_{2,3}$ = 3.3, 1 H, H-2), 3.95 (dd, $^2J_{4,4}$ = 10.6, $^3J_{4,3a}$ = 1.2 Hz, 1 H, one of H-4), 4.02 (dd, $^2J_{4,4}$ = 10.6, $^3J_{4,3a}$ = 5.3 Hz, 1 H, the other of H-4), 4.07 (d, $^3J_{9b,3a}$ = 5.9 Hz, 1 H, H-9b), 4.18 (dq, ^3J = 7.3, ^2J = 2.3 Hz, 2 H, OCH_2CH_3), 6.98−7.28 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 13.8 [$NCH_2(CH_2)_2CH_3$], 14.6 (OCH_2CH_3), 20.2 [$N(CH_2)_2CH_2CH_3$], 28.7 ($NCH_2CH_2-CH_2CH_3$), 30.7 (C-3), 35.4 (C-3a), 46.4 ($NCH_2(CH_2)_2CH_3$), 58.3 (C-2), 60.1 (C-9b), 60.4 (OCH_2CH_3), 68.2 (C-4), 117.3−157.1 (arom. CH and C_q), 173.9 (C=O) ppm. EI-MS: *m*/*z* (%) = 305.6 (5) [M^+ + H], 304.1 (18) [M^+], 302.3 (5), 260.2 (12), 231.8 (13), 230.4 (100), 186.1 (7), 173.2 (16), 144.6 (21), 131.0 (45), 115.1 (12), 107.0 (11), 90.9 (9), 56.9 (11), 40.8 (18). $C_{18}H_{25}NO_3$ (303.4): calcd. C 71.26, H 8.31, N 4.62; found C 71.18, H 8.27, N 4.57.

Ethyl (2*R,3a*S**,9b*R**)-1-Isopropyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrolo-2-carboxylate (5d):** Flash chromatography (6:1) gave **5d** as a yellowish oil (570 mg, 79%). IR (film): $\tilde{\nu}$ = 3034 (m), 2967 (s), 2935 (s), 2878 (m), 1727 (s, C=O), 1610 (m), 1582 (m), 1487 (m), 1454 (m), 1383 (w), 1175 (w), 1117 (w), 1031 (w), 963 (w), 757 (w) cm^{-1}. ^1H NMR (300 MHz): δ = 1.09 [dd, ^3J = 6.8, 2.6 Hz, 6 H, $NCH(CH_3)_2$], 1.33 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 1.89 (ddd, $^2J_{3',3}$ = 13.1, $^3J_{3',2}$ = 8.7, $^3J_{3',3a}$ = 4.6 Hz, 1 H, H-3′), 2.10 (ddd, $^2J_{3,3'}$ = 13.1, $^3J_{3,3a}$ = 8.3, $^3J_{3,2}$ = 2.6 Hz, 1 H, H-3), 2.68 (m, 1 H, H-3a), 3.28 [p, ^3J = 6.6 Hz, 1 H, $NCH(CH_3)_2$], 3.83 (dd, $^2J_{4,4}$ = 10.2, $^3J_{4,3a}$ = 1.3, 1 H, one of H-4), 3.88 (dd, $^3J_{2,3'}$ = 8.3, $^3J_{2,3}$ = 2.6 Hz, 1 H, H-2), 3.97 (dd, $^2J_{4,4}$ = 10.6, $^3J_{4,3a}$ = 4.6 Hz, 1 H, the other of H-4), 4.19 (dq, ^3J = 7.3, ^2J = 2.3 Hz, 2 H, OCH_2CH_3), 4.49 (d, $^3J_{9b,3a}$ = 6.3 Hz, 1 H, H-9b), 6.82−7.62 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 14.6 (OCH_2CH_3), 17.8 and 22.4 [$NCH(CH_3)_2$], 31.4 (C-3), 35.7 (C-3a), 45.7 [$NCH(CH_3)_2$], 55.1 (C-9b), 57.3 (C-2), 61.0 (OCH_2CH_3), 68.8 (C-4), 117.8−156.6 (arom. CH and C_q), 178.4 (C=O) ppm. EI-MS: *m*/*z* (%) = 290.5 (7) [M^+ + H], 289.4 (18) [M^+], 252.5 (16), 202.4 (15), 192.4 (100), 165.2 (16), 121.3 (25), 101.3 (35), 89.2 (12), 76.9 (11), 55.4 (12), 40.8 (18). $C_{17}H_{23}NO_3$ (289.4): calcd. C 70.56, H 8.01, N 4.84; found C 70.50, H 7.94, N 4.78.



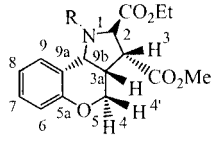
2-Ethyl 3-Methyl (2*R,3*S**,3a*S**,9b*R**)-1-Benzyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (6a):** Flash chromatography (7:1) gave **6a** as a yellowish oil (620 mg, 62%). IR (film): $\tilde{\nu}$ = 3067 (m), 3020 (m), 2945 (s), 2876 (s), 1725 (s, C=O), 1608 (m), 1580 (m), 1490 (m), 1445 (m), 1230 (w), 1189 (w), 1049 (w), 762 (w) cm^{-1}. ^1H NMR (300 MHz): δ = 1.31 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 3.39 (dddd, $^3J_{3a,3}$ = 9.3, $^3J_{3a,9b}$ = 8.3, $^3J_{3a,4'}$ = 3.6, $^3J_{3a,4}$ = 1.7 Hz, 1 H, H-3a), 3.43 (dd, $^3J_{3,3a}$ = 9.3, $^3J_{3,2}$ = 6.6 Hz, 1 H, H-3), 3.58 (d, ^2J = 13.2 Hz, 1 H, one of NCH_2Ph), 3.72 (s, 3 H, OCH_3), 3.93 (d, $^3J_{2,3}$ = 6.6 Hz, 1 H, H-2), 3.97 (dd, $^3J_{4',4}$ = 11.6, $^3J_{4',3a}$ = 3.6 Hz, 1 H, H-4′), 4.11 (d, $^3J_{9b,3a}$ = 8.3 Hz, 1 H, H-9b), 4.22 (d, ^3J = 13.2 Hz, 2 H, NCH_2Ph), 4.27 (q, ^3J = 7.3 Hz, 2 H, OCH_2CH_3), 4.31 (dd, $^3J_{4,4'}$ = 11.6, $^3J_{4,3a}$ = 1.7 Hz, 1 H, H-4), 6.90−7.41 (m, 9 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 14.6 (OCH_2CH_3), 41.4 (C-3a), 47.7 (C-3), 52.1 (NCH_2Ph), 52.1 (OCH_3), 58.8 (C-9b), 60.6 (OCH_2CH_3), 63.6 (C-2), 69.8 (C-4), 116.0−157.7 (m, 9 H, arom. CH and C_q), 171.5 and 172.1 (C=O) ppm. EI-MS: *m*/*z* (%) = 396.8 (1) [M^+ + H], 395.1 (1) [M^+], 324.2 (15), 222.3 (95), 320.5 (15), 260.5 (5), 174.2 (2), 173.1 (14), 172.1 (15), 131.0 (13), 92.1 (8), 90.9 (100), 64.8 (18). $C_{23}H_{25}NO_5$ (395.4): calcd. C 69.86, H 6.37, N 3.54; found C 69.81, H 6.32, N 3.49.

2-Ethyl 3-Methyl (2*R,3*S**,3a*S**,9b*R**)-1-Ethyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (6b):** Flash chromatography (4:1) gave **6b** as a yellowish oil (540 mg, 65%). IR (film): $\tilde{\nu}$ = 3022 (m), 2950 cm^{-1} (s), 2878 (s), 1721 (s, C=O), 1608 (m), 1568 (m), 1440 (m), 1451 (m), 1230 (w), 1185 (w), 1048 (w), 761 (w) cm^{-1}. ^1H NMR (300 MHz): δ = 1.06 (t, ^3J = 7.3 Hz, 3 H, NCH_2CH_3), 1.33 (t, ^3J = 7.3 Hz, 3 H, OCH_2CH_3), 2.53 (q, ^3J = 7.3 Hz, 2 H, one of NCH_2CH_3), 2.96 (q, ^3J = 7.3 Hz, 2 H, the other of NCH_2CH_3), 3.40 (dddd, $^3J_{3a,3}$ = 9.2, $^3J_{3a,9b}$ = 8.9, $^3J_{3a,4'}$ = 3.6, $^3J_{3a,4}$ = 1.3 Hz, 1 H, H-3a), 3.46 (dd, $^3J_{3,3a}$ = 9.2, $^3J_{3,2}$ = 6.9 Hz, 1 H, H-3), 3.75 (s, 3 H, OCH_3), 3.90 (dd, $^2J_{4',4}$ = 10.2, $^3J_{4',3a}$ = 3.6 Hz, 1 H, H-4′), 4.06 (d, $^3J_{2,3}$ = 6.9 Hz, 1 H, H-2),4.15 (d, $^3J_{9b,3a}$ = 8.9 Hz, 1 H, H-9b), 4.18 (q, ^3J = 7.3 Hz, 2 H, OCH_2CH_3), 4.32 (dd, $^2J_{4,4'}$ = 10.2, $^3J_{4,3a}$ = 1.3 Hz, 1 H, H-4), 6.88−7.24 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 13.9 (NCH_2CH_3), 14.6 (OCH_2CH_3), 41.4 (C-3a), 42.6 (NCH_2CH_3), 47.9 (C-3), 52.2 (OCH_3), 59.3 (C-9b), 60.6 (OCH_2CH_3), 63.7 (C-2), 70.2 (C-4), 116.1−157.7 (arom. CH and C_q), 171.5 and 172.4 (C=O) ppm. EI-MS: *m*/*z* (%) = 335.6 (15) [M^+ + H], 334.4 (25) [M^+], 275.3 (9), 261.2 (100), 210.7 (7), 173.2 (15), 159.0 (21), 144.5 (22), 131.0 (45), 115.7 (12), 107.1 (13), 55.9 (15). $C_{18}H_{23}NO_5$ (333.4): calcd. C 64.85, H 6.95, N 4.20; found C 64.76, H 6.90, N 4.17.

2-Ethyl 3-Methyl (2*R,3*S**,3a*S**,9b*R**)-1-Butyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (6c):** Flash chromatography (6:1) gave **6c** as a yellowish oil (590 mg, 65%). IR (film): $\tilde{\nu}$ = 3025 (m), 2942 (s), 2882 (s), 1725 (s, C=O), 1608 (m), 1508 (m), 1490 (m), 1451 (m), 1219 (w), 1145 (w), 1048 (w), 759 (w)

cm^{-1}. ^{1}H NMR (300 MHz): δ = 0.80 [, ^3J = 7.2 Hz, 3 H, NCH$_2$(CH$_2$)$_2$C*H*$_3$] 1.11 (m, 4 H, NCH$_2$(C*H*$_2$)$_2$CH$_3$), 1.31 (t, ^3J = 7.3 Hz, 3 H, OCH$_2$C*H*$_3$), 2.53 [, ^3J = 7.3 Hz, 2 H, one of NC*H*$_2$(CH$_2$)$_2$CH$_3$] 2.96 [, ^3J = 7.3 Hz, 2 H, the other of NC*H*$_2$(CH$_2$)$_2$CH$_3$] 3.31 (dddd, $^3J_{3a,3}$ = 9.1, $^3J_{3a,9b}$ = 8.7, $^3J_{3a,4'}$ = 3.7, $^3J_{3a,4}$ = 2.1 Hz, 1 H, H-3a), 3.46 (dd, $^3J_{3,3a}$ = 9.1, $^3J_{3,2}$ = 6.3 Hz, 1 H, H-3), 3.73 (s, 3 H, OC*H*$_3$), 3.95 (dd, $^2J_{4',4}$ = 11.6, $^3J_{4',3a}$ = 3.7 Hz, 1 H, H-4′), 4.03 (d, $^3J_{2,3}$ = 6.3 Hz, 1 H, H-2), 4.13 (d, $^3J_{9b,3a}$ = 8.7 Hz, 1 H, H-9b), 4.19 (q, ^3J = 7.3 Hz, 2 H, OC*H*$_2$CH$_3$), 4.31 (dd, $^2J_{4,4'}$ = 11.6, $^3J_{4,3a}$ = 2.1 Hz, 1 H, H-4), 6.88−7.24 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 13.8 (NCH$_2$(CH$_2$)$_2$*C*H$_3$), 14.2 (OCH$_2$*C*H$_3$), 20.3 (CH$_2$), 29.9 (CH$_2$), 41.3 (C-3a), 47.8 (N*C*H$_2$(CH$_2$)$_2$CH$_3$), 47.8 (C-3), 52.6 (O*C*H$_3$), 61.0 (C-9b), 63.9 (O*C*H$_2$CH$_3$), 64.8 (C-2), 69.6 (C-4), 118.0−157.7 (arom. CH and C$_q$), 176.1 and 172.1 (C=O) ppm. EI-MS: *m*/*z* (%) = 360.3 (9) [M$^+$ + H], 332.3 (29) [M$^+$], 318.3 (29), 288.2 (100), 256.2 (21), 230.2 (18), 228.2 (18), 203.1 (61), 171.0 (42), 145.0 (31), 131.0 (95), 115.0 (38), 77.0 (22), 55.0 (28), 44.0 (42). C$_{20}$H$_{27}$NO$_5$ (361.4): calcd. C 66.46, H 7.53, N 3.88; found C 66.39, H 7.48, N 3.79.

2-Ethyl 3-Methyl (2*R,3*S**,3a*S**,9b*R**)-1-Isopropyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (6d):** Flash chromatography (9:1) gave **6d** as a yellowish oil (530 mg, 61%). IR (film): ṽ = 3025 (m), 2967 (s), 2935 (s), 2878 (s), 1722 (s, C=O), 1610 (m), 1592 (m), 1477 (m), 1453 (m), 1379 (w), 1185 (w), 1117 (w), 1031 (w), 963 (w), 757 (w) cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.02 [d, ^3J = 6.6 Hz, 3 H, one of NCH(C*H*$_3$)$_2$], 1.10 [d, ^3J = 6.6 Hz, 3 H, the other of NCH(C*H*$_3$)$_2$], 1.32 (t, ^3J = 7.3 Hz, 3 H, OCH$_2$C*H*$_3$), 3.13 [h, ^3J = 6.6 Hz, 1 H, NC*H*(CH$_3$)$_2$], 3.37 (dddd, $^3J_{3a,3}$ = 9.6, $^3J_{3a,9b}$ = 9.2, $^3J_{3a,4'}$ = 4.1, $^3J_{3a,4}$ = 2.1 Hz, 1 H, H-3a), 3.43 (dd, $^3J_{3,3a}$ = 9.6, $^3J_{3,2}$ = 6.1 Hz, 1 H, H-3), 3.71 (s, 3 H, OC*H*$_3$), 3.95 (dd, $^2J_{4',4}$ = 11.2, $^3J_{4',3a}$ = 4.1 Hz, 1 H, H-4′), 4.08 (d, $^3J_{2,3}$ = 6.1 Hz, 1 H, H-2), 4.17 (d, $^3J_{9b,3a}$ = 9.2 Hz, 1 H, H-9b), 4.23 (q, ^3J = 7.3 Hz, 2 H, OC*H*$_2$CH$_3$), 4.26 (dd, $^2J_{4',4}$ = 11.2, $^3J_{4',3a}$ = 2.1 Hz, 1 H, H-4), 6.88−7.24 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 14.3 (OCH$_2$*C*H$_3$), 15.4 and 21.4 [NCH(*C*H$_3$)$_2$], 41.7 [N*C*H(CH$_3$)$_2$], 45.3 (C-3a), 48.1 (C-3), 52.1 (O*C*H$_3$), 54.2 (C-2), 60.2 (C-2), 60.7 (C-4), 70.6 (O*C*H$_2$CH$_3$), 118.2−158.1 (arom. CH and C$_q$), 172.2 and 174.8 (C=O) ppm. EI-MS: *m*/*z* (%) = 347.5 (15) [M$^+$], 274.2 (18), 273.4 (100), 202.9 (16), 192.8 (45), 164.8 (20), 121.9 (35), 101.3 (25), 89.1 (12), 77.0 (15), 54.6 (21), 40.8 (18). C$_{19}$H$_{25}$NO$_5$ (347.4): calcd. C 65.69, H 7.25, N 4.03; found C 65.61, H 7.19, N 3.99.



2-Ethyl 3-Methyl (2*R,3*R**,3a*R**,9b*R**)-1-Benzyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (7a):** Flash chromatography (7:1) gave **7a** as a yellowish oil (170 mg, 17%). IR (film): ṽ = 3067 (m), 3020 (m), 2945 (s), 2876 (s), 1727 (s, C=O), 1608 (m), 1578 (m), 1467 (m), 1445 (m), 1230 (w), 1189 (w), 1049 (w), 762 (w) cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.19 (t, ^3J = 7.3 Hz, 3 H, OCH$_2$C*H*$_3$), 2.80 (dddd, $^3J_{3a,3}$ = 11.0, $^3J_{3a,9b}$ = 11.0, $^3J_{3a,4}$ = 10.5, $^3J_{3a,4'}$ = 2.0 Hz, 1 H, H-3a), 3.22 (dd, $^3J_{3a,3}$ = 10.9, $^3J_{3a,2}$ = 5.4 Hz, 1 H, H-3), 3.59 (d, ^2J = 13.2 Hz, 1 H, one of NC*H*$_2$Ph), 3.79 (s, 3 H, OC*H*$_3$), 4.10 (dd, $^3J_{4',4}$ = 9.9, $^3J_{4',3a}$ = 2.0 Hz, 1 H, H-4′), 4.18 (d, $^3J_{2,3}$ = 5.4 Hz, 1 H, H-2), 4.21 (d, ^3J = 11.0 Hz, 2 H, H-9b), 4.25 (q, ^3J = 7.3 Hz, 2 H, OC*H*$_2$CH$_3$), 4.34 (d, ^2J = 13.2 Hz, 1 H, the other of NC*H*$_2$Ph), 4.52 (dd, $^3J_{4,3a}$ = 10.9, $^3J_{4,4'}$ = 9.9 Hz, 1 H, H-4), 6.90−7.49 (m, 9 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 14.2 (OCH$_2$*C*H$_3$), 42.5 (C-3), 49.4 (C-3a), 52.7 (O*C*H$_3$), 53.4 (N*C*H$_2$Ph), 52.1 58.8 (C-9b), 61.1 (O*C*H$_2$CH$_3$), 64.8 (C-2), 69.8 (C-4), 116.9−155.2 (arom. CH and C$_q$), 172.3 and 173.4 (C=O) ppm. EI-MS: *m*/*z* (%) = 396.8 (1) [M$^+$ +1], 395.1 (1) [M$^+$], 324.2 (12), 323.2 (25), 222.3 (80), 320.5 (16), 260.5 (7), 174.2 (5), 173.1 (20), 172.1 (10), 131.0 (15), 92.1 (5), 90.9 (100), 64.8 (18). C$_{23}$H$_{25}$NO$_5$ (395.4): calcd. C 69.86, H 6.37, N 3.54; found C 69.80, H 6.33, N 3.51.

2-Ethyl 3-Methyl (2*R,3*R**,3a*R**,9b*R**)-1-Ethyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (7b):** Flash chromatography (4:1) gave **7b** as a yellowish oil (140 mg, 17%). IR (film): ṽ = 3022 (m), 2950 (s), 2878 (s), 1725 (s, C=O), 1608 (m), 1568 (m), 1440 (m), 1451 (m), 1230 (w), 1185 (w), 1048 (w), 761 (w) cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.19 (t, ^3J = 7.3 Hz, 3 H, NCH$_2$C*H*$_3$), 1.33 (t, ^3J = 7.3 Hz, 3 H, OCH$_2$C*H*$_3$), 2.39 (m, 1 H, one of NC*H*$_2$CH$_3$), 2.61 (m, 1 H, the other of NC*H*$_2$CH$_3$), 3.02 (dddd, $^3J_{3a,3}$ = 11.7, $^3J_{3a,9b}$ = 11.7, $^3J_{3a,4}$ = 10.6, $^3J_{3a,4'}$ = 4.4 Hz, 1 H, H-3a), 3.17 (dd, $^3J_{3,3a}$ = 11.7, $^3J_{3,2}$ = 5.9 Hz, 1 H, H-3), 3.77 (s, 3 H, OC*H*$_3$), 3.90 (d, $^3J_{2,3}$ = 5.9 Hz, 1 H, H-2), 4.08 (d, $^3J_{9b,3a}$ = 11.7 Hz, 1 H, H-9b), 4.20 (q, ^3J = 7.3 Hz, 2 H, OC*H*$_2$CH$_3$), 4.25 (dd, $^3J_{4',4}$ = 10.2, $^3J_{4',3a}$ = 4.4 Hz, 1 H, H-4′), 4.56 (dd, $^3J_{4,3a}$ = 11.7, $^3J_{4,4'}$ = 10.2 Hz, 1 H, the other of H-4), 6.83−7.26 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 13.3 (NCH$_2$*C*H$_3$), 14.6 (OCH$_2$*C*H$_3$), 42.1 (N*C*H$_2$CH$_3$), 43.8 (C-3), 49.2 (C-3a), 52.7 (O*C*H$_3$), 61.6 (O*C*H$_2$CH$_3$), 64.8 (C-9b), 69.1 (C-2), 70.2 (C-4), 116.9−153.9 (arom. CH and C$_q$), 172.3 and 173.2 (C=O) ppm. EI-MS: *m*/*z* (%) = 335.6 (15) [M$^+$ + H], 334.4 (24) [M$^+$], 275.3 (11), 261.2 (100), 210.7 (4), 173.2 (14), 159.5 (20), 144.5 (19), 131.0 (45), 115.6 (12), 107.1 (13), 55.8 (15). C$_{18}$H$_{23}$NO$_5$ (333.4): calcd. C 64.85, H 6.95, N 4.20; found C 64.78, H 6.89, N 4.17.

2-Ethyl 3-Methyl (2*R,3*R**,3a*R**,9b*R**)-1-Butyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*] pyrrole-2,3-dicarboxylate (7c):** Flash chromatography (6:1) gave **5c** as a yellowish oil (150 mg, 16%). IR (film): ṽ = 3025 (m), 2945 (s), 2872 (s), 1728 (s, C=O), 1608 (m), 1508 (m), 1490 (m), 1441 (w), 1230 (w), 1150 (w), 1048 (w), 759 (w) cm^{-1}. ^{1}H NMR (300 MHz): δ = 0.91 [t, ^3J = 7.2 Hz, 3 H, NCH$_2$(CH$_2$)$_2$C*H*$_3$], 1.28 (t, ^3J = 7.3 Hz, 3 H, OCH$_2$C*H*$_3$), 1.45 [m, 4 H, NCH$_2$(C*H*$_2$)$_2$CH$_3$], 2.39 [m, 1 H, one of NC*H*$_2$(CH$_2$)$_2$CH$_3$], 2.61 [m, 1 H, the other of NC*H*$_2$(CH$_2$)$_2$CH$_3$], 3.17 (dddd, $^3J_{3a,4}$ = 11.5, $^3J_{3a,9b}$ = 11.5, $^3J_{3a,3}$ = 10.4, $^3J_{3a,4}$ = 4.3 Hz, 1 H, H-3a), 3.26 (dd, $^3J_{3,3a}$ = 11.5, $^3J_{3,2}$ = 5.7 Hz, 1 H, H-3), 3.79 (s, 3 H, OC*H*$_3$), 3.85 (d, $^3J_{2,3}$ = 5.7 Hz, 1 H, H-2), 4.09 (d, $^3J_{9b,3a}$ = 11.5 Hz, 1 H, H-9b), 4.18 (q, ^3J = 7.3 Hz, 2 H, OC*H*$_2$CH$_3$), 4.29 (dd, $^3J_{4',4}$ = 10.1, $^3J_{4',3a}$ = 4.3 Hz, 1 H, H-4′), 4.66 (dd, $^3J_{4,3a}$ = 11.5, $^3J_{4,4'}$ = 10.1 Hz, 1 H, the other of H-4), 6.83−7.26 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 14.1 [NCH$_2$(CH$_2$)$_2$*C*H$_3$], 14.2 (OCH$_2$*C*H$_3$), 20.7 (CH$_2$), 28.2 (CH$_2$), 42.0 (C-3a), 49.2 [N*C*H$_2$(CH$_2$)$_2$CH$_3$], 49.0 (C-3), 52.6 (O*C*H$_3$), 61.0 (O*C*H$_2$CH$_3$), 61.4 (C-9b), 69.0 (C-2), 70.2 (C-4), 116.9−156.2 (arom. CH and C$_q$), 173.2 and 174.1 (C=O) ppm. EI-MS: *m*/*z* (%) = 360.3 (2) [M$^+$], 318.3 (8), 289.4 (15), 288.3 (100), 256.2 (10), 228.2 (5), 203.1 (11), 171.1 (11), 145.1 (8), 131.0 (31), 115.0 (8), 107.0 (4), 57.1 (4), 44.0 (9). C$_{20}$H$_{27}$NO$_5$ (361.4): calcd. C 66.46, H 7.53, N 3.88; found C 66.39, H 7.50, N 3.86.

2-Ethyl 3-Methyl (2*R,3*R**,3a*R**,9b*R**)-1-Isopropyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-*b*]pyrrole-2,3-dicarboxylate (7d):** Flash chromatography (9:1) gave **7d** as a yellowish oil (180 mg, 21%). IR (film): ṽ = 3025 (m), 2967 (s), 2935 (s), 2878 (s), 1726 (s, C=O), 1720 (s, C=O), 1608 (m), 1582 (m), 1465 (m), 1448 (m), 1382 (w), 1174 (w), 1118 (w), 1021 (w), 963 (w), 758 (w) cm^{-1}. ^{1}H NMR (300 MHz): δ = 1.06 [d, ^3J = 6.6 Hz, 3 H, one of NCH(C*H*$_3$)$_2$], 1.11 [d, ^3J = 6.6 Hz, 3 H, the other of NCH(C*H*$_3$)$_2$], 1.31 (t, ^3J =

7.3 Hz, 3 H, OCH_2CH_3), 2.83 [h, ^3J = 6.6 Hz, 1 H, $NCH(CH_3)_2$], 3.17 (dddd, $^3J_{3a,3}$ = 11.2, $^3J_{3a,9b}$ = 11.2, $^3J_{3a,4}$ = 11.0, $^3J_{3a,4'}$ = 3.6 Hz, 1 H, H-3a), 3.26 (dd, $^3J_{3,3a}$ = 11.2, $^3J_{3,2}$ = 5.4 Hz, 1 H, H-3), 3.78 (s, 3 H, OCH_3), 3.85 (d, $^3J_{2,3}$ = 5.4 Hz, 1 H, H-2), 4.09 (d, $^3J_{9b,3a}$ = 11.2 Hz, 1 H, H-9b), 4.18 (q, ^3J = 7.3 Hz, 2 H, OCH_2CH_3), 4.29 (dd, $^3J_{4,3a}$ = 11.0, $^3J_{4,4'}$ = 10.1 Hz, 1 H, H-4), 4.66 (dd, $^3J_{4',4}$ = 10.1, $^3J_{4',3a}$ = 3.6 Hz, 1 H, the other of H-4), 6.83−7.26 (m, 4 H, arom. CH) ppm. ^{13}C NMR (75 MHz): δ = 14.1 (OCH_2CH_3), 17.6 and 21.2 [$NCH(CH_3)_2$], 40.8 [$NCH(CH_3)_2$], 45.2 (C-3), 50.7 (C-3a), 52.1 (OCH_3), 56.9 (C-2), 61.0 (OCH_2CH_3), 63.4 (C-9b), 70.1 (C-4), 116.9−154.5 (arom. CH and C_q), 173.6 and 174.0 (C=O) ppm. EI-MS: *m*/*z* (%) = 347.5 (16) [M^+], 274.8 (15), 273.4 (100), 202.1 (14), 192.4 (35), 165.2 (15), 121.7 (25), 101.3 (28), 88.5 (9), 77.0 (15), 55.2 (11), 40.8 (8). $C_{19}H_{25}NO_5$ (347.4): calcd. C 65.69, H 7.25, N 4.03; found C 65.64, H 7.21, N 3.98.

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