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Synthesis of 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones by cyclization of 1,1-bis(trimethylsiloxy)ketene acetals with pyrazine and quinoxaline

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Abstract—1,4-Diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones were prepared by cyclization of 1,1-bis(trimethylsiloxy)ketene acetals with pyrazine and quinoxaline.

1. Introduction

1,1-Bis(trimethylsiloxy)ketene acetals represent interesting synthetic building blocks, which can be regarded as masked carboxylic acid dianions.[1–3] Rudler et al. were the first to report the use of 1,1-bis(trimethylsiloxy)ketene acetals as 1,3-dinucleophiles in cyclization reactions: In 1999, they reported the synthesis of lactones by reaction of 1,1-bis(trimethylsiloxy)ketene acetals with chromium(0) complexes.[4] In 2000, Rudler et al. developed the palladium(0) catalysed reaction of 1,1-bis(trimethylsiloxy)ketene acetals with allyl acetates to give γ-unsaturated carboxylic acids, which were transformed into 5-(hydroxymethyl)-γ-lactones by addition of H_2O_2 in the presence of catalytic amounts of methyltrioxorhenium (MTO).[5] Rudler et al. also reported interesting reactions of 1,1-bis(trimethylsiloxy)ketene acetals with tropylium derivatives.[6] We reported the cyclocondensation of 1,1-bis(trimethylsiloxy)ketene acetals with oxalyl chloride[7] and 3-(siloxy)alk-2-en-1-ones to give maleic anhydrides and pyran-2-ones, respectively.[8]

Pyridinium salts represent important synthetic building blocks, which can be generated in situ by acylation of pyridines.[9] They have been used in various reactions with Grignard reagents, cyanide (Reissert reaction), trimethylsilylacetonitrile, allylsilanes, silyl enol ethers or diazoesters.[10] We reported the cyclization of 1,3-bis(silyl enol ethers)[11]—masked 1,3-dicarbonyl dianions—with isoquinoline.[12] In 2002, Rudler et al. reported the first cyclocondensations of 1,1-bis(trimethylsiloxy)ketene acetals with pyridine[13a] and later extended this interesting concept to other *N*-heterocycles.[13b] We reported the cyclocondensation of 1,1-bis(trimethylsiloxy)ketene acetals with isoquinoline.[14] Recently, Rudler et al. reported the first cyclizations of 1,1-bis(trimethylsiloxy)ketene acetals with pyrazine[13b,15] and quinoxaline.[15] These reactions provide a facile access to 2,3-benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones and 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones, respectively. Herein, we report our own findings in this field. With regard to the previous report of Rudler et al.,[15] we extensively studied the preparative scope of the reactions. In addition, 2-monosubstituted 1,1-bis(trimethylsiloxy)ketene acetals have been employed by us, which give rise to questions of stereochemistry. The isomeric products could be successfully separated for the first time and their structure unambiguously assigned.

2,3-Benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones and 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones are of biological relevance as they represent analogues of clofazimine, riboflavin (vitamin B_2) and lumiflavin. The substituted dihydrophenazine clofazimine represents an important drug against leprosy and is also effective against a number of diseases related to the autoimmune system.[16] However, there are serious problems, such as bacterial resistance.[16] Therefore, the development of suitable clofazimine analogues is of pharmacological relevance.

Keywords: Cyclizations; Heterocycles; Iminium salts; Pyrazine; Quinoxaline; Silyl enol ethers.
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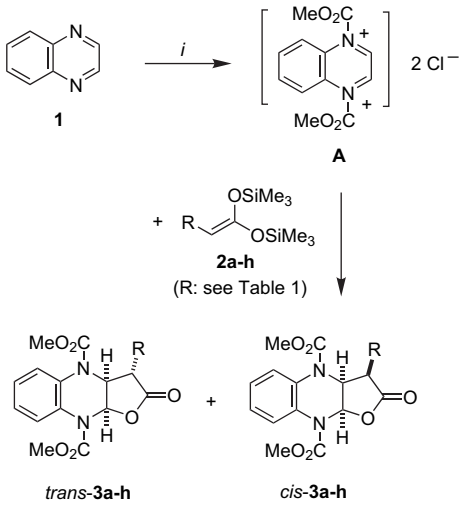
2. Results and discussion

The reaction of 1,1-bis(trimethylsiloxy)ketene acetal **2a** (1.4 equiv)[17] with quinoxaline (**1**) (1.0 equiv) in the presence of methyl chloroformate (4.0 equiv) afforded the 2,3-benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-one **3a** as a separable mixture of diastereomers *trans*-**3a** and *cis*-**3a** (Scheme 1 and Table 1). During the optimization of the cyclocondensation, the activating agent, stoichiometry, temperature and concentration played an important role. The formation of **3a** can be explained by formation of bis(iminium salt) **A**, attack of the carbon atom of **2a** onto **A** and subsequent cyclization. Alternatively, the reaction may proceed by formation of a simple iminium salt, reaction of the latter with **2a**, acylation of the second nitrogen atom and subsequent cyclization.



Scheme 1. Cyclization of 1,1-bis(siloxy)ketene acetals **2a–h** with **1**. *i*, **1** (1.0 equiv), **2** (1.4 equiv), $ClCO_2Me$ (4.0 equiv), CH_2Cl_2, 20 °C, 12 h.

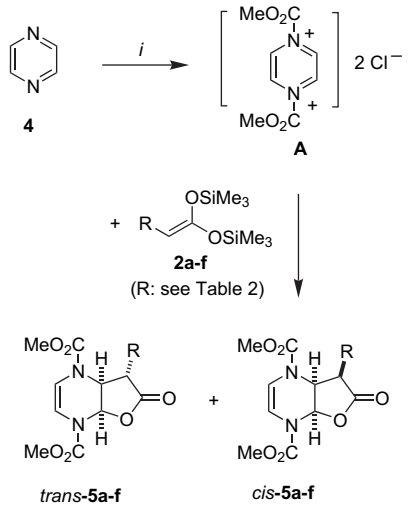
The preparative scope of the methodology was studied (Scheme 1 and Table 1). The reaction of **1** with 1,1-bis(trimethylsiloxy)ketene acetals **2b–h**, prepared from the corresponding alkanoic acids, afforded the 2,3-benzo-1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones **3b–h** as separable mixtures of diastereomers. As expected, a cis-annulation was observed for all 5,6-bicyclic products, due to steric reasons. In contrast to the reaction of isoquinoline with 1,1-bis(trimethylsiloxy)ketene acetals, the reaction of the latter with quinoxaline proceeded with low 1,2-diastereoselectivity. However, the isomers could be separated by chromatography, due to their different polarity.

Table 1. Products and yields

3	R	% (*trans*-**3**)[a]	% (*cis*-**3**)[a]
a	Et	19	28
b	^{n}Pr	29	21
c	^{n}Bu	11	25
d	^{n}Dodec	30	15
e	^{i}Pr	27	33
f	^{c}Hex	28	27
g	$CH_2(^{c}Pent)$	32	24
h	$(CH_2)_2(^{c}Hex)$	25	12

[a] Yields of isolated products.

The reaction of 1,1-bis(trimethylsiloxy)ketene acetal **2a** (1.4 equiv) with pyrazine (**4**) (1.0 equiv) in the presence of methyl chloroformate (4.0 equiv) afforded the 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-one **5a** as a separable mixture of diastereomers *trans*-**5a** and *cis*-**5a** (Scheme 2 and Table 2). The reaction of **4** with 1,1-bis(trimethylsiloxy)-ketene acetals **2b–f** afforded the 1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones **5b–f** as separable mixtures of diastereomers.



Scheme 2. Cyclization of 1,1-bis(siloxy)ketene acetals **2a–f** with **4**: *i*, **4** (1.0 equiv), **2** (1.4 equiv), $ClCO_2Me$ (4.0 equiv), CH_2Cl_2, 20 °C, 12 h.

The relative configurations for chinoxalines **3** and pyrazines **5** were proved by NOESY experiments. In the NOESY spectra recorded for **3b**, **3f**, **3g** and **5e** cross peaks could be observed for the hydrogen atoms H-2 with H-9 (**3b**, **3f**, **3g**) and H-2 with H-7 (**5e**), respectively, only in the case of cis-compounds. The atom numbering for NMR assignment of **3** and **5** is given in Scheme 3. The cis- or trans-configuration of the other compounds **3** and **5** could be confirmed based on chemical shifts. Thus, the H-3 signals for the cis-compounds are generally shifted downfield compared to the trans-compounds. It should be noted that some signals in the ^{1}H and ^{13}C spectra appeared as broadened or doubled signals due to dynamic processes (hindered rotation about the NCO bonds).

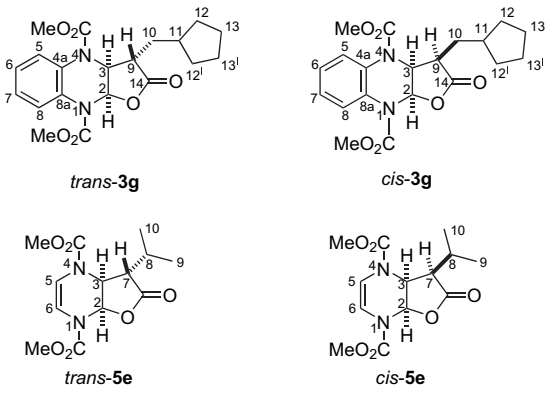
The configuration of *cis*-**5e** was independently confirmed by X-ray crystal structure analysis (Fig. 1).[18] The trans-isomers generally proved to be less polar (R_f value) than the cis-isomers.

In conclusion, we have reported—based on previous work of Rudler et al.[15]—the synthesis of a number of

Table 2. Products and yields

5	R	% (*trans*-**5**)[a]	% (*cis*-**5**)[a]
a	Et	24	0
b	^{n}Pr	40	26
c	^{n}Bu	30	39
d	^{n}Dodec	26	20
e	^{i}Pr	20	35
f	^{c}Hex	38	11

[a] Yields of isolated products.



Scheme 3. Atom numbering of quinoxaline **3g** and pyrazine **5e** for NMR assignment.

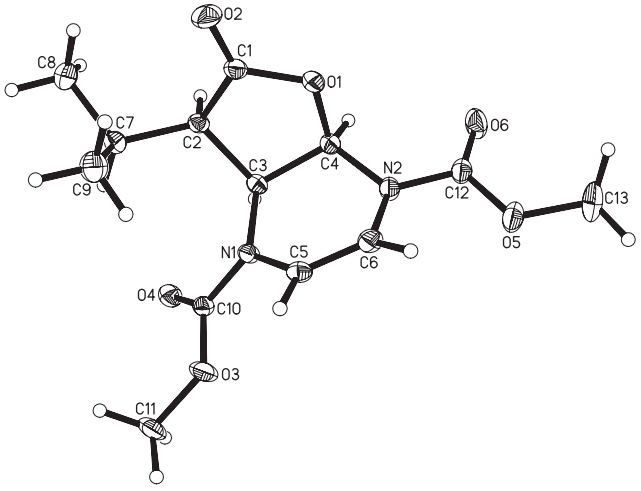


Figure 1. Ortep plot of *cis*-**5e**. The thermal ellipsoids of 50% probability are shown for the non-hydrogen atoms.

1,4-diaza-7-oxabicyclo[4.3.0]non-2-en-6-ones by cyclization of 1,1-bis(trimethylsiloxy)ketene acetals with pyrazine and quinoxaline.

3. Experimental

3.1. General

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^{1}H and ^{13}C NMR, the deuterated solvents indicated were used. The ^{1}H NMR (250.13 and 300.13 MHz) and ^{13}C NMR (62.9 and 75.5 MHz) were recorded on Bruker spectrometers AC 250 and ARX 300, respectively, at 300 K. In addition to the routine measurements, the spectra of **3b**, **3f**, **3g** and **5e** were recorded on a Bruker spectrometer AVANCE 500 (^{1}H: 500.13 MHz and ^{13}C: 125.8 MHz). Calibration of spectra was carried out on solvent signals ($CDCl_3$: δ ^{1}H=7.25, δ ^{13}C=77.0; DMSO-d_6: δ ^{1}H=2.50, δ ^{13}C=39.7). The NMR signals were assigned by DEPT and two-dimensional $^{1}H,^{1}H$ COSY, $^{1}H,^{1}H$ NOESY and $^{1}H,^{13}C$ correlation spectra (HSQC, HMBC). Mass spectrometric data (MS) were obtained by electron ionization (70 eV), chemical ionization (CI, H_2O) or electrospray ionization (ESI). For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

3.1.1. Typical procedure for the synthesis of 2-oxo-3,3a-dihydrofuro[2,3-*b*]quinoxalines 3a–h and 6-oxo-7,7a-dihydrofuro[3,2-*b*]pyrazines 5a–f. To a CH_2Cl_2 solution (50 mL) of quinoxaline (0.325 g, 2.5 mmol) and 2-methylcyclopentyl-1,1-bis(trimethylsilyloxy)ethene (1.003 g 3.5 mmol) was slowly added methyl chloroformate (0.945 g, 10.0 mmol) at 20 °C. The solution was stirred for 12 h at 20 °C. The solvent was removed in vacuo and the residue was purified by chromatography (silica gel, *n*-heptane/EtOAc 20:1 to 5:1) to give *trans*-**3g** (0.315 g, 32%) and *cis*-**3g** (0.225 g, 24%) as colourless solids. Due to the restricted rotation in the urethane moiety, compounds **3** and **5** appeared as mixtures of two rotamers. All compounds were formed as racemates.

3.1.1.1. Dimethyl 3-ethyl-2-oxo-3,3a-dihydrofuro[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3a). Starting with quinoxaline (**1**) (0.261 g, 2.00 mmol), 2-ethyl-1,1-bis-(trimethylsilyloxy)ethene (**2a**) (0.650 g, 2.80 mmol) and methyl chloroformate (0.67 mL, 8.00 mmol), *trans*-**3a** (0.125 g, 19%) was isolated as a colourless solid, mp 147 °C; *cis*-**3a** (0.185 g, 27%) was isolated as a colourless solid, mp 147 °C.

Data of *trans*-**3a**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.52 (br, 1H, Ar), 7.33 (br, 1H, Ar), 7.23–7.17 (m, 2H, Ar), 6.70 (d, 1H, $^{3}J_{2,3}$=8.8 Hz, H-2), 5.50 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.45–2.36 (m, 1H, H-9), 1.92–1.84 (m, 1H, CH_2), 1.82–1.65 (m, 1H, CH_2), 1.03 (t, 3H, ^{3}J=7.3 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.6 (COO), 153.9 (br) (2NCO), 130.5, 130.3 (C_{Ar}), 126.5, 126.2, 126.1, 125.9 (CH_{Ar}), 86.0 (C-2), 59.1 (C-3), 53.9, 53.7 (OCH_3), 43.2 (C-9), 22.7 (CH_2), 10.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422 (br), 2965 (m), 1715 (s), 1506 (m), 1325 (s), 1165 (s), 950 (s), 755 (w). MS (EI; 70 eV): *m*/*z* (%)=334 ([M]$^+$, 100), 306 (39), 247 (43), 235 (54), 145 (25), 59 (21). HRMS (EI) calcd for $C_{16}H_{18}N_2O_6$ ([M]$^+$): 334.1159; found: 334.1154.

Data of *cis*-**3a**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.43 (br, 1H, Ar), 7.33 (br, 1H, Ar), 7.30–7.19 (m, 2H, Ar), 6.92 (d, 1H, $^{3}J_{2,3}$=8.0 Hz, H-2), 5.73 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.77 (br s, 3H, OCH_3), 2.66 (m, 1H, H-9), 1.71–1.50 (m, 2H, CH_2), 1.12 (t, 3H, ^{3}J=7.3 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.3 (COO), 155.0, 153.6 (2NCO), 130.9, 130.3 (C_{Ar}), 126.8, 126.4, 126.3, 125.6 (CH_{Ar}), 86.4 (C-2), 58.9 (C-3), 53.9, 53.8 (OCH_3), 44.7 (C-9), 19.1 (CH_2), 12.5 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422 (br), 2965 (m), 1715 (s), 1506 (m), 1325 (s), 1165 (s), 950 (s), 755 (w). MS (EI; 70 eV): *m*/*z* (%)=334 ([M]$^+$, 100), 306 (39), 247 (43), 235 (54), 145 (25), 59 (21). HRMS (EI) calcd for $C_{16}H_{18}N_2O_6$ ([M]$^+$): 334.1159; found: 334.1153.

3.1.1.2. Dimethyl 3-propyl-2-oxo-3,3a-dihydrofuro-[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3b). Starting with quinoxaline (**1**) (0.325 g, 2.50 mmol), 2-propyl-1,1-bis-(trimethylsilyloxy)ethene (**2b**) (0.863 g, 3.5 mmol) and methyl

chloroformate (0.78 mL, 10.25 mmol), *trans*-**3b** (0.252 g, 29%) was isolated as a colourless solid, mp 99–100 °C; *cis*-**3b** (0.183 g, 21%) was isolated as a colourless solid, mp 142–143 °C.

Data of *trans*-**3b**: ^{1}H NMR (500 MHz, DMSO-d_6): δ=7.51–7.48 (m, 1H, H-8), 7.41 (br, 1H, H-5), 7.28–7.23 (m, 2H, H-6,7), 6.73 (d, 1H, $^3J_{2,3}$=8.8 Hz, H-2), 5.53 (br t, 1H, H-3), 3.78 (s, 3H, OCH_3), 3.73 (br s, 3H, OCH_3), 2.34 (m, 1H, H-9), 1.70–1.59 (m, 2H, CH_2), 1.45–1.36 (m, 2H, CH_2), 0.84 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ=175.1 (COO), 153.8, 153.5 (br) (2NCO), 130.8 (C-4a), 130.6 (C-8a), 126.5 (br), 126.3 (br), 126.2, 125.6 (C-5,6,7,8), 86.6 (C-2), 59.6 (C-3), 53.9, 53.5 (OCH_3), 41.6 (C-9), 31.4, 19.2 (CH_2), 13.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3427 (br, w), 2961 (m), 2974 (w), 1792 (s), 1730 (br, s), 1596 (w), 1505 (s), 1441 (s). MS (EI, 70 eV): *m*/*z* (%)=348 ([M]$^+$, 100), 320 (68), 291 (97), 261 (34), 235 (77), 145 (30). Anal. Calcd for $C_{17}H_{20}N_2O_6$ (348.35): C, 58.61; H, 5.79; N, 8.04. Found: C, 58.37; H, 5.81; N, 7.85.

Data of *cis*-**3b**: ^{1}H NMR (500 MHz, DMSO-d_6): δ=7.47–7.43 (m, 1H, H-8), 7.39 (br, 1H, H-5), 7.27–7.22 (m, 2H, H-6,7), 6.92 (d, 1H, $^3J_{2,3}$=8.0 Hz, H-2), 5.61 (br t, 1H, H-3), 3.80 (s, 3H, OCH_3), 3.70 (br s, 3H, OCH_3), 3.00 (ddd, 1H, $^3J_{3,9}$=9.5 Hz, $^3J_{9,10a}$=7.5 Hz, $^3J_{9,10b}$=6.3 Hz, H-9), 1.53–1.30 (m, 4H, CH_2), 0.87 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ=175.1 (COO), 154.3 (br, NCO), 153.4 (NCO), 131.2 (C-4a), 130.7 (C-8a), 126.6 (br), 126.5 (br), 126.2 (C-5,6,7), 125.3 (C-8), 86.8 (C-2), 59.1 (C-3), 53.9 (OCH_3), 53.7 (br, OCH_3), 41.9 (C-9), 27.2, 20.3 (CH_2), 13.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422 (br, w), 2963 (m), 2867 (w), 1774 (s), 1713 (br, s), 1597 (m), 1508 (s), 1441 (s), 1330 (br, s). MS (EI, 70 eV): *m*/*z* (%)=348 ([M]$^+$, 94), 320 (55), 291 (100), 261 (25), 235 (55), 145 (37). Anal. Calcd for $C_{17}H_{20}N_2O_6$ (348.35): C, 58.61; H, 5.79; N, 8.04. Found: C, 58.23; H, 5.91; N, 7.97.

3.1.1.3. Dimethyl 3-butyl-2-oxo-3,3a-dihydrofuro[2,3-*b*]-quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3c). Starting with quinoxaline (**1**) (0.261 g, 2.00 mmol), 2-butyl-1,1-bis(trimethylsilyloxy)ethene (**2c**) (0.728 g, 2.80 mmol) and methyl chloroformate (0.67 mL, 8.00 mmol), *trans*-**3c** (0.083 g, 11%) was isolated as a colourless solid, mp 125–126 °C; *cis*-**3c** (0.180 g, 25%) was isolated as a colourless oil.

Data of *trans*-**3c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.50 (br, 1H, Ar), 7.32 (br, 1H, Ar), 7.25–7.17 (m, 2H, Ar), 6.69 (d, 1H, $^3J_{2,3}$=8.8 Hz, H-2), 5.48 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.48–2.34 (m, 1H, H-9), 1.90–1.78 (m, 1H, CH_2), 1.71–1.56 (m, 1H, CH_2), 1.46–1.22 (m, 4H, CH_2), 1.03 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=175.0 (COO), 154.0 (2NCO), 130.6, 130.3 (C_{Ar}), 126.5, 126.2 (2), 126.0 (CH_{Ar}), 86.0 (C-2), 59.6 (C-3), 54.0, 53.7 (OCH_3), 41.8 (C-9), 29.4, 28.2, 22.2 (CH_2), 13.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3425 (br), 2960 (m), 1789 (s), 1507 (s), 1332 (s), 1162 (s), 971 (s), 745 (w). MS (EI; 70 eV): *m*/*z* (%)=362 ([M]$^+$, 100), 291 (65), 275 (33), 235 (55), 189 (14), 145 (26), 59 (20). HRMS (EI) calcd for $C_{18}H_{22}N_2O_6$ ([M]$^+$): 362.1472; found: 362.1461.

Data of *cis*-**3c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.43 (br, 1H, ArH), 7.23–7.19 (m, 3H, ArH), 6.92 (d, 1H, $^3J_{2,3}$=8.2 Hz, H-2), 5.74 (br, 1H, H-3), 3.87 (s, 3H, OCH_3), 3.78 (br s, 3H, OCH_3), 2.75–2.66 (m, 1H, H-9), 1.59–1.29 (m, 6H, CH_2), 0.91 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.4 (COO), 154.9 (br) (2NCO), 131.0, 130.3 (C_{Ar}), 126.8, 126.4, 126.3, 125.6 (CH_{Ar}), 86.5 (C-2), 58.8 (C-3), 53.9, 53.7 (OCH_3), 43.0 (C-9), 29.7, 25.2, 22.5 (CH_2), 13.7 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3420 (br), 2954 (m), 1715 (s), 1508 (s), 1331 (s), 1160 (s), 965 (s), 754 (w). MS (EI; 70 eV): *m*/*z* (%)=362 ([M]$^+$, 100), 291 (63), 275 (32), 235 (51), 189 (17), 145 (28), 59 (21). HRMS (EI) calcd for $C_{18}H_{22}N_2O_6$ ([M]$^+$): 362.1472; found: 362.1462.

3.1.1.4. Dimethyl 3-dodecyl-2-oxo-3,3a-dihydrofuro-[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3d). Starting with quinoxaline (**1**) (0.325 g, 2.50 mmol), 2-dodecyl-1,1-bis-(trimethylsilyloxy)ethene (**2d**) (1.304 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**3d** (0.355 g, 30%) was isolated as a colourless solid, mp 100–101 °C; *cis*-**3d** (0.178 g, 15%) was isolated as a colourless solid, mp 119–120 °C.

Data of *trans*-**3d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.52 (br, 1H, Ar), 7.31 (br, 1H, Ar), 7.26–7.21 (m, 2H, Ar), 6.70 (d, 1H, $^3J_{2,3}$=8.7 Hz, 1H, H-2), 5.49 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.82 (br s, 3H, OCH_3), 2.47–2.42 (m, 1H, H-9), 1.85–1.60 (br m, 2H, CH_2), 1.46–1.39 (m, 2H, CH_2), 1.38–1.24 (m, 18H, CH_2), 0.88 (t, 3H, ^3J=6.7 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=175.0 (COO), 154.1, 154.0 (NCO), 130.6, 130.4 (C_{Ar}), 126.6, 126.2 (2), 125.9 (CH_{Ar}), 86.0 (C-2), 59.7 (C-3), 53.9, 53.7 (OCH_3), 41.8 (C-9), 31.9, 29.7, 29.6 (3), 29.5, 29.4, 29.3, 29.2, 26.1, 22.7 (CH_2), 14.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3413 (br, w), 2919 (s), 2849 (m), 1771 (s), 1716 (br, s), 1595 (w), 1508 (s), 1441 (m). MS (EI, 70 eV): *m*/*z* (%)=474 ([M]$^+$, 100), 387 (19), 291 (62), 235 (55), 145 (20). HRMS (EI) calcd for $C_{26}H_{38}N_2O_6$ ([M]$^+$): 474.27244; found: 474.27190.

Data of *cis*-**3d**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.43 (br, 1H, Ar), 7.26–7.19 (m, 3H, Ar), 6.92 (d, 1H, $^3J_{2,3}$=8.3 Hz, H-2), 5.73 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.77 (br s, 3H, OCH_3), 2.71 (m, 1H, H-9), 1.62–1.52 (m, 4H, CH_2), 1.47–1.13 (m, 18H, CH_2), 0.87 (t, 3H, ^3J=6.7 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.4 (COO), 153.6 (2NCO), 131.0, 130.4 (C_{Ar}), 126.8, 126.4 (2), 125.6 (CH_{Ar}), 86.4 (C-2), 58.8 (C-3), 53.8, 53.7 (br) (OCH_3), 43.1 (C-9), 31.9, 29.6 (3), 29.5 (2), 29.3 (2), 27.5, 25.6, 22.7 (CH_2), 14.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3419 (br, w), 2918 (s), 2849 (m), 1773 (s), 1715 (br, s), 1596 (w), 1509 (s), 1472 (m). MS (EI, 70 eV): *m*/*z* (%)=474 ([M]$^+$, 100), 387 (13), 291 (40), 235 (34), 145 (15). Anal. Calcd for $C_{17}H_{20}N_2O_6$ (474.58): C, 65.80; H, 8.07; N, 5.90. Found: C, 66.00; H, 8.20; N, 5.59.

3.1.1.5. Dimethyl 3-isopropyl-2-oxo-3,3a-dihydrofuro-[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3e). Starting with quinoxaline (**1**) (0.261 g, 2.00 mmol), 2-isopropyl-1,1-bis(trimethylsilyloxy)ethene (**2e**) (0.728 g, 2.80 mmol) and methyl chloroformate (0.67 mL, 8.00 mmol), *trans*-**3e** (0.185 g, 27%) was isolated as a brownish solid, mp

159–160 °C; *cis*-**3e** (0.232 g, 33%) was isolated as a brownish solid, mp 168–169 °C.

Data of *trans*-**3e**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.50 (br, 1H, Ar), 7.26–7.19 (m, 3H, Ar), 6.67 (d, 1H, $^3J_{2,3}$=8.9 Hz, H-2), 5.60 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.80 (br s, 3H, OCH_3), 2.40 (dd, 1H, $^3J_{3,9}$=7.6 Hz, $^3J_{9,CH}$=4.2 Hz, H-9), 2.32–2.22 (m, 1H, CH), 1.03 (d, 3H, ^3J=7.0 Hz, CH_3), 1.00 (d, 3H, ^3J=6.8 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.1 (COO), 153.8 (2NCO), 130.7, 130.4 (C_{Ar}), 126.5, 126.2 (2), 125.7 (CH_{Ar}), 86.2 (C-2), 56.2 (C-3), 53.9, 53.6 (OCH_3), 48.0 (C-9), 28.2 (CH), 19.5, 18.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3413 (br), 2959 (m), 1715 (s), 1507 (m), 1330 (s), 1165 (s), 959 (s), 766 (w). MS (EI; 70 eV): *m*/*z* (%)=348.1 ([M]$^+$, 100), 320 (48), 305 (49), 261 (73), 235 (64), 145 (27). HRMS (EI) calcd for $C_{17}H_{20}N_2O_6$ ([M]$^+$): 348.13159; found: 348.13137.

Data of *cis*-**3e**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.44 (br, 1H, Ar), 7.26–7.14 (m, 3H, Ar), 6.84 (d, 1H, $^3J_{2,3}$=7.8 Hz, H-2), 5.77 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.75 (br s, 3H, OCH_3), 2.56 (dd, 1H, $^3J_{3,9}$=9.2 Hz, $^3J_{9,CH}$=6.1 Hz, H-9), 2.08–2.00 (m, 1H, CH), 1.11 (d, 3H, ^3J=6.8 Hz, CH_3), 1.04 (d, 3H, ^3J=6.8 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.3 (COO), 153.8 (2NCO), 130.8, 130.5 (C_{Ar}), 127.1, 127.0, 126.0, 125.4 (CH_{Ar}), 85.4 (C-2), 59.7 (C-3), 53.8 (2 OCH_3), 49.0 (C-9), 25.5 (CH), 22.7, 19.6 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3428 (br), 2954 (m), 1711 (s), 1507 (m), 1328 (s), 1161 (s), 1008 (s), 765 (w). MS (EI; 70 eV): *m*/*z* (%)=348.1 ([M]$^+$, 100), 320 (81), 305 (58), 261 (78), 235 (68), 145 (29). Anal. Calcd for $C_{19}H_{22}N_2O_6$ (348.35): C, 58.61; H, 5.79, N, 8.04. Found: C, 58.98; H, 5.86; N, 7.83.

3.1.1.6. Dimethyl 3-cyclohexyl-2-oxo-3,3a-dihydrofuro-[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3f). Starting with quinoxaline (**1**) (0.190 g, 1.45 mmol), 2-cyclohexyl-1,1-bis(trimethylsilyloxy)ethene (**2f**) (0.580 g, 2.03 mmol) and methyl chloroformate (0.54 mL, 5.80 mmol), *trans*-**3f** (0.160 g, 28%) was isolated as a colourless solid, mp 169–170 °C; *cis*-**3f** (0.150 g, 27%) was isolated as a colourless solid, mp 205–206 °C.

Data of *trans*-**3f**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.60 (br, 1H, Ar), 7.27 (br, 1H, Ar), 7.23–7.18 (m, 2H, Ar), 6.66 (d, 1H, $^3J_{2,3}$=8.5 Hz, H-2), 5.62 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.40 (dd, 1H, $^3J_{3,9}$=7.0 Hz, $^3J_{9,10}$=4.5 Hz, H-9), 1.89–1.55 (m, 6H, ring CH, ring CH_2), 1.31–1.15 (m, 5H, ring CH_2). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=174.2 (COO), 153.9 (br, 2NCO), 130.7, 130.4 (C-4a,8a), 126.7, 126.5, 126.2, 125.9 (CH_{Ar}), 86.3 (C-2), 56.9 (C-3), 53.9, 53.7 (OCH_3), 48.2 (C-9), 38.4 (CH), 30.0, 28.5, 26.3, 26.0, 25.8 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3432 (br), 2927 (m), 1715 (s), 1506 (m), 1329 (s), 1157 (s), 960 (s), 751 (w). MS (EI; 70 eV): *m*/*z* (%)=388.1 ([M]$^+$, 100), 360 (21), 301 (21), 252 (25), 192 (19), 145 (18). Anal. Calcd for $C_{20}H_{24}N_2O_6$ (388.41): C, 61.84; H, 6.23; N, 7.21. Found: C, 61.81; H, 6.16; N, 6.77.

Data of *cis*-**3f**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.45 (br, 1H, Ar), 7.30 (br, 1H, Ar), 7.24–7.15 (m, 2H, Ar), 6.83 (d, 1H, $^3J_{2,3}$=7.9 Hz, H-2), 5.76 (br s, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.57 (dd, 1H, $^3J_{3,9}$=9.5 Hz, $^3J_{9,10}$=5.4 Hz, H-9), 1.75–1.61 (m, 6H, ring CH, ring CH_2), 1.28–1.12 (m, 5H, ring CH_2). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=172.5 (COO), 155.2, 153.5 (NCO), 131.1, 130.5 (C-4a,8a), 127.0 (br), 126.8 (br), 126.0, 125.5 (CH_{Ar}), 85.6 (C-2), 59.5 (C-3), 53.8 (2C, OCH_3), 48.2 (C-9), 35.5 (CH), 32.7, 29.1, 26.6, 26.2, 25.9 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3428 (br), 2928 (m), 1714 (s), 1506 (s), 1327 (s), 1159 (m), 966 (s), 753 (w). MS (EI; 70 eV): *m*/*z* (%)=388.1 ([M]$^+$, 100), 360 (25), 301 (19), 252 (24), 235 (40), 192 (20), 145 (22). Anal. Calcd for $C_{20}H_{24}N_2O_6$ (388.41): C, 61.84; H, 6.23; N, 7.21. Found: C, 61.80; H, 6.08; N, 6.62.

3.1.1.7. Dimethyl 3-(cyclopentylmethyl)-2-oxo-3,3a-dihydrofuro[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3g). Starting with quinoxaline (**1**) (0.325 g, 2.5 mmol), 2-methylcyclopentyl-1,1-bis(trimethylsilyloxy)ethene (1.003 g, 3.5 mmol) and methyl chloroformate (0.945 g, 10.0 mmol), *trans*-**3g** (0.315 g, 32%) was isolated as a colourless solid, mp 129 °C; *cis*-**3g** (0.225 g, 24%) was isolated as a colourless solid, mp 174 °C.

Data of *trans*-**3g**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.51 (br, 1H, Ar), 7.30 (br, 1H, Ar), 7.24–7.19 (m, 2H, Ar), 6.69 (d, 1H, $^3J_{2,3}$=8.5 Hz, H-2), 5.50 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.80 (br s, 3H, OCH_3), 2.43 (m, 1H, H-9), 2.06 (br m, 1H, H-11), 1.82–1.48 (m, 8H, H-10,12a,12′a,13,13′), 1.09–0.97 (m, 2H, H-12b,12′b). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=175.2 (C-14), 154.1 (br, NCO), 154.0 (NCO), 126.6 (CH_{Ar}), 126.3 (br, CH_{Ar}), 126.2, 125.9 (CH_{Ar}), 86.0 (C-2), 60.1 (C-3), 53.9 (OCH_3), 53.7 (br, OCH_3), 40.9 (C-9), 36.7 (C-11), 36.3 (C-10), 32.9, 31.8 (C-12,12′), 25.1, 25.0 (C-13,13′). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3421 (br, w), 2958 (m), 2870 (w), 1787 (s), 1725 (s), 1593 (m), 1507 (s). MS (EI, 70 eV): *m*/*z* (%)=388 ([M]$^+$, 99), 291 (100), 235 (45), 189 (25), 145 (28). Anal. Calcd for $C_{20}H_{24}N_2O_6$ (388.41): C, 61.84; H, 6.23; N, 7.21. Found: C, 62.16; H, 6.43; N, 6.84.

Data of *cis*-**3g**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.44 (br, 1H, Ar), 7.27 (br, 1H, Ar), 7.23–7.17 (m, 2H, Ar), 6.92 (d, 1H, $^3J_{2,3}$=8.2 Hz, H-2), 5.73 (br, 1H, H-3), 3.76 (br s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 2.76 (m, 1H, H-9), 2.16 (m, 1H, H-11), 1.78 (m, 2H, H-12a,12′a), 1.65–1.43 (m, 6H, H-10,13,13′), 1.08 (m, 2H, H-12b,12′b). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=174.5 (C-14), 155.0, 153.5 (NCO), 126.8 (br, CH_{Ar}), 126.5 (br, CH_{Ar}), 126.3, 125.6 (CH_{Ar}), 86.4 (C-2), 59.0 (C-3), 53.8 (OCH_3), 53.7 (br, OCH_3), 42.1 (C-9), 37.1 (C-11), 32.5, 32.4 (C-12,12′), 31.6 (C-10), 25.1, 25.0 (C-13,13′). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3427 (br, w), 2955 (m), 2867 (w), 1785 (s), 1719 (s), 1594 (m), 1506 (s). MS (EI, 70 eV): *m*/*z* (%)=388 ([M]$^+$, 100), 291 (97), 235 (43), 189 (20), 145 (23). Anal. Calcd for $C_{20}H_{24}N_2O_6$ (388.41): C, 61.84; H, 6.23; N, 7.21. Found: C, 61.90; H, 6.38; N, 6.90.

3.1.1.8. Dimethyl 3-(2-cyclohexylethyl)-2-oxo-3,3a-dihydrofuro[2,3-*b*]quinoxaline-4,9(2*H*,9a*H*)-dicarboxylate (3h). Starting with quinoxaline (**1**) (0.325 g, 2.50 mmol), 4-cyclohexyl-1,1-bis(trimethylsilyloxy)but-1-ene (**2h**) (1.100 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**3h** (0.258 g, 25%) was isolated as a

colourless solid, mp 128–130 °C; *cis*-**3h** (0.123 g, 12%) was isolated as a colourless solid, mp 115–116 °C.

Data of *trans*-**3h**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.52 (br, 1H, Ar), 7.33 (br, 1H, Ar), 7.24–7.20 (m, 2H, Ar), 6.70 (d, 1H, $^3J_{2,3}$=8.8 Hz, 1H, H-2), 5.49 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.81 (br s, 3H, OCH_3), 2.47–2.33 (m, 1H, H-9), 1.99–1.80 (br m, 1H, CH), 1.78–1.51 (m, 6H, CH_2), 1.39–1.05 (m, 6H, CH_2), 1.00–0.75 (m, 2H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=175.0 (COO), 154.0 (br, 2NCO), 130.6, 130.4 (C_{Ar}), 126.5, 126.2 (2), 125.9 (CH_{Ar}), 86.0 (C-2), 59.5 (C-3), 53.9, 53.6 (br) (OCH_3), 41.9 (C-9), 37.2 (CH), 33.4, 33.1, 32.8, 26.9, 26.4, 26.2, 26.1 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3448 (br, m), 2923 (s), 2852 (m), 1771 (s), 1716 (br, s), 1593 (w), 1507 (s), 1441 (s). MS (EI, 70 eV): *m*/*z* (%)=416 ([M]$^+$, 100), 357 (3), 291 (11), 235 (27), 188 (30), 145 (16). HRMS (EI) calcd for $C_{22}H_{28}N_2O_6$ ([M]$^+$): 416.19419; found: 416.19472.

Data of *cis*-**3h**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.44 (br, 1H, Ar), 7.31 (br, 1H, Ar), 7.23–7.20 (m, 2H, Ar), 6.93 (d, 1H, $^3J_{2,3}$=8.0 Hz, 1H, H-2), 5.75 (br, 1H, H-3), 3.86 (s, 3H, OCH_3), 3.78 (br s, 3H, OCH_3), 2.75–2.61 (br m, 1H, H-9), 1.77–1.53 (m, 7H, CH, CH_2), 1.38–1.05 (m, 6H, CH_2), 1.01–0.75 (m, 2H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.3 (COO), 155.0, 153.5 (NCO), 131.0, 130.4 (C_{Ar}), 126.8 (br), 126.5 (br), 126.3, 125.6 (CH_{Ar}), 86.5 (C-2), 58.8 (C-3), 53.8, 53.7 (br) (OCH_3), 43.4 (C-9), 37.6 (CH), 33.2, 33.1, 32.9, 26.5, 26.3, 26.2 (2) (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3420 (br, m), 2920 (s), 2851 (s), 1773 (s), 1717 (br, s), 1597 (w), 1508 (s), 1440 (s), 1338 (br, s). MS (EI, 70 eV): *m*/*z* (%)=416 ([M]$^+$, 100), 388 (3), 291 (11), 235 (26), 145 (17). HRMS (EI) calcd for $C_{22}H_{28}N_2O_6$ ([M]$^+$): 416.19419; found: 416.19437. Anal. Calcd for $C_{22}H_{28}N_2O_6$ (416.47): C, 63.45; H, 6.78; N, 6.73. Found: C, 64.11; H, 7.07; N, 6.44.

3.1.1.9. Dimethyl 7-ethyl-6-oxo-7,7a-dihydrofuro[3,2-*b*]-pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5a). Starting with pyrazine (**4**) (0.200 g, 2.5 mmol), 2-ethyl-1,1-bis(trimethylsilyloxy)ethene (**2a**) (0.650 g, 2.80 mmol) and methyl chloroformate (0.67 mL, 8.00 mmol), *trans*-**5a** (0.170 g, 24%) was isolated as a colourless oil.

Data of *trans*-**5a**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.20 (br, 3H, H-2,5,6), 4.72 (br, 1H, H-3), 3.84 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.84 (br, 1H, H-7), 1.85–1.79 (m, 1H, CH_2), 1.62–1.53 (m, 1H, CH_2), 1.10 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.5 (COO), 153.1 (NCO), 152.7 (NCO), 108.7 (br, 2CH), 80.4 (C-2), 56.0 (br, C-3), 53.8, 53.7 (OCH_3), 46.0 (br, C-7), 21.4 (CH_2), 10.6 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br), 2960 (s), 1716 (s), 1443 (s), 1339 (s), 1127 (s), 974 (s), 766 (w). MS (EI; 70 eV): *m*/*z* (%)=284.1 ([M]$^+$, 100), 240 (10), 185 (76), 139 (44), 95 (44), 59 (30). Anal. Calcd for $C_{12}H_{16}N_2O_6$ (284.00): C, 50.70; H, 6.63; N, 9.85. Found: C, 50.86; H, 6.09; N, 9.21.

3.1.1.10. Dimethyl 7-propyl-6-oxo-7,7a-dihydrofuro-[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5b). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-propyl-1,1-bis(trimethylsilyloxy)ethene (**2b**) (0.863 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**5b** (0.299 g, 40%) was isolated as a colourless oil; *cis*-**5b** (0.196 g, 26%) was isolated as a colourless solid, mp 71–72 °C.

Data of *trans*-**5b**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.24 (br, 3H, H-2,5,6), 4.66 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.91 (br, 1H, H-7), 1.81–1.71 (m, 2H, CH_2), 1.64–1.45 (m, 2H, CH_2), 0.97 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.8 (COO), 153.0 (br, NCO), 152.7 (NCO), 108.8 (br), 108.0 (br) (CH), 80.5 (C-2), 57.1 (br, C-3), 54.0, 53.7 (OCH_3), 46.2 (br), 45.0 (br) (C-7), 30.6, 19.7 (CH_2), 13.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3546 (br, w), 3160 (s), 2960 (br, s), 2875 (s), 1785 (br, s), 1717 (br, s), 1540 (w), 1443 (br, s). MS (EI, 70 eV): *m*/*z* (%)=298 ([M]$^+$, 73), 198 (12), 185 (100), 139 (68), 95 (48). Anal. Calcd for $C_{13}H_{18}N_2O_6$ (298.29): C, 52.34; H, 6.08; N, 9.39. Found: C, 52.06; H, 6.19; N, 9.19.

Data of *cis*-**5b**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.27 (br, 3H, H-2,5,6), 5.28 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.83 (br m, 1H, H-7), 1.71–1.39 (m, 4H, CH_2), 0.92 (t, 3H, ^3J=7.3 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.7 (COO), 153.1 (2NCO), 110.6 (2CH), 81.7 (br, C-2), 54.0 (C-3), 54.0, 53.9 (OCH_3), 42.3 (C-7), 28.4, 20.5 (CH_2), 13.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3545 (br, w), 3138 (m), 2960 (br, s), 2874 (s), 1783 (br, s), 1717 (br, s), 1540 (w), 1438 (br, s). MS (EI, 70 eV): *m*/*z* (%)=298 ([M]$^+$, 27), 198 (15), 185 (61), 139 (49), 95 (43), 59 (100). HRMS (EI) calcd for $C_{13}H_{18}N_2O_6$ ([M]$^+$): 298.11594; found: 298.11537. Anal. Calcd for $C_{13}H_{18}N_2O_6$ (298.29): C, 52.34; H, 6.08; N, 9.39. Found: C, 51.83; H, 6.09; N, 8.84.

3.1.1.11. Dimethyl 7-butyl-6-oxo-7,7a-dihydrofuro[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5c). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-butyl-1,1-bis(trimethylsilyloxy)ethene (**2c**) (0.912 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**5c** (0.234 g, 30%) was isolated as a colourless oil; *cis*-**5c** (0.297 g, 39%) was isolated as a colourless oil.

Data of *trans*-**5c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.24 (br, 3H, H-2,5,6), 4.68 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.90 (br m, 1H, H-7), 1.82–1.73 (m, 2H, CH_2), 1.63–1.25 (m, 4H, CH_2), 0.93 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.8 (COO), 153.0 (br, NCO), 152.7 (NCO), 108.9 (br), 108.8 (br) (CH), 80.5 (C-2), 56.9 (C-3), 54.0, 53.7 (OCH_3), 46.5 (br), 44.9 (br) (C-7), 28.4, 28.2, 22.5 (CH_2), 13.8 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3432 (br, s), 3140 (m), 2959 (s), 2863 (s), 1792 (br, s), 1734 (br, s), 1539 (w), 1437 (br, s), 1368 (br, s). MS (EI, 70 eV): *m*/*z* (%)=312 ([M]$^+$, 100), 268 (10), 185 (79), 139 (61), 95 (21), 59 (17). HRMS (EI) calcd for $C_{14}H_{20}N_2O_6$ ([M]$^+$): 312.13159; found: 312.13168. Anal. Calcd for $C_{14}H_{20}N_2O_6$ (312.32): C, 53.84; H, 6.45; N, 8.97. Found: C, 53.20; H, 6.42; N, 8.63.

Data of *cis*-**5c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.27 (br, 3H, H-2,5,6), 5.29 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.82 (br m, 1H, H-7), 1.64-1.24 (m, 6H, CH_2), 0.89 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=174.8 (COO), 153.4 (br, NCO), 153.1 (NCO), 110.6 (2 CH), 81.6 (br, C-2), 54.0 (C-3), 54.0, 53.8 (OCH_3), 42.5 (C-7), 29.4, 26.0, 22.5 (CH_2), 13.7 (CH_3). IR (KBr, cm^{-1}):

$\tilde{\nu}$ = 3545 (br, w), 3435 (br, w), 3137 (m), 2958 (br, s), 2871 (s), 1782 (br, s), 1716 (br, s), 1540 (w), 1444 (br, s). MS (EI, 70 eV): *m/z* (%)=312 ([M]$^+$, 100), 198 (19), 185 (83), 139 (46), 95 (23), 59 (21). HRMS (EI) calcd for $C_{14}H_{20}N_2O_6$ ([M]$^+$): 312.13159; found: 312.13136.

3.1.1.12. Dimethyl 7-dodecyl-6-oxo-7,7a-dihydrofuro-[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5d). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-dodecyl-1,1-bis(trimethylsilyloxy)ethene (**2d**) (1.304 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**5d** (0.275 g, 26%) was isolated as a colourless oil; *cis*-**5d** (0.214 g, 20%) was isolated as a colourless oil.

Data of *trans*-**5d**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.23 (br, 3H, H-2,5,6), 4.67 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.89 (m, 1H, H-7), 1.82–1.71 (m, 2H, CH_2), 1.67–1.45 (br m, 2H, CH_2), 1.38–1.21 (m, 18H, CH_2), 0.88 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.8 (COO), 153.0 (br, NCO), 152.7 (NCO), 108.9 (br, 2CH), 80.5 (C-2), 56.9 (C-3), 54.0, 53.7 (OCH_3), 46.6, 45.1 (br) (C-7), 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.3, 29.3, 26.3, 22.7 (CH_2), 14.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3140 (w), 2924 (s), 2854 (s), 1790 (s), 1724 (br, s), 1540 (w), 1444 (s), 1344 (br, s). MS (EI, 70 eV): *m/z* (%)=424 ([M]$^+$, 100), 380 (5), 281 (4), 185 (20), 139 (15). HRMS (EI) calcd for $C_{22}H_{36}N_2O_6$ ([M]$^+$): 424.25679; found: 424.25793.

Data of *cis*-**5d**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.27 (br, 3H, H-2,5,6), 5.28 (br, 1H, H-3), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.81 (br m, 1H, H-7), 1.75–1.55 (m, 2H, CH_2), 1.55–1.37 (m, 2H, CH_2), 1.37–1.18 (m, 18H, CH_2), 0.88 (t, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.8 (COO), 153.3 (br, NCO), 153.0 (NCO), 110.6, 110.3 (br) (CH), 81.6 (C-2), 54.1 (C-3), 54.0, 53.8 (OCH_3), 42.5 (br, C-7), 31.9, 29.6 (3), 29.5, 29.4, 29.3 (2), 27.3, 26.3, 22.6 (CH_2), 14.1 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3447 (br, w), 3144 (w), 2957 (m), 2920 (s), 2850 (s), 1763 (s), 1748 (s), 1678 (m), 1449 (s), 1349 (br, s). MS (EI, 70 eV): *m/z* (%)=424 ([M]$^+$, 100), 380 (1), 280 (3), 185 (40), 139 (28). HRMS (EI) calcd for $C_{22}H_{36}N_2O_6$ ([M]$^+$): 424.25679; found: 424.25795.

3.1.1.13. Dimethyl 7-isopropyl-6-oxo-7,7a-dihydrofuro-[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5e). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-isopropyl-1,1-bis-(trimethylsilyloxy)ethene (**2e**) (0.616 g, 3.5 mmol) and methyl chloroformate (0.78 mL, 10.25 mmol), *trans*-**5e** (0.146 g, 20%) was isolated as a colourless solid, mp 102–103 °C; *cis*-**5e** (0.265 g, 35%) was isolated as a colourless solid, mp 92–93 °C.

Data of *trans*-**5e**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.30–6.05 (br, 3H, H-2,5,6), 4.79 (br, 1H, H-3), 3.80 (s, 3H, OCH_3), 3.77 (br s, 3H, OCH_3), 2.75 (br s, 1H, H-7), 2.17 (br s, 1H, H-8), 1.12 (d, 3H, ^3J=7.0 Hz, CH_3), 1.04 (d, 3H, ^3J= 7.0 Hz, CH_3). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=173.7 (COO), 152.9 (br, NCO), 152.6 (NCO), 108.7 (br, C-5,6), 80.5 (C-2), 55.4 (br), 54.6 (br) (C-3), 53.9, 53.5 (OCH_3), 52.1 (br), 50.1 (br) (C-7), 27.7 (C-8), 19.7, 18.9 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br, w), 3139 (w), 2964 (m), 1783 (s), 1727 (br, s), 1683 (m), 1441 (s), 1347 (br, s). MS (EI, 70 eV): *m/z* (%)=298 ([M]$^+$, 100), 211 (40), 198 (15), 185 (74), 139 (60). Anal. Calcd for $C_{13}H_{18}N_2O_6$ (298.29): C, 52.34; H, 6.08; N, 9.39. Found: C, 52.14; H, 6.08; N, 9.05.

Data of *cis*-**5e**: ^{1}H NMR (500 MHz, $CDCl_3$): δ=6.25–6.18 (br, 3H, H-2,5,6), 5.25 (br s, 1H, H-3), 3.82 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 2.79 (br s, 1H, H-7), 1.96 (br s, 1H, H-8), 1.13 (d, 3H, ^3J=7.0 Hz, CH_3), 0.94 (d, 3H, ^3J=7.0 Hz, CH_3). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ=173.1 (COO), 153.4 (br, NCO), 153.0 (NCO), 110.8 (br), 110.2 (C-5,6), 81.2 (C-2), 54.4 (C-3), 53.9, 53.8 (OCH_3), 48.5 (C-7), 25.0 (C-8), 23.0, 18.5 (CH_3). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br, m), 3137 (w), 2965 (m), 1780 (s), 1728 (br, s), 1442 (s), 1337 (br, s). MS (EI, 70 eV): *m/z* (%)=298 ([M]$^+$, 92), 211 (24), 198 (45), 185 (100), 139 (67). Anal. Calcd for $C_{13}H_{18}N_2O_6$ (298.29): C, 52.34; H, 6.08; N, 9.39. Found: C, 52.24; H, 6.10; N, 9.20.

3.1.1.14. Dimethyl 7-cyclohexyl-6-oxo-7,7a-dihydrofuro-[3,2-*b*]pyrazine-1,4(4a*H*,6*H*)-dicarboxylate (5f). Starting with pyrazine (**4**) (0.200 g, 2.50 mmol), 2-cyclohexyl-1,1-bis(trimethylsilyloxy)ethene (**2f**) (0.989 g, 3.46 mmol) and methyl chloroformate (0.94 mL, 10.0 mmol), *trans*-**5f** (0.320 g, 38%) was isolated as a colourless solid, mp 129–130 °C; *cis*-**5f** (0.060 g, 11%) was isolated as a colourless oil.

Data of *trans*-**5f**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.22 (br, 3H, H-2,5,6), 4.73 (br, 1H, H-3), 3.83 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.76 (br, 1H, H-7), 1.78–1.64 (m, 6H, CH_2, ring CH), 1.46–1.11 (m, 5H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.0 (COO), 153.0, 152.7 (NCO), 109.4 (br) (C-5,6), 80.9 (C-2), 56.4 (br, C-3), 54.0, 53.6 (br) (OCH_3), 48.2 (br, C-7), 37.7 (ring CH), 30.2, 29.6, 26.3, 26.2, 25.8 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br), 2931 (s), 1721 (s), 1449 (s), 1341 (s), 1120 (s), 956 (s), 765 (w). MS (EI; 70 eV): *m/z* (%)=388.1 ([M]$^+$, 100), 211 (26), 185 (59), 139 (37), 95 (15), 59 (12). HRMS (EI) calcd for $C_{16}H_{22}N_2O_6$ ([M]$^+$): 338.1472; found: 338.1466.

Data of *cis*-**5f**: ^{1}H NMR (250 MHz, $CDCl_3$): δ=6.29–6.12 (br m, 3H, H-2,5,6), 5.22 (br, 1H, H-3), 3.84 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 2.75 (br, 1H, H-7), 1.76–1.53 (m, 6H, CH_2, ring CH), 1.24–1.12 (m, 5H, CH_2). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=173.3 (COO), 153.1 (2NCO), 110.1 (C-5,6), 81.0 (C-2), 53.9 (C-3), 53.9 (2 OCH_3), 48.4 (C-7), 35.5 (CH), 33.2, 28.8, 27.0, 26.4, 25.7 (CH_2). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3434 (br), 2931 (s), 1733 (s), 1428 (s), 1341 (s), 1121 (s), 957 (s), 766 (w). MS (EI; 70 eV): *m/z* (%)=388.1 ([M]$^+$, 100), 211 (26), 185 (59), 139 (37), 95 (15), 59 (12). HRMS (EI) calcd for $C_{16}H_{22}N_2O_6$ ([M]$^+$): 338.14724; found: 338.14659.

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