Synthesis of Pyrrolo[1,2-*a*]quinoxaline Derivatives by Lewis Acid-Catalyzed Reactions of 1-(2-Isocyanophenyl)pyrroles

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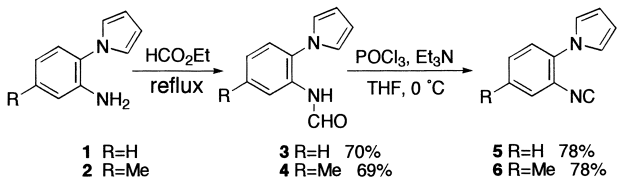
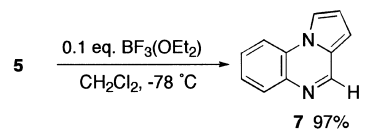
1-(2-Isocyanophenyl)pyrroles have been prepared. They react in moderate to good isolated yields with aldehydes (or ketones), oxiranes, and acetals in the presence of catalytic amounts of diethyl ether–boron trifluoride to give pyrrolo[1,2-*a*]quinoxalines carrying an oxyalkyl substituent, such as α-hydroxyalkyl, β-hydroxyalkyl, or α-alkoxyalkyl, at the 4-position.

Pyrrolo[1,2-*a*]quinoxaline derivatives have held considerable interest for not only organic but also medicinal chemists because of their enzyme inhibitory,[1a] antiallergic,[1b,c] antagonistic,[1d–f] and other biological activities.[1c,g] A number of methods for the preparation of this class of molecules have been reported.[2] For example, Weidner and co-workers have recently reported a pyrrolo[1,2-*a*]quinoxaline derivative using the reaction of diphenylcyclopropenone with quinoxaline.[2k] Most of previous methods involve either multi-steps and/or incomplete generality. For these reasons we have embarked upon development of a new efficient method for synthesizing substituted pyrrolo[1,2-*a*]quinoxalines. In our preliminary communication, we reported on a synthesis of 4-(1-hydroxyalkyl)pyrrolo[1,2-*a*]quinoxalines by a boron trifluoride-catalyzed reaction of 1-(2-isocyanophenyl)pyrrole with aldehydes or ketones, which involve two carbon–carbon bond formations in one-pot procedure.[3,4] We have found that pyrrolo[1,2-*a*]quinoxalines carrying an oxyalkyl substituent, such as β-hydroxyalkyl or α-alkoxyalkyl, at the 4-position could be prepared by using oxiranes[5] or acetals[6] as well as aldehydes (or ketones). In this paper we wish to describe the full details concerning these boron trifluoride-catalyzed heterocyclization reactions.

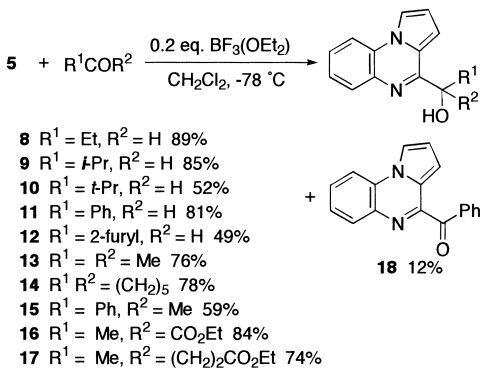
The preparation of the starting isocyanides **5** and **6** is outlined in Scheme 1. Thus, formylation of 1-(2-aminophenyl)pyrroles, which are commercially available (**1**) or easily prepared by the reported method (**2**),[2a] in refluxing ethyl formate gave 1-(2-formylaminophenyl)pyrroles **3** and **4**[2b] in good yields. These pyrroles were dehydrated with phosphoryl chloride/triethylamine in THF to afford **5** and **6**, respectively, in excellent yields as pale-yellow needles after recrystallization from pentane. These isocyanides are relatively stable and storable at refrigerator temperature under argon for several weeks.



Scheme 1.



Scheme 2.



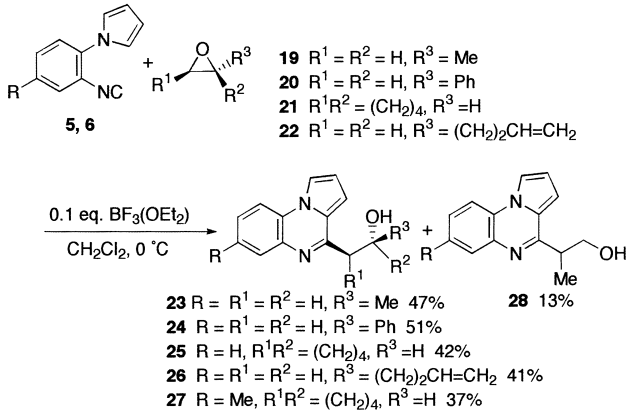
Scheme 3.

The starting isocyanide **5** with 0.1 molar amount of diethyl ether–boron trifluoride under mild conditions (in CH_2Cl_2, 0 °C, 1 h) resulted in smooth (1 h) and almost quantitative conversion into pyrrolo[1,2-*a*]quinoxaline (**7**),[2a] as shown in Scheme 2.

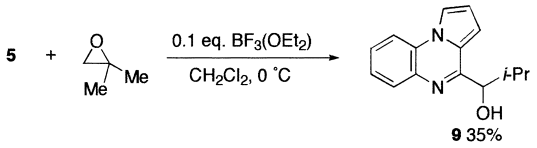
We next examined the reaction of isocyanide **5** with carbonyl compounds, such as aldehydes and ketones, as outlined in Scheme 3. The boron trifluoride-catalyzed reactions of **5** with aldehydes or ketones also proceeded under the above conditions to give the corresponding 4-(1-hydroxyalkyl)pyrrolo[1,2-*a*]quinoxalines **8**–**17** but in low yields. For example, in the reaction of **5** with propanal (propionaldehyde), only 32% yield of the expected product **8** was isolated from a complex mix-

ture, which included some starting isocyanyde (56%). The use of an equimolar amount of the Lewis acid gave somewhat increased yield of **8** (48%) along with the formation of fairly large quantities of pyrrolo[1,2-*a*]quinoxaline (**7**) (48%). The use of other Lewis acids gave much inferior results; $TiCl_4$ and $SnCl_4$ gave **8** in about 5% yields, and $ZnCl_2$ and $AlCl_3$ gave no more than a trace amount of **8**. However, we found that the yield of **8** was considerably improved (89%) when two portions of 0.1 molar amount each of the catalyst were added at 20 min intervals. The results using a range of ketones and aldehydes are summarized in Scheme 3, which shows that generally good yields of products are obtained. 2,2-Dimethylpropanal could also be used to give the expected quinoxaline derivative **10** in fair yield. With benzaldehyde, the expected product **11** was obtained in high yield, along with a small quantity of the corresponding 4-benzoyl derivatives **18**. Furan-2-carbaldehyde and acetophenone gave the corresponding products **12** and **15** in modest yields, presumably due to the acid-lability of the furan ring of furan-2-carbaldehyde and the low reactivity of acetophenone, respectively. The ester moieties of keto esters proved to be inert under the present reaction conditions and the hydroxy ester products **16** and **17** could be obtained in good yields.

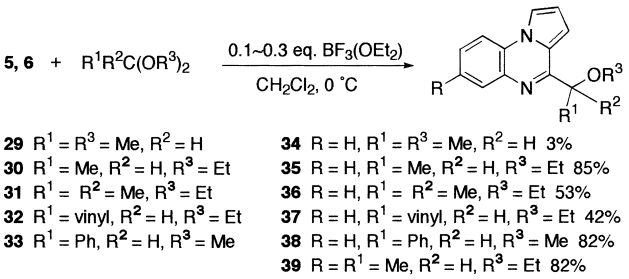
In order to evaluate the generality of the present pyrroloquinoxaline formation, we then investigated the boron trifluoride-catalyzed reaction of the (isocyanophenyl)pyrroles **5** and **6** with oxiranes **19**–**22** (Scheme 4). These oxiranes had a tendency of low electropilicity to the isocyano moiety under the above conditions. Only modest yields of the desired 4-(2-hydroxyalkyl)pyrrolo[1,2-*a*]quinoxalines **23**–**28** were obtained for these reactions even at an intermitting adding of boron trifluoride. The preferred formation of **23** over **28** from 1-methyloxirane (**19**) and the exclusive formation of **24** from 1-phenyloxirane (**20**) appear to result from a S_N2-like mechanism rather than from a S_N1-like mechanism. Isocyanides **5** and **6** reacted with cyclohexene oxide (**21**) with complete stereoselectivity to give *trans* (tentatively determined) isomers **25** and **27**, in each case. It was interesting to find that treatment of **5** with 2,2-dimethyloxirane under the same conditions gave only 4-(1-hydroxy-2-methylpropyl)pyrrolo[1,2-*a*]quinoxaline (**9**) in moderate yield, as shown in Scheme 5. Presumably, the boron trifluoride catalyzed-isomerization of 2,2-dimethyloxirane to



Scheme 4.



Scheme 5.

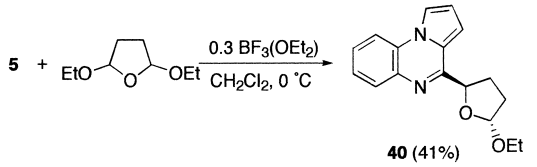


Scheme 6.

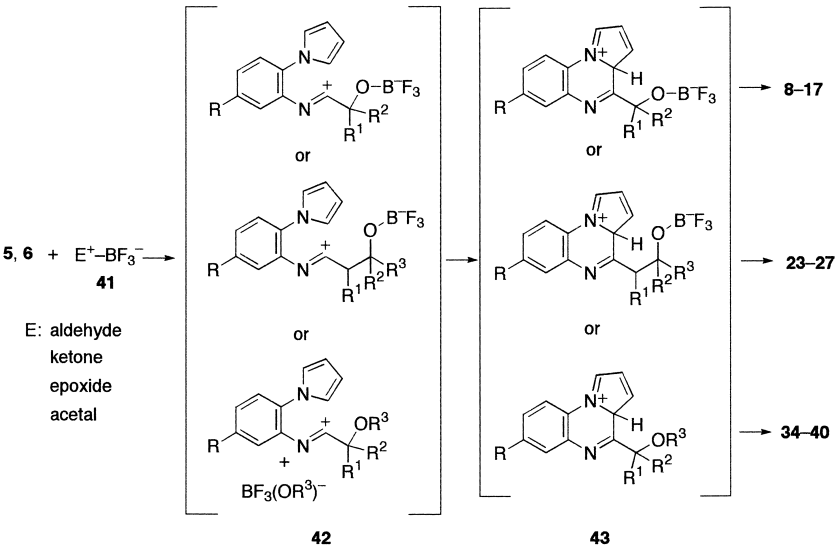
2-methylpropanal took place prior to the reaction with the isocyanide **5** to give rise to **9**. A limitation of the present method is indicated by the reaction with 2-methoxymethyl oxirane and 2-chloromethyloxirane giving only intractable mixtures.

We extend this new method to the synthesis of 4-(1-alkoxyalkyl)pyrrolo[1,2-a]quinoxalines **34**–**39**. Thus, isocyano pyrroles **5** and **6** were treated with acetals **29**–**33** in the presence of diethyl ether–boron trifluoride, as outlined in Scheme 6. First **5** was allowed to react with acetaldehyde dimethyl acetal (**29**) in the presence of 0.1 molar amount of diethyl ether–boron trifluoride. However, this reaction did not proceed cleanly, and only a very low yield (3%) of the desired product **34** (along with 4-methylpyrrolo[1,2-*a*]quinoxaline; 19%) was isolated from the complicated reaction mixture. Diethyl acetals proved to show superior results by using intermitting addition of 0.3 molar amount of boron trifluoride. Thus, although a complex product mixture, including starting material, was obtained in each reaction when 0.1 molar amount of catalyst was used, a much cleaner reaction resulted when three portions of 0.1 molar amount of catalyst were added at 30 min intervals. Phenylacetaldehyde dimethyl acetal (**33**) gave a modest yield of the desired product **38** with a negligible quantity of 4-methylpyrrolo[1,2-*a*]quinoxaline. A limitation was again indicated by the formation of an intractable mixture in the reaction with bromoacetaldehyde diethyl acetal.

We planned to prepare a tetrahydrofuran derivative bearing two pyrrolo[1,2-*a*]quinoxaline substituents. Thus, 2,5-diethoxytetrahydrofuran was treated with 2 molar amounts of isocyanide **5** under the above intermitting addition conditions, and 4-(*trans*-5-ethoxytetrahydrofuran-2-yl)pyrrolo[1,2-*a*]quinoxaline (**40**) (the stereochemistry was tentative) (Scheme 7)



Scheme 7.



Scheme 8.

was obtained as a sole isolated product in moderate yield; however, no trace amount of its diastereomer or the desired bis(pyrroloquinoxanyl)tetrahydrofuran could be obtained. Failure of **40** to react with **5** is probably the result of unfavorable steric interactions between the pyrroloquinoxalinyl group of **40** and **5**.

The pathway which led to the substituted pyrroloquinoxalines **8**–**17**, **23**–**27**, and **34**–**40** from the 1-(2-isocyanophenyl)pyrroles **5** and **6** is outlined in Scheme 8. Thus, attack of the isocyano carbon to the activated electrophile **41** generates the intermediate **42**. An intramolecular combination of the 2-carbon of the pyrrole and the cation center of **42** affords **43**, which gives rise to the pyrroloquinoxaline derivatives.

From the synthetic point of view, we now have a sequence of reactions whereby pyrrolo[1,2-*a*]quinoxaline derivatives carrying an oxy functional group at the 4-position can be prepared efficiently. Since the method employs readily available starting materials and is experimentally simple, it may prove useful in organic synthesis.

Experimental

General. The mps were recorded with a Laboratory Devices MEL-TEMP II melting point apparatus and are uncorrected. The IR spectra were determined for KBr disks (unless stated otherwise) with a Perkin-Elmer 1600 Series FT IR spectrometer. The ^{1}H NMR spectra were determined using $SiMe_4$ as an internal reference with a JEOL JNM-GX270 FT NMR spectrometer operating at 270 MHz in $CDCl_3$, unless otherwise stated. Low-resolution mass spectra were recorded on a JEOL AUTOMASS 20 spectrometer (Center for Joint Research and Development, this University). High-resolution MS analyses were performed a JEOL JMS-AX505 HA spectrometer (Faculty of Agriculture, this University). Column chromatography was carried out on Merck Kieselgel 60 F_{254}. Thin-layer chromatography (TLC) was carried out on Merck Kieselgel 60 PF_{254}. All of the solvents used were dried over appropriate drying agents and distilled under argon prior to use. All reactions were carried out under argon.

1-[(2-Formylamino)phenyl]pyrrole 3.[2b] 1-(2-Aminophenyl)pyrrole (**1**) (29 mmol, 4.5 g; commercially available) was dissolved in ethyl formate (48 mL) and the solution was heated under reflux for 9 d. After cooling, the solvent was removed using a rotary evaporator. The residual solid was recrystallized from hexane–AcOEt to give the title compound **3** as pale-yellow needles (3.7 g, 70%); mp 123–124 °C; IR 3279, 1693, and 1659 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 6.27 (2H, t, J = 2.1 Hz), 6.91 (2H, t, J = 2.1 Hz), 7.2–7.8 (4H, m), 8.16 (1H, br s), and 9.00 (1H, br s).

1-(2-Isocyanophenyl)pyrrole 5. To a stirred solution of the above fromamide **3** (5.0 mmol, 0.93 g) in THF (20 mL) containing Et_3N (22 mmol, 2.3 g) at 0 °C under argon was added dropwise $POCl_3$ (3.3 mmol, 0.51 g), and the mixture was stirred for 12 min at the same temperature. Aqueous $NaHCO_3$ was added to the reaction mixture, and the organic materials were extracted with Et_2O. The extract was dried over anhydrous K_2CO_3. Evaporation of the solvent gave a residual solid, which was recrystallized from hexane to give the title compound **5** (0.66 g, 78%); mp 42–43 °C; IR 2122 cm^{-1}; ^{1}H NMR δ 6.39 (2H, t, J = 2.1 Hz), 7.02 (2H, t, J = 2.1 Hz), and 7.3–7.55 (4H, m); MS m/z (%) 168 (M^+, 100). Found: m/z 168.0676. $C_{11}H_8N_2$: M, 168.0688.

1-(2-Amino-4-methylphenyl)pyrrole 2. This compound was prepared according to the procedure reported by Cheeseman et al.[2a] ^{1}H NMR δ 2.30 (3H, s), 3.63 (2H, br), 6.32 (2H, t, J = 2.1 Hz), 6.55–6.65 (2H, m), 6.80 (2H, t, J = 2.1 Hz), and 7.03 (1H, d, J = 7.9 Hz).

1-(2-Formylamino-4-methylphenyl)pyrrole 4. This compound was prepared under conditions similar to those described above for the preparation of **3**. Mp 73–75 °C (hexane–AcOEt); IR 3271 and 1667 cm^{-1}; ^{1}H NMR δ 2.41 (3H, s), 6.38 (2H, t, J = 2.1 Hz), 6.75 (2H, t, J = 2.1 Hz), 6.99 (1H, d, J = 7.4 Hz), 7.1–7.2 (2H, m), 8.29 (1H, s), and 8.29 (1H, br. s); MS m/z (%) 200 (M^+, 75) and 171 (100). Found: C, 71.75; H, 6.07; N, 14.22%. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99%.

1-(2-Isocyano-4-methylphenyl)pyrrole 6. This compound was prepared under conditions similar to those described above for the preparation of **5**. Mp 97–99 °C (hexane); IR 2125 cm^{-1}; ^{1}H NMR δ 2.39 (3H, s), 6.36 (2H, t, J = 2.1 Hz), 6.97 (2H, t, J = 2.1 Hz), 7.25 (2H, s), and 7.31 (1H, s); MS m/z (%) 182 (M^+, 100). Found: m/z 182.0841. Calcd for $C_{12}H_{10}N_2$: M, 182.0845.

Pyrrolo[1,2-*a*]quinoxaline 7. To a magnetically stirred solution of the isocyanide **5** (1.0 mmol, 0.17 g) in CH_2Cl_2 (20 mL) at 0

°C under argon was added dropwise diethyl ether–boron trifluoride (14 mg, 0.10 mmol). After the mixture was stirred for 20 min at the same temperature, aqueous $NaHCO_3$ was added to it. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined extracts were dried over anhydrous Na_2SO_4 and evaporated. The residue was recrystallized from hexane to give the title compound **7** (0.16 g, 97%); mp 130–132 °C (Ref. 2b, 131–134 °C); IR 3093, 1618, 1340, and 747 cm^{-1}; ^1H NMR δ 6.85–6.95 (2H, m), 7.4–7.6 (2H, m), 7.77 (1H, dd, J = 7.9 and 1.8 Hz), 7.9–7.95 (1H, m), 7.96 (1H, dd, J = 7.9 and 1.6 Hz), and 8.82 (1H, s).

4-(1-Hydroxylpropyl)pyrrolo[1,2-*a*]quinoxaline 8. Typical Procedure for the Reaction of 1-(2-Isocyanophenyl)pyrroles 5 and 6 with Aldehydes or Ketones. To a magnetically stirred solution of the isocyanide **5** (1.0 mmol, 0.17 g) and propanal (58 mg, 1.0 mmol) in CH_2Cl_2 (20 mL) at 0 °C under argon was added dropwise diethyl ether–boron trifluoride (14 mg, 0.10 mmol). After 20 min, diethyl ether–boron trifluoride (14 mg, 0.10 mmol) was added to the reaction mixture, and stirring was continued for an additional 20 min at the same temperature before the same workup as employed for the preparation of **7**. The residue was purified by column chromatography on SiO_2 to give the title compound **8** (0.20 g, 89%): R_f 0.68 (1 : 1 hexane–EtOAc); IR (neat) 3395, 3158, 1613, 1365, and 756 cm^{-1}; ^1H NMR δ 1.03 (3H, t, J = 7.4 Hz), 1.75–1.9 (1H, m), 2.1–2.2 (1H, m), 4.82 (1H, d, J = 6.3 Hz), 5.0–5.1 (1H, m), 6.85–6.9 (2H, m), 7.4–7.6 (2H, m), 7.87 (1H, dd, J = 8.4 and 1.6 Hz), and 7.9–8.0 (2H, m); MS *m/z* (%) 226 (M^+, 37) and 198 (100). Found: *m/z* 226.1124. Calcd for $C_{14}H_{14}N_2O$: M, 226.1107.

Compounds **9**–**17** were prepared similarly with the above-mentioned Typical Procedure.

4-(1-Hydroxy-2-methylpropyl)pyrrolo[1,2-*a*]quinoxaline 9: R_f 0.58 (1 : 2 EtOAc–hexane); IR (neat) 3400, 3136, and 1614 cm^{-1}; ^1H NMR δ 0.75 (3H, d, J = 6.9 Hz), 1.23 (3H, d, J = 6.9 Hz), 2.3–2.4 (1H, m), 4.68 (1H, br. s), 4.94 (1H, d, J = 3.2 Hz), 6.85–6.9 (2H, m), 7.44 (1H, td, J =7.9 and 1.6 Hz), 7.52 (1H, td, J =7.9 and 1.6 Hz), 7.86 (1H, dd, J = 7.9 and 1.6 Hz), and 7.9–8.0 (2H, m); MS *m/z* (%) 240 (M^+, 15), 223 (29), and 197 (100). Found: *m/z* 240.1263. $C_{15}H_{16}N_2O$: M, 240.1264.

4-(1-Hydroxy-2,2-dimethylpropyl)pyrrolo[1,2-*a*]quinoxaline 10: R_f 0.61 (1 : 2 EtOAc–hexane); IR (neat) 3439, 3138, 1612, 1364, and 756 cm^{-1}; ^1H NMR δ 1.04 (9H, s), 4.22 (1H, br. d, J = 5.9 Hz), 4.76 (1H, br d, J = 5.9 Hz), 6.86 (1H, dd, J = 4.1 and 2.7 Hz), 6.92 (1H, dd, J = 4.1 and 1.4 Hz), 7.43 (1H, td, J = 7.8 and 1.6 Hz), 7.50 (1H, td, J = 7.8 and 1.6 Hz), 7.85 (1H, dd, J = 7.8 and 1.6 Hz), and 7.9–7.95 (2H, m); MS *m/z* (%) 254 (M^+, 7.6) and 197 (100). Found: *m/z* 254.1426. $C_{16}H_{18}N_2O$: M, 254.1420.

4-(α-Hydroxybenzyl)pyrrolo[1,2-*a*]quinoxaline 11, along with 4-Benzoylpyrrolo[1,2-*a*]quinoxaline 18.[2c] **11:** mp 125–134 °C (hexane–Et_2O); IR 3334, 3133, 1613, 1368, and 763 cm^{-1}; ^1H NMR δ 5.9–5.95 (2H, m), 6.64 (1H, dd, J = 4.2 and 1.1 Hz), 6.75 (1H, dd, J = 4.2 and 2.6 Hz), 7.25–7.35 (3H, m), 7.45–7.6 (4H, m), 7.85 (1H, dd, J = 7.9 and 1.6 Hz), 7.89 (1H, dd, J = 2.6 and 1.1 Hz) and 8.05 (1H, dd, J = 7.9 and 1.6 Hz); MS *m/z* (%) 274 (M^+, 28) and 257 (100). Found: C, 78.61; H, 5.22; N, 10.20%. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21%. **18**: mp 169–171 °C (hexane–AcOEt) (Ref. 1b, 170–171 °C); IR 3136, 1666, 1374, and 758 cm^{-1}; ^1H NMR δ 6.97 (1H, dd, J = 4.2 and 2.6 Hz), 7.22 (1H, dd, J = 4.2 and 1.6 Hz), 7.45–7.55 (3H, m), 7.6–7.7 (2H, m), 7.94 (1H, dd, J = 7.9 and 1.1 Hz), 8.0–8.1 (2H, m), and 8.18 (2H, dd, J = 8.4 and 1.6 Hz); MS *m/z* (%) 272 (M^+, 60), 243 (68), and 77 (100).

4-(2-Furyl-1-hydroxymethyl]pyrrolo[1,2-*a*]quinoxaline 12: mp 111–116 °C (hexane–EtOAc); IR 3352, 3138, 1365, and 755 cm^{-1}; ^1H NMR δ 5.79 (1H, br s), 6.05 (1H, br s), 6.34 (1H, dd, J = 4.3 and 1.1 Hz), 6.42 (1H, d, J = 4.3 and 1.1 Hz), 6.73 (1H, dd, J = 4.3 and 2.6 Hz), 6.80 (1H, dd, J = 4.3 and 2.6 Hz), 7.45–7.6 (2H, m), 7.86 (1H, dd, J = 8.1 and 1.7 Hz), 7.9–8.0 (2H, m), and 8.02 (1H, dd, J = 7.7 and 1.7 Hz); MS *m/z* (%) 264 (M^+, 1.5), 262 (49), and 234 (100). Found: C, 73.01; H, 4.39; N, 10.79%. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60%.

4-(1-Hydroxy-1-methylethyl)pyrrolo[1,2-*a*]quinoxaline 13: mp 151–153 °C (hexane–EtOAc); IR 3355, 3123, 1612, 1362, and 749 cm^{-1}; ^1H NMR δ 1.75 (6H, s), 6.24 (1H, s), 6.90 (1H, dd, J = 4.2 and 2.6 Hz), 7.00 (1H, dd, J = 4.2 and 1.6 Hz), 7.45 (1H, td, J = 7.4 and 1.6 Hz), 7.54 (1H, td, J = 7.4 and 2.1 Hz), 7.87 (1H, dd, J = 7.4 and 1.6 Hz), and 7.9–8.0 (2H, m); MS *m/z* (%) 226 (M^+, 42) and 211 (100). Found: C, 74.55; 6.36; N, 12.13%. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38%.

4-(1-Hydroxycyclohexyl)pyrrolo[1,2-*a*]quinoxaline 14: mp 162–163 °C (hexane–EtOAc); IR 3302, 3146, 1611, 1368, and 738 cm^{-1}; ^1H NMR δ 1.5–2.05 (8H, m), 2.25–2.4 (2H, m), 6.10 (1H, s), 6.90 (1H, dd, J = 4.2 and 2.6 Hz), 7.12 (1H, dd, J = 4.2 and 1.6 Hz), 7.4–7.55 (2H, m), 7.86 (1H, d, J = 7.9 Hz), 7.94 (1H, dd, J = 7.9 and 1.6 Hz) and 7.96 (1H, dd, J = 2.6 and 1.6 Hz); MS *m/z* (%) 266 (M^+, 46) and 211 (100). Found: C, 76.41; H, 6.75; N, 10.50%. $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.51%.

4-(1-Hydroxy-1-phenylethyl)pyrrolo[1,2-*a*]quinoxaline 15: mp 196–198 °C (hexane–EtOAc); IR 3293, 3135, 1610, 1363, and 756 cm^{-1}; ^1H NMR δ 2.12 (3H, s), 2.61 (1H, s), 6.43 (1H, dd, J = 4.2 and 2.6 Hz), 6.69 (1H, dd, J = 4.2 and 1.6 Hz), 7.25–7.35 (3H, m), 7.45–7.6 (4H, m), 7.84 (1H, dd, J = 7.4 and 1.6 Hz), 7.86 (1H, dd, J = 2.6 and 1.6 Hz), and 8.04 (1H, dd, J = 7.9 and 1.6 Hz); MS *m/z* (%) 288 (M^+, 38), 271 (82), and 168 (100). Found: C, 79.14; H, 5.64; N, 9.65%. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72%.

Ethyl 2-Hydroxy-2-methyl-2-(pyrrolo[1,2-*a*]quinoxalin-4-yl)acetate 16: R_f 0.56 (2 : 1 hexane–EtOAc); IR (neat) 3356, 3136, 1736, 1613, 1361, and 758 cm^{-1}; ^1H NMR δ 1.16 (3H, t, J = 7.4 Hz), 1.95 (3H, s), 4.1–4.25 (2H, m), 6.27 (1H, s), 6.88 (1H, dd, J = 4.2 and 2.6 Hz), 7.03 (1H, dd, J = 4.2 and 1.6 Hz), 7.46 (1H, td, J = 7.9 and 1.0 Hz), 7.46 (1H, td, J = 7.9 and 1.6 Hz), 7.87 (1H, dd, J = 7.9 and 1.0 Hz), and 7.95–8.05 (2H, m); MS *m/z* (%) 284 (M^+, 30) and 211 (100). Found: *m/z* 284.1150. Calcd for $C_{16}H_{16}N_2O_3$: M, 284.1162.

Ethyl 4-Hydroxy-4-methyl-4-(pyrrolo[1,2-*a*]quinoxalin-4-yl)butylate 17: R_f 0.33 (1 : 1 hexane–EtOAc); IR (neat) 3340, 3135, 1731, 1621, 1375, and 761 cm^{-1}; ^1H NMR δ 1.15 (3H, t, J = 6.8 Hz), 1.84 (3H, s), 2.09 (1H, ddd, J = 15.8, 11.1, and 5.3 Hz), 2.35–2.6 (3H, m), 2.72 (1H, ddd, J = 15.8, 10.0, and 5.3 Hz), 3.95–4.1 (2H, m), 7.17 (1H, dd, J = 4.2 and 2.6 Hz), 7.40 (1H, dd, J = 4.2 and 1.0 Hz), 7.61 (1H, td, J = 7.9 and 1.0 Hz), 7.72 (1H, td, J = 7.9 and 1.0 Hz), 8.00 (1H, dd, J = 7.9 and 1.0 Hz), 8.26 (1H, dd, J = 2.6 and 1.0 Hz), and 8.41 (1H, dd, J = 7.9 and 1.0 Hz); MS *m/z* (%) 266 [$(M-EtOH)^+$, 35%] and 195 (100). Found: *m/z* 266.1070. $C_{16}H_{14}N_2O_2$: M−EtOH, 266.1056.

4-(2-Hydroxypropyl)pyrrolo[1,2-*a*]quinoxaline 23 and 4-(2-Hydroxy-1-methylethyl)pyrrolo[1,2-*a*]quinoxaline 28. Typical Procedure for the Reaction of 1-(2-Isocyanophenyl)pyrroles 5 and 6 with Oxiranes 19–22. To a stirred solution of **5** (0.91 mmol, 0.15 g) and 2-methyloxirane (**19**) (0.91 mmol, 53 mg) in CH_2Cl_2 (10 mL) at −0 °C under argon was added dropwise diethyl ether–boron trifluoride (0.091 mmol, 13 mg). After stir-

ring for 40 min at the same temperature, the reaction mixture was diluted with CH_2Cl_2 (20 mL), and aqueous Na_2CO_3 (20 mL) successively, and the organic phase was separated and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by column chromatography on silica gel to give **23** (0.10 g, 47%) and **28** (27 mg, 13%). **23**: mp 90–91 °C (hexane); IR 3350, 3130 and 1614 cm^{-1}; ^1H NMR δ 1.39 (3H, d, J = 6.3 Hz), 2.99 (1H, dd, J = 16.4 and 9.5 Hz), 3.17 (1H, dd, J = 16.4 and 2.1 Hz), 4.45–4.55 (1H, m), 5.40 (1H, br s), 6.8–6.9 (2H, m), 7.42 (1H, td, J = 7.9 and 1.6 Hz), 7.52 (1H, td, J = 7.9 and 1.6 Hz), 7.84 (1H, dd, J = 7.9 and 1.6 Hz), 7.88 (1H, dd, J = 7.9 and 1.6 Hz), and 7.92 (1H, dd, J = 2.6 and 1.1 Hz); MS m/z (%) 226 (M^+, 7.4) and 182 (100). Found: C, 74.11; H, 6.32; N, 12.16%. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38%. **28**: R_f 0.31 (1 : 2 EtOAc–hexane); IR (neat) 3335, 3127, and 1614 cm^{-1}; ^1H NMR δ 1.52 (3H, d, J = 7.4 Hz), 3.25–3.55 (2H, m), 4.00 (1H, dd, J = 11.1 and 4.8 Hz), 4.19 (1H, dd, J = 11.1 and 3.2 Hz), 6.87 (1H, dd, J = 4.2 and 2.6 Hz), 6.93 (1H, dd, J = 4.2 and 1.1 Hz), 7.43 (1H, td, J = 7.9 and 1.6 Hz), 7.50 (1H, td, J = 7.9 and 1.6 Hz), 7.84 (1H, dd, J = 7.9 and 1.6 Hz), 7.88 (1H, dd, J = 7.9 and 1.6 Hz) and 7.93 (1H, dd, J = 2.6 and 1.1 Hz); MS m/z (%) 226 (M^+, 36), 209 (85) and 168 (100). Found: m/z 226.1127. Calcd for $C_{14}H_{14}N_2O$: M, 226.1107.

4-(2-Hydroxy-2-phenylethyl)pyrrolo[1,2-*a*]quinoxaline 24: mp 114–115 °C (hexane); IR 3330, 3179, and 1610 cm^{-1}; ^1H NMR δ 3.08 (1H, dd, J = 13.7 and 7.9 Hz), 3.36 (1H, dd, J = 13.7 and 7.9 Hz), 4.7–4.8 (1H, m), 5.25–5.35 (1H, m), 6.85–6.95 (2H, m), 7.2–7.3 (5H, m), 7.44 (1H, td, J = 7.9 and 1.6 Hz), 7.53 (1H, td, J = 7.9 and 1.6 Hz), 7.89 (1H, dd, J = 7.9 and 1.6 Hz), 7.92 (1H, dd, J = 7.9 and 1.6 Hz), and 7.97 (1H, dd, J = 2.1 and 1.6 Hz); MS m/z (%) 288 (M^+, 25), 168 (60), and 197 (100). Found: C, 79.39; H, 5.42; N, 10.00%. Calcd for $C_{19}H_{16}N_2O$: C, 79.16; H, 5.59; N, 9.72%.

***trans*-4-(2-Hydroxycyclohxyl)pyrrolo[1,2-*a*]quinoxaline 25:** mp 164–167 °C (hexane–Et_2O); IR 3350, 3131, and 1614 cm^{-1}; ^1H NMR δ 1.45–1.55 (4H, m), 1.8–1.95 (2H, m), 2.15–2.3 (2H, m), 3.05–3.2 (2H, m), 4.35–4.5 (1H, m), 6.85 (1H, dd, J = 4.0 and 2.6 Hz), 6.93 (1H, dd, J = 4.0 and 1.5 Hz), 7.41 (1H, td, J = 7.9 and 1.6 Hz), 7.47 (1H, td, J = 7.9 and 1.6 Hz), 7.83 (1H, dd, J = 7.9 and 1.6 Hz), and 7.85–7.95 (2H, m); MS m/z (%) 266 (M^+, 17) and 195 (100). Found: C, 76.68; H, 6.81; N, 10.55. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.51%.

4-(2-Hydroxy-5-hexenyl)pyrrolo[1,2-*a*]quinoxaline 26: mp 79–82 °C (hexane–Et_2O); IR 3440, 3143, 1638, and 1614 cm^{-1}; ^1H NMR δ 1.6–1.9 (3H, m), 2.2–2.4 (2H, m), 3.01 (1H, dd, J = 15.8 and 8.9 Hz), 3.19 (1H, dd, J = 15.8 and 2.6 Hz), 4.25–4.4 (1H, m), 4.95–5.15 (2H, m), 5.8–6.0 (1H, m), 6.86 (1H, dd, J = 3.7 and 2.6 Hz), 6.90 (1H, dd, J = 3.7 and 1.5 Hz), 7.42 (1H, td, J = 7.9 and 1.6 Hz), 7.49 (1H, td, J = 7.9 and 1.6 Hz), 7.83 (1H, dd, J = 7.9 and 1.6 Hz), 7.89 (1H, dd, J = 7.9 and 1.6 Hz), and 7.93 (1H, J = 2.6 and 1.5 Hz); MS m/z (%) 266 (M^+, 0.02), 248 (62), and 207 (100). Found: C, 76.64; H, 6.84; N, 10.80%. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.51%.

***trans*-4-(2-Hydroxycyclohxyl)-7-methylpyrrolo[1,2-*a*]quinoxaline 27:** mp 127–129 °C (hexane); IR 3414, 3144, and 1614 cm^{-1}; ^1H NMR δ 1.4–1.55 (4H, m), 1.8–1.95 (2H, m), 2.15–2.3 (2H, m), 2.48 (3H, s), 3.0–3.15 (1H, m), 3.19 (1H, s), 4.35–4.5 (1H, m), 6.82 (1H, dd, J = 4.0 and 2.6 Hz), 6.90 (1H, dd, J = 4.0 and 1.5 Hz), 7.29 (1H, dd, J = 7.9 and 2.1 Hz), 7.71 (1H, d, J = 7.9 Hz), 7.73 (1H, br s), and 7.86 (1H, dd, J = 2.6 and 1.5 Hz); MS m/z (%) 280 (M^+, 41), 209 (91), and 183 (100). Found: C, 76.99; H, 7.15; N, 10.17%. Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99%.

The reaction of **5** with 2,2-dimethyloxirane under conditions similar to those described for the preparations of **23**–**28** gave **9**.

4-(1-Ethoxyethyl)pyrrolo[1,2-*a*]quinoxaline 35. Typical Procedure for the Reaction of 1-(2-Isocyanophenyl)pyrroles 5 or 6 with Acetals 29–33. To a stirred solution of **5** (1.0 mmol, 0.17 g) and actaldehyde diethyl acetal **30** (1.0 mmol, 0.12 g) in CH_2Cl_2 (10 ml) at 0 °C under argon was added dropwise three portions of 14 mg (0.10 mmol) each of diethyl ether–boron trifluoride at 30 min intervals. After completion of the addition of diethyl ether–boron trifluoride, stirring was continued for 40 min at the same temperature. The reaction mixture was worked up in a manner similar to that described above, and the crude product was purified by column chromatography on silica gel to give **35** (0.21 g, 85%): R_f 0.52 (1 : 2 EtOAc–hexane); IR (neat) 3143 and 1612 cm^{-1}; ^1H NMR δ 1.22 (3H, t, J = 6.9 Hz), 1.67 (3H, d, J = 6.9 Hz), 3.4–1.69 (2H, m), 4.78 (1H, q, J = 6.9 Hz), 6.86 (1H, dd, J = 4.2 and 2.6 Hz), 7.27 (1H, dd, J = 4.2 and 1.1 Hz), 7.42 (1H, td, J = 7.9 and 1.6 Hz), 7.49 (1H, td, J = 7.9 and 1.6 Hz), 7.83 (1H, dd, J = 7.9 and 1.6 Hz), and 7.9–8.0 (2H, m); MS m/z (%) 240 (M^+, 15) and 195 (100). Found: m/z 240.1270. Calcd for $C_{15}H_{16}N_2O$: M, 240.1264.

4-(1-Methoxyethyl)pyrrolo[1,2-*a*]quinoxaline 34: R_f 0.49 (1 : 2 EtOAc–hexane); IR (neat) 3134 and 1613 cm^{-1}; ^1H NMR δ 1.67 (3H, d, J = 6.9 Hz), 3.39 (3H, s), 4.70 (1H, q, J = 6.9 Hz), 6.79 (1H, dd, J = 4.2 and 2.6 Hz), 7.21 (1H, dd, J = 4.2 and 1.1 Hz), 7.43 (1H, td, J = 7.9 and 1.6 Hz), 7.52 (1H, td, J = 7.9 and 1.6 Hz), 7.86 (1H, dd, J = 7.9 and 1.6 Hz), and 7.9–8.0 (2H, m); MS m/z (%) 226 (M^+, 17), 196 (92), and 195 (100). Found: m/z 226.1107. Calcd for $C_{14}H_{14}N_2O$: M, 226.1107.

4-Methylpyrrolo[1,2-*a*]quinoxaline.[2a] This compound was obtained along with **34**, and identified by a comparison of its ^1H NMR spectrum with that reported by Cheeseman et al.;[2a] mp 138–140 °C (Ref. 2a, 137 °C).

4-(1-Ethoxy-1-methylethyl)pyrrolo[1,2-*a*]quinoxaline 36: R_f 0.74 (1 : 2 EtOAc–hexane); IR (neat) 3143 and 1608 cm^{-1}; ^1H NMR δ 1.15 (3H, t, J = 6.9 Hz), 1.73 (6H, s), 3.30 (2H, q, J = 6.9 Hz), 6.85 (1H, dd, J = 4.2 and 2.6 Hz), 7.35–7.45 (2H, m), 7.49 (1H, td, J = 7.9 and 1.6 Hz), 7.83 (1H, dd, J = 7.9 and 1.6 Hz), and 7.85–7.95 (2H, m); MS m/z (%) 254 (M^+, 5) and 210 (100). Found: m/z 254.1433. Calcd for $C_{16}H_{18}N_2O$: M, 254.1420.

4-(1-Ethoxy-2-propenyl)pyrrolo[1,2-*a*]quinoxaline 37: R_f 0.15 (1 : 10 EtOAc–hexane); IR (neat) 3135, 1643, and 1613 cm^{-1}; ^1H NMR δ 1.26 (3H, t, J = 6.9 Hz), 3.5–3.7 (2H, m), 5.12 (1H, dt, J = 6.0 and 1.3 Hz), 5.27 (1H, dt, J = 10.3 and 1.3 Hz), 5.54 (1H, dt, J = 17.1 and 1.3 Hz), 6.23 (1H, dt, J = 17.1, 10.3, and 6.0 Hz), 6.86 (1H, dd, J = 4.2 and 2.6 Hz), 7.22 (1H, dd, J = 4.2 and 1.1 Hz), 7.42 (1H, td, J = 7.9 and 1.6 Hz), 7.50 (1H, td, J = 7.9 and 1.6 Hz), 7.84 (1H, dd, J = 7.9 and 1.6 Hz), 7.92 (1H, dd, J = 2.6 and 1.1 Hz), and 7.97 (1H, dd, J = 7.9 and 1.6 Hz); MS m/z (%) 252 (M^+, 4), 223 (9), and 207 (100). Found: m/z 254.1254. Calcd for $C_{16}H_{16}N_2O$: M, 252.1264.

4-(α-Methoxybenzyl)pyrrolo[1,2-*a*]quinoxaline 38: mp 139–142 °C (EtOAc–hexane); IR 3141 and 1602 cm^{-1}; ^1H NMR δ 3.54 (3H, s), 5.64 (1H, s), 6.80 (1H, dd, J = 4.2 and 2.6 Hz), 7.12 (1H, dd, J = 4.2 and 1.1 Hz), 7.15–7.35 (3H, m), 7.4–7.55 (2H, m), 7.62 (2H, d, J = 7.4 Hz), 7.82 (1H, dd, J = 7.9 and 1.6 Hz), 7.88 (1H, dd, J = 2.6 and 1.1 Hz), and 8.04 (1H, dd, J = 7.9 and 1.6 Hz); MS m/z (%) 288 (M^+, 9), 273 (16), and 258 (100). Found: C, 79.11; H, 5.70 N, 9.75%. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72%.

4-(1-Ethoxyethyl)-7-methylpyrrolo[1,2-*a*]quinoxaline 39:

R_f 0.63 (1 : 2 EtOAc–hexane); IR (neat) 3134 and 1613 cm^{-1}; ^1H NMR δ 1.21 (3H, t, J = 7.4 Hz), 1.66 (3H, d, J = 6.8 Hz), 2.48 (3H, s), 3.4–3.65 (2H, m), 4.76 (1H, q, J = 6.8 Hz), 6.84 (1H, dd, J = 4.2 and 2.6 Hz), 7.24 (1H, dd, J = 4.2 and 1.1 Hz), 7.31 (1H, dd, J = 8.4 and 1.6 Hz), 7.7–7.75 (2H, m), and 7.89 (1H, dd, J = 2.6 and 1.1 Hz); MS *m/z* (%) 254 (M^+, 5) and 209 (100). Found: *m/z* 254.1436. Calcd for $C_{16}H_{18}N_2O$: M, 254.1420.

4-(*trans*-5-Ethoxytetrahydrofuran-2-yl)pyrrolo[1,2-*a*]quinoxaline 40: This compound was prepared by treating **5** with 2 molar amounts of 2,5-diethoxytetrahydrofuran in the presence of 0.3 molar amount of diethyl ether–boron trifluoride under the same conditions as described above for the preparation of **35**. R_f 0.52 (1 : 2 EtOAc–hexane); IR 3138 and 1619 cm^{-1}; ^1H NMR δ 1.27 (3H, t, J = 7.3 Hz), 2.0–2.1 (1H, m), 2.25–2.4 (2H, m), 2.5–2.6 (1H, m), 3.5–3.65 (1H, m), 3.8–3.95 (1H, m), 5.45–5.55 (2H, m), 6.86 (1H, dd, J = 4.2 and 2.6 Hz), 7.02 (1H, dd, J = 4.2 and 1.1 Hz), 7.35–7.55 (2H, m), 7.83 (1H, dd, J = 7.9 and 1.6 Hz), 7.93 (1H, dd, J = 2.6 and 1.1 Hz), and 7.99 (1H, dd, J = 7.9 and 1.6 Hz); MS *m/z* (%) 282 (M^+, 2), 237 (7), and 195 (100). Found: *m/z* 282.1349. Calcd for $C_{17}H_{18}N_2O_2$: M, 282.1369.

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