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N^1-Allyl-3-substituted-6,7-dimethyl-1, 2-dihydro-2-quinoxalinone as Key Intermediate for New Acyclonucleosides and Their Regioisomer *O*-Analogues

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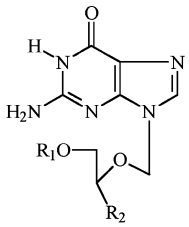
ABSTRACT: *The key intermediates allyloxyquinoxaline* **2a–c** *and N-allylquinoxaline* **3a–c** *were used to synthesize a number of acyclonucleosides whose chemical modifications include quinoxaline ring and the acyclic part is either N^1-propanediol or 3-hydroxypropyl substituents and their O-analogues. These compounds were characterized by elemental analysis, MALDI MS, and NMR data.* © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:280–288, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20203

INTRODUCTION

The successful development of acyclovir I (ACV) [1,2], 9-[(2-hydroxyethoxy)-methyl]guanine, and ganciclovir II (DHPG) [3,4] as excellent antiviral agents have stimulated the synthesis and biological evaluation of a wide variety of acyclic nucleosides modified either in the base moiety or the acyclic part.



I $R_1 = R_2 = H$
II $R_1 = H$, $R_2 = CH_2OH$

Acyclovir

Conventional and common synthetic methods for the preparation of acyclic nucleosides and nucleotides involve the coupling reaction of heterocyclic bases with α-halo [5–7] or acetoxymethyl ethers catalyzed by various Lewis acids or bases [7,8], e.g., HMDS [5,6], $SnCl_4$, $Hg(CN)_2$, $(CH_3)_3SiClO_4$, $(CH_3)_3SiSO_3C_4F_9$ [9,10], and natural phosphates (NP) [6] to afford the regioselective *N*-alkylation of the nucleobases, i.e., acyclonucleoside.

Quinoxaline derivatives have attracted interest as biologically active materials [11–13]. They also find considerable application as angiotensin II receptor antagonists [14], NMDA antagonists [15], anti-inflammatory [16], antidepressant-tranquilizing agents [17], and antitumor drugs [18,19]. El Ashry et al. [7] described the synthesis

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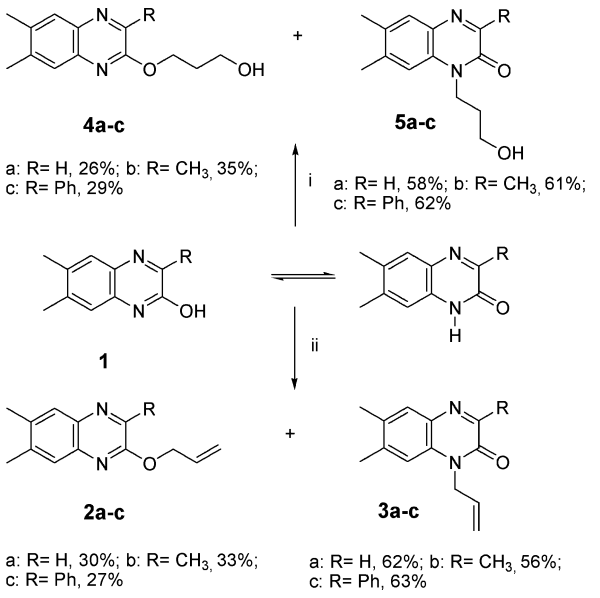
of some homoacyclovir analogues of 2-(1*H*)-quinoxalinone bases and their activity against Hepatitis B virus (HBV). The tested compounds showed high viral replication inhibition with low cytotoxicity. Therefore, a continuous need for new quinoxaline acyclonucleosides are still of great interest.

RESULTS AND DISCUSSION

In this paper, we report the results related to the synthesis of the acyclonucleosides whose chemical modifications include quinoxaline as the heterocyclic base and the acyclic part (acyclic sugar residue) is either N^1-propanediol or 3-hydroxypropyl substituents and their *O*-analogues. The *N*-acyclonucleosides and the *O*-regioisomers could be useful for the antiviral evaluation and SAR study.

As part of our continuing interest toward the regioselective reactions of ambident nucleophiles, i.e., thioamides [20–22], we have studied the reaction of quinoxalines **1a–c** [23–25] with electrophiles. Thus, the reaction of the ambident nucleophile **1a–c** with allyl bromide in the presence of NaH in *N*,*N*-dimethylformamide always afforded a mixture of *O*- and *N*-allyl substituted quinoxalines **2a–c** and **3a–c**, respectively (Scheme 1). The two alkylated isomers were easily separated by column chromatography using petroleum ether/ethylacetate (6:1) as eluent to afford **2a–c** in 27–33% yield and **3a–c** in 56–62% yield. The elemental analysis together with



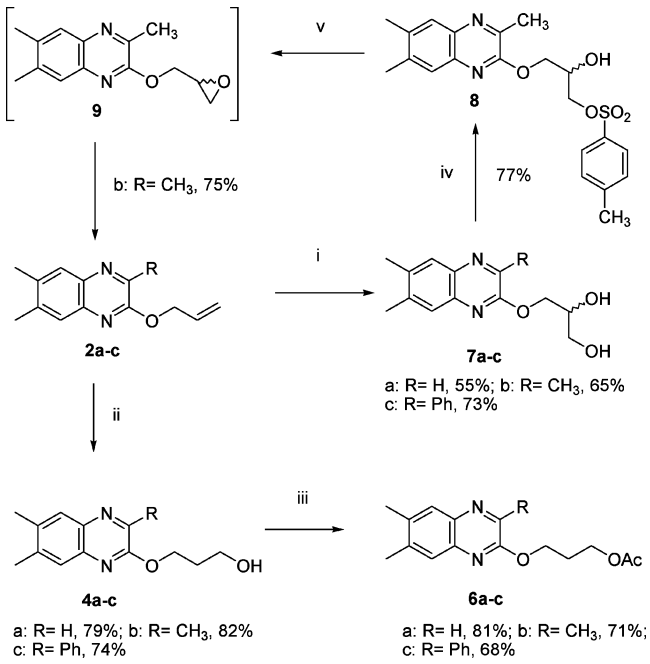
SCHEME 1 Reagents and conditions: (i) 3-bromopropanol, NaH, DMF, 100°C, 3 h; (ii) allyl bromide, NaH, DMF, 100°C, 3 h.

MALDI MS of both alkylated couples **2a–c** and **3a–c** gave identical results agreed with the molecular formula of these compounds. This made us conclude that these compounds are isomeric alkylated products. Thus, the MALDI of **2a** and **3a** gave 237.4 and 237.5, respectively, corresponding to $(M + Na)^+$. The ^{1}H NMR spectra of compounds **2** and **3** gave small evidence to deduce the site of alkylation. The ^{1}H NMR spectrum of **2a** showed a doublet at δ 4.89 attributed to $OC\underline{H}_2$, while that of **3a** gave δ 5.00 attributed to $NC\underline{H}_2$. The ^{13}C NMR clearly deduce the alkylation site; it shows a chemical shift at δ 66.7 corresponding to $OC\underline{H}_2$ for **2a** while a shift at δ 43.4 corresponding to $NC\underline{H}_2$ for **3a**. The ^{1}H NMR spectra of the *N*-alkylated quinoxaline gave an interesting pattern due to an anisotropy caused by the adjacent alkyl substituent toward both methyl groups and the aromatic protons. Thus, the ^{1}H NMR spectrum of **2a** showed δ at 2.33, 7.48, and 7.65 attributed to $2CH_3$, CH_{Ar}, and CH_{Ar}, respectively, while the ^{13}C NMR showed δ 19.8, 20.1, 118.1, 126.6, 128.2, and 132.8 corresponding to (CH_3), (CH_3), $(CH{=}CH_2)$, (CH_{Ar}), (CH_{Ar}), and $(\underline{C}H{=}CH_2)$, respectively. On the other hand, the ^{1}H NMR spectrum of **3a** gave δ 2.47, 2.53, 7.20, and 7.71 attributed to CH_3, CH_3, CH_{Ar}, and CH_{Ar}, respectively, while the ^{13}C NMR showed δ 18.6, 20.1, 114.3, 117.3, 130.0, and 130.2, corresponding to (CH_3), (CH_3), (CH_{Ar}), $(CH{=}CH_2)$, (CH_{Ar}), and $(\underline{C}H{=}CH_2)$, respectively.

The presence of the allyl group on oxygen rather than on the nitrogen of the quinoxaline can be explained as being due to rearrangement of the *N*-allyl group via a Claisen rearrangement to afford the *O*-allyl derivative **2a–c** [8]. The *N*/*O* alkylation products were once again produced in a similar manner by the reaction of the ambident nucleophile **1** with 3-bromopropanol under the same reaction condition to afford the *O*-substituted propanol **4a–c** in 26–35% yield and *N*-substituted propanol **5a–c** in 58–62% yield (Scheme 1).

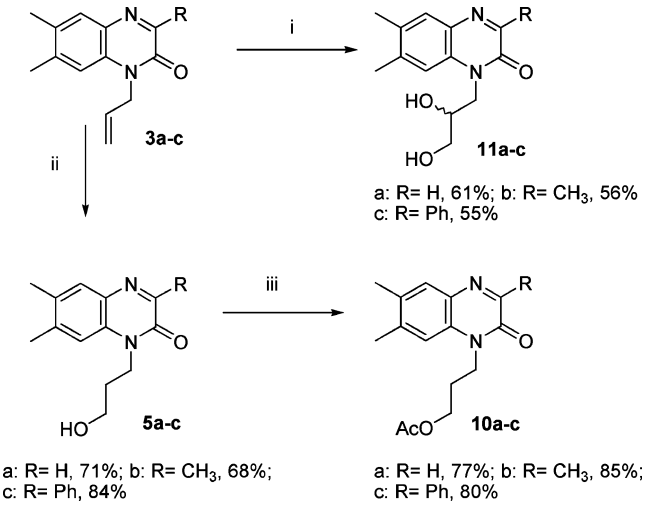
The basic physicochemical features described above for allyl derivatives **2** and **3** were also found for compounds **4a–c** and **5a–c**. The *O*-alkylation site were confirmed from the ^{13}C NMR spectrum that shows δ 58.6 and 60.7 attributed to two OCH_2 groups of compound **4a**. The ^{13}C NMR spectrum of **5a** gave δ 38.5 and 58.0 attributed to NCH_2 and OCH_2 groups, respectively.

The structure of these compounds was chemically confirmed by an equivocal synthesis of these compounds from the allyl derivatives **2a–c** and **3a–c**. Thus, The borohydride hydroxylation of the allyl key intermediate **2a–c** and **3a–c** using $BH_3{\cdot}$DMS under inert atmosphere gave the *N*- and *O*-3-hydroxypropyl derivatives **4a–c** and **5a–c**, respectively, in good



SCHEME 2 Reagents and conditions: (i) AD-mix β, ^{t}BuOH, H_2O, 0°C, 2 days; (ii) BH_3·DMS, THF, 4 h, NaOH, H_2O_2, 0°C; (iii) acetic anhydride, pyridine, 15 h; (iv) *p*-toluenesulfonyl chloride, dichloromethane, pyridine, 0°C, 1 h; (v) NaH, THF, room temperature, 24 h.

yields 74–82% (Schemes 2 and 3). Acetylation of compounds **4a–c** and **5a–c** afforded the propyl acetate derivatives **6a–c** and **10a–c**, respectively, in good to moderate yields, which gave an additional chemical evidence of the products formed (Schemes 2 and 3).



SCHEME 3 Reagents and conditions: (i) AD-mix β, ^{t}BuOH, H_2O, 0°C, 2 days; (ii) BH_3·DMS, THF, 4 h, NaOH, H_2O_2, 0°C; (iii) acetic anhydride, pyridine, 15 h.

The key intermediate allyloxy quinoxaline **2a–c** and *N*-allyl quinoxaline **3a–c** prepared in a single step were designed to produce acyclonucleosides mainly from the *N*-allyl quinoxaline, in addition to *O*-regioisomer analogues. The allyl group is an excellent precursor for various chemical modifications as described above.

Another type of acyclonucleoside classified as tetra seco type, possessing a glycerol-1-yl side-chain and their *O*-analogues were prepared. Thus, stirring allyl derivatives **2a–c** and **3a–c** with AD-mix β in *tert*-butyl alcohol for 2 days at ambient temperature afforded *O*- and *N*-propanediol **7a–c** and **11a–c**, respectively, in moderate yield [26]. The ^{1}H NMR spectra of diol derivative **7a–c** gave completely different pattern compared to the *N*-substituted propanediol **11a–c** (Schemes 2 and 3). The ^{1}H NMR spectrum of **7b** gave multiplet centered at δ 3.71, 4.12 and a doublet at δ 4.56 corresponding to C$\underline{H}_2$OH, C$\underline{H}$OH, and OC$\underline{H}_2$, respectively. On the other hand, the ^{1}H NMR of propanediol **11b** gave two doublets of doublets at δ 3.50 and 3.68 attributed to NCH_2 and two doublets of doublets at δ 4.23 and 4.51 attributed to OCH_2.

The selective tosylation of the primary alcohol of the diol **7b** afforded tosylate **8**. Treatment of tosylate with NaH failed to give the epoxide by smooth displacement of the tosyl group and instead it afforded the 2-allyloxyquinoxaline **2b**.

EXPERIMENTAL

Solvents were purified and dried in the usual way. The boiling range of the petroleum ether used was 35–65°C. Thin layer chromatography (TLC): silica gel 60 F_{254} plastic plates (E. Merck, layer thickness 0.2 mm) detected by UV absorption. Melting points were determined on a Büchi 510 melting-point apparatus and the values are uncorrected. NMR spectra measured with Bruker AC 250 (250 MHz). TMS (0.00 ppm) or the signal of the deuterated solvent was used as internal standard. FAB-MS modified Finningan MAT 312/AMD 5000 spectrometer at 790 eV and $T = 70$ MALDI-MS, the mass spectra were measured with a KRATOS Analytical Kompact.

General Procedure of Allylation Reaction

A mixture of quinoxaline derivatives (14 mmol) and NaH (0.30 g, 14 mmol) in dry DMF (20 mL) was stirred at 100°C for 0.5 h, and then cooled to room temperature. Allyl bromide (1.4 mL, 16 mmol) was added and the mixture was stirred at 100°C for 3 h. The reaction mixture was evaporated to dryness under reduced pressure, and the residue

was chromatographed on silica gel column with petroleum ether/ethylacetate as eluent to give the products.

2-(Allyloxy)-6,7-dimethylquinoxaline **2a**. Yellow powder (0.90 g, 30%); $R_f = 0.73$ (petroleum ether/ethylacetate, 3:1); mp 45°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.32$ (s, 1H, CH), 7.65 (s, 1H, Ar-H), 7.48 (s, 1H, Ar-H), 6.17–6.00 (m, 1H, CH=CH_2), 5.43 (d, 1H, $J = 17.2$ Hz, CH), 5.25 (d, 1H, $J = 10.4$ Hz, CH), 4.89 (m, 2H, OC$\underline{H}_2$), 2.33 (s, 6H, 2CH_3). ^{13}C NMR (62.8 MHz): $\delta = 156.6$ (C=N), 140.1 (C=N), 138.7 (C_q), 138.2 (CH), 137.7 (C_q), 136.1 (C_q), 132.8 ($\underline{C}$H=CH_2), 128.2 (CH_{Ar}), 126.6 (CH_{Ar}), 118.13 (CH=CH_2), 66.7 (OCH_2), 20.1 (CH_3), 19.8 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 237.4$ $(M + Na)^+$. $C_{13}H_{14}N_2O$ (214.27): C, 72.87; H, 6.59; N, 13.07; Found: C, 73.11; H, 6.63; N, 13.42.

2-(Allyloxy)-3,6,7-trimethylquinoxaline **2b**. White powder (1.05 g, 33%); $R_f = 0.78$ (petroleum ether/ethylacetate, 3:1); mp 72°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.59$ (s, 1H, Ar-H), 7.46 (s, 1H, Ar-H), 6.18–6.05 (m, 1H, CH=CH_2), 5.41 (d, 1H, $J = 17.4$ Hz, CH), 5.24 (d, 1H, $J = 10.8$ Hz, CH), 4.91 (m, 2H, OC$\underline{H}_2$), 2.56 (s, 3H, CH_3), 2.33 (s, 6H, 2CH_3). ^{13}C NMR (62.8 MHz): $\delta = 155.4$ (C=N), 146.5 (C=N), 138.5 (C_q), 138.2 (C_q), 137.2 (C_q), 135.8 (C_q), 132.9 ($\underline{C}$H=CH_2), 127.4 (CH_{Ar}), 126.2 (CH_{Ar}), 117.4 (CH=CH_2), 66.6 (OCH_2), 20.1 (CH_3), 19.9 (CH_3), 19.7 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 251.2$ $(M + Na)^+$. $C_{14}H_{16}N_2O$ (228.29): C, 73.66; H, 7.06; N, 12.27; Found: C, 73.43; H, 6.98; N, 12.56.

2-(Allyloxy)-6,7-dimethyl-3-phenylquinoxaline **2c**. Yellow powder (1.10 g, 27%); $R_f = 0.82$ (petroleum ether/ethylacetate, 3:1); mp 55°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.07$–8.03 (m, 2H, Ar-H), 7.59 (s, 1H, Ar-H), 7.46 (s, 1H, Ar-H), 7.44–7.35 (m, 4H, Ar-H), 6.14–6.01 (m, 1H, CH=CH_2), 5.36 (d, 1H, $J = 17.2$ Hz, CH), 5.19 (d, 1H, $J = 10.5$ Hz, CH), 4.95 (d, 2H, $J = 5.4$ Hz, OCH_2), 2.31 (s, 6H, 2CH_3). ^{13}C NMR (62.8 MHz): $\delta = 154.9$ (C=N), 145.2 (C=N), 139.9 (C_q), 138.5 (C_q), 137.9 (C_q), 136.5 (C_q), 133.0 (C_q), 129.8 (CH_{Ar}), 129.4 ($\underline{C}$H=CH_2), 129.04 (CH_{Ar}), 128.4 (CH_{Ar}), 128.1 (CH_{Ar}), 126.2 (CH_{Ar}), 117.7 (CH=CH_2), 67.1 (OCH_2), 20.3 (CH_3), 20.0 (CH_3), 20.3 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 313.8$ $(M + Na)^+$. $C_{19}H_{18}N_2O$ (290.36): C, 78.59; H, 6.25; N, 9.65; Found: C, 78.13; H, 6.56; N, 10.2.

1-Allyl-6,7-dimethyl-1,2-dihydro-2-quinoxalinone **3a**. White powder (1.87 g, 62%); $R_f = 0.27$ (petroleum ether/ethylacetate, 3:1); mp 142°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.33$ (s, 1H, CH), 7.71 (s, 1H, Ar-H), 7.20 (s, 1H, Ar-H), 6.15–6.00 (m, 1H, CH=CH_2), 5.46 (d, 1H, $J = 10.4$ Hz, CH), 5.29 (d, 1H, $J = 17.3$ Hz, CH), 5.00 (d, 2H, $J = 5.1$ Hz, NC$\underline{H}_2$), 2.53 (s, 3H, CH_3), 2.47 (s, 3H, CH_3). ^{13}C NMR (62.8 MHz): $\delta = 154.1$ (C=O), 148.4 (CH), 140.4 (C=N), 132.1 (C_q), 131.5 (C_q), 130.2 ($\underline{C}$H=CH_2), 130.0 (CH_{Ar}), 117.3 (CH=CH_2), 114.3 (CH_{Ar}), 43.4 (NCH_2), 20.1 (CH_3), 18.6 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 237.5$ $(M + Na)^+$. $C_{13}H_{14}N_2O$ (214.27): C, 72.87; H, 6.59; N, 13.07; Found: C, 73.11; H, 6.26; N, 12.82.

1-Allyl-3,6,7-trimethyl-1,2-dihydro-2-quinoxalinone **3b**. White powder (1.80 g, 56%); $R_f = 0.33$ (petroleum ether/ethylacetate, 3:1); mp 98°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.73$ (s, 1H, Ar-H), 7.22 (s, 1H, Ar-H), 6.24–6.09 (m, 1H, CH=CH_2), 5.48 (d, 1H, $J = 10.4$ Hz, CH), 5.38 (d, 1H, $J = 17.2$ Hz, CH), 5.07 (d, 2H, $J = 5.2$ Hz, NC$\underline{H}_2$), 2.79 (s, 3H, CH_3), 2.59 (s, 3H, CH_3), 2.53 (s, 3H, CH_3). ^{13}C NMR (62.8 MHz): $\delta = 156.4$ (C=O), 154.2 (C=N), 138.6 (C_q), 131.8 (C_q), 130.8 (C_q), 130.5 ($\underline{C}$H=CH_2), 129.9 (C_q), 129.1 (CH_{Ar}), 117.3 (CH=CH_2), 114.1 (CH_{Ar}), 43.8 (NCH_2), 20.9 (CH_3), 20.0 (CH_3), 18.7 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 251.5$ $(M + Na)^+$. $C_{14}H_{16}N_2O$ (228.29): C, 73.66; H, 7.06; N, 12.27; Found: C, 73.76; H, 7.23; N, 12.01.

1-Allyl-6,7-dimethyl-3-phenyl-1,2-dihydro-2-quinoxalinone **3c**. Yellow powder (2.55 g, 63%); $R_f = 0.55$ (petroleum ether/ethylacetate, 3:1); mp 129°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.26$–8.22 (m, 2H, Ar-H), 7.52 (s, 1H, Ar-H), 7.34–7.31 (m, 4H, Ar-H), 6.86 (s, 1H, Ar-H), 5.90–5.75 (m, 1H, CH=CH_2), 5.13 (d, 1H, $J = 10.3$ Hz, CH), 5.04 (d, 1H, $J = 17.0$ Hz, CH), 4.76 (m, 2H, NC$\underline{H}_2$), 2.21 (s, 3H, CH_3), 2.19 (s, 3H, CH_3). ^{13}C NMR (62.8 MHz): $\delta = 154.3$ (C=O), 152.5 (C=N), 140.2 (C_q), 136.3 (C_q), 132.6 (C_q), 131.7 (C_q), 131.0 (CH_{Ar}), 130.7 (C_q), 130.6 ($\underline{C}$H=CH_2), 130.0 (CH_{Ar}), 129.6 (CH_{Ar}), 128.0 (CH_{Ar}), 117.9 (CH=CH_2), 114.6 (CH_{Ar}), 44.5 (NCH_2), 20.7 (CH_3), 19.2 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 313.6$ $(M + Na)^+$. $C_{19}H_{18}N_2O$ (290.36): C, 78.59; H, 6.25; N, 9.65; Found: C, 79.01; H, 6.43; N, 9.36.

N- and O-Substituted Propanol Derivatives

Method A. A mixture of quinoxaline derivatives (14 mmol) and NaH (0.30 g, 14 mmol) in dry DMF (20 mL) was stirred at 100°C for 0.5 h, and then cooled to room temperature. 3-Bromopropanol (14 mmol) was added and the mixture was stirred at 100°C for 3 h. The reaction mixture was evaporated to dryness under reduced pressure, and the residue was chromatographed on silica gel column

with petroleum ether/ethylacetate as eluent to give the products.

Method B. To a solution of allyl quinoxaline derivatives (14 mmol) in dry THF (50 mL) at 0°C under argon atmosphere, BH_3·DMS (7 mL, 14 mmol, 2 M solution in THF) was added and the reaction mixture was allowed to warm to room temperature and stirred for 4 h. The reaction flask was cooled to 0°C and then a solution of NaOH (7 g, 28 mmol) in EtOH/H_2O (2:1, 18 mL) followed by H_2O_2 (4.7 mL, 42 mmol, 30%, w/v solution in water) were added dropwise over 30 min. It was then allowed to stir at room temperature for 3 h. The product was taken up in EtOAc and aqueous layer extracted with EtOAc (3×50 mL). The combined organic layers were washed with brine, water, dried (Na_2SO_4), and concentrated. The crude product was chromatographed using petroleum ether/ethylacetate (3:1) as eluent.

3-((6,7-Dimethyl-2-quinoxalinyl)oxy)-1-propanol **4a** *(Method A).* Yellow powder (0.84 g, 26%); $R_f = 0.21$ (petroleum ether/ethylacetate, 2:1); mp 79°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.27$ (s, 1H, CH), 7.63 (s, 1H, Ar-H), 7.41 (s, 1H, Ar-H), 4.55 (m, 2H, CH_2), 3.65 (m, 2H, CH_2), 3.10 (bs, 1H, OH), 2.32 (s, 6H, $2CH_3$), 1.90 (m, 2H, CH_2). ^{13}C NMR (62.8 MHz): $\delta = 157.1$ (C=N), 142.2 (C_q), 140.4 (C_q), 138.1 (C_q), 136.4 (C_q), 127.9 (CH_{Ar}), 126.2 (CH_{Ar}), 60.7 (CH_2), 58.6 (CH_2), 32.0 (CH_2), 20.1 (CH_3), 19.2 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 269.5$ $(M + Na)^+$. $C_{14}H_{18}N_2O_2$ (246.31): C, 68.27; H, 7.37; N, 11.37; Found: C, 68.11; H, 7.71; N, 10.98.

Method B: (2.56 g, 79%).

3-((3,6,7-Trimethyl-2-quinoxalinyl)oxy)-1-propanol **4b** *(Method A).* White powder (1.20 g, 35%); $R_f = 0.25$ (petroleum ether/ethylacetate, 2:1); mp 104°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.59$ (s, 1H, Ar-H), 7.42 (s, 1H, Ar-H), 4.56 (t, 2H, $J = 5.9$ Hz, CH_2), 3.74 (t, 2H, $J = 5.9$ Hz, CH_2), 3.50 (bs, 1H, OH), 2.51 (s, 3H, CH_3), 2.34 (s, 6H, $2CH_3$), 2.07–1.93 (m, 2H, CH_2). ^{13}C NMR (62.8 MHz): $\delta = 156.3$ (C=N), 146.8 (C=N), 139.1 (C_q), 138.1 (C_q), 137.3 (C_q), 136.3 (C_q), 127.5 (CH_{Ar}), 126.1 (CH_{Ar}), 63.3 (CH_2), 58.9 (CH_2), 32.8 (CH_2), 20.3 (CH_3), 20.2 (CH_3), 20.0 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 269.5$ $(M + Na)^+$. $C_{14}H_{18}N_2O_2$ (246.31): C, 68.27; H, 7.37; N, 11.37; Found: C, 68.11; H, 7.71; N, 10.98.

Method B: (2.82 g, 82%).

3-((6,7-Dimethyl-3-phenyl-2-quinoxalinyl)oxy)-1-propanol **4c** *(Method A).* Yellow powder (1.25 g, 29%); $R_f = 0.32$ (petroleum ether/ethylacetate, 2:1); mp 185°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.06$–7.97 (m, 2H, Ar-H), 7.81 (s, 1H, Ar-H), 7.54 (s, 1H, Ar-H), 7.49–7.39 (m, 3H, Ar-H), 4.70 (t, 2H, $J = 5.8$ Hz, CH_2), 3.72 (m, 2H, CH_2), 3.11 (bs, 1H, OH), 2.41 (s, 6H, $2CH_3$), 2.12–2.00 (m, 2H, CH_2). ^{13}C NMR (62.8 MHz): $\delta = 155.7$ (C=N), 145.7 (C=N), 140.6 (C_q), 138.3 (C_q), 138.1 (C_q), 137.1 (C_q), 130.5 (C_q), 129.8 (CH_{Ar}), 129.7 (CH_{Ar}), 128.7 (CH_{Ar}), 128.5 (CH_{Ar}), 126.1 (CH_{Ar}), 63.9 (CH_2), 59.5 (CH_2), 32.6 (CH_2), 20.5 (CH_3), 20.3 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 347.6$ $(M + K)^+$. $C_{19}H_{20}N_2O_2$ (308.38): C, 74.00; H, 6.54; N, 9.08; Found: C, 74.34; H, 7.01; N, 9.21.

Method B: (3.19 g, 74%).

1-(3-Hydroxypropyl)-6,7-dimethyl-1,2-dihydro-2-quinoxalinone **5a** *(Method A).* White powder (1.68 g, 58%); $R_f = 0.12$ (petroleum ether/ethylacetate, 2:1); mp 125°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.25$ (s, 1H, CH), 7.65 (s, 1H, Ar-H), 7.20 (s, 1H, Ar-H), 4.48 (t, 2H, $J = 5.9$ Hz, $OC\underline{H}_2$), 3.72 (bs, 1H, OH), 3.56 (m, 2H, $NC\underline{H}_2$), 2.44 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.14–1.93 (m, 2H, CH_2). ^{13}C NMR (62.8 MHz): $\delta = 155.7$ (C=O), 148.7 (CH), 141.3 (C=N), 133.1 (C_q), 132.1 (C_q), 130.7 (CH_{Ar}), 129.9 (C_q), 114.2 (CH_{Ar}), 58.0 ($O\underline{C}H_2$), 38.5 ($N\underline{C}H_2$), 29.9 (CH_2), 20.6 (CH_3), 19.0 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 255.4$ $(M + Na)^+$. $C_{13}H_{16}N_2O_2$ (232.28): C, 67.22; H, 6.94; N, 12.06; Found: C, 67.01; H, 7.21; N, 11.82.

Method B: (2.30 g, 71%).

1-(3-Hydroxypropyl)-3,6,7-trimethyl-1,2-dihydro-2-quinoxalinone **5b** *(Method A).* White powder (2.05 g, 61%); $R_f = 0.15$ (petroleum ether/ethylacetate, 2:1); mp 148°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.48$ (s, 1H, Ar-H), 7.07 (s, 1H, Ar-H), 4.33 (t, 2H, $J = 6.5$ Hz, $OC\underline{H}_2$), 3.80 (bs, 1H, OH), 3.50 (m, 2H, $NC\underline{H}_2$), 2.49 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.03–1.90 (m, 2H, CH_2). ^{13}C NMR (62.8 MHz): $\delta = 156.3$ (C=O), 155.6 (C=N), 139.4 (C_q), 132.7 (C_q), 131.5 (C_q), 129.9 (C_q), 129.7 (CH_{Ar}), 114.1 (CH_{Ar}), 58.2 ($\underline{C}H_2OH$), 38.8 ($N\underline{C}H_2$), 30.0 (CH_2), 21.2 (CH_3), 20.4 (CH_3), 19.0 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 268.1$ $(M + Na)^+$. $C_{14}H_{18}N_2O_2$ (246.31): C, 68.27; H, 7.37; N, 11.37; Found: C, 67.88; H, 7.51; N, 11.13.

Method B: (2.34 g, 68%).

1-(3-Hydroxypropyl)-6,7-dimethyl-3-phenyl-1,2-dihydro-2-quinoxalinone **5c** *(Method A).* Yellow

powder (2.67 g, 62%); $R_f = 0.19$ (petroleum ether/ethylacetate, 2:1); mp 210°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.32$–8.25 (m, 2H, Ar-H), 7.72 (s, 1H, Ar-H), 7.47–7.44 (m, 3H, Ar-H), 7.16 (s, 1H, Ar-H), 4.47 (t, 2H, $J = 6.1$ Hz, CH_2), 3.75 (bs, 1H, OH), 3.58 (m, 2H, CH_2), 2.35 (s, 3H, CH_3), 2.17–2.03 (m, 2H, CH_2), 2.42 (s, 3H, CH_3). ^{13}C NMR (62.8 MHz): $\delta = 155.3$ (C=O), 152.4 (C=N), 140.5 (C_q), 136.1 (C_q), 133.1 (C_q), 132.1 (C_q), 130.7 (CH_{Ar}), 130.0 (CH_{Ar}), 129.4 (CH_{Ar}), 128.2 (C_q), 127.9 (CH_{Ar}), 114.0 (CH_{Ar}), 58.2 (CH_2), 39.0 (CH_2), 30.2 (CH_2), 20.6 (CH_3), 19.06 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 331.4$ $(M + Na)^+$. $C_{19}H_{20}N_2O_2$ (308.38): C, 74.00; H, 6.54; N, 9.08; Found: C, 74.21; H, 6.62; N, 9.42.

Method B: (3.62 g, 84%).

General Procedure of Acetylation Reaction

The quinoxaline derivatives (2 mmol) were treated with acetic anhydride (20 mL) and pyridine (20 mL). The reaction mixture was stirred for 15 h, and then concentrated and purified by flash chromatography (petroleum ether/ethylacetate, 2:1).

3-((6,7-Dimethyl-2-quinoxalinyl)oxy)propyl Acetate **6a**. White powder (0.43 g, 81%); $R_f = 0.35$ (petroleum ether/ethylacetate, 2:1); mp 65°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.15$ (s, 1H, CH); 7.52 (s, 1H, Ar-H), 7.35 (s, 1H, Ar-H), 4.35 (t, 2H, $J = 6.2$ Hz, CH_2), 4.20 (t, 2H, $J = 6.2$ Hz, CH_2), 2.23 (s, 6H, $2CH_3$), 2.04–2.00 (m, 2H, CH_2), 1.92 (s, 3H, OAc). ^{13}C NMR (62.8 MHz): $\delta = 170.7$ (C=O), 156.8 (C=N), 138.7 (C_q), 138.6 (C_q), 138.1(C_q), 136.1 (C_q), 128.2 (CH_{Ar}), 126.5 (CH_{Ar}), 62.6 (CH_2), 61.1 (CH_2), 28.0 (CH_2), 20.7 (CH_3), 20.0 (CH_3), 19.7 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 297.2$ $(M + Na)^+ + 313.3$ $(M + K)^+$. $C_{15}H_{18}N_2O_3$ (274.32): C, 65.68; H, 6.61; N, 10.21; Found: C, 66.12; H, 6.32; N, 10.41.

3-((3,6,7-Trimethyl-2-quinoxalinyl)oxy)propyl Acetate **6b**. White powder (0.40 g, 71%); $R_f = 0.41$ (petroleum ether/ethylacetate, 2:1); mp 87°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.63$ (s, 1H, Ar-H), 7.50 (s, 1H, Ar-H), 4.50 (t, 2H, $J = 6.3$ Hz, CH_2), 4.25 (t, 2H, $J = 6.3$ Hz, CH_2), 2.56 (s, 3H, CH_3), 2.37 (s, 6H, $2CH_3$), 2.28–2.11 (m, 2H, CH_2), 2.02 (s, 3H, OAc). ^{13}C NMR (62.8 MHz): $\delta = 170.9$ (C=O), 155.8 (C=N), 146.6 (C=N), 138.7 (C_q), 138.3 (C_q), 137.2 (C_q), 135.9 (C_q), 127.5 (CH_{Ar}), 126.2 (CH_{Ar}), 62.7 (CH_2), 61.4 (CH_2), 28.2 (CH_2), 20.8 (CH_3), 20.1 (CH_3), 20.0 (CH_3), 19.8 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 311.5$ $(M + Na)^+$. $C_{16}H_{20}N_2O_3$ (288.34): C, 66.65; H, 6.99; N, 9.72; Found: C, 66.31; H, 7.21; N, 9.43.

3-((6,7-Dimethyl-3-phenyl-2-quinoxalinyl)oxy)propyl Acetate **6c**. Yellow powder (0.47 g, 68%); $R_f = 0.52$ (petroleum ether/ethylacetate, 2:1); mp 95°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.06$ (s, 1H, Ar-H), 7.94–7.89 (m, 2H, Ar-H), 7.79 (s, 1H, Ar-H), 7.62–7.49 (m, 3H, Ar-H), 4.63 (t, 2H, $J = 6.2$ Hz, CH_2), 4.29 (t, 2H, $J = 6.2$ Hz, CH_2), 2.51 (s, 6H, $2CH_3$), 2.26–2.18 (m, 2H, CH_2), 2.04 (s, 3H, OAc). ^{13}C NMR (62.8 MHz): $\delta = 168.5$ (C=O), 145.3 (C=N), 141.1 (C=N), 140.4 (C_q), 138.4 (C_q), 129.5 (CH_{Ar}), 128.9 (CH_{Ar}), 128.1 (CH_{Ar}), 127.3 (CH_{Ar}), 126.1 (CH_{Ar}), 63.2 (CH_2), 61.6 (CH_2), 28.2 (CH_2), 21.1 (CH_3), 20.3 (CH_3), 19.9 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 373.4$ $(M + Na)^+$. $C_{21}H_{22}N_2O_3$ (350.41): C, 71.98; H, 6.33; N, 7.99; Found: C, 72.14; H, 6.52; N, 8.35.

3-(6,7-Dimethyl-2-oxo-1,2-dihydro-1-quinoxalinyl)propyl Acetate **10a**. Yellow powder (0.41 g, 77%); $R_f = 0.2$ (petroleum ether/ethylacetate, 2:1); mp 80°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.16$ (s, 1H, CH), 7.58 (s, 1H, Ar-H), 7.12 (s, 1H, Ar-H), 4.35 (t, 2H, $J = 6.0$ Hz, OCH_2), 4.20 (t, 2H, $J = 6.0$ Hz, $NC\underline{H}_2$), 2.43 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.15–2.09 (m, 5H, OAc, CH_2). ^{13}C NMR (62.8 MHz): $\delta = 170.3$ (C=O), 154.4 (C=O), 148.4 (CH), 140.6 (C=N), 132.2 (C_q), 131.7 (C_q), 130.3 (C_q), 129.9 (CH_{Ar}), 113.1 (CH_{Ar}), 61.5 ($O\underline{C}H_2$), 38.5 ($N\underline{C}H_2$), 26.1 (CH_2), 20.4 (CH_3), 20.3 (CH_3), 18.6 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 297.2$ $(M + Na)^+$. $C_{15}H_{18}N_2O_3$ (274.32): C, 65.68; H, 6.61; N, 10.21; Found: C, 65.73; H, 6.52; N, 10.43.

3-(3,6,7-Trimethyl-2-oxo-1,2-dihydro-1-quinoxalinyl)propyl Acetate **10b**. White powder (0.48 g, 85%); $R_f = 0.22$ (petroleum ether/ethylacetate, 2:1); mp 121°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.48$ (s, 1H, Ar-H), 6.99 (s, 1H, Ar-H), 4.26 (t, 2H, $J = 6.1$ Hz, $OC\underline{H}_2$), 4.14 (t, 2H, $J = 6.1$ Hz, $NC\underline{H}_2$), 2.49 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 2.08–1.99 (m, 5H, OAc, CH_2). ^{13}C NMR (62.8 MHz): $\delta = 170.7$ (C=O), 156.8 (C=O), 154.9 (C=N), 139.1 (C_q), 132.3 (C_q), 131.3 (C_q), 130.2 (C_q), 129.8 (CH_{Ar}), 113.7 (CH_{Ar}), 61.8 (CH_2), 39.1 (CH_2), 26.5 (CH_2), 21.2 (CH_3), 20.7 (CH_3), 20.5 (CH_3), 19.0 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 311.6$ $(M + Na)^+$. $C_{16}H_{20}N_2O_3$ (288.34): C, 66.65; H, 6.99; N, 9.72; Found: C, 66.84; H, 7.22; N, 9.54.

3-(6,7-Dimethyl-2-oxo-3-phenyl-1,2-dihydro-1-quinoxalinyl)propyl Acetate **10c**. Yellow powder (0.56 g, 80%); $R_f = 0.30$ (petroleum ether/ethylacetate, 2:1); mp 175°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.33$–8.24 (m, 2H, Ar-H), 7.65 (s, 1H, Ar-H), 7.48–7.41 (m, 3H, Ar-H), 7.06 (s, 1H, Ar-H), 4.36 (t, 2H, $J = 5.9$ Hz, $OC\underline{H}_2$), 4.21 (t, 2H, $J = 5.9$ Hz, $NC\underline{H}_2$), 2.39 (s, 3H, CH_3),

2.32 (s, 3H, CH_3), 2.18 (m, 2H, CH), 2.10 (s, 3H, OAc). ^{13}C NMR (62.8 MHz): $\delta = 170.8$ (C=O), 154.5 (C=O), 152.7 (C=N), 140.3 (C_q), 136.2 (C_q), 132.6 (CH_{Ar}), 131.9 (C_q), 130.8 (CH_{Ar}), 130.5 (C_q), 129.5 (CH_{Ar}), 127.9 (CH_{Ar}), 62.1 (O<u>C</u>H$_2$), 39.6 (N<u>C</u>H$_2$), 26.6 (CH_2), 20.8 (CH_3), 20.2 (CH_3), 19.1 (CH_3). (MALDI, positive mode, Matrix: DHB): $m/z = 373.5$ $(M + Na)^+$. $C_{21}H_{22}N_2O_3$ (350.42): C, 71.98; H, 6.33; N, 7.99; Found: C, 72.31; H, 6.29; N, 7.75.

General Procedure (O- and N-Propanediol **7** *and* **11***)*

To a mixture of AD-mix β (0.7 g), *tert*-butyl alcohol (3 mL) and water (5 mL) were added and the mixture was stirred vigorously for 20 min before being cooled to 0°C. Allyl quinoxaline derivatives (0.5 mmol) in *tert*-butyl alcohol (2 mL) was added and the mixture was stirred for 2 days. Sodium sulfite (0.62 g, 5 mmol) and water (20 mL) were added and crude product was extracted with dichloromethane (3×20 mL). The solvent was removed at reduced pressure and purified by flash chromatography (methanol/chloroform, 3%).

3-((6,7-Dimethyl-2-quinoxalinyl)oxy)-1,2-propanediol **7a**. White powder (0.07 g, 55%); $R_f = 0.53$ (methanol/chloroform, 5%); mp 119°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.40$ (s, 1H, CH), 7.71 (s, 1H, Ar-H), 7.50 (s, 1H, Ar-H), 4.54 (d, 2H, $J = 4.5$ Hz, OC<u>H</u>$_2$), 4.14–4.10 (m, 1H, C<u>H</u>OH), 3.76–3.71 (m, 2H, C<u>H</u>$_2$OH), 4.05 (bs, 1H, OH), 3.40 (bs, 1H, OH), 2.36 (s, 6H, $2CH_3$). ^{13}C NMR (62.8 MHz): $\delta = 156.7$ (C=N), 140.7 (C=N), 137.9 (CH), 137.5 (C_q), 136.8 (C_q), 127.9 (CH_{Ar}), 126.0 (CH_{Ar}), 70.5 (<u>C</u>HOH), 67.7 (O<u>C</u>H$_2$), 63.1 (<u>C</u>H$_2$OH), 20.0 (CH_3), 19.7 (CH_3). EI-MS: $m/z = 248.0$; $C_{13}H_{16}N_2O_3$ (248.28): C, 62.89; H, 6.50; N, 11.28; Found: C, 63.21; H, 6.59; N, 11.32.

3-((3,6,7-Trimethyl-2-quinoxalinyl)oxy)-1,2-propanediol **7b**. White powder (0.08 g, 65%); $R_f = 0.58$ (methanol/chloroform, 5%); mp 178°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.61$ (s, 1H, Ar-H), 7.43 (s, 1H, Ar-H), 4.56 (d, 2H, $J = 4.5$ Hz, CH_2), 4.18–4.08 (m, 1H, C<u>H</u>OH), 4.04 (bs, 1H, OH), 3.77–3.66 (m, 2H, C<u>H</u>$_2$OH), 3.21 (bs, 1H, OH), 2.54 (s, 3H, CH_3), 2.35 (s, 6H, $2CH_3$). ^{13}C NMR (62.8 MHz): $\delta = 155.9$ (C=N), 146.7 (C=N), 139.4 (C_q), 137.5 (C_q), 137.4 (C_q), 138.7 (C_q), 127.5 (CH_{Ar}), 125.8 (CH_{Ar}), 70.9 (<u>C</u>HOH), 68.2 (O<u>C</u>H$_2$), 63.5 (<u>C</u>H$_2$OH), 20.2 (CH_3), 20.1 (CH_3), 19.9 (CH_3). EI-MS: $m/z = 262.0$; $C_{14}H_{18}N_2O_3$ (262.31): C, 64.11; H, 6.92; N, 10.68; Found: C, 64.43; H, 6.75; N, 11.01.

3-((6,7-Dimethyl-3-phenyl-2-quinoxalinyl)oxy)-1,2-propanediol **7c**. White powder (0.12 g, 73%); $R_f = 0.63$ (methanol/chloroform, 5%); mp 115°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.05$–7.98 (m, 2H, Ar-H), 7.82 (s, 1H, Ar-H), 7.55 (s, 1H, Ar-H), 7.47–7.42 (m, 3H, Ar-H), 4.56 (m, 2H, CH_2), 4.19–4.12 (m, 1H, C<u>H</u>OH), 4.07 (bs, 1H, OH), 3.78–3.65 (m, 2H, C<u>H</u>$_2$OH), 3.26 (bs, 1H, OH), 2.40 (s, 6H, $2CH_3$). ^{13}C NMR (62.8 MHz): $\delta = 155.1$ (C=N), 145.4 (C=N), 140.6 (C_q), 138.0 (C_q), 137.7 (C_q), 137.3 (C_q), 136.1 (C_q), 129.6 (CH_{Ar}), 128.4 (CH_{Ar}), 128.3 (CH_{Ar}), 125.8 (CH_{Ar}), 70.8 (<u>C</u>HOH), 68.4 (O<u>C</u>H$_2$), 63.7 (<u>C</u>H$_2$OH), 20.4 (CH_3), 20.1 (CH_3). EI-MS: $m/z = 324.0$; $C_{19}H_{20}N_2O_3$ (324.38): C, 70.35; H, 6.21; N, 8.64; Found: C, 70.41; H, 6.32; N, 8.81.

1-(2,3-Dihydroxypropyl)-6,7-dimethyl-1,2-dihydro-2-quinoxalinone **11a**. White powder (0.08 g, 61%); $R_f = 0.32$ (methanol/chloroform, 5%); mp 164°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.20$ (s, 1H, CH), 7.58 (s, 1H, Ar-H),), 7.25 (s, 1H, Ar-H), 4.89–4.78 (bs, 1H, OH), 4.47 (dd, 1H, $J_{gem} = 12.0$ Hz, $J_{1,2'} = 7.6$ Hz, OC<u>H</u>$_2$), 4.25 (dd, 1H, $J_{gem} = 12.0$ Hz, $J_{1,2'} = 6.2$ Hz, OC<u>H</u>$_2$), 4.16–4.02 (m, 1H, C<u>H</u>OH), 3.78–3.48 (bs, 1H, OH), 3.68 (dd, 1H, $J_{gem} = 10.9$ Hz, $J_{1,2'} = 3.6$ Hz, NC<u>H</u>$_2$), 3.53 (dd, 1H, $J_{gem} = 11.0$ Hz, $J_{1',2'} = 2.9$ Hz, NC<u>H</u>$_2$), 2.37 (s, 3H, CH_3), 2.29 (s, 3H, CH_3). ^{13}C NMR (62.8 MHz): $\delta = 156.0$ (C=O), 148.1 (CH), 141.5 (C=N), 133.4 (C_q), 132.3 (C_q), 130.4 (CH_{Ar}), 118.1 (C_q), 114.7 (CH_{Ar}), 69.5 (<u>C</u>HOH), 63.2 (O<u>C</u>H$_2$), 44.3 (N<u>C</u>H$_2$), 20.5 (CH_3), 19.0 (CH_3). EI-MS: $m/z = 248.0$; $C_{13}H_{16}N_2O_3$ (248.28): C, 62.89; H, 6.50; N, 11.28; Found: C, 63.09; H, 6.63; N, 11.40.

1-(2,3-Dihydroxypropyl)-3,6,7-trimethyl-1,2-dihydro-2-quinoxalinone **11b**. White powder (0.08 g, 56%); $R_f = 0.42$ (methanol/chloroform, 5%); mp 211°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.56$ (s, 1H, Ar-H), 7.23 (s, 1H, Ar-H), 4.51 (dd, 1H, $J_{gem} = 12.6$ Hz, $J_{1',2'} = 7.6$ Hz, OC<u>H</u>$_2$), 4.23 (dd, 1H, $J_{gem} = 12.6$ Hz, $J_{1',2'} = 5.8$ Hz, OC<u>H</u>$_2$), 4.18–4.00 (m, 1H, C<u>H</u>OH), 3.72–3.70 (bs, 2H, 2OH), 3.68 (dd, 1H, $J_{gem} = 12.5$ Hz, $J_{1',2'} = 3.2$ Hz, NC<u>H</u>$_2$), 3.50 (dd, 1H, $J_{gem} = 12.5$ Hz, $J_{1',2'} = 3.2$ Hz, NC<u>H</u>$_2$), 2.48 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 2.33 (s, 3H, CH_3). ^{13}C NMR (62.8 MHz): $\delta = 156.3$ (C=O), 156.2 (C=N), 139.9 (C_q), 133.3 (C_q), 131.6 (C_q), 130.3 (C_q), 129.8 (CH_{Ar}), 114.3 (CH_{Ar}), 69.5 (<u>C</u>HOH), 63.0 (<u>C</u>H$_2$OH), 44.5 (N<u>C</u>H$_2$), 21.3 (CH_3), 20.5 (CH_3), 19.1 (CH_3). EI-MS: $m/z = 262.0$; $C_{14}H_{18}N_2O_3$ (262.31): C, 64.11; H, 6.92; N, 10.68; Found: C, 63.76; H, 6.74; N, 10.53.

1-(2,3-Dihydroxypropyl)-6,7-dimethyl-3-phenyl-1,2-dihydro-2-quinoxalinone **11c**. White powder (0.05 g, 55%); $R_f = 0.51$ (methanol/chloroform, 5%);

mp 130°C. ^{1}H NMR ($CDCl_3$): $\delta = 8.29$–8.19 (m, 2H, Ar-H), 7.64 (s, 1H, Ar-H), 7.46–7.32 (m, 3H, Ar-H), 7.23 (s, 1H, Ar-H), 4.96–4.76 (bs, 1H, OH), 4.47 (dd, 1H, $J_{gem} = 12.5$ Hz, $J_{1',2'} = 7.8$ Hz, OC$\underline{H}_2$), 4.28 (dd, 1H, $J_{gem} = 12.5$ Hz, $J_{1',2'} = 6.5$ Hz, OC$\underline{H}_2$), 4.18–3.95 (bs, 2H, C$\underline{H}$OH, CHO$\underline{H}$), 3.71 (dd, 1H, $J_{gem} = 10.8$ Hz, $J_{1',2'} = 3.7$ Hz, NC$\underline{H}_2$), 3.53 (dd, 1H, $J_{gem} = 10.7$ Hz, $J_{1',2'} = 3.5$ Hz, NC$\underline{H}_2$), 2.42 (s, 3H, CH_3), 2.30 (s, 3H, CH_3). ^{13}C NMR (62.8 MHz): $\delta = 155.6$ (C=O), 154.3 (C=N), 140.9 (C_q), 135.9 (C_q), 133.4 (C_q), 132.0 (C_q), 130.9 (C_q), 130.5 (CH_{Ar}), 130.0 (CH_{Ar}), 129.5 (CH_{Ar}), 127.9 (CH_{Ar}), 114.6 (CH_{Ar}), 69.5 ($\underline{C}$HOH), 63.3 (O$\underline{C}H_2$), 44.6 (N$\underline{C}H_2$), 20.6 (CH_3), 19.1 (CH_3). EI-MS: $m/z = 324.0$; $C_{19}H_{20}N_2O_3$ (324.38): C, 70.35; H, 6.21; N, 8.64; Found: C, 69.87; H, 6.43; N, 8.54.

2-Hydroxy-3-((3,6,7-trimethyl-2-quinoxalinyl)oxy)-propyl-p-toluenesulfonate **8**. To a mixture of diol derivative **7b** (0.15 g, 0.59 mmol) and *p*-toluenesulfonyl chloride (0.12 g, 0.65 mmol) in dichloromethane (10 mL) cooled to 0°C, pyridine (0.2 mL, 2.5 mmol) was added with stirring for 1 h. The mixture was allowed to warm to room temperature, stirred for 24 h, then poured into water. The aqueous layer was extracted with dichloromethane (3×20 mL) and the combined organic extracts washed with hydrochloric acid (1 M), water, and brine. After drying over anhydrous magnesium sulfate, the solvent was removed at reduced pressure and the crude product was purified by flash chromatography using petroleum ether/ethyacetate as eluent. White powder (0.18 g, 77%); $R_f = 0.36$ (petroleum ether/ethyacetate, 3:1); mp 83°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.91$ (d, 2H, $J = 8.2$ Hz, Ar-H), 7.61 (s, 1H, Ar-H), 7.50 (s, 1H, Ar-H), 7.35 (d, 2H, $J = 8.2$ Hz, Ar-H), 6.23–6.03 (m, 1H, CH), 5.43 (d, 1H, $J = 17.2$ Hz, CH), 5.26 (d, 1H, $J = 10.5$ Hz, CH), 4.94 (d, 2H, $J = 5.4$ Hz, OC$\underline{H}_2$), 2.58 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.37 (s, 6H, $2CH_3$). ^{13}C NMR (62.8 MHz): $\delta = 155.6$ (C=N), 146.6 (C=N), 141.7 (C_q), 138.7 (C_q), 138.3 (C_q), 137.3 (C_q), 135.9 (C_q), 133.0 (CH_{Ar}), 130.1 (CH_{Ar}), 127.5 (CH_{Ar}), 126.9 (CH_{Ar}), 126.3 (CH), 117.5 (CH_2), 66.7 (CH_2), 21.7 (CH_3), 20.2 (CH_3), 20.0 (CH_3), 19.8 (CH_3). EI-MS: $m/z = 416.0$; $C_{21}H_{24}N_2O_5S$ (416.49): C, 60.56; H, 5.81; N, 6.70; Found: C, 60.75; H, 5.90; N, 6.83.

Attempted Cyclization of **8**

2-(Allyloxy)-3,6,7-trimethylquinoxaline **2b**. To a solution of monotosylate derivative **8** (0.05 g, 0.11 mmol) in tetrahydrofuran (20 mL) at room temperature, sodium hydride (20 mg, of a 60% dispersion in mineral oil, 0.4 mmol) was added and the mixture was stirred for 24 h. Water (50 mL) was added slowly and the mixture was extracted with dichloromethane (3×30 mL). The combined extracts were washed with water (2×20 mL), brine (2×30 mL), and dried over anhydrous magnesium sulfate. The solvent was removed at reduced pressure and the crude product was purified by flash chromatography. White powder (0.021 g, 75%); $R_f = 0.78$ (petroleum ether/ethylacetate, 3:1); mp 72°C. ^{1}H NMR ($CDCl_3$): $\delta = 7.59$ (s, 1H, Ar-H), 7.46 (s, 1H, Ar-H), 6.18–6.05 (m, 1H, CH=CH_2), 5.41 (d, 1H, $J = 17.4$ Hz, CH), 5.24 (d, 1H, $J = 10.8$ Hz, CH), 4.91 (m, 2H, OC$\underline{H}_2$), 2.56 (s, 3H, CH_3), 2.33 (s, 6H, $2CH_3$).

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