Synthesis of 9-ethyl[1,2,5]selenadiazolo[3,4-*h*]quinolones by the application of modified Gould-Jacobs reaction to *N*-ethyl-2,1,3-benzoselenadiazol-4-amine

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Abstract
An effective method for the synthesis of *N*-ethyl-2,1,3-benzoselenadiazolamines **11** and **15** has been described. Modified Gould-Jacobs reaction of *N*-ethylbenzoselenadiazol-4-amine **15** provided 9-ethylselenadiazoloquinolone derivatives **2** and **19** in high yields. Acid-promoted ring closure of enamine **18c** unexpectedly afforded completely deacetylated product – 9-ethylselenadiazoloquinolone **2**. Identical product was obtained by ethylation of selenadiazolo[3,4-*h*]quinolone **1** and by basic hydrolysis of ethyl ester **19b** followed by thermal decarboxylation of the corresponding acid **20**.

Keywords: Cyclization, deacetylation, Gould-Jacobs reaction, nucleophilic vinylic substitution, selenadiazoloquinolones

Introduction

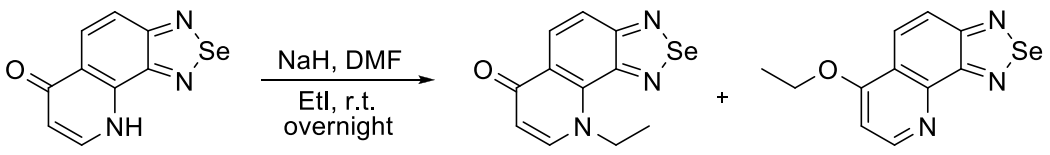
Antibacterial agents containing 4-oxoquinoline (4-quinolone) moiety found a broad application in the treatment of bacterial infections in human and veterinary medicine.[1,2] In the last decades, anti-cancer activity of 4-quinolone derivatives has been revealed and studied intensively.[3,4] The presence of selenium in the structure of 4-quinolones can bring new characteristics, and plenty of selenaheterocyclic compounds showed positive biological impact.[5,6] In our previous research, 7-substituted selenadiazolo[3,4-*h*]quinolones and 8-substituted selenadiazolo[3,4-*f*]quinolones (R_7, R_8 = H, CN, $COCH_3$, COOMe, COOEt, COOH) were successfully synthetized by the Gould-Jacobs reaction[7,8] and their biological/photobiological activity was investigated together with their EPR spectroscopy.[9-12] Antimicrobial activity of 7-substituted selenadiazolo[3,4-

h]quinolones was demonstrated on Gram positive and Gram negative bacteria, yeasts and filamentous fungi.[7] Ultraviolet A photoexcitation of all selenadiazoloquinolones in DMSO or acetonitrile led to the formation of paramagnetic intermediates coupled with activation of molecular oxygen generating the superoxide anion or singlet oxygen. The ability to form paramagnetic species was evidenced by means of EPR spectroscopy employing the spin-trapping technique or oxidation of sterically hindered amines. The cytotoxic/photocytotoxic effect on murine and human cancer cell lines was demonstrated on 7-acetyl-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinolin-6-one.[9] Upon anodic oxidation of selenadiazoloquinolones in alkaline solutions, the selenadiazole ring was replaced with paramagnetic *ortho* semiquinone radical anions which was confirmed by EPR spectroscopy and quantum chemical calculations.[10]

Based on our previous results obtained for 7- and 8-substituted selenadiazoloquinolones, we decided to synthesize their analogues ethylated at nitrogen atom of the pyridone ring to improve their biological/photobiological and physicochemical properties. Prepared ethylselenadiazoloquinolones showed different redox behaviour which was studied in detail by *in situ* EPR/UV-vis cyclovoltammetric experiments.[12] Recently, the cytotoxic/photocytotoxic effects of ethylselenadiazoloquinolones on cancer human (HeLa) and murine (L1210) and non-cancer (NIH-3T3) cell lines were investigated.[13] In this paper, the synthesis of ethylselenadiazoloquinolones by ethylation of selenadiazoloquinolones and modified Gould-Jacobs reaction applied to *N*-ethylbenzoselenadiazolamines is discussed in detail.

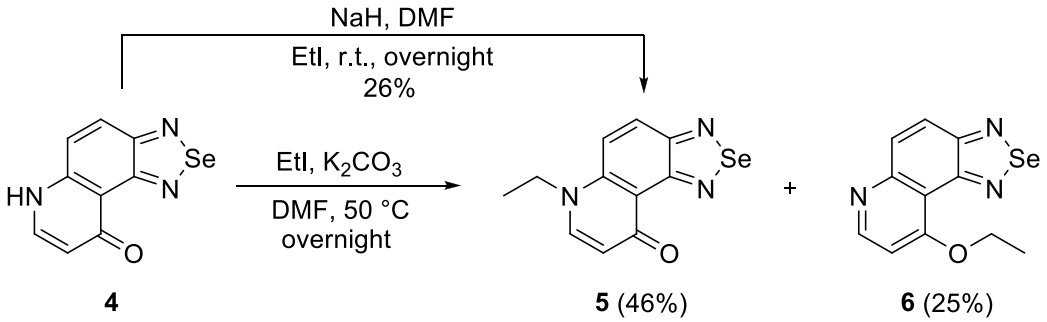
Results and Discussion

Usually, 4-oxoquinolone derivatives are *N*-ethylated with an excess of iodoethane in DMF at room or elevated temperature in the presence of K_2CO_3 or NaH as a base.[14] Rarely, diethylsulfate,[15] triethylphosphate[16] and ethyl tosylate[17] are employed as the ethylating agents. Hence, the most straightforward route towards 6- and 9-ethylselenadiazoloquinolones seemed to be the ethylation of selenadiazoloquinolones prepared in our previous papers.[7,8] However, the ethylation of selenadiazoloquinolone **1**, as a representative compound, with the excess of EtI (3-4 eq.) in DMF at 50 °C in the presence of K_2CO_3 led to a mixture of polyethylated products in a very low yield. When NaH was used as the base instead of K_2CO_3 and the amount of EtI was reduced to 1.5 equivalents, the mixture of *N*- and *O*-ethylated products **2** and **3** was formed in the 3:2 ratio (Scheme 1).



Scheme 1

Analogously, treatment of selenadiazoloquinolone **4** with EtI in the presence of K_2CO_3 afforded a mixture of *N*- and *O*-ethylated products **5** and **6** in almost the same ratio as in the previous case. Despite the fact that formation of selanadiazoloquinoline **6** was not observed when NaH was applied as the base, desired 6-ethylselenadiazoloquinolone **5** was isolated only in 26% yield (Scheme 2).



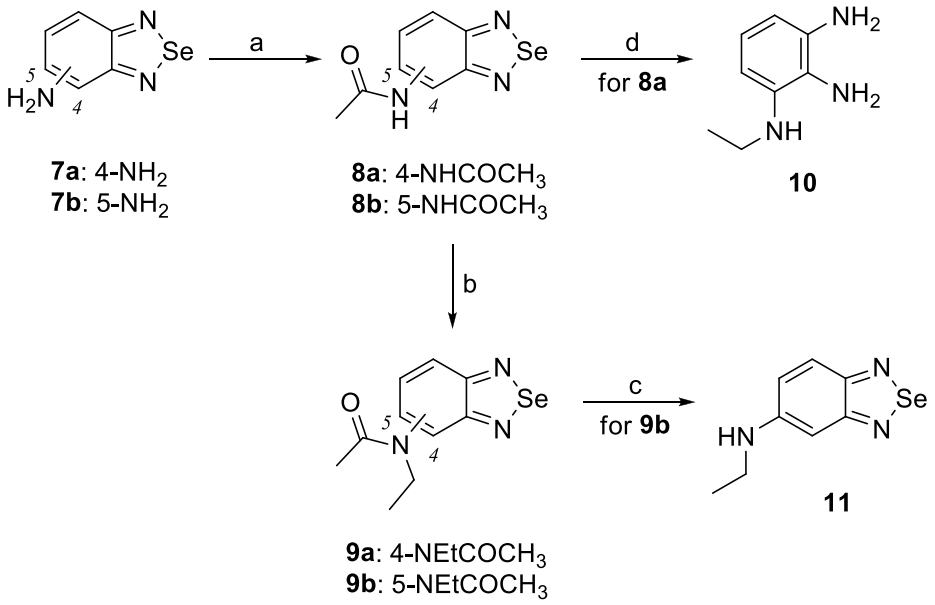
Scheme 2

Because of the poor regioselectivity as well as relatively low yields of target *N*-ethylated derivatives **2** and **5**, the ethylation of selenadiazoloquinolones did not seem to be the perspective method for the preparation of ethylselenadiazoloquinolones.

Another approach to ethylselenadiazoloquinolones could represent ethylation of precursors of selenadiazoloquinolones under the same reaction conditions which were applied to selenadiazoloquinolones **1** and **4**. The products obtained after ethylation might be cyclized to target compounds in various acidic media. However, selected precursors did not undergo ethylation with an excess of EtI in the presence of K_2CO_3 even at higher temperature (70 °C) and only starting materials were recovered. On the other hand, using NaH as the base led to complex reaction mixtures of practically inseparable products.

In modified Gould-Jacobs reaction,[14] *N*-substituted (hetero)aromatic amines play the role of the starting materials. In such a case the enamines formed in nucleophilic vinylic substitution, no longer bear a hydrogen at the amino nitrogen, thus making thermal cyclization impossible. These enamines can be cyclized into the quinolones in a range of acidic media such as polyphosphoric acid (PPA), ethyl polyphosphate (PPE), $BF_3{\cdot}OEt_2$, Ac_2O/H_2SO_4, P_2O_5 in benzene or $POCl_3$.[18-20] Although the preparation of *N*-substituted (hetero)aromatic amines is more laborious, the regioselectivity of the alkylation is no longer a problem. Thus we focused our attention on the synthesis of *N*-ethylbenzoselenadiazolamines **11** and **15**. First, we excluded classical ethylation of benzoselenadiazolamines **7** with EtI because that would probably give a mixture of polyethylated products. Since benzoselenadiazole ring is very sensitive to reductive conditions, a reductive amination of benzoselenadiazolamines **7** was not considered as a suitable method for preparation of ethylamines **11** and **15**. Treatment of benzoselenadiazolamines **7** with concentrated H_2SO_4 in triethyl orthoformate did not provide the appropriate *N*-ethylformamides.

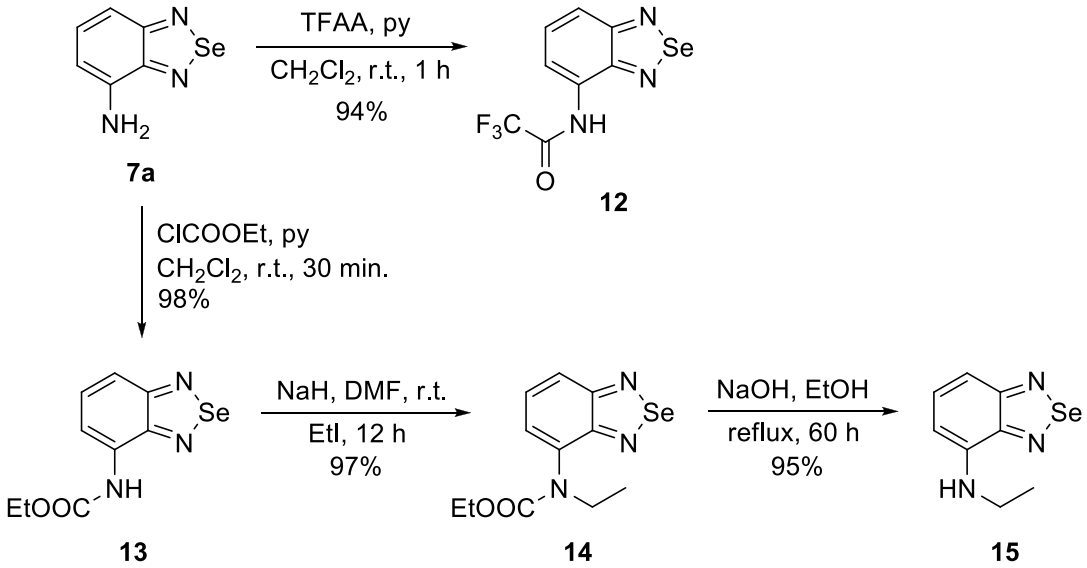
The latter ones could yield *N*-ethylbenzoselenadiazolamines **11** and **15** after acid hydrolysis.[21] Monoethylation of amines **7** according to Katritzky's protocol[22-24] failed already at the preparation of benzotriazole ethylating agent. Another route for preparation of ethylamines **11** and **15** could include ethylation of acetamides **8** followed by hydrolysis of the resulting *N*-ethylacetamides **9** (Scheme 3).



Scheme 3. Reagents and conditions: a) for **8a**: Ac_2O, 100 °C, 30 min., 96%; for **8b**: Ac_2O, 45 °C, 1 h, 77%; b) NaH, DMF, then EtI, r.t., 2 h, 90% for **9a** and 83% for **9b**; c) MeONa, MeOH, reflux 3.5 h, 76%; d) $BH_3 \cdot Me_2S$, THF, reflux, 1 h, 84%.

Acetamides **8** were obtained by a simple acetylation of amines **7** in acetic anhydride according to procedures described in the literature.[25] Before ethylation of acetamides **8**, we tried to take advantage of their direct reduction into ethylamines **11** and **15**. The reduction of acetamides **8** with $LiAlH_4$ in refluxing THF resulted in a mixture of unidentified products of decomposition. On the other hand, their treatment with $BH_3 \cdot SMe_2$ in refluxing THF caused besides reduction of acetamide moiety even reductive deselenation of benzoselanadiazole ring to form corresponding benzenetriamines. These were extremely unstable and sensitive to air oxidation. Despite their instability we were able to isolate triamine **10** as a pale brown semisolid. Due to its instability it was characterized only by ^1H NMR spectroscopy (Scheme 3). To our knowledge, reductive deselenation of benzoselenadiazole ring with $BH_3 \cdot SMe_2$ was not described in the literature up to date. Immediate dissolution of triamine **10** in EtOH and treatment with stoichiometric amount of SeO_2 dissolved in water resulted in a black mixture of reaction products in which desired ethylamine **15** was observed only in traces along with decomposition and oxidation products. In our next strategy, the acetamides **8** underwent deprotonation with NaH in DMF followed by treatment with EtI to access *N*-ethylacetamides **9** in high yields.

Alcoholysis of *N*-ethylacetamide **9b** with one equivalent of MeONa in refluxing MeOH proceeded smoothly affording *N*-ethylbenzoselenadiazol-5-amine **11** in a good yield (Scheme 3). On the contrary, basic hydrolysis of *N*-ethylacetamide **9a** with a large excess of MeONa in MeOH proceeded very slowly and starting material was still identified (TLC) in the reaction mixture even after 7 days of reflux. Moreover, hydrolysis of *N*-ethylacetamide **9a** under basic ($NaOH/H_2O/EtOH$/reflux, NaOH/EtOH/reflux), acidic (20% HCl/reflux, 20% HCl/dioxane/reflux) or neutral ($N_2H_4 \cdot H_2O$/EtOH/reflux) conditions failed or led to complex reaction mixtures. Since hydrolysis of acetamide group was not successful, it was replaced by trifluoroacetyl group which is more susceptible to basic hydrolysis. Nevertheless, trifluoroacetamide **12** obtained by trifluoroacetylation of amine **7a** did not undergo ethylation under the same reaction conditions described for acetamide **8a** (Scheme 4).

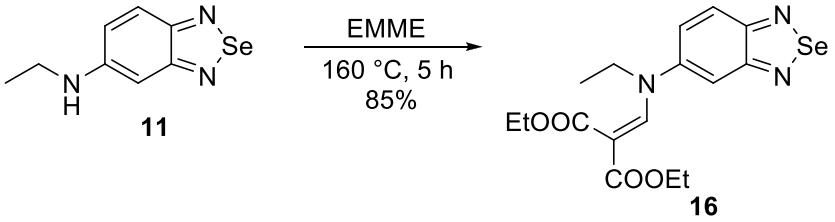


Scheme 4

Finally, the ethoxycarbonyl group was successfully employed as a protecting group in the synthesis of ethylamine **15**. Ethylation of carbamate **13** smoothly yielded ethylcarbamate **14** which was subjected to basic hydrolysis to provide *N*-ethylbenzoselenadiazol-4-amine **15**. Even under very hard reaction conditions for the removal of ethoxycarbonyl group, (reflux of ethylcarbamate **14** with 10 equivalents of NaOH in EtOH for 60 h), ethylamine **15** was isolated in 90% yield over three steps (Scheme 4).

Next, ethylamines **11** and **15** entered into the nucleophilic vinylic substitution[26] with the appropriate alkoxymethylidene derivatives **17** (activated enol ethers). Generally, this substitution proceeds smoothly with primary amines in refluxing alcohol (MeOH, EtOH) with a small excess of the activated enol ether. In our case, nucleophilic vinylic substitution of diethyl 2-(ethoxymethylidene)propanedioate **17b** (EMME) with ethylamines **11** and **15** in refluxing EtOH did not proceed at all, even if EMME was used in an excess. Therefore the substitution was

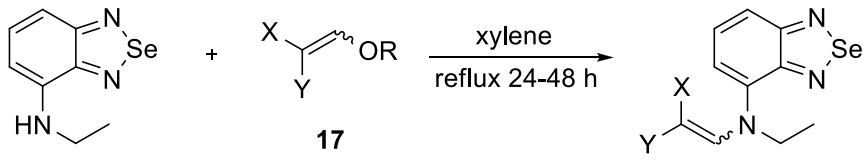
performed under solvent free conditions by a simple heating of ethylamines **11** and **15** in an excess of EMME at 160 °C. In case of ethylamine **11**, the reaction was complete within 5 hours and desired enamine **16** was isolated in 85% yield (Scheme 5).



11 **16**

Scheme 5

On the other hand, the heating of ethylamine **15** with the excess of EMME at 150-160 °C was not effective since ethylamine **15** is somewhat volatile and condenses on the walls of the reaction vessel or condenser preventing thus reaction with EMME which is much less volatile and remains at the bottom of the reaction vessel. To avoid this obstacle, xylene became the solvent of choice. Reflux of ethylamine **15** and two equivalents of suitable activated enol ether **17** during 24-48 h was found as the optimal reaction conditions for preparation of [(2,1,3-benzoselenadiazol-4-ylamino)(ethyl)amino]methylidene derivatives **18** (Scheme 6).



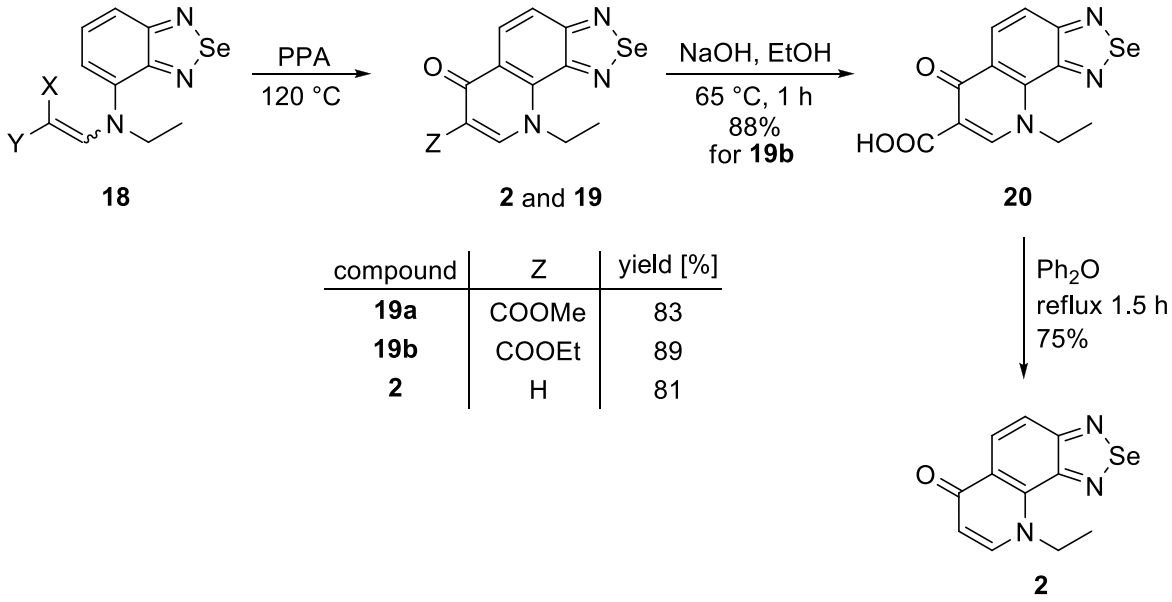
15 **17** **18**

compound **17** and **18**	R	X	Y	yield of **18** [%] (*E*:*Z*)
a	Me	COOMe	COOMe	82
b	Et	COOEt	COOEt	83
c	Et	COOEt	COMe	85 (*10*:*1*)

Scheme 6

The unwillingness of ethylamines **11** and **15** to substitute the alkoxy group of the activated enol ethers **17** can be explained by the larger steric demands. Enamines **18a** and **18b** bear identical substituents X and Y, whereas enamine **18c** with different substituents X and Y exist as a mixture of *E* and *Z* isomers. The relative ratio of the particular geometric isomers (*E*:*Z* 10:1) was estimated from its NMR spectral data considering intensities of the signals. We assume, on the basis of steric hindrance, that *E*-isomer strongly prevails.

Obtained enamines **16** and **18** were subjected to acid-catalysed pyridone ring closure. Heating of enamine **16** in PPA at 120 °C did not yield angularly and/or linearly annulated ethylselenadiazoloquinolones instead ethylamine **11** was isolated. Thus a cleavage of the bond between nitrogen and methylidene carbon atom occurred before the closure to pyridone ring. Our next attempts on cyclization to pyridone ring using various acidic media such as PPE, $BF_3 \cdot OEt_2$ and $POCl_3$ also failed. In case of enamines **18** cyclization in PPA at 120 °C smoothly afforded 9-ethylselenadiazoloquinolones **2** and **19** in high yields (Scheme 7).



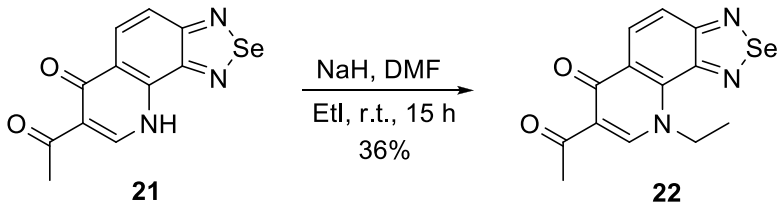
compound	Z	yield [%]
19a	COOMe	83
19b	COOEt	89
2	H	81

Scheme 7

To our surprise, enamine **18c** after the treatment with PPA gave completely deacetylated product **2**. ^1H and ^{13}C NMR spectra as well as physicochemical properties of the product of deacetylation were in accordance with those of 9-ethylselenadiazoloquinolone **2** prepared by ethylation of selenadiazoloquinolone **1** (Scheme 1). Basic hydrolysis of ethyl ester **19b** readily provided acid **20** in high yield (Scheme 7). Next we decided to examine decarboxylation of the acid **20**. Decarboxylation promoted by cyanide ions in hot DMSO or DMF[27] did not proceed at all. Although, decarboxylation conducted in boiling quinoline was complete in about 1 hour, the isolation of the product was troublesome since it did not precipitated from the reaction mixture. Moreover, basic quinoline caused difficulties in the separation by FLC. Finally, decarboxylation was successfully performed in boiling Ph_2O (Scheme 7). In this case precipitation of the product also did not occur but non-polar Ph_2O can be easily removed by FLC. In this way 9-ethylselenadiazoloquinolone **2** was isolated in 75 % yield and the structure of product obtained after the ring closure of enamine **18c** was confirmed.

Since 7-acetylselenadiazoloquinolone **21** exhibited significant cytotoxic/photocytotoxic activity, our goal was to prepare 7-acetyl-9-ethylselenadiazoloquinolone **22** which could be even

more promising in this respect. The desired 7-acetyl-9-ethylselenadiazoloquinolone **22** was obtained by ethylation of quinolone **21** in low yield (Scheme 8).



Scheme 8

Conclusions

The ethylation of selenadiazolodiazoloquinolones **1**, **4** and **21** was found to be ineffective (low yields) due to the poor regioselectivity. The synthesis of *N*-ethylbenzoselanadiazolamines **11** and **15** by ethylation of benzoselenadiazolamines **7** was developed. Modified Gould-Jacobs reaction of *N*-ethylbenzoselanadiazol-4-amine **15** gave three 9-ethylselenadiazoloquinolone derivatives **2**, **19a** and **19b**. Surprisingly, acid-catalysed cyclization of enamine **18c** resulted in totally deacetylated product – 9-ethylselenadiazoloquinolone **2**. Basic hydrolysis of ethyl ester **19b** followed by thermal decarboxylation of the resulting acid **20** yielded identical product as the acid-promoted ring closure of enamine **18c**.

Experimental Section

General. Thin-layer chromatography (TLC) was performed on aluminium plates pre-coated with 0.2 mm silica gel (25 μm) containing fluorescent indicator 254 nm (Fluka) and stains were visualized by UV light (254 nm or 366 nm). Flash column liquid chromatography (FLC) was performed on silica gel Normasil 60 (43-60 μm). Melting points were measured on Koffler block and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian Mercury 300-MHz spectrometer at 25 °C. The operation frequencies were 300 MHz for ^{1}H and 75.5 MHz for ^{13}C nuclei. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) are given in Hz. Elemental analyses were determined using a Thermo Finnigan Flash EA 1112 instrument.
The starting compounds **1, 4, 7** and **21** were prepared according to procedures described in our previous papers.[7,8] The alkoxymethylidene derivatives **17a** and **17b** are commercially available (AlfaAesar®, Sigma-Aldrich®) while derivative **17c** was synthesized by condensation of ethyl 3-oxobutanoate with triethyl orthoformate.[28,29]

Ethylation of selenadiazoloquinolones 1, 4 and 21

9-Ethyl-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinolin-6-one (2) and 6-ethoxy-[1,2,5]selenadiazolo[3,4-*h*]quinoline (3). NaH (60 % suspension in mineral oil, 23 mg, 0.57 mmol) was added to a stirred suspension of selenadiazoloquinolone **1** (100 mg, 0.4 mmol) in dry DMF (2 mL) under the Ar atmosphere at room temperature and stirring was continued for 1 hour. Then ethyl iodide (0.05 mL, 0.62 mmol) was added dropwise and the reaction mixture was stirred at room temperature overnight. Once the reaction was complete, it was diluted with water (25 mL) and extracted with $CHCl_3$ (30 mL). Organic phase was dried with Na_2SO_4, filtered and the voletiles were evaporated under reduced pressure. Particular isomers **2** and **3** were separated by FLC (SiO_2, $CHCl_3$/MeOH 40:1).

9-Ethyl-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinolin-6-one (2). Yellow solid, yield 40%, 44 mg, R_f ($CHCl_3$/MeOH 9:1) 0.28, mp 185-186 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.53 (t, 3H, *J* 7.0 Hz, NCH_2CH_3), 5.05 (q, 2H, *J* 7.0 Hz, NCH_2CH_3), 6.59 (d, 1H, *J* 7,6 Hz, H-7), 7.58 (d, 1H, *J* 7.6 Hz, H-8), 7.65 (d, 1H, *J* 9.4 Hz, H-4), 8.51 (d, 1H, *J* 9.4 Hz, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 16.5 (NCH_2CH_3), 52.8 (NCH_2CH_3), 116.0, 119.0, 125.8, 128.2, 134.8, 143.5, 153.2, 162.3, 176.1 (CO). Anal. Calcd for $C_{11}H_9N_3OSe$ (278.17): C, 47.50; H, 3.26; N, 15.11. Found: C, 47.41; H, 3.29; N, 15.04.

6-Ethoxy-[1,2,5]selenadiazolo[3,4-*h*]quinoline (3). Brownish solid, yield 26%, 29 mg, R_f ($CHCl_3$/MeOH 9:1) 0.45, mp 226-228 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.57 (t, 3H, *J* 6.9 Hz, OCH_2CH_3), 4.27 (q, 2H, *J* 6.9 Hz, OCH_2CH_3), 6.98 (d, 1H, *J* 5.5 Hz, H-7), 7.68 (d, 1H, *J* 9.7 Hz, H-4), 8.17 (d, 1H, *J* 9.7 Hz, H-5), 8.83 (d, 1H, *J* 5.5 Hz, H-8). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 14.4 (OCH_2CH_3), 64.5 (OCH_2CH_3), 105.3, 119.7, 121.2, 124.6, 151.6, 145.4, 158.6, 160.9, 161.4. Anal. Calcd for $C_{11}H_9N_3OSe$ (278.17): C, 47.50; H, 3.26; N, 15.11. Found: C, 47.55; H, 3.24; N, 15.12.

6-Ethyl-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*f*]quinolin-9-one (5) and 9-ethoxy-[1,2,5]selenadiazolo[3,4-*f*]quinoline (6). *Method A* (with K_2CO_3 as the base). Ethyl iodide (0.045 mL, 0.56 mmol) was added to a stirred suspension of selenadiazoloquinolone **4** (100 mg, 0.4 mmol) and anhydrous K_2CO_3 (200 mg, 1.6 mmol) in DMF (1 mL) heated to 50 °C and stirring was continued at this temperature overnight. After cooling down, reaction mixture was diluted with water (20 mL) and extracted with $CHCl_3$ (4×15 mL). Combined extracts were dried with Na_2SO_4, filtered and the voletiles were evaporated to under reduced pressure. Particular isomers **5** and **6** were separated by FLC (SiO_2, $CHCl_3$/MeOH 100:1 → 20:1).

6-Ethyl-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*f*]quinolin-9(6*H*)-one (5). Yellow solid, yield 46%, 44 mg, R_f ($CHCl_3$/MeOH 5:1) 0.22, mp 253-256 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.47 (t, 3H, *J* 7.2 Hz, NCH_2CH_3), 4.22 (q, 2H, *J* 7.2 Hz, NCH_2CH_3), 7.46 (d, 1H, *J* 7.7 Hz, H-7), 7.56 (d, 1H, *J* 10.0 Hz, H-4), 6.58 (d, 1H, *J* 7.7 Hz, H-8), 7.88 (d, 1H, *J* 10.0 Hz, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 15.2 (NCH_2CH_3), 49.6 (NCH_2CH_3), 118.41, 118.47, 120.2, 127.5, 140.2, 142.3, 156.8, 157.4, 176.0 (CO). Anal. Calcd for $C_{11}H_9N_3OSe$ (278.17): C, 47.50; H, 3.26; N, 15.11. Found: C, 47.55; H, 3.21; N, 15.15.

9-Ethoxy-[1,2,5]selenadiazolo[3,4-*f*]quinoline (6). Brownish solid, yield 25%, 28 mg, R_f ($CHCl_3$/MeOH 100:1) 0.16, mp 183-185 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.67 (t, 3H, *J* 7.0 Hz, OCH_2CH_3), 4.47 (q, 2H, *J* 7.0 Hz, OCH_2CH_3), 7.08 (d, 1H, *J* 5.7 Hz, H-8), 7.88 (d, 1H, *J* 9.6 Hz, H-4), 7.94 (d, 1H, *J* 9.6 Hz, H-5), 8.79 (d, 1H, *J* 5.7 Hz, H-7). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 14.4 (OCH_2CH_3), 65.1 (OCH_2CH_3), 105.9, 114.7, 125.3, 133.8, 151.8, 152.6, 156.4, 159.5, 163.5. Anal. Calcd for $C_{11}H_9N_3OSe$ (278.17): C, 47.50; H, 3.26; N, 15.11. Found: C, 47.44; H, 3.23; N, 15.17.

Method B (with NaH as the base). NaH (60% suspension in mineral oil, 0.23 mg, 5.7 mmol) was added to a stirred suspension of selenadiazoloquinolone **4** (1.0 g, 4.0 mmol) in dry DMF (25 mL) under the Ar atmosphere at room temperature and stirring was continued for 1 hour. Then ethyl iodide (0.5 mL, 6.2 mmol) was added dropwise and the reaction mixture was stirred at room temperature overnight. Once the reaction was complete, it was diluted with water (100 mL) and extracted with $CHCl_3$ (2×100 mL). Combined extracts were dried with Na_2SO_4, filtered and the voletiles were evaporated under reduced pressure. The residual solid was subjected to FLC (SiO_2, $CHCl_3$/MeOH 20:1, R_f 0.11) to give compound **5** (0.28 g, 26%) as yellow solid; mp 254-256 °C. NMR spectral data were in accordance with those of ethylselenadiazoloquinolone **5** prepared by ethylation of selenadiazoloquinolone **4** in presence of K_2CO_3 as the base.

7-Acetyl-9-ethyl-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinolin-6-one (22). NaH (60% suspension in mineral oil, 100 mg, 2.50 mmol) was added to a stirred suspension of selenadiazoloquinolone **21** (500 mg, 1.71 mmol) in dry DMF (10 mL) under the Ar atmosphere at room temperature and stirring was continued for 1 hour. Then ethyl iodide (0.20 mL, 2.50 mmol) was added dropwise and the reaction mixture was stirred at room temperature overnight. Once the reaction was complete, it was diluted with water (25 mL) and the resulting brown precipitate was collected by suction, washed with water and allowed to dry. Mother liquor was extracted with $CHCl_3$ (60 mL), chloroform layer was washed with water (60 mL), dried with Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. Combined solids were subjected to FLC (SiO_2, $CHCl_3$, R_f 0.10) to afford compound **22** (197 mg, 36%) as yellow solid; mp 242-246 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.56 (t, 3H, *J* 7.0 Hz, NCH_2CH_3), 2.81 (s, 3H, CH_3), 5.13 (q, 2H, *J* 7.0 Hz, NCH_2CH_3), 7.75 (d, 1H, *J* 9.5 Hz, H-5), 8.48 (s, 1H, H-8), 8.57 (d, 1H, *J* 9.5 Hz, H-4). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 16.6 (NCH_2CH_3), 31.6 (CH_3), 53.8 (NCH_2CH_3), 120.3, 122.8, 127.9, 129.4, 133.9, 148.2, 152.8, 162.3, 174.2 (CO), 197.5 ($COCH_3$). Anal. Calcd for $C_{13}H_{11}N_3O_2Se$ (320.21): C, 48.76; H, 3.46; N, 13.12. Found: C, 48.72; H, 3.42; N, 13.14.

Synthesis of *N*-Ethyl-2,1,3-benzoselenadiazol-5-amine (11)

***N*-(2,1,3-Benzoselenadiazol-5-yl)acetamide (8b).** A mixture of benzoselenadiazol-5-amine **7b** (10.0 g, 50.5 mmol) and acetic anhydride (40 mL) was stirred for 1 h at 45 °C. Then the reaction mixture was cooled in an ice bath, water (50 mL) was added and stirring continued for additional 1.5 h. The mixture was then made alkaline with 27% NH_4OH solution while cooling in the ice

bath. Pale brown precipitate was collected by suction, washed with water and dried in a vacuum oven at 40 °C for 6 hours. This crude material was characterized and used in the next reaction without further purification. Yield 77%, 9.4 g, mp 260-264 °C (ref.[25] mp 259 °C, ref.[30] mp 268-270 °C). ^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ_H 2.12 (s, 3H, CH_3), 7.51 (dd, 1H, *J* 9.5, 2.0 Hz, H-6), 7.76 (d, 1H, *J* 9.5 Hz, H-7), 8.32 (d, 1H, *J* 1.6 Hz, H-4), 10.29 (br s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-*d*$_6$): δ_C 24.2 (CH_3), 107.6, 123.0, 125.6, 139.8, 157.1, 160.3, 169.4 (CO).

***N*-(2,1,3-Benzoselenadiazol-5-yl)-*N*-ethylacetamide (9b).** NaH (60% suspension in mineral oil, 0.7 g, 17.5 mmol) was added in one portion to a stirred suspension of acetamide **8b** (3.0 g, 12.5 mmol) in dry DMF (30 mL) under the Ar atmosphere at room temperature and stirring was continued for 20 min. Then ethyl iodide (1.1 mL, 13.7 mmol) was added dropwise and the reaction mixture was stirred at room temperature for 2 hours. Once the reaction was complete, it was carefully quenched with water (2 mL), subsequently diluted with brine (300 mL) and extracted with ethyl acetate (300 mL). Organic phase was washed with brine (2×300 mL), dried with Na_2SO_4, filtered and evaporated under reduced pressure. The resulting brown oil was subjected to FLC (SiO_2, EtOAc/hexanes 3:1, R_f 0.17) to afford compound **9b** (2.8 g, 83%) as yellow-brown oil which solidified on standing in the fridge; mp 64-65 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.19 (t, 3H, *J* 7.1 Hz, $NCH_2C\mathit{H}_3$), 2.00 (s, 3H, $COCH_3$), 3.85 (q, 2H, *J* 7.1 Hz, $NC\mathit{H}_2CH_3$), 7.31 (dd, 1H, *J* 9.4, 2.0 Hz, H-6), 7.66 (d, 1H, *J* 2.0 Hz, H-4), 7.89 (d, 1H, *J* 9.4 Hz, H-7). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 13.2 ($NCH_2\mathit{C}H_3$), 22.9 ($CO\mathit{C}H_3$), 43.8 ($N\mathit{C}H_2CH_3$), 121.4, 124.0, 130.1, 144.0, 159.2, 160.2, 169.5 (CO). Anal. Calcd for $C_{10}H_{11}N_3OSe$ (268.17): C, 44.79; H, 4.13; N, 15.67. Found: C, 44.72; H, 4.10; N, 15.63.

***N*-Ethyl-2,1,3-benzoselenadiazol-5-amine (11).** Acetamide **9b** (2.8 g, 10.4 mmol) was dissolved in methanolic solution of MeONa prepared from sodium (0.24 g, 10.4 mmol) and methanol (40 mL). The resulting solution was refluxed for 3.5 h, charcoaled while hot and filtered into a beaker. To the filtrate cooled in an ice bath, water (300 mL) was added and the precipitated yellow needles were collected by suction, washed with water and dried. This crude material was characterized and used in the next reaction without further purification. Yield 76%, 1.8 g, mp 90-92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.33 (t, 3H, *J* 7.1 Hz, $NCH_2C\mathit{H}_3$), 3.23 (q, 2H, *J* 7.1 Hz, $NC\mathit{H}_2CH_3$), 4.09 (br s, 1H, NH), 6.55 (s, 1H, H-4), 6.90 (dd, 1H, ^{3}*J* 9.4, 1.8 Hz, H-6), 7.53 (d, 1H, *J* 9.4 Hz, H-7). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 14.1 ($NCH_2\mathit{C}H_3$), 38.1 ($N\mathit{C}H_2CH_3$), 94.6, 123.2, 126.5, 148.5, 157.0, 162.3 ppm. Anal. Calcd for $C_8H_9N_3Se$ (226.14): C, 42.49; H, 4.01; N, 18.58. Found: C, 42.44; H, 4.07; N, 18.61.

Synthesis of *N*-Ethyl-2,1,3-benzoselenadiazol-4-amine (15)

***N*-(2,1,3-Benzoselenadiazol-4-yl)acetamide (8a).** A mixture of benzoselenadiazol-4-amine **7a** (5.0 g, 25.2 mmol) and acetic anhydride (20 mL) was stirred for 30 min. at 100 °C. Then water (70 mL) was added to the reaction mixture and heating was continued for 30 min. The mixture was made alkaline with 27% NH_4OH solution while cooling in an ice bath. Pale yellow-brown precipitate was collected by suction, washed with water and dried in a vacuum oven at 40 °C for 6 hours. This crude material was characterized and used in the next reaction without further

purification. Yield 96%, 5.8 g, mp 175-176 °C (ref.[25] mp 175-176 °C, ref.[30] mp 177-178 °C). ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.22 (s, 3H, CH_3), 7.50 (d, 1H, *J* 4.7 Hz, H-7), 7.51 (t, 1H, *J* 9.0 Hz, H-6), 8.11 (dd, 1H, *J* 8.2, 4.3 Hz, H-5), 10.05 (br s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 24.0 (CH_3), 114.9, 117.4, 130.5, 131.4, 153.6, 159.6, 169.3 (CO).

1-*N*-Ethylbenzene-1,2,3-triamine (10). $BH_3 \cdot SMe_2$ comlex (1.31 mL, 12.48 mmol, technical grade >90% in dimethyl sulfide) was added dropwise under Ar atmosphere to a solution of acetamide **8a** (0.5 g, 2.08 mmol) in dry THF (40 mL) and the reaction mixture was refluxed for 1 h. After cooling down in an ice bath, a precipitated black solid was filtered off. The filtrate was carefully quenched with water (40 mL), stirred for 15 min. and made alkaline with 20% NaOH solution. The resulting brownish solution was extracted with ethyl acetate (40 mL). Organic phase was separated, dried with Na_2SO_4, filtered and evaporated under reduced pressure to afford compound **10** (0.26 g, 82%) as an unstable pale brown semisolid. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 1.18 (t, 3H, *J* 7.1 Hz, NCH_2CH_3), 2.99 (q, 2H, *J* 7.1 Hz, NCH_2CH_3), 5.90 (dd, 1H, *J* 7.88, 0.82 Hz, H-6), 6.02 (dd, 1H, *J* 7.80, 1.10 Hz, H-4), 6.35 (t, 1H, *J* 7.84 Hz, H-5).

***N*-(2,1,3-Benzoselenadiazol-4-yl)-*N*-ethylacetamide (9a).** NaH (60% suspension in mineral oil, 100 mg, 2.5 mmol) was added in one portion to a stirred suspension of acetamide **8a** (0.5 g, 2.08 mmol) in dry DMF (5 mL) under the Ar atmosphere at room temperature and stirring was continued for 20 min. Then ethyl iodide (0.2 mL, 2.5 mmol) was added dropwise and reaction mixture was stirred at room temperature for 2 hours. After the reaction was complete, it was carefully quenched with water (2 mL), diluted with brine (50 mL) and extracted with ethyl acetate (50 mL). Organic phase was washed with brine (2×50 mL) and water (2×50 mL), dried with Na_2SO_4, filtered and evaporated under reduced pressure. The resulting yellow solid was subjected to FLC (SiO_2, EtOAc/hexanes 3:1, R_f 0.24) to afford compound **9a** (0.5 g, 90%) as pale yellow solid; mp 108-110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.14 (t, 3H, *J* 7.3 Hz, NCH_2CH_3), 1.83 (s, 3H, $COCH_3$), 3.69 (br s, 1H, NCH_2CH_3), 4.11 (br s, 1H, NCH_2CH_3), 7.30 (d, 1H, *J* 6.6 Hz, H-5), 7.53 (dd, 1H, *J* 9.5, 6.6 Hz, H-6), 7.88 (d, 1H, *J* 9.5 Hz, H-7). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 13.4 (NCH_2CH_3), 22.5 ($COCH_3$), 43.4 (NCH_2CH_3), 123.7, 128.4, 129.1, 136.2, 157.8, 161.3, 170.2 (CO). Anal. Calcd for $C_{10}H_{11}N_3OSe$ (268.17): C, 44.79; H, 4.13; N, 15.67. Found: C, 44.85; H, 4.11; N, 15.70.

***N*-(2,1,3-Benzoselenadiazol-4-yl)-2,2,2-trifluoroacetamide (12).** A solution of trifluoroacetic anhydride (2.0 mL, 14.1 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a stirred solution of benzoselenadiazol-4-amine **7a** (2.0 g, 10.0 mmol) and pyridine (1.0 mL, 12.4 mmol) in CH_2Cl_2 (200 mL) and the mixture was stirred at room temperature for 1 hour. Once the reaction was complete, the reaction mixture was washed with water (2×200 mL), organic phase was dried with Na_2SO_4, filtered and evaporated under reduced pressure to afford compound **12** as yellow-brown needles. This crude material was characterized without further purification. Yield 94%, 2.8 g, mp 136-138 °C (ref.[30] mp 140-141 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.55 (t, 1H, *J* 8.7 Hz, H-6), 7.65 (d, 1H, *J* 9.0 Hz, H-7), 8.33 (d, 1H, *J* 7.0 Hz, H-5), 9.35 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 115.4 (q, *J* 288,5 Hz, CF_3), 116.0, 119.9, 128.3, 130.5, 153.1, 154.7 (q, *J* 37.9 Hz, CO), 159.7.

Ethyl *N*-(2,1,3-benzoselenadiazol-4-yl)carbamate (13). Ethyl chloroformate (2.6 mL, 27.3 mmol) was added dropwise to a stirred solution of benzoselenadiazol-4-amine **7a** (5.0 g, 25.2 mmol) and pyridine (5.0 mL, 62.0 mmol) in CH_2Cl_2 (400 mL) and the mixture was stirred at room temperature for 30 min. After the reaction was complete, the reaction mixture was washed with water (2×400 mL), organic phase was dried with Na_2SO_4, filtered and evaporated under reduced pressure. The resulting brown oil was subjected to FLC (SiO_2, EtOAc/hexanes 1:4, R_f 0.35) to afford compound **13** (6.7 g, 98%) as yellow solid; mp 87-88 °C (ref.[30] mp 89-90 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.36 (t, 3H, *J* 7.1 Hz, OCH_2CH_3), 4.30 (q, 2H, *J* 7.1 Hz, OCH_2CH_3), 7.44 (dd, 1H, *J* 9.1, 1.8 Hz, H-7), 7.48 (t, 1H, *J* 9.1 Hz, H-6), 7.97 (br d, 1H, *J* 5.7 Hz, H-5), 8.05 (br s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 14.5 (OCH_2CH_3), 61.6 (OCH_2CH_3), 111.9, 116.6, 131.1, 131.3, 153.1, 153.6, 160.2.

Ethyl *N*-(2,1,3-benzoselenadiazol-4-yl)-*N*-ethylcarbamate (14). NaH (60% suspension in mineral oil, 1.4 g, 35.0 mmol) was added in one portion to a stirred suspension of carbamate **13** (6.7 g, 24.8 mmol) in dry DMF (70 mL) under the Ar atmosphere at room temperature and stirring was continued for 30 min. Then ethyl iodide (3.0 mL, 37.5 mmol) was added dropwise and reaction mixture was stirred overnight at room temperature. Once the reaction was complete, it was carefully quenched with water (2 mL), diluted with brine (400 mL) and extracted with ethyl acetate (400 mL). Organic phase was washed with brine (2×400 mL) and water (2×400 mL), dried with Na_2SO_4, filtered and evaporated under reduced pressure. The resulting orange oil was subjected to FLC (SiO_2, EtOAc/hexanes 1:4, R_f 0.25) to afford compound **14** (7.2 g, 97%) as yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.08 (br s, 3H, NCH_2CH_3), 1.10 (t, 3H, *J* 7.1 Hz, OCH_2CH_3), 3.79 (q, 2H, *J* 7.1 Hz, OCH_2CH_3), 4.07 (q, 2H, *J* 6.8 Hz, NCH_2CH_3), 7.21 (d, 1H, *J* 6.5 Hz, H-7), 7.41 (dd, 1H, *J* 9.0, 6.9 Hz, H-6), 7.72 (dd, 1H, *J* 9.0, 0.9 Hz, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 14.2 (NCH_2CH_3), 14.7 (OCH_2CH_3), 45.2 (NCH_2CH_3), 61.9 (OCH_2CH_3), 122.9, 127.9, 129.5, 135.4, 155.8, 158.0, 161.6.

***N*-Ethyl-2,1,3-benzoselenadiazol-4-amine (15).** A mixture of carbamate **14** (7.2 g, 24.1 mmol) and NaOH (9.9 g, 0.25 mol) in EtOH (225 mL) was refluxed for 60 hours. Once the reaction was complete, EtOH (150-170 mL) was evaporated under reduced pressure and the residue was taken up into CH_2Cl_2 (400 mL). Organic phase was washed with water (3×400 mL), dried with Na_2SO_4, filtered and evaporated under reduced pressure to yield compound **15** as dark red oil which solidified on standing in the fridge. This crude material was characterized and used in next reactions without further purification. Yield 95%, 5.2 g, mp 49-50 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.38 (t, 3H, *J* 7.2 Hz, NCH_2CH_3), 3.32 (q, 2H, *J* 7.2 Hz, NCH_2CH_3), 6.14 (d, 1H, *J* 7.2 Hz, H-5), 7.07 (d, 1H, *J* 9.0 Hz, H-7), 7.34 (dd, 1H, *J* 9.0, 7.2 Hz, H-6). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 14.2 (NCH_2CH_3), 38.1 (NCH_2CH_3), 100.0, 110.2, 132.4, 140.9, 154.2, 161.2. Anal. Calcd for $C_8H_9N_3Se$ (226.14): C, 42.49; H, 4.01; N, 18.58. Found: C, 42.41; H, 4.06; N, 18.53.

Synthesis of 2-[(2,1,3-benzoselenadiazolyl)(ethyl)amino]methylidene derivatives 16 and 18

1,3-Diethyl 2-{[(2,1,3-benzoselenadiazol-5-yl)(ethyl)amino]methylidene}propanedioate (16). A mixture of ethylamine **11** (0.40 g, 1.77 mmol) and diethyl ethoxymethylidenepropanedioate **17b**

(2.0 mL, 10 mmol) was heated at 160 °C for 5 hours. After cooling down, the reaction mixture was subjected to FLC (SiO_2, EtOAc/hexanes 1:2, R_f 0.13) to afford compound **16** (0.59 g, 85%) as yellow-orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.08 (t, 3H, *J* 7.1 Hz, NCH_2CH_3), 1.27 (t, 3H, *J* 7.1 Hz, OCH_2CH_3), 1.31 (t, 3H, *J* 7.1 Hz, OCH_2CH_3), 3.76 (q, 2H, *J* 7.1 Hz, NCH_2CH_3), 3.84 (q, 2H, *J* 7.1 Hz, OCH_2CH_3), 4.21 (q, 2H, *J* 7.1 Hz, OCH_2CH_3), 7.37 (dd, 1H, *J* 9.5, 2.1 Hz, H-6), 7.52 (d, 1H, *J* 2.1 Hz, H-4), 7.73 (s, 1H, =CH-), 7.77 (d, 1H, *J* 9.5 Hz, H-7). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 13.8 (NCH_2CH_3), 13.9 (OCH_2CH_3), 14.3 (OCH_2CH_3), 49.9 (NCH_2CH_3), 60.5 (OCH_2CH_3), 60.8 (OCH_2CH_3), 100.4, 114.6, 123.5, 126.5, 145.4, 147.0, 158.4, 160.2, 166.2 (CO), 166.6 (CO).

General procedure for the preparation of 2-[(2,1,3-benzoselenadiazol-4-yl)(ethyl)amino]methylidene derivatives (18). A mixture of ethylamine **15** (2.0 g, 8.84 mmol) and corresponding alkoxymethylidene derivative **17** (17.68 mmol) was refluxed in xylene (20 mL) for 24-48 hours (TLC) followed by the evaporation of xylene under reduced pressure. The crude products were subjected to FLC (SiO_2, EtOAc/hexanes 1:2) to yield compounds **18**.

1,3-Dimethyl 2-{[(2,1,3-benzoselenadiazol-4-yl)(ethyl)amino]methylidene}propanedioate (18a). Yellow solid, yield 82%, 2.67 g, R_f (EtOAc/hexanes 1:2) 0.15, mp 98-100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.25 (t, 3H, *J* 7,2 Hz, NCH_2CH_3), 2.88 (br s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 3.95 (q, 2H, *J* 7.2 Hz, NCH_2CH_3), 7.21 (d, 1H, *J* 6.9 Hz, H-5), 7.46 (dd, 1H, *J* 9.0, 7.0 Hz, H-6), 7.80 (d, 1H, *J* 9.0 Hz, H-7), 7.90 (s, 1H, =CH-). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 51.1 (OCH_3), 51.6 (OCH_3), 51.8 (NCH_2CH_3), 96.7, 123.0, 126.0, 129.0, 135.7, 150.4, 156.2, 161.2, 166.5 (CO), 167.1 (CO). Anal. Calcd for $C_{14}H_{15}N_3O_4Se$ (368.25): C, 45.66; H, 4.11; N, 11.41. Found: C, 45.53; H, 4.17; N, 11.50.

1,3-Diethyl 2-{[(2,1,3-benzoselenadiazol-4-yl)(ethyl)amino]methylidene}propanedioate (18b). Yellow solid, yield 83%, 2.90 g, R_f (EtOAc/hexanes 1:2) 0.15, mp 95-97 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 0.79 (t, 3H, *J* 7.1 Hz, OCH_2CH_3), 1.22 (t, 3H, *J* 7.1 Hz, NCH_2CH_3), 1.28 (t, 3H, *J* 7.1 Hz, OCH_2CH_3), 3.40 (br s, 2H, OCH_2CH_3), 3.95 (q, 2H, *J* 7.1 Hz, NCH_2CH_3), 7.83 (s, 1H, =CH-), 4.14 (q, 2H, *J* 7.1 Hz, OCH_2CH_3), 7.22 (dd, 1H, *J* 6.9 Hz, H-5), 7.45 (dd, 1H, *J* 9.0, 6.9 Hz, H-6), 7.78 (dd, 1H, *J* 9.0, 0.9 Hz, H-7). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 13.5 (NCH_2CH_3), 14.2 (OCH_2CH_3), 14.3 (OCH_2CH_3), 51.5 (NCH_2CH_3), 60.2 (OCH_2CH_3), 60.3 (OCH_2CH_3), 97.7, 122.9, 126.2, 128.9, 135.8, 149.3, 156.2, 161.3, 166.3 (CO), 166.7 (CO). Anal. Calcd for $C_{16}H_{19}N_3O_4Se$ (396.30): C, 48.49; H, 4.83; N, 10.60. Found: C, 48.40; H, 4.88; N, 10.66.

Ethyl (2*E*/2*Z*)-2-{[(2,1,3-benzoselenadiazol-4-yl)(ethyl)amino]methylidene}-3-oxobutanoate (18c). Yellow-brown solid, yield 85%, 2.82 g, R_f (EtOAc/hexanes 1:2) 0.10, mp 108-109 °C, *E*/*Z* 10:1. ^{1}H NMR (300 MHz, $CDCl_3$), *E*-isomer: δ_H 0.81 (t, 3H, *J* 6.6 Hz, OCH_2CH_3), 1.24 (t, 3H, *J* 7.2 Hz, NCH_2CH_3), 2.15 (s, 3H, CH_3), 3.43 (br q, 2H, *J* 6.8 Hz, OCH_2CH_3), 4.00 (q, 2H, *J* 6.6 Hz, NCH_2CH_3), 7.19 (d, 1H, *J* 6.8 Hz, H-5), 7.46 (dd, 1H, *J* 9.0, 7.0 Hz, H-6), 7.80 (d, 1H, *J* 9.0 Hz, H-7), 8.95 (s, 1H, =CH-). Z-isomer (observable signals): δ_H 1.35 (t, 3H, *J* 7.1 Hz, OCH_2CH_3), 1.44 (t, 3H, *J* 7.2 Hz, NCH_2CH_3), 2.57 (s, 3H, CH_3), 4.28 (q, 2H, *J* 7.1 Hz, NCH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$), *E*-isomer: δ_C 13.5 (NCH_2CH_3), 14.2 (OCH_2CH_3), 28.2 ($COCH_3$), 52.2

(N*C*H$_2$CH$_3$), 60.1 (O*C*H$_2$CH$_3$), 107.1, 123.0, 125.5, 128.9, 136.1, 151.2, 155.9, 161.2, 167.7 (CO), 187.3 (COCH$_3$). Signals for *Z*-isomer in ^{13}C NMR spectra were not observed. Anal. Calcd for $C_{15}H_{17}N_3O_3Se$ (366.27): C, 49.19; H, 4.68; N, 11.47. Found: C, 49.24; H, 4.73; N, 11.42.

General procedure for the preparation of 9-ethylselenadiazolo[3,4-*h*]quinolone derivatives 2 and 19. A mixture of the corresponding enamine **18** (2.0 g) and polyphosphoric acid (15 g) was mechanically stirred with a glass rod at 120 °C for 15-20 min. After cooling down, ice water (35 mL) was added to the reaction mixture and mechanical stirring was continued until a gummy residue dissolved to form yellow-brown suspension. This suspension was made alkaline with 30% NaOH solution or 27% NH_4OH solution while cooling in an ice bath. Obtained precipitate was collected by suction, washed with water and dried. In case of derivative **18c**, mother liquor was extracted with $CHCl_3$ (2×70 mL). Combined extracts were dried with Na_2SO_4, filtered and evaporated under reduced pressure. Purification by FLC (SiO_2, $CHCl_3$/MeOH) gave compounds **2** and **19**.

Methyl 9-ethyl-6-oxo-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinoline-7-carboxylate (19a). Yellow solid, yield 83%, 1.51 g, R_f ($CHCl_3$/MeOH 30:1) 0.32, mp 203-207 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.57 (t, 3H, *J* 7.0 Hz, NCH$_2$C*H*$_3$), 3.96 (s, 3H, OCH$_3$), 5.13 (q, 2H, *J* 7.0 Hz, NC*H*$_2$CH$_3$), 7.74 (d, 1H, *J* 9.5 Hz, H-4), 8.52 (s, 1H, H-8), 8.60 (d, 1H, *J* 9.5 Hz, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 16.6 (NCH$_2$*C*H$_3$), 52.4 (OCH$_3$), 53.8 (N*C*H$_2$CH$_3$), 115.5, 120.4, 128.0, 128.6, 133.9, 149.4, 152.7, 162.3, 166.0 (COOMe), 172.6 (CO). Anal. Calcd for $C_{13}H_{11}N_3O_3Se$ (336.20): C, 46.44; H, 3.30; N, 12.50. Found: C, 46.48; H, 3.35; N, 12.53.

Ethyl 9-ethyl-6-oxo-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinoline-7-carboxylate (19b). Yellow solid, yield 89%, 1.57 g, R_f ($CHCl_3$/MeOH 50:1) 0.18, mp 182-184 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.45 (t, 3H, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.58 (t, 3H, *J* 7.0 Hz, NCH$_2$C*H*$_3$), 4.45 (q, 2H, *J* 7,1 Hz, OC*H*$_2$CH$_3$), 5.16 (q, 2H, *J* 7.0 Hz, NC*H*$_2$CH$_3$), 7.74 (d, 1H, *J* 9.5 Hz, H-4), 8.55 (s, 1H, H-8), 8.60 (d, 1H, *J* 9.5 Hz, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 14.4 (OCH$_2$*C*H$_3$), 16.6 (NCH$_2$*C*H$_3$), 53.7 (O*C*H$_2$CH$_3$), 61.4 (N*C*H$_2$CH$_3$), 116.0, 120.3, 128.1, 128.6, 133.9, 149.2, 152.8, 162.3, 165.3 (COOEt), 172.6 (CO). Anal. Calcd for $C_{14}H_{13}N_3O_3Se$ (350.23): C, 48.01; H, 3.74; N, 12.00. Found: C, 47.95; H, 3.77; N, 12.08.

9-Ethyl-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinolin-6-one (2). Yellow solid, yield 81%, 1.23 g, R_f ($CHCl_3$/MeOH 40:1) 0.10, mp 185-187 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.52 (t, 3H, *J* 7.0 Hz, NCH$_2$C*H*$_3$), 5.05 (q, 2H, *J* 7.0 Hz, NC*H*$_2$CH$_3$), 6.63 (d, 1H, *J* 7,6 Hz, H-7), 7.61 (d, 1H, *J* 7.4 Hz, H-8), 7.63 (d, 1H, *J* 9.4 Hz, H-4), 8.48 (d, 1H, *J* 9.5 Hz, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 16.5 (NCH$_2$*C*H$_3$), 52.8 (N*C*H$_2$CH$_3$), 116.0, 119.0, 125.8, 128.2, 134.8, 143.5, 153.2, 162.3, 176.1 (CO). Anal. Calcd for $C_{11}H_9N_3OSe$ (278.17): C, 47.50; H, 3.26; N, 15.11. Found: C, 47.56; H, 3.21; N, 15.16.

9-Ethyl-6-oxo-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinoline-7-carboxylic acid (20). A mixture of ethyl ester **19b** (1.0 g, 2.85 mmol) and NaOH (0.3 g, 7.50 mmol) in EtOH (20 mL) was heated at 65 °C for 1.5 h. After cooling down, the mixture was diluted with water (30 mL) and acidified with 20% HCl. The resulting pale yellow precipitate was collected by suction, washed with water and dried to give acid **20**. This crude material was characterized and used in next reaction

without further purification. Yield 88%, 0.8 g, mp 321-325 °C. ^{1}H NMR (300 MHz, TFA-*d*): δ_H 1.89 (t, 3H, *J* 6.8 Hz, NCH_2CH_3), 5.86 (q, 2H, *J* 6.8 Hz, NCH_2CH_3), 8.37 (d, 1H, *J* 9.6 Hz, H-4), 8.73 (d, 1H, *J* 9.6 Hz, H-5), 9.58 (s, 1H, H-8). ^{13}C NMR (75 MHz, TFA-*d*): δ_C 16.0 (NCH_2CH_3), 59.8 (NCH_2CH_3), 110.3, 124.2, 125.1, 126.1, 138.4, 151.0, 151.4, 162.4, 169.9 (COOH), 172.1 (CO). Anal. Calcd for $C_{12}H_9N_3OSe$ (322.18): C, 44.74; H, 2.82; N, 13.04. Found: C, 44.77; H, 2.81; N, 12.99.

Decarboxylation of the acid 20

9-Ethyl-6*H*,9*H*-[1,2,5]selenadiazolo[3,4-*h*]quinolin-6-one (2). A mixture of acid **20** (0.20 g, 0.62 mmol) and Ph_2O (4 mL) was refluxed for 1.5 h. After cooling down, the mixture was diluted with $CHCl_3$ (40 mL) and filtered. Silica gel (6 g) was added to the filtrate and the solvent was evaporated under reduced pressure. The rest was loaded on silicagel column and was eluted with the mixture of $CHCl_3$/MeOH 30:1 (R_f 0.12) to afford compound **2** (0.13 g, 75%) as yellow-orange solid; mp 184-186 °C. NMR spectral characteristics were in accordance with those of ethylselenadiazoloquinolone **2** prepared by ethylation of selenadiazoloquinolone **1** and cyclization of enamine **18c**.

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