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Synthesis of Multisubstituted Dihydroquinoxaline Derivatives by Tandem *N*-Alkylation and Addition Reactions of 3-Oxoquinoxaline-2-carboxylates

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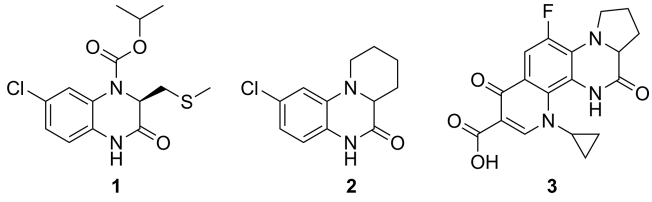
This report describes a one-pot synthesis of multisubstituted dihydroquinoxalin-2-ones using an umpolung *N*-alkylation followed by oxidation and *C*-alkylation reactions. Moreover, the synthesis of tricyclic compounds containing a dihydroquinoxaline skeleton was carried out by ring closing metathesis (RCM) of the resulting *N*,*C*-bis-addition products containing olefins.

Introduction

Compounds containing a nitrogen atom often have a wide variety of important biological activities. Those with a dihydroquinoxaline skeleton are used in many biologically active compounds.[1] Examples are used as pharmaceuticals, including antiviral compound **1**, used for the treatment of HIV,[2] anticancer compound **2**,[3] antitumor agent **3**,[4] and they are also used as agrochemicals[5] (Scheme 1).



Scheme 1. Valuable compounds containing a dihydroquinoxaline skeleton.

Various approaches to the synthesis of dihydroquinoxalin-2-ones have been reported. For example copper-catalysed couplings,[3,6] palladium-catalysed intramolecular *N*-arylation,[7] Ugi four-component reactions followed by palladium-assisted intramolecular *N*-arylation,[8] and bifunctional inverse-electron-demand hetero-Diels–Alder reactions using Lewis acids.[2] However, the synthesis of simple multisubstituted dihydroquinoxalin-2-ones has rarely been reported.

An umpolung reaction of an α-imino ester involving nucleophilic addition to the nitrogen atom is difficult due to the electron-withdrawing effect of the imino group. We have developed umpolung reactions of α-imino esters using organometallic reagents to give *N*-alkylated products, and the subsequent C–C bond formation was carried out using the iminium salt formed by oxidation of the intermediate metal enolate producted in the *N*-alkylation.[9] In this paper, we report a one-pot synthesis of multisubstituted di hydroquinoxalin-2-ones by *N*-alkylation/*C*-alkylation reactions of 3-oxo-quinoxalin-2-carboxylate derivatives.

Results and Discussion

For the initial *N*-alkylation step, the optimum reaction conditions were examined using quinoxaline derivatives **4**. As shown in Table 1, the reaction of quinoxaline derivative **4a** (0.15 mmol) with ethylmagnesium bromide (3 equiv.) in EtCN at –78 °C for 15 min led to the formation of *N*-ethylated product **5a** in 48% yield (Table 1, entry 1). The protecting group of the amide nitrogen was next examined (Table 1, entries 2 and 3). The use of a methyl group as a protecting group did not give the desired product (Table 1, entry 2), whereas the *tert*-butoxycarbonyl (Boc) derivative gave *N*-ethylated product **5a** in good yield, presumably due to the ability of the electron-withdrawing Boc group to enhance the reactivity of the imine nitrogen (Table 1, entry 3). Next, we examined various solvents using the *N*-Boc-protected substrate (i.e., **4c**). The use of polar solvents such as EtCN, THF, DME (1,2-dimethoxyethane), and MeCN (Table 1, entries 3–6) gave the product (i.e., **5a**) in good yields, whereas the use of nonpolar (Table 1, entries 7 and 8) solvents such as CH_2Cl_2 and toluene gave **5a** in moderate yields. When the reaction was carried out for a longer reaction time, the desired product was obtained in 90% yield (Table 1, entry 9). The amount of the nucleophile is very important: when the amount of EtMgBr was decreased (Table 1, entries 10 and 11), the yield of *N*-alkylated product **5a** decreased, and the yield of *N*-Et-*N*′-Boc product **6c**

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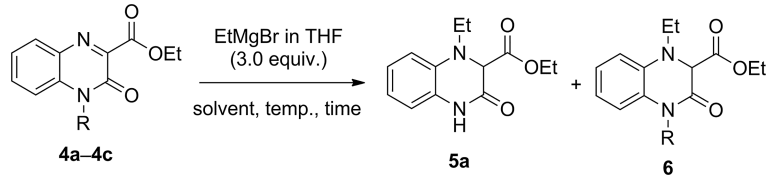
Table 1. Optimization of reaction conditions.



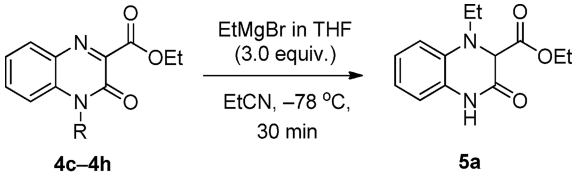
Entry	4	R	Solvent	Temp. °[C]	Time [min]	Yield [%] 5a		6
1	**4a**	H	EtCN	–78	15	48		–
2	**4b**	Me	EtCN	–78	15	0[a]	**6b**	0
3	**4c**	Boc	EtCN	–78	15	73	**6c**	0
4	**4c**	Boc	THF	–78	15	69	**6c**	7
5	**4c**	Boc	DME	–78	15	60	**6c**	11
6	**4c**	Boc	MeCN	–40	15	58	**6c**	13
7	**4c**	Boc	CH_2Cl_2	–78	15	27	**6c**	20
8	**4c**	Boc	Toluene	–78	15	48	**6c**	9
9	**4c**	Boc	EtCN	–78	30	90	**6c**	4
10[b]	**4c**	Boc	EtCN	–78	30	71	**6c**	8
11[c]	**4c**	Boc	EtCN	–78	30	10	**6c**	49

[a] A complex mixture was obtained. [b] EtMgBr (2.5 equiv.) was used. [c] EtMgBr (1.5 equiv.) was used.

increased. However, the combined yield of *N*-ethylated products **5a** and **6c** was not satisfactory (Table 1, entries 10 and 11).

Under the optimized conditions (Table 1, entry 9), several electron-withdrawing *N*-protecting groups were examined. Quinoxaline derivatives **4c**–**4g** with *N*-protecting groups containing a carbonyl moiety gave the desired *N*-ethylated product (i.e., **5a**) in moderate to good yields (Table 2, entries 1–5). An *N*-tosyl derivative gave the desired *N*-ethylated product (i.e., **5a**) in low yield with concomitant formation of many by-products, which suggests that an Mg^{II}-chelated intermediate between the lactam and the

Table 2. Examination of various electron-withdrawing *N*-protecting groups.



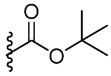
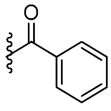
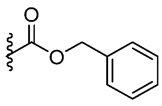
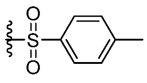
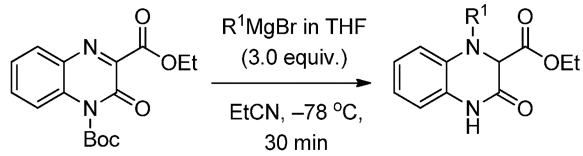
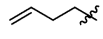
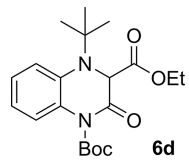
Entry	4	R		Yield [%]
1	**4c**		(Boc)	90
2	**4d**		(Bz)	78
3	**4e**		(Ac)	74
4	**4f**		(Cbz)	61
5	**4g**			55
6	**4h**		(Ts)	20

Table 3. Scope of Grignard reagents for *N*-alkylation.

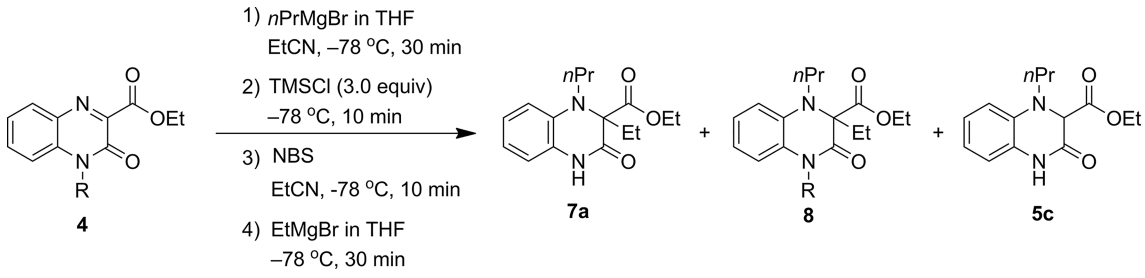


Entry	R^1	5	Yield [%]	Entry	R^1	5	Yield [%]
1	Et	**5a**	90	6	*i*Pr	**5f**	20
2	Me	**5b**	65	7	Ph	**5g**	15
3	*n*Pr	**5c**	69	8[a]	*t*Bu	**5h**	0 (9)[b]
4	*n*Bu	**5d**	73	9		**5i**	79
5	*n*Hex	**5e**	76	10		**5j**	69



[a] *t*BuMgCl was used. [b] Yield of *N*-*t*Bu-*N*′-Boc product **6d** is given in parentheses.

Table 4. Optimization of the tandem *N*,*C*-dialkylation.



Entry	4	R	*n*PrMgBr [equiv.]	NBS [equiv.]	EtMgBr [equiv.]	Yield [%] 7a		8	5c
1[a]	**4c**	Boc	3.0	2.5	3.0	22 (17)[b]	**8c**	0	3
2[a]	**4c**	Boc	1.5	2.5	2.0	28	**8c**	0	44
3	**4c**	Boc	1.5	2.5	2.0	22	**8c**	24	0
4	**4e**	Ac	1.5	2.0	2.0	40	**8e**	6	11
5	**4e**	Ac	1.5	2.0	3.0	56	**8e**	0	7
6	**4e**	Ac	1.5	2.4	3.0	65	**8e**	0	8
7[c]	**4e**	Ac	1.5	2.4	3.0	71	**8e**	0	9
8[c]	**4e**	Ac	1.5	2.4	1.5	29	**8e**	0	25
9[c,d]	**4e**	Ac	1.5	2.4	3.0	75	**8e**	0	0

[a] TMSCl was not used. [b] *N*,*C*-Dipropylation product **7j** was obtained. [c] TMSCl was added first. [d] NCS was used instead of NBS.

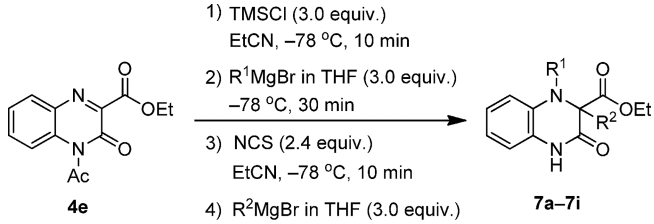
carbonyl oxygens of the protecting group plays an important role (Table 2, entry 6).

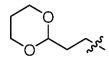
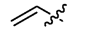
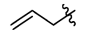
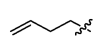
The scope of the reaction in terms of the Grignard reagents was examined next (Table 3). Linear primary alkyl Grignard reagents gave the desired *N*-alkylation products (i.e., **5a**–**5e**) in good yields (Table 3, entries 1–5). In contrast, bulky nucleophiles such as secondary, tertiary alkyl, and phenyl Grignard reagents gave the desired products (i.e., **5f**–**5h**) in low yields (Table 3, entries 6–8). When primary Grignard reagents with functional groups such as a terminal alkene or a cyclic acetal were used, the desired products (i.e., **5i** and **5j**) were also obtained in good yields (Table 3, entries 9 and 10).

Further studies were carried out on the oxidation of the intermediate enolate into an iminium salt, and the subsequent addition of another Grignard reagent. As expected, the *N*,*C*-dialkylated products were obtained (Table 4).

The initial *N*-alkylation reaction was carried out under the optimized conditions, and this was followed by the addition of *N*-bromosuccinimide (NBS) as an oxidant (2.5 equiv.) and EtMgBr (3.0 equiv.) (Table 4, entry 1). However, the reaction gave the *N*-propyl *C*-ethylated product (i.e., **7a**) in low yield, and the *N*,*C*-dipropylated product was obtained as a by-product in 17% yield. When the amount of *n*PrMgBr (1.5 equiv.) was decreased, none of the *N*,*C*-dipropylated product was obtained (Table 4, entry 2). When trimethylsilyl chloride (TMSCl) was used as an additive, the *N*-propyl *C*-ethylated products (i.e., **7a** and **8c**) were obtained in moderate yields, which suggests that a TMS enol derivative generated by silylation of the magnesium enolate intermediate would be suitable for oxidation into an iminium salt (Table 4, entry 3). When quinoxaline derivative **4e** bearing an acetyl group was subjected to the reaction conditions, the *N*-propyl *C*-ethylated product (i.e., **7a**) was obtained in 40% yield (Table 4, entry 4). Next, the effect of the amounts of reagents was examined using quinoxaline derivative **4e** as a starting material. When the

Table 5. Scope of Grignard reagents for *N*,*C*-dialkylation.[a]



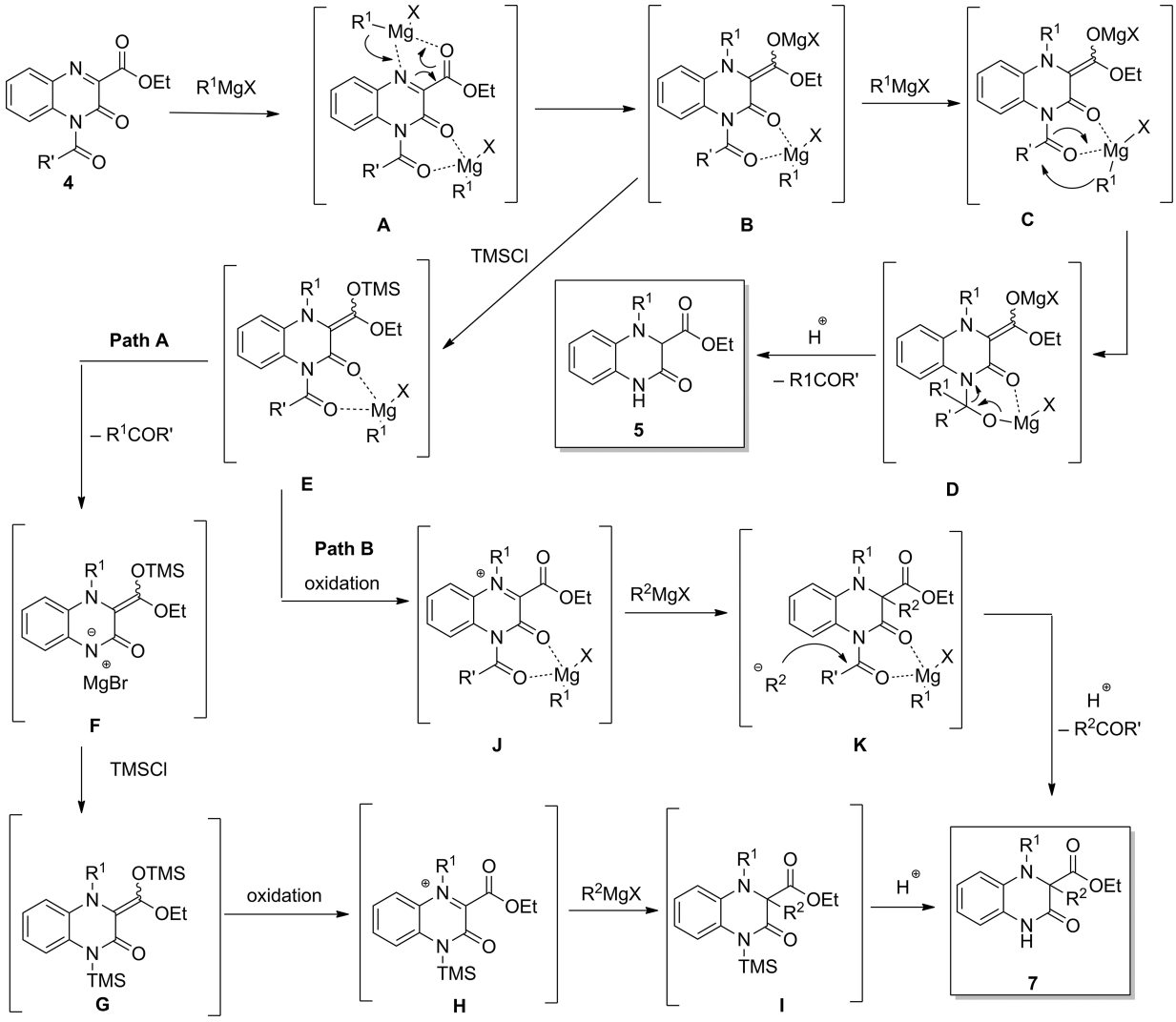
Entry	R^1	R^2	7	Yield [%]
1	*n*Pr	Et	**7a**	75
2	*n*Pr	Me	**7b**	66
3	*n*Pr	*i*Pr	**7c**	40
4	Et	Me	**7d**	58
5	Et	*n*Pr	**7e**	64
6	Et		**7f**	40
7[a]			**7g**	67
8[a][b]			**7h**	68
9[a]			**7i**	66

[a] TMSCl was added after the addition of R^1MgBr. [b] Using tetraallyltin instead of allylmagnesium bromide.

amounts of the nucleophile and the oxidant were increased, the desired product (i.e., **7a**) was obtained in good yields (Table 4, entries 5 and 6). Furthermore, when TMSCl was added initially, the *N*-propyl-*C*-ethylated product (i.e., **7a**) was obtained in 71% yield (Table 4, entry 7). Decreasing the amount of EtMgBr (1.5 equiv.) led to the formation of the desired product (i.e., **7a**) in low yield, while the yield of *N*-alkylated product **5c** increased (Table 4, entry 8). When NCS (*N*-chlorosuccinimide) was used as the oxidant instead of NBS, the best yield of 75% was obtained (Table 4, entry 9).

The scope of the reaction in terms of the Grignard reagents was next examined under the optimized conditions (Table 5). Primary alkyl Grignard reagents gave *N*,*C*-dialkylated products in good yields (Table 5, entries 1, 2, 4, and 5), while *i*PrMgBr and the Grignard reagent containing a cyclic acetal gave the desired products in moderate yields (Table 5, entries 3 and 6). In order to synthesize dihydroquinoxaline derivatives containing tricyclic structures, homoallyl and vinyl Grignard reagents, and tetraallyltin were used. As a result, the desired *N*,*C*-dialkylated products (i.e., **7g**–**7i**) were obtained in good yields (Table 5, entries 7–9).

A proposed reaction mechanism for the *N*-alkylation and *N*,*C*-dialkylation reaction is shown in Scheme 2. The electron density of the nitrogen atom of the imino group of intermediate **A** decreases as a result of chelation with the magnesium halide, and therefore, the electrophilicity of the nitrogen atom increases. *N*-Alkylation of quinoxaline derivative **4** generates magnesium enolate **B**. The addition of another Grignard reagent to the carbonyl group of the protecting group proceeds to form bis-magnesium species **D**, and hydrolysis of salt **D** gives the *N*-alkylated product (i.e., **5**). Regarding the *N*,*C*-dialkylation, *N*-alkylation/silylation of quinoxaline derivative **4** generates ketene silyl acetal **E** via magnesium enolate **B**. Two reaction pathways are possible. Deacetylation of ketene silyl acetal **E** with the Grignard reagent forms dianion **F** (Path A). Dianion **F** reacts with an excess of TMSCl to give bis-trimethylsilyl derivative **G**. Bis-trimethylsilyl derivative **G** is oxidized to give iminium salt **H**, which reacts with another Grignard reagent to give *N*,*C*-dialkylated product **7** after hydrolysis

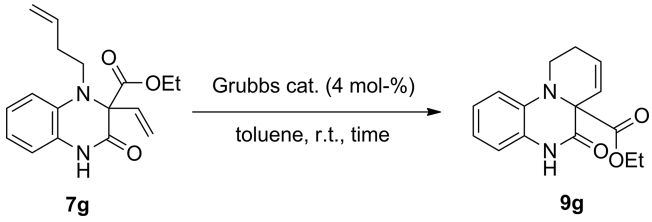


Scheme 2. Proposed reaction mechanism.

of silylated product **I**. Alternatively, ketene silyl acetal **E** is oxidized before the deacetylation to form iminium salt **J**, which reacts with another Grignard reagent to give *N*,*C*-dialkylated product **K**. Deacetylation of **K** with an extra Grignard reagent gives *N*,*C*-dialkylated product **7** (Path B).

Finally, we examined a synthesis of tricyclic compounds through a ring closing metathesis (RCM) reaction of *N*-homoallyl-*C*-vinyl compound **7g** with Grubbs catalysts (Table 6).[10] First, the reaction of the *N*-homoallyl-*C*-vinyl compound **7g** with Grubbs first-generation catalyst (4 mol-%) in toluene at reflux for 12 h gave tricyclic product **9g** in 55% yield (Table 6, entry 1). By using Grubbs second-generation catalyst or Hoveyda–Grubbs' second-generation catalyst, the desired tricyclic product (i.e., **9g**) was obtained in high yields (Table 6, entries 2 and 3).

Table 6. Synthesis of tricyclic compounds by RCM.

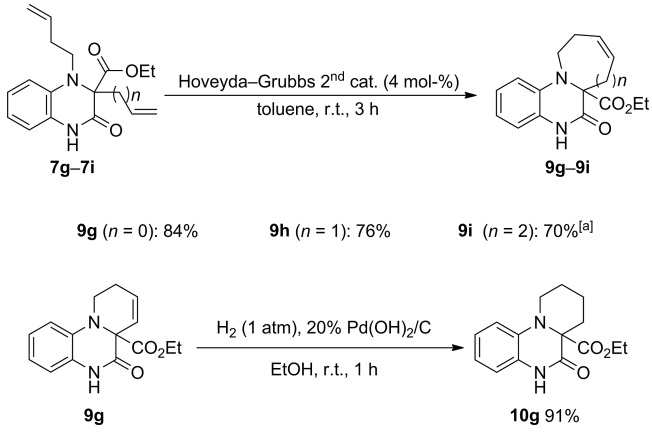


7g **9g**

Entry	Catalyst	Time [h]	Yield [%]
1	Grubbs 1st	12	55[a]
2	Grubbs 2nd	3	78
3	Hoveyda–Grubbs 2nd	3	84

[a] Carried out at reflux for 12 h.

Furthermore, the RCM of *N*,*C*-dialkylated compounds **7g**–**7i** was examined under the optimized conditions (Scheme 3). The reaction of *N*-homoallyl *C*-vinyl product **7g** and *N*-homoallyl *C*-allyl derivative **7h** gave the desired tricyclic products (i.e., **9g** and **9h**) in good yields. Using the *N*,*C*-dihomoallyl compound as substrate, the desired product (i.e., **9i**) was obtained in good yield under the influence of the Grubbs first-generation catalyst in CH_2Cl_2. Reduction of the newly formed olefin was readily carried out.



Scheme 3. Scope of the approach to tricyclic compounds. [a] Reaction conditions: Grubbs first-generation catalyst (4 mol-%), CH_2Cl_2 (10 mL), room temp., 16 h.

The reaction of tricyclic compound **9g** under H_2 (1 atm) in the presence of $Pd(OH)_2/C$ (Pearlman's catalyst, 4 mol-%) in EtOH for 1 h gave the desired product (i.e., **10g**) in 91% yield.

Conclusions

In summary, we have developed a one-pot synthesis of multisubstituted dihydroquinoxalin-2-ones using an umpolung *N*-alkylation and *N*,*C*-dialkylation. This method is useful because it enables the introduction of two substituents into a dihydroquinoxaline skeleton in a one-pot procedure. Tricyclic compounds containing a dihydroquinoxaline skeleton are attractive, because many of them show a wide variety of biological activities. These compounds are also readily accessible by the method described here.

Experimental Section

General Information: Infrared spectra were determined with a JASCO FTIR 460 plus spectrometer. ^1H and ^{13}C NMR spectra were recorded with a JEOL ECX-400P or a JEOL A-500 spectrometer using tetramethylsilane as an internal standard. Mass spectra were recorded with a JEOL MS-700D spectrometer. Tetrahydrofuran (THF) was distilled from benzophenone ketyl immediately before use. Dimethoxyethane (DME) was distilled from calcium hydride and then from copper(I) chloride, and stored over sodium. Toluene was dried with calcium chloride, distilled, and stored over molecular sieves (4 Å). Propionitrile (EtCN) and acetonitrile (MeCN) were distilled from phosphorus pentaoxide and then from calcium hydride, and stored over molecular sieves (4 Å). Dichloromethane (CH_2Cl_2) was distilled from calcium hydride, and stored over molecular sieves (4 Å). Products were purified by column chromatography on silica gel (Kanto silica Gel 60N) and/or preparative TLC on silica gel (Merck Kieselgel GF254).

Ethyl 2-Hydroxy-3-quinoxalinecarboxylate (4a): A 100 mL two-necked round-bottomed flask was equipped with a magnetic stirrer bar, a rubber septum, and an argon balloon. 1,2-Benzenediamine (7.0 g, 40 mmol) was dissolved in EtOH (50 mL), and diethyl 2-ozomalonete (36.1 mL, 20 mmol) was added. The reaction mixture was heated at reflux for 1 h with azeotropic removal of water, and then it was concentrated in vacuo to give ethyl 2-hydroxy-3-quinoxalinecarboxylate **4a** (8.8 g, 95%) as a yellow solid, m.p. 175.5–176.5 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.48 (t, J = 7.1 Hz, 3 H), 4.55 (q, J = 7.1 Hz, 2 H), 7.37–7.43 (m, 2 H), 7.61–7.65 (m, 1 H), 7.96–7.98 (m, 1 H), 11.72 (br., 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 62.5, 116.5, 125.0, 130.1, 132.0, 132.1, 132.7, 148.4, 154.7, 163.4 ppm. IR (neat): $\tilde{\nu}$ = 2965, 1741, 1658, 1611, 1300, 1254, 1133, 1092, 902, 767, 755 cm^{-1}. HRMS (EI): calcd. for $C_{11}H_{10}N_2O_3$ $[M]^+$ 218.0691; found 218.0686.

Ethyl 4-Methyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4b): A 200 mL two-necked round-bottomed flask was equipped with a magnetic stirrer bar, a rubber septum, and an argon balloon. A solution of ethyl 2-hydroxy-3-quinoxalinecarboxylate (**4a**; 2.1 g, 9.2 mmol) in DME (50 mL) was stirred at –5 °C to 5 °C, and then NaH (60% in oil; 0.41 g, 10.2 mmol) was added. The resulting mixture was stirred at room temperature. After 1 h, CH_3I (0.86 mL, 13.8 mmol) was added, and the mixture was stirred for 16 h. The reaction was quenched with H_2O (50 mL), and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined extracts

were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (*n*-hexane/ethyl acetate, 2:3) to give **4b** (1.9 g, 88%) as a white solid, m.p. 124.5–125.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (t, J = 7.3 Hz, 3 H), 3.74 (s, 3 H), 4.51 (q, J = 7.3 Hz, 2 H), 7.35–7.42 (m, 2 H), 7.64–7.69 (m, 1 H), 7.94–7.97 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 29.1, 62.3, 113.8, 124.2, 131.3, 132.5, 134.0, 149.0, 152.6, 163.8 ppm. IR (neat): $\tilde{\nu}$ = 2997, 1740, 1666, 1469, 1309, 1367, 1246, 1167, 1082, 761 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{12}N_2O_3$ $[M]^+$ 232.0848; found 232.08412.

Ethyl 4-*tert*-Butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4c): A 100 mL two-necked round-bottomed flask was equipped with a magnetic stirrer bar, a rubber septum, and an argon balloon Ethyl 2-hydroxy-3-quinoxalinecarboxylate **(4a**; 1.2 g, 5.0 mmol) and DMAP (4-dimethylaminopyridine; 61.0 mg, 0.5 mmol) were dissolved in THF (40 mL), and then Boc_2O (5.7 mL, 25 mmol), DMF (8.0 mL), and Et_3N (0.7 mL, 5.0 mmol) were added. The resulting mixture was stirred at room temperature for 3 h, then the reaction was quenched with H_2O (20 mL). The mixture was extracted with ethyl acetate (2× 20 mL). The combined extracts were dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (*n*-hexane/ethyl acetate, 7:2) to give **4c** (1.3 g, 81%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.49 (t, J = 7.3 Hz, 3 H), 1.60 (s, 9 H), 4.55 (q, J = 7.3 Hz, 2 H), 7.82–7.91 (m, 2 H), 8.06–8.08 (m, 1 H), 8.28–8.30 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 27.6, 62.7, 85.1, 128.4, 129.9, 130.5, 132.8, 138.6, 140.4, 141.5, 149.9, 150.4, 162.9 ppm. IR (neat): $\tilde{\nu}$ = 2983, 1761, 1728, 1574, 1469, 1372, 1345, 1244, 1138, 1084, 768 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{18}N_2O_5$ $[M]^+$ 318.1216; found 318.1230.

Ethyl 4-Benzoyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4d): A 200 mL two-necked round-bottomed flask was equipped with a magnetic stirrer bar, a rubber septum, and an argon balloon. Ethyl 2-hydroxy-3-quinoxalinecarboxylate (**4a**; 0.93 g, 4.0 mmol) was dissolved in Et_2O (25 mL), and NaH (60% in oil; 0.41 g, 10.2 mmol) was added. The mixture was stirred for 1 h at room temperature, then benzoyl chloride (0.7 mL, 6.0 mmol) was added. The mixture was stirred at room temperature for 14 h, and then it was concentrated in vacuo. The crude product was purified by silica gel column chromatography (*n*-hexane/ethyl acetate, 4:1) to give **4d** (1.0 g, 79%) as a white solid, m.p. 134.5–135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3 H), 4.41 (q, J = 7.1 Hz, 2 H), 7.54–7.58 (m, 2 H), 7.68–7.72 (m, 1 H), 7.85–7.94 (m, 2 H), 8.10–8.12 (m, 1 H), 8.28–8.35 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 62.7, 128.4, 128.7, 130.1, 130.6, 132.9, 134.3, 138.8, 140.6, 141.8, 150.6, 162.8, 164.9 ppm. IR (neat): $\tilde{\nu}$ = 2989, 1744, 1724, 1148, 1327, 1240, 1210, 1140, 1088, 10545, 765, 744 cm^{-1}. HRMS (EI): calcd. for $C_{18}H_{14}N_2O_4$ $[M]^+$ 322.0954; found 322.0945.

Ethyl 4-Acetyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4e): A 50 mL two-necked round-bottomed flask was equipped with a magnetic stirrer bar, a rubber septum, and an argon balloon. Ethyl 2-hydroxy-3-quinoxalinecarboxylate (**4a**; 0.93 g, 4.0 mmol) was dissolved in THF (35 mL), and NaH (60% in oil; 0.41 g, 10.2 mmol) was added. The mixture was stirred at room temperature for 1 h, then acetyl chloride (0.43 mL, 6.0 mmol) was added. The mixture was stirred at room temperature for 18 h, and then it was concentrated in vacuo. The crude product was purified by silica gel column chromatography (*n*-hexane/ethyl acetate, 7:3) to give **4e** (466 mg, 44%) as a yellow solid, m.p. 86.7–87.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (t, J = 7.2 Hz, 3 H), 2.47 (s, 3 H), 4.54 (q, J = 7.2 Hz, 2 H), 7.82–7.91 (m, 2 H), 8.05–8.07 (m, 1 H), 8.28–8.30 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 21.0, 62.7, 128.3, 130.0, 130.5, 132.9, 138.2, 140.4, 141.7, 150.3, 162.8, 169.1 ppm. IR (neat): $\tilde{\nu}$ = 2985, 1941, 1767, 1722, 1569, 1374, 1326, 1186, 1135, 1084, 1011, 896, 770 cm^{-1}. HRMS (EI): calcd. for $C_{13}H_{12}N_2O_4$ $[M]^+$ 260.0797; found 260.0784.

Ethyl 4-Benzyloxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4f): A 50 mL two-necked round-bottomed flask was equipped with a magnetic stirrer bar, a rubber septum, and an argon balloon. Ethyl 2-hydroxy-3-quinoxalinecarboxylate (**4a**; 0.93 g, 4.0 mmol) was dissolved in THF (35 mL), and NaH (60% in oil; 0.41 g, 10.2 mmol) was added. The mixture was stirred for 1 h at room temperature, then benzyl chloroformate (0.86 mL, 6.0 mmol) was added. The mixture was stirred at room temperature for 4 h, and the precipitate was removed by filtration with the aid of ethyl acetate. The filtrate was concentrated in vacuo. The crude product was purified by silica gel column chromatography (toluene/ethyl acetate, 10:1) to give **4f** (332 mg, 26%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (t, J = 7.0 Hz, 3 H), 4.46 (q, J = 7.3 Hz, 2 H), 5.36 (s, 2 H), 7.36–7.42 (m, 3 H), 7.46–7.48 (m, 2 H), 7.84–7.92 (m, 2 H), 8.06–8.07 (m, 1 H), 8.29–8.30 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 62.8, 71.1, 128.3, 128.6, 128.8, 129.9, 130.7, 133.0, 134.1, 138.1, 140.6, 141.3, 149.6, 152.3, 162.6 ppm. IR (neat): $\tilde{\nu}$ = 2983, 1766, 1728, 1574, 1468, 1330, 1211, 1142, 1093, 785 cm^{-1}. HRMS (EI): calcd. for $C_{19}H_{16}N_2O_5$ $[M]^+$ 352.1059; found 352.1064.

Ethyl 4-(Dimethylcarbamoyl)-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4g): A 50 mL two-necked round-bottomed flask was equipped with a magnetic stirrer bar, a rubber septum, and an argon balloon. Ethyl 2-hydroxy-3-quinoxalinecarboxylate (**4a**; 1.2 g, 5.0 mmol), DMAP (61.0 mg, 0.5 mmol), and Et_3N (0.84 mL, 6.0 mmol) were dissolved in CH_2Cl_2 (30 mL), and dimethylcarbamoyl chloride (0.7 mL, 7.5 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 19 h, then at room temperature for 14 h, and then it was concentrated in vacuo. The crude product was purified by silica gel column chromatography (toluene/ethyl acetate, 10:2) to give **4g** (151 mg, 10%) as a yellow solid, m.p. 97.1–97.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (t, J = 7.1 Hz, 3 H), 3.06 (s, 3 H), 3.24 (s, 3 H), 4.49 (q, J = 7.1 Hz, 2 H), 7.78–7.88 (m, 2 H), 8.04–8.28 (m, 1 H), 8.26–8.28 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 36.8, 62.5, 128.2, 129.9, 130.0, 132.5, 139.2, 140.0, 141.6, 150.6, 153.4, 163.2 ppm. IR (neat): $\tilde{\nu}$ = 2978, 1730, 1574, 1486, 1384, 1329, 1261, 1216, 1161, 776 cm^{-1}. HRMS (EI): calcd. for $C_{14}H_{15}N_3O_4$ $[M]^+$ 289.1063; found 289.1057.

Ethyl 3-Oxo-4-tosyl-3,4-dihydroquinoxaline-2-carboxylate (4h): A 200 mL two-necked round-bottomed flask was equipped with a magnetic stirrer bar, a rubber septum, and an argon balloon. Ethyl 2-hydroxy-3-quinoxalinecarboxylate (**4a**; 0.93 g, 4.0 mmol) was dissolved in THF (30 mL), and NaH (60% in oil; 0.19 g, 4.8 mmol) was added. The mixture was stirred for 30 min at room temperature, then *p*-toluenesulfonyl chloride (0.92 g, 4.8 mmol) was added. The mixture was stirred at room temperature for 3 h, and then it was concentrated in vacuo. The crude product was purified by silica gel column chromatography (*n*-hexane/ethyl acetate, 5:2) to give **4h** (1.07 g, 71%) as yellow crystals, m.p. 110–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (t, J = 7.1 Hz, 3 H), 2.48 (s, 3 H), 4.54 (q, J = 7.1 Hz, 2 H), 7.39–7.41 (m, 2 H), 7.79–7.87 (m, 2 H), 7.92–7.95 (m, 1 H), 8.04–8.06 (m, 2 H), 8.20–8.23 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 21.7, 62.9, 128.1, 129.1, 129.7, 129.8, 130.5, 132.7, 133.7, 138.7, 134.0, 140.5, 145.8, 148.7, 162.7 ppm. IR (neat): $\tilde{\nu}$ = 2989, 1733, 1466, 1571, 1368, 1326, 1266,

1202, 1070, 779 cm^{-1}. HRMS (EI): calcd. for $C_{18}H_{16}N_2O_5S$ [M]$^+$ 372.0780; found 372.0791.

***N*-Ethylation of Ethyl 4-*tert*-Butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4c):** (Table 1, entry 9): Under an argon atmosphere, a suspension of ethyl 4-*tert*-butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (**4c**; 47.7 mg, 0.15 mmol) in EtCN (1.0 mL) was stirred at –78 °C for 5 min, and then EtMgBr (1.03 N in THF; 0.44 mL, 0.45 mmol, 3.0 equiv.) was added slowly. The mixture was stirred for 25 min at that temperature, and then it was stirred further at room temperature for 5 min. The reaction was quenched with satd. aq. $NaHCO_3$ (20 mL), and the mixture was extracted with ethyl acetate (3× 10 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified on silica gel TLC (*n*-hexane/ethyl acetate, 7:3) to give **5a** (33.6 mg, 90%) and **6c** (2.1 mg, 4%).

Ethyl 1-Ethyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (5a): White solid, m.p. 119.5–120.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (dd, *J* = 7.1, 7.1 Hz, 3 H), 1.27 (dd, *J* = 7.3, 7.3 Hz, 3 H), 3.29 (dq, *J* = 14.1, 7.1 Hz, 1 H), 3.58 (dq, *J* = 14.1, 7.1 Hz, 1 H), 4.13 (dq, *J* = 7.3, 7.3 Hz, 2 H), 6.75–6.83 (m, 3 H), 6.99–7.03 (m, 1 H), 9.46 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.3, 14.0, 43.7, 61.8, 64.3, 112.4, 115.9, 119.1, 124.4, 125.5, 133.7, 163.2, 167.8 ppm. IR (neat): $\tilde{\nu}$ = 3186, 3058, 2975, 2918, 1748, 1692, 1593, 1506, 1472, 1435, 1343, 1252, 744 cm^{-1}. HRMS (EI): calcd. for $C_{13}H_{16}N_2O_3$ [M]$^+$ 248.1611; found 248.1153.

Ethyl 4-*tert*-Butoxycarbonyl-1-ethyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (6c): Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (dq, *J* = 7.2, 7.2 Hz, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.56 (s, 9 H), 3.30 (dq, *J* = 14.4, 7.2 Hz, 1 H), 3.56 (dq, *J* = 14.4, 7.2 Hz, 1 H), 4.14 (q, *J* = 7.1 Hz, 2 H), 4.93 (s, 1 H), 6.74–6.81 (m, 2 H), 7.12–7.23 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.1, 14.0, 27.6, 43.8, 59.3, 61.8, 84.8, 111.2, 118.5, 127.5, 128.7, 130.2, 136.1, 148.7, 148.8, 167.3 ppm. IR (neat): $\tilde{\nu}$ = 2980, 1742, 1693, 1490, 1371, 1250, 1200, 1130, 748 cm^{-1}. HRMS (EI): calcd. for $C_{18}H_{24}N_2O_5$ [M]$^+$ 348.1685; found 348.1686.

***N*-Methylation of Ethyl 4-*tert*-Butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4c):** (Table 3, entry 2): Under an argon atmosphere, a suspension of ethyl 4-*tert*-butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (**4c**; 47.7 mg, 0.15 mmol) in EtCN (1.0 mL) was stirred at –78 °C for 5 min, and then MeMgBr (0.97 N in THF; 0.46 mL, 0.45 mmol, 3.0 equiv.) was added slowly. The mixture was stirred for 25 min at that temperature, and then it was stirred further at room temperature for 5 min. The reaction was quenched with satd. aq. $NaHCO_3$ (20 mL), and the mixture was extracted with ethyl acetate (3× 10 mL). The combined extracts were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified on silica gel TLC (*n*-hexane/ethyl acetate, 7:3) to give ethyl 1-methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (**5b**; 23.0 mg, 65%) as a white solid, m.p. 146.5–147.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (t, *J* = 7.1 Hz, 3 H), 3.02 (s, 3 H), 4.14 (q, *J* = 7.1 Hz, 2 H), 4.53 (s, 1 H), 6.73–6.82 (m, 3 H), 7.00–7.06 (m, 1 H), 9.02 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 36.8, 61.9, 67.0, 112.1, 115.5, 119.3, 124.5, 125.2, 134.4, 162.6, 167.0 ppm. IR (neat): $\tilde{\nu}$ = 3073, 2976, 2872, 1729, 1685, 1441, 1406, 1305, 1227, 738 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{14}N_2O_3$ [M]$^+$ 234.1004; found 234.1002.

Ethyl 3-Oxo-1-propyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (5c): White solid (26.7 mg, 69%), m.p. 126–128.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (q, *J* = 7.6 Hz, 3 H), 1.18 (dd, *J* = 7.1, 7.1 Hz, 3 H), 1.60–1.78 (m, 2 H), 3.12 (ddd, *J* = 14.0, 8.5, 6.4 Hz, 1 H), 3.52 (ddd, *J* = 14.0, 8.6, 5.6 Hz, 1 H), 4.14 (dq, *J* = 7.2, 1.9 Hz, 2 H), 4.60 (s, 1 H), 6.74–6.80 (m, 3 H), 7.00–7.04 (m, 1 H), 8.23 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.4, 14.1, 20.0, 51.3, 61.9, 65.2, 112.6, 115.6, 119.0, 124.4, 125.3, 133.9, 162.4, 167.7 ppm. IR (neat): $\tilde{\nu}$ = 3194, 2964, 2871, 1745, 1697, 1650, 1506, 1468, 1432, 1387, 1205, 750 cm^{-1}. HRMS (EI): calcd. for $C_{14}H_{18}N_2O_3$ [M]$^+$ 262.1317; found 262.1329.

Ethyl 1-Butyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (5d): White solid (30.3 mg, 73%), m.p. 105.0–105.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.4 Hz, 3 H), 1.18 (dd, *J* = 7.2, 7.1 Hz, 3 H), 1.39 (tq, *J* = 14.6, 7.4 Hz, 2 H), 1.55–1.73 (m, 2 H), 3.16 (ddd, *J* = 14.5, 8.3, 6.2 Hz, 1 H), 3.56 (ddd, *J* = 14.5, 8.3, 5.7 Hz, 1 H), 4.13 (dq, *J* = 7.2, 1.7 Hz, 2 H), 4.61 (s, 1 H), 6.75–6.81 (m, 3 H), 6.99–7.03 (m, 1 H), 7.26 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.1, 20.2, 28.9, 49.2, 61.9, 65.1, 112.6, 115.7, 119.0, 124.4, 125.4, 133.9, 162.7, 167.7 ppm. IR (neat): $\tilde{\nu}$ = 3203, 3127, 2962, 2930, 2869, 1745, 1697, 1505, 1430, 1385, 1207, 1178, 754 cm^{-1}. HRMS (EI): calcd. for $C_{15}H_{20}N_2O_3$ [M]$^+$ 276.1474; found 276.1477.

Ethyl 1-Hexyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (5e): Yellow oil (34.7 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 6.9 Hz, 3 H), 1.17 (dd, *J* = 7.5, 7.5 Hz, 3 H), 1.26–1.39 (m, 6 H), 1.56–1.73 (m, 2 H), 3.15 (ddd, *J* = 14.1, 8.5, 5.9 Hz, 1 H), 3.54 (ddd, *J* = 14.1, 8.5, 5.9 Hz, 1 H), 4.14 (dq, *J* = 7.5, 1.6 Hz, 2 H), 4.61 (s, 1 H), 6.78–6.79 (m, 3 H), 6.99–7.03 (m, 1 H), 8.71 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 14.1, 22.5, 26.7, 26.7, 31.5, 49.5, 61.9, 65.1, 112.5, 119.0, 124.4, 125.3, 133.8, 162.7, 167.7 ppm. IR (neat): $\tilde{\nu}$ = 3208, 2955, 2868, 1742, 1695, 1505, 1469, 1429, 1385, 1207, 1031, 755 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{24}N_2O_3$ [M]$^+$ 304.1787; found 304.1793.

Ethyl 1-Isopropyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (5f): White solid (7.6 mg, 20%), m.p. 108.5–109.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (dd, *J* = 7.1, 7.1 Hz, 3 H), 1.26 (d, *J* = 1.4 Hz, 3 H), 1.27 (d, *J* = 0.9 Hz, 3 H), 4.01–4.15 (m, 3 H), 4.71 (s, 1 H), 6.73–6.80 (m, 2 H), 6.90–6.92 (m, 1 H), 7.00–7.04 (m, 1 H), 8.01 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 19.9, 20.8, 49.9, 59.3, 61.9, 114.1, 115.8, 119.1, 124.4, 125.9, 134.1, 163.0, 168.9 ppm. IR (neat): $\tilde{\nu}$ = 3186, 3050, 2979, 2914, 2871, 1737, 1677, 1505, 1438, 1396, 1367, 1296, 1193, 748 cm^{-1}. HRMS (EI): calcd. for $C_{14}H_{18}N_2O_3$ [M]$^+$ 262.1317; found 262.1328.

Ethyl 3-Oxo-1-phenyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (5g): White solid (7.6 mg, 20%), m.p. 191.0–192.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (dd, *J* = 7.1, 7.1 Hz, 3 H), 4.21 (dq, *J* = 7.1, 3.0 Hz, 2 H), 5.10 (s, 1 H), 6.91–6.97 (m, 3 H), 7.10–7.14 (m, 2 H), 7.22–7.25 (m, 2 H), 7.32–7.77 (m, 2 H), 9.00 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 62.3, 65.6, 116.6, 117.8, 121.5, 121.7, 123.9, 124.1, 126.9, 129.5, 131.3, 144.3, 163.1, 167.7 ppm. IR (neat): $\tilde{\nu}$ = 179, 3073, 3045, 2983, 2916, 1740, 1684, 1597, 1502, 1373, 1281, 1127, 756 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{16}N_2O_3$ [M]$^+$ 296.1161; found 296. 1164.

Ethyl 4-*tert*-Butoxycarbonyl-1-*tert*-butyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (6d): Yellow oil (4.9 mg, 9%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (t, *J* = 7.1 Hz, 3 H), 1.29 (s, 9 H), 1.62 (s, 9 H), 4.10 (q, *J* = 7.1 Hz, 2 H), 4.62 (s, 1 H), 6.80–6.85 (m, 3 H), 6.94–6.98 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 26.0, 27.6, 37.8, 61.8, 70.9, 85.2, 115.5, 115.9, 120.4, 124.5, 124.7, 133.5, 151.0, 163.1, 170.1 ppm. IR (neat): $\tilde{\nu}$ = 2980, 2873, 1764, 1739, 1705, 1493, 1456, 1396, 1369, 1242, 1150 cm^{-1}. HRMS (EI): calcd. for $C_{20}H_{28}N_2O_5$ [M]$^+$ 376.1998; found 376.1991.

Ethyl 1-(But-3-en-1-yl)-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (5i): Yellow solid (32.5 mg, 79%), m.p. 102.5–103.5 °C ^{1}H

NMR (400 MHz, $CDCl_3$): δ = 1.16 (dd, J = 7.1, 7.1 Hz, 3 H), 2.34–2.49 (m, 2 H), 3.24 (ddd, J = 14.2, 8.2, 6.3 Hz, 1 H), 3.65 (ddd, J = 14.2, 8.2, 6.3 Hz, 1 H), 4.14 (dq, J = 7.1, 2.1 Hz, 2 H), 4.62 (s, 1 H), 5.08 (dd, J = 10.3, 1.4 Hz, 1 H), 5.13 (dd, J = 17.2, 1.4 Hz, 1 H), 5.81 (dddd, J = 17.2, 10.3, 6.8, 6.7 Hz, 1 H), 6.79–6.68 (m, 3 H), 6.99–7.06 (m, 1 H), 8.71 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 31.2, 49.0, 62.0, 65.2, 112.6, 115.7, 117.1, 119.2, 124.5, 125.4, 133.5, 134.8, 162.5, 167.7 ppm. IR (neat): $\tilde{\nu}$ = 3143, 3081, 2980, 2919, 2872, 1742, 1701, 1652, 1506, 1433, 1384, 1252, 1208, 1021, 780 cm^{-1}. HRMS (EI): calcd. for $C_{15}H_{18}N_2O_3$ $[M]^+$ 274.1317; found 274.1311.

Ethyl 1-[2-(1,3-Dioxan-2-yl)ethyl]-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (5j): White solid (34.8 mg, 69%), m.p. 109–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (dd, J = 7.1, 7.1 Hz, 3 H), 1.31–1.35 (m, 1 H), 1.82–1.90 (m, 1 H), 1.93–1.21 (m, 2 H), 3.32 (ddd, J = 14.6, 7.5, 7.4 Hz, 1 H), 3.68–3.78 (m, 3 H), 4.06–4.17 (m, 4 H), 4.60–4.62 (m, 2 H), 6.73–6.79 (m, 2 H), 6.82–6.84 (m, 1 H), 6.99–7.03 (m, 1 H), 8.12 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 25.7, 32.4, 44.7, 62.0, 66.2, 66.9, 100.1, 112.7, 115.6, 119.0, 124.5, 125.2, 133.3, 162.1, 167.8 ppm. IR (neat): $\tilde{\nu}$ = 3196, 3077, 2966, 2853, 1730, 1686, 1509, 1438, 1360, 1308, 1223, 1142, 1076, 744 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{22}N_2O_5$ $[M]^+$ 334.1529; found 334.1543.

***N*-*n*-Propylation *C*-Ethylation of Ethyl 4-*tert*-Butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4c):** (Table 4, entry 1): Under an argon atmosphere, a suspension of ethyl 4-*tert*-butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (**4c**; 47.7 mg, 0.15 mmol) in EtCN (1.0 mL) was stirred at –78 °C for 5 min, and then *n*PrMgBr (0.88 N in THF; 0.51 mL, 0.45 mmol, 3.0 equiv.) was added slowly. The mixture was stirred for 30 min, and then EtCN (1.0 mL) and NBS (66.7 mg, 0.38 mmol) were added at –78 °C. The mixture was stirred for 10 min at –78 °C, and then EtMgBr (0.99 N in THF; 0.45 mL, 0.45 mmol, 3.0 equiv.) was added. The mixture was stirred for 30 min at –78 °C, then the reaction was quenched with satd. aq. $NaHCO_3$ (20 mL), and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined extracts were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified on silica gel TLC (*n*-hexane/ethyl acetate, 7:3) to give **7a** (9.8 mg, 22%), **7j** (8.1 mg, 17%), and **5c** (1.2 mg, 3%).

Ethyl 2-Ethyl-3-oxo-1-propyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (7a): White crystals, m.p. 152.5–153.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (dd, J = 7.3, 7.3 Hz, 3 H), 0.94 (dd, J = 7.3, 7.3 Hz, 3 H), 1.14 (t, J = 7.1 Hz, 3 H), 1.57 (m, 2 H), 2.12 (dq, J = 14.6, 7.3 Hz, 1 H), 2.47 (dq, J = 14.6, 7.3 Hz, 1 H), 3.01–3.18 (m, 2 H), 4.16 (q, J = 7.1 Hz, 2 H), 6.56–6.58 (m, 1 H), 6.67–7.73 (m, 2 H), 6.94–6.98 (m, 1 H), 9.30 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.2, 11.2, 13.9, 20.1, 26.1, 48.0, 61.8, 73.0, 111.4, 115.3, 117.9, 124.0, 124.3, 133.5, 165.8, 169.8 ppm. IR (neat): $\tilde{\nu}$ = 3190, 3053, 2979, 1878, 1738, 1677, 1510, 1438, 1408, 1347, 1209, 747 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{22}N_2O_3$ $[M]^+$ 290.1630; found 290.1616.

Ethyl 3-Oxo-1,2-dipropyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (7j): White solid, m.p. 120–120.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (dd, J = 6.9, 6.9 Hz, 3 H), 0.93 (t, J = 6.9, 6.9 Hz, 3 H), 1.14 (t, J = 7.3 Hz, 3 H), 1.35 (ddq, J = 12.6, 12.6, 6.8 Hz, 2 H), 1.62 (m, 2 H), 1.99–2.07 (m, 1 H), 2.35–2.43 (m, 1 H), 3.00–3.17 (m, 2 H), 4.16 (q, J = 7.3 Hz, 2 H), 6.54–6.56 (m, 1 H), 6.66–6.74 (m, 2 H), 6.93–6.98 (m, 1 H), 9.58 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.2, 13.9, 14.1, 17.0, 20.1, 35.3, 48.1, 61.8, 72.6 111.2, 115.4, 117.8, 123.9, 124.3, 133.3, 166.0, 169.9 ppm. IR (neat): $\tilde{\nu}$ = 3065, 2960, 2872, 1744, 1679, 1592, 1505, 1437, 1232, 746 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{24}N_2O_3$ $[M]^+$ 304.1787; found 304.1793.

***N*-*n*-Propylation *C*-Ethylation of Ethyl 4-*tert*-Butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4c):** (Table 4, entry 3): Under an argon atmosphere, a suspension of ethyl 4-*tert*-butoxycarbonyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (**4c**; 47.7 mg, 0.15 mmol) in EtCN (1.0 mL) was stirred at –78 °C for 5 min, and *n*PrMgBr (1.02 N in THF; 0.22 mL, 0.45 mmol, 1.5 equiv.) was added slowly. The mixture was stirred for 30 min, then TMSCl (0.06 mL, 0.45 mmol) was added at –78 °C. The mixture was stirred for 10 min at –78 °C, then EtCN (1.0 mL) and NBS (66.7 mg, 0.38 mmol) were added at –78 °C. The mixture was stirred for 10 min at –78 °C, then EtMgBr (0.98 N in THF; 0.31 mL, 0.3 mmol, 2.0 equiv.) was added. The mixture was stirred for 30 min at –78 °C, then the reaction was quenched with satd. aq. $NaHCO_3$ (20 mL), and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by preparative silica gel TLC (*n*-hexane/ethyl acetate, 7:3) to give **7a** (9.7 mg, 22%) and **8c** (14.0 mg, 24%).

Ethyl 4-*tert*-Butoxycarbonyl-2-ethyl-3-oxo-1-propyl-3,4-dihydroquinoxaline-2-carboxylate (8c): Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (dd, J = 7.3, 7.3 Hz, 3 H), 0.97 (dd, J = 7.4, 7.4 Hz, 3 H), 1.25 (dd, J = 7.1, 7.1 Hz, 3 H), 1.54–1.66 (m, 11 H), 2.06 (dq, J = 15.1, 7.4, Hz, 1 H), 2.15 (dq, J = 15.1, 7.4 Hz, 1 H), 2.94–3.08 (m, 2 H), 4.14–4.31 (m, 2 H), 6.44–6.46 (m, 1 H), 6.64–6.67 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0, 11.2, 14.0, 20.1, 26.4, 27.5, 47.5, 62.1, 69.7, 84.6, 109.4, 117.2, 127.7, 128.0, 128.7, 136.3, 148.1, 151.4, 168.8 ppm. IR (neat): $\tilde{\nu}$ = 2979, 2878, 2769, 1744, 1686, 1506, 1462, 1370, 1294, 742 cm^{-1}. HRMS (EI): calcd. for $C_{21}H_{30}N_2O_5$ $[M]^+$ 390.2155; found 390.2149.

***N*-*n*-Propylation *C*-Ethylation of Ethyl 4-Acetyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4e):** (Table 4, entry 4): Under an argon atmosphere, a suspension of ethyl 4-acetyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (**4e**; 39.0 mg, 0.15 mmol) in EtCN (1.0 mL) was stirred at –78 °C for 5 min, and then *n*PrMgBr (1.02 N in THF; 0.22 mL, 0.45 mmol, 1.5 equiv.) was added slowly. The mixture was stirred for 30 min, then TMSCl (0.06 mL, 0.45 mmol) was added at –78 °C. The mixture was stirred for 10 min at –78 °C, then EtCN (1.0 mL) and NBS (53.4 mg, 0.3 mmol) were added at –78 °C. The mixture was stirred for 10 min at –78 °C, then EtMgBr (0.98 N in THF; 0.31 mL, 0.3 mmol, 2.0 equiv.) was added. The mixture was stirred for 30 min at –78 °C, then the reaction was quenched with satd. aq. $NaHCO_3$ (20 mL), and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by preparative silica gel TLC (*n*-hexane/ethyl acetate, 7:3) to give **7a** (17.5 mg, 40%), **8e** (3.2 mg, 6%), and **5c** (4.3 mg, 11%).

Ethyl 4-Acetyl-3-oxo-1,2-dipropyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (8e): Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (dd, J = 7.3, 7.3 Hz, 3 H), 0.98 (dd, J = 7.3, 7.3 Hz, 3 H), 1.00 (dd, J = 7.3, 7.3 Hz, 3 H), 2.18 (dq, J = 14.8, 7.3 Hz, 1 H), 2.39 (dq, J = 148.8, 7.3 Hz, 1 H), 2.66 (s, 3 H), 3.10–3.26 (m, 2 H), 3.96–4.05 (m, 2 H), 6.85–6.93 (m, 2 H), 7.11–7.15 (m, 1 H), 7.39–7.41 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.4, 11.3, 13.8, 20.7, 25.5, 27.7, 46.9, 61.6, 75.0, 115.2, 119.9, 122.6, 125.1, 126.1, 137.5, 169.5, 169.9, 172.3 ppm. IR (neat): $\tilde{\nu}$ = 2962, 2933, 1874, 1737, 1723, 1797, 1499, 1460, 1366, 1247, 1185, 746 cm^{-1}. HRMS (EI): calcd. for $C_{18}H_{24}N_2O_4$ $[M]^+$ 332.1736; found 332.1732.

***N*-*n*-Propylation *C*-Ethylation of Ethyl 4-Acetyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4e):** (Table 4, entry 9): Under an argon atmosphere, a suspension of ethyl 4-acetyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (**4e**; 39.0 mg, 0.15 mmol) in EtCN (1.0 mL) was stirred at –78 °C for 5 min, and TMSCl (0.06 mL, 0.45 mmol) was added at –78 °C. The mixture was stirred for 10 min, then *n*PrMgBr (0.97 N in THF; 0.23 mL, 0.23 mmol, 1.5 equiv.) was added slowly. The mixture was stirred for 30 min, then EtCN (1.0 mL) and NCS (48.1 mg, 0.36 mmol) were added at –78 °C. The mixture was stirred for 10 min at –78 °C, then EtMgBr (0.86 N in THF; 0.52 mL, 0.45 mmol, 3.0 equiv.) was added. The mixture was stirred for 30 min at –78 °C, then the reaction was quenched with satd. aq. $NaHCO_3$ (20 mL), and the mixture was extracted with ethyl acetate (3× 10 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by preparative silica gel TLC (*n*-hexane/ethyl acetate, 7:3) to give **7a** (32.5 mg, 75%) as white crystals, m.p. 152.5–153.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (dd, *J* = 7.3, 7.3 Hz, 3 H), 0.94 (dd, *J* = 7.3, 7.3 Hz, 3 H), 1.14 (t, *J* = 7.1 Hz, 3 H), 1.57 (m, 2 H), 2.12 (dq, *J* = 14.6, 7.3 Hz, 1 H), 2.47 (dq, *J* = 14.6, 7.3 Hz, 1 H), 3.01–3.18 (m, 2 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 6.56–6.58 (m, 1 H), 6.67–7.73 (m, 2 H), 6.94–6.98 (m, 1 H), 9.30 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.2, 11.2, 13.9, 20.1, 26.1, 48.0, 61.8, 73.0, 111.4, 115.3, 117.9, 124.0, 124.3, 133.5, 165.8, 169.8 ppm. IR (neat): $\tilde{\nu}$ = 3190, 3053, 2979, 1878, 1738, 1677, 1510, 1438, 1408, 1347, 1209, 747 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{22}N_2O_3$ [M]$^+$ 290.1630; found 290.1616.

***N*-*n*-Propyl *C*-Methylation of Ethyl 4-Acetyl-3-oxo-3,4-dihydroquinoxaline-2-carboxylate (4e):** (Table 5, entry 2): Under an argon atmosphere, a suspension of ethyl 4-acetyl-3-oxo-3,4-dihydroquinoxalin-2-carboxylate (**4e**; 39.0 mg, 0.15 mmol) in EtCN (1.0 mL) was stirred at –78 °C for 5 min, and TMSCl (0.06 mL, 0.45 mmol) was added at –78 °C. The mixture was stirred for 10 min, then *n*PrMgBr (1.08 N in THF; 0.21 mL, 0.23 mmol, 1.5 equiv.) was added slowly. The mixture was stirred for 30 min, then EtCN (1.0 mL) and NCS (48.1 mg, 0.36 mmol) were added at –78 °C. The mixture was stirred for 10 min at –78 °C, then MeMgBr (1.08 N in THF; 0.49 mL, 0.45 mmol, 3.0 equiv.) was added. The mixture was stirred for 30 min at –78 °C, then the reaction was quenched with satd. aq. $NaHCO_3$ (20 mL), and the mixture was extracted with ethyl acetate (3× 10 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was purified by preparative silica gel TLC (*n*-hexane/ethyl acetate, 7:3) to give ethyl 2-methyl-3-oxo-1-propyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (**7b**; 27.4 mg, 66%) as a white solid, m.p. 143.5–146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.6 Hz, 3 H), 1.15 (t, *J* = 7.2 Hz, 3 H), 1.59–1.69 (m, 2 H), 1.73 (s, 3 H), 3.09–3.27 (m, 2 H), 4.16 (q, *J* = 7.2 Hz, 2 H), 6.69–6.67 (m, 1 H), 6.76–6.77 (m, 2 H), 6.96–7.02 (m, 1 H), 7.26 8.97 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.2, 13.9, 18.6, 20.9, 47.9, 61.8, 68.7, 112.8, 115.6, 118.9, 124.1, 125.1, 133.4, 166.5, 170.2 ppm. IR (neat): $\tilde{\nu}$ = 3191, 2984, 2877, 1740, 1675, 1617, 1444, 1353, 748 cm^{-1}. HRMS (EI): calcd. for $C_{15}H_{20}N_2O_3$ [M]$^+$ 276.1474; found 276.1469.

Ethyl 2-Isopropyl-3-oxo-1-propyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (7c): White crystals (18.3 mg, 40%), m.p. 148–149 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (dd, *J* = 7.6, 7.6 Hz, 3 H), 0.96 (d, *J* = 6.9 Hz, 3 H), 1.10 (d, *J* = 6.9 Hz, 3 H), 1.24 (dd, *J* = 7.1 Hz, 3 H), 1.45–1.58 (m, 2 H), 1.67–1.78 (m, 1 H), 2.63 (q, *J* = 6.9 Hz, 1 H), 2.99 (ddd, *J* = 15.2, 11.4, 5.0 Hz, 1 H), 3.33 (ddd, *J* = 15.2, 10.7, 5.0 Hz, 1 H), 4.20–4.29 (m, 2 H), 6.56–6.58 (m, 1 H), 6.65–6.71 (m, 2 H), 6.93–6.98 (m, 1 H), 9.14 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.1, 13.9, 18.1, 19.0, 19.9, 34.3, 49.0, 61.7, 75.7, 111.2, 115.2, 117.7, 124.3, 124.4, 133.2, 164.7, 168.9 ppm. IR (neat): $\tilde{\nu}$ = 3184, 3060, 2980, 2979, 1744, 1674, 1613, 1505, 1435, 1387, 1348, 1236, 753 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{24}N_2O_3$ [M]$^+$ 304.1787; found 304.17822.

Ethyl 1-Ethyl-2-methyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (7d): Yellow solid (22.7 mg, 58%), m.p. 97.5–98.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (dd, *J* = 7.2, 7.2 Hz, 3 H), 1.22 (t, *J* = 7.0 Hz, 3 H), 1.72 (s, 3 H), 3.23 (dq, *J* = 14.4, 7.2 Hz, 1 H), 3.39 (dq, *J* = 14.4, 7.2 Hz, 1 H), 4.18 (q, *J* = 7.1 Hz, 2 H), 6.71–6.73 (m, 1 H), 6.76–6.77 (m, 2 H), 6.97–7.01 (m, 1 H), 9.00 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4, 14.0, 18.5, 40.7, 61.9, 68.8, 112.6, 115.5, 118.7, 124.2, 125.0, 133.0, 166.3, 170.2 ppm. IR (neat): $\tilde{\nu}$ = 3195, 3064, 2989, 2933, 1736, 1677, 1508, 1412, 1313, 1235, 1114, 738 cm^{-1}. HRMS (EI): calcd. for $C_{14}H_{18}N_2O_3$ [M]$^+$ 262.1317; found 262.1312.

Ethyl 1-Ethyl-3-oxo-2-propyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (7e): White solid (27.9 mg, 64%), m.p. 119–120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (dd, *J* = 7.3, 7.3 Hz, 3 H), 1.15 (dd, *J* = 7.1, 7.1 Hz, 3 H), 1.19 (dd, *J* = 6.9, 6.9 Hz, 3 H), 1.29–1.43 (m, 2 H), 2.40 (ddd, *J* = 14.4, 11.3, 5.6 Hz, 1 H), 2.4 (ddd, *J* = 14.3, 11.2, 5.6 Hz, 1 H), 3.18–3.36 (m, 2 H), 4.16 (dq, *J* = 7.1, 1.1 Hz, 2 H), 6.63–6.71 (m, 3 H), 6.94–7.00 (m, 1 H), 9.02 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.5, 14.0, 14.2, 17.0, 36.3, 40.3, 61.8, 72.6, 111.3, 115.3, 117.8, 124.0, 124.3, 133.0, 165.8, 169.8 ppm. IR (neat): $\tilde{\nu}$ = 3194, 3069, 2931, 2872, 1735, 1678, 1503, 1460, 1301, 1221, 1183, 1021, 744 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{22}N_2O_3$ [M]$^+$ 290.1630; found 290.1636.

Ethyl 2-[2-(1,3-Dioxan-2-yl)ethyl]-1-ethyl-1,2,3,4-tetrahydro-quinoxaline-2-carboxylate (7f): White solid (21.5 mg, 40%), m.p. 127.5–128.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (dd, *J* = 7.1, 7.1 Hz, 3 H), 1.20 (t, *J* = 7.0 Hz, 3 H), 1.29–1.32 (m, 1 H), 1.58–1.73 (m, 2 H), 1.98–2.10 (m, 1 H), 3.24 (dq, *J* = 15.2, 7.3 Hz, 1 H), 3.35 (dq, *J* = 15.4, 7.3 Hz, 1 H), 3.73 (t, *J* = 12.4 Hz, 2 H), 4.06 (ddd, *J* = 11.3, 10.5, 4.9 Hz, 2 H), 4.15 (q, *J* = 7.0 Hz, 2 H), 4.54 (dd, *J* = 6.0 Hz, 1 H), 6.64–6.71 (m, 3 H), 6.94–6.98 (m, 1 H), 8.36 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.4, 13.9, 25.7, 27.4, 29.4, 40.2, 61.8, 66.8, 66.8, 72.2, 101.8, 111.6, 115.3, 117.9, 124.0, 124.3, 132.9, 165.3, 169.7 ppm. IR (neat): $\tilde{\nu}$ = 3204, 2983, 2853, 1741, 1687, 1508, 1447, 1395, 1334, 1313, 1245, 1141, 1110, 749 cm^{-1}. HRMS (EI): calcd. for $C_{19}H_{26}N_2O_5$ [M]$^+$ 362.1842; found 362.1856.

Ethyl 1-(But-3-en-1-yl)-3-oxo-2-vinyl-1,2,3,4-tetrahydro-quinoxaline-2-carboxylate (7g): Yellow solid (30.0 mg, 67%), m.p. 96.5–97.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.22 (dd, *J* = 7.2, 7.2 Hz, 3 H), 2.28–2.46 (m, 2 H), 3.22 (ddd, *J* = 15.2, 9.9, 5.1 Hz, 1 H), 3.51 (ddd, *J* = 15.2, 9.9, 6.0 Hz, 1 H), 4.24 (dq, *J* = 7.2, 4.8 Hz, 2 H), 5.06–5.11 (m, 2 H), 5.24 (d, *J* = 17.8 Hz, 1 H), 5.48 (d, *J* = 10.7 Hz, 1 H), 5.79 (dddd, *J* = 17.1, 10.5, 6.8, 6.8 Hz, 1 H), 6.22 (dd, *J* = 17.8, 10.7 Hz, 1 H), 6.74–6.80 (m, 3 H), 7.00–7.05 (m, 1 H), 9.05 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 31.7, 46.9, 62.2, 74.4, 112.3, 115.8, 116.7, 119.1, 119.6, 124.5, 124.6, 132.9, 133.2, 134.9, 164.3, 168.8 ppm. IR (neat): $\tilde{\nu}$ = 3204, 3079, 2981, 2871, 1730, 1694, 1643, 1503, 1450, 1385, 917, 749 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{20}N_2O_3$ [M]$^+$ 300.1474; found 300.1460.

Ethyl 2-Allyl-1-(but-3-en-1-yl)-3-oxo-1,2,3,4-tetrahydro-quinoxaline-2-carboxylate (7h): Yellow oil (32.3 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 (t, *J* = 7.1 Hz, 3 H), 2.29–2.44 (m, 2 H), 2.87 (dd, *J* = 15.1, 7.5 Hz, 1 H), 3.14–3.22 (m, 2 H), 3.36 (ddd, *J* = 15.2, 10.1, 5.5 Hz, 1 H), 4.12 (q, *J* = 7.1 Hz, 2 H), 5.04 (d, *J* = 10.0 Hz, 1 H), 5.09 (dd, *J* = 9.6, 1.4 Hz, 1 H), 5.12 (dd, *J* = 15.6, 1.4 Hz, 1

H), 5.16 (dd, J = 16.8, 1.6 Hz, 1 H), 5.71–5.84 (m, 2 H), 6.61–6.64 (m, 1 H), 6.71–6.76 (m, 2 H), 6.96–7.00 (m, 1 H), 8.65 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 31.2, 37.2, 45.8, 62.0, 72.4, 111.8, 115.5, 116.7, 118.5, 119.5, 124.3, 124.4, 131.8, 132.9, 134.7, 165.36, 169.3 ppm. IR (neat): $\tilde{\nu}$ = 3208, 3078, 2980, 2913, 1741, 1684, 1640, 1612, 1507, 1434, 1230, 917, 744 cm^{-1}. HRMS (EI): calcd. for $C_{18}H_{22}N_2O_3$ $[M]^+$ 314.1630; found 314.1624.

Ethyl 1,2-Di(but-3-en-1-yl)-3-oxo-1,2,3,4-tetrahydro-quinoxaline-2-carboxylate (7i): Yellow solid (32.3 mg, 66%), m.p. 96–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, J = 7.1 Hz, 3 H), 2.11 (m, 3 H), 2.31 (m, 2 H), 2.49, 2.57 (m, 1 H), 3.15–3.32 (m, 2 H), 4.17 (q, J = 7.1 Hz, 2 H), 4.95 (d, J = 10.1 Hz, 1 H), 4.99 (dd, J = 17.0, 1.4 Hz, 1 H), 5.11 (d, J = 17.0, 1.4 Hz, 1 H), 5.75 (m, 2 H), 6.62–6.64 (m, 1 H), 6.69–6.76 (m, 2 H), 6.97–7.02 (m, 1 H), 8.65 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 27.9, 31.2, 32.1, 45.6, 62.0, 72.3, 111.6, 115.6, 115.4, 117.0, 118.3, 124.0, 124.4, 132.9, 134.6, 137.1, 165.4, 169.5 ppm. IR (neat): $\tilde{\nu}$ = 3202, 3078, 2981, 2923, 2868, 1729, 1695, 1503, 1431, 1385, 1303, 1256, 917, 748 cm^{-1}. HRMS (EI): calcd. for $C_{19}H_{24}N_2O_3$ $[M]^+$ 328.1787; found 328.1800.

RCM Reaction of Ethyl 1-(But-3-en-1-yl)-3-oxo-2-vinyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (7g): (Table 6, entry 3 and structure): Under an argon atmosphere, a suspension of ethyl 1-(but-3-en-1-yl)-3-oxo-2-vinyl-1,2,3,4-tetrahydroquinoxaline-2-carboxylate (**7g**; 23.9 mg, 0.08 mmol) in toluene (4.5 mL) was stirred at room temperature. A solution of Hoveyda–Grubbs second-generation catalyst (2.0 mg, 3.2 μmmol) in toluene (2.0 mL) was added. The mixture was stirred for 3 h at room temperature, then it was filtered through a pad of Celite, and concentrated in vacuo. The crude product was purified by preparative silica gel TLC (toluene/ethyl acetate, 20:1) to give ethyl 6-oxo-5,6,9,10-tetrahydro-6aH-pyrido[1,2-*a*]quinoxaline-6a-carboxylate (**9g**; 18.2 mg, 84%) as a white solid, m.p. 186.5–187.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (dd, J = 7.1, 7.1 Hz, 3 H), 2.28 (ddd, J = 17.7, 5.1, 5.1 Hz, 1 H), 2.40–2.50 (m, 1 H), 3.59 (ddd, J = 11.2, 11.2, 4.5 Hz, 1 H), 3.69 (dd, J = 11.3, 4.5 Hz, 1 H), 3.96–4.11 (m, 2 H), 6.20 (ddd, J = 10.2, 5.9, 2.1 Hz, 1 H), 6.32 (dd, J = 10.2, 5.9, 2.1 Hz, 1 H), 6.79–6.93 (m, 3 H), 7.04–7.08 (m, 1 H), 8.24 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 24.0, 40.0, 61.8, 65.5, 113.0, 115.7, 120.0, 121.8, 124.2, 125.8, 128.2, 136.0, 164.4, 168.8 ppm. IR (neat): $\tilde{\nu}$ = 3192, 3061, 2989, 2924, 2859, 1738, 1683, 1612, 1503, 1463, 1366, 1503, 1463, 1366, 1214, 754 cm^{-1}. HRMS (EI): calcd. for $C_{15}H_{16}N_2O_3$ $[M]^+$ 272.1161; found 272.1155.

Ethyl 6-Oxo-5,6,10,11-tetrahydroazepino[1,2-*a*]quinoxaline-6a(7*H*)-carboxylate (9h): White solid (19.7 mg, 76%), m.p. 165–166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (dd, J = 7.1, 7.1 Hz, 3 H), 2.40–2.54 (m, 2 H), 3.06–3.22 (m, 2 H), 3.83 (ddd, J = 8.9, 3.6, 3.6 Hz, 1 H), 3.94–4.01 (m, 2 H), 4.02–4.14 (m, 2 H), 6.72–6.78 (m, 2 H), 6.89–6.91 (m, 1 H), 6.99–7.03 (m, 1 H), 8.22 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 29.8, 30.6, 43.4, 61.7, 72.5, 113.3, 115.7, 118.7, 123.4, 124.3, 125.1, 131.3, 134.6, 163.8, 170.1 ppm. IR (neat): $\tilde{\nu}$ = 3185, 3072, 2973, 2951, 1750, 1679, 1506, 1436, 1376, 1181, 749 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{18}N_2O_3$ $[M]^+$ 286.1317; found 286.1301.

Ethyl 6-Oxo-5,6,7,8,11,12-hexahydro-6aH-azocino[1,2-*a*]quinoxaline-6a-carboxylate (9i): White solid (17.0 mg, 70%), m.p. 100–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, J = 7.1 Hz, 3 H), 2.04 (ddd, J = 10.8, 10.9, 6.1 Hz, 1 H), 2.20–2.27 (m, 3 H), 2.46–2.57 (m, 1 H), 3.52 (ddd, J = 16.1, 6.9, 3.5 Hz, 1 H), 3.72 (ddd, J = 15.9, 6.7, 3.5 Hz, 1 H), 4.28 (q, J = 7.1 Hz, 2 H), 5.65–5.75 (m, 2 H), 6.70–6.79 (m, 3 H), 6.97–7.01 (m, 1 H), 8.71 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 22.9, 26.4, 34.0, 47.7, 62.0, 71.4, 112.7, 115.2, 118.3, 124.3, 127.9, 132.2, 133.9, 166.4, 168.3 ppm. IR (neat): $\tilde{\nu}$ = 3185, 3072, 2973, 2951, 1750, 1679, 1506, 1436, 1376, 1181, 749 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{20}N_2O_3$ $[M]^+$ 300.1474; found 300.1468.

Hydrogenation of Ethyl 6-Oxo-5,6,9,10-tetrahydro-6a*H*-pyrido[1,2-*a*]quinoxaline-6a-carboxylate (9g): (Table 6 structure): A suspension of ethyl 6-oxo-5,6,9,10-tetrahydro-6a*H*-pyrido[1,2-*a*]quinoxaline-6a-carboxylate (**9g**; 12.8 mg, 0.05 mmol) and $Pd(OH)_2$/C (20 wt.-%; 1.4 mg, 2.0 μmol) in EtOH (5 mL) was stirred at room temperature. The reaction mixture was stirred under a hydrogen atmosphere at room temperature for 1 h. The mixture was then filtered through a pad of Celite, and concentrated in vacuo to give ethyl 6-oxo-5,6,7,8,9,10-hexahydro-6a*H*-pyrido[1,2-*a*]quinoxaline-6a-carboxylate (**10g**; 12.5 mg, 91%) as a yellow solid, m.p. 160.5–161.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (dd, J = 7.1, 7.1 Hz, 3 H), 1.46–1.71 (m, 2 H), 1.83–2.07 (m, 3 H), 2.64–2.68 (m, 1 H), 3.29–3.36 (m, 1 H), 3.50–3.53 (m, 1 H), 3.98–4.401 (m, 2 H), 6.76–6.86 (3 H), 7.00–7.04 (m, 1 H), 8.68 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 19.8, 24.2, 44.3, 61.5, 65.9, 112.8, 115.2, 119.7, 124.2, 125.3, 136.5, 165.5, 165.5, 169.6 ppm. IR (neat): $\tilde{\nu}$ = 3192, 3074, 2981, 2860, 1737, 1687, 1591, 1507, 1383, 1209, 958, 748 cm^{-1}. HRMS (EI): calcd. for $C_{15}H_{18}N_2O_3$ $[M]^+$ 274.1317; found 274.1316.

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