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A New Efficient Route for the Formation of Quinoxaline *N*-Oxides and *N*,*N*′-Dioxides Using HOF·CH_3CN

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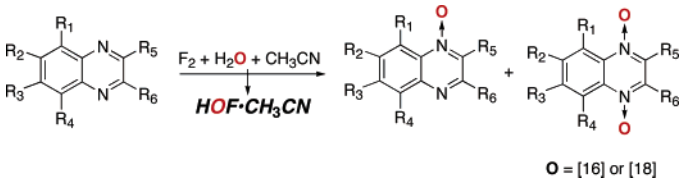


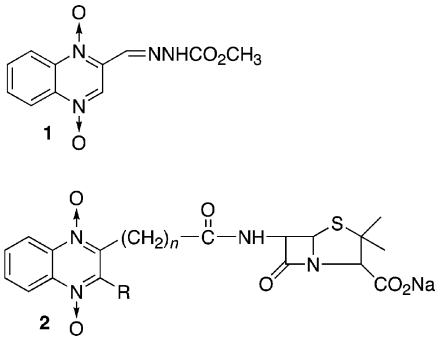
HOF·CH_3CN, a very efficient oxygen-transfer agent made readily from fluorine and aqueous acetonitrile, was reacted with various quinoxaline derivatives to give the corresponding mono *N*-oxides and especially the *N*,*N*′-dioxides in very good yields under mild conditions and short reaction times.

Introduction

Quinoxaline *N*,*N*′-dioxides and phenazine 5,10-*N*,*N*′-dioxides have found application as antibacterial agents, possessing a wide range of activities.[1] Methyl 3-[(2-quinoxalinyl)methylene]carbazate *N*,*N*′-dioxide (**1**), for example, known commercially as Carbadox,[2] has proven to be an efficient antibacterial and growth-promoting material. Another example is a series of penicillin derivatives of quinoxaline *N*,*N*′-dioxide carboxylic acids such as **2**,[3] which exhibit exceptional activity against *Salmonella* and *Proteus* species (Scheme 1).[4]

One of the most common methods for generating some quinoxaline mono- and *N*,*N*′-dioxides consists in the total synthesis based on the reaction of carbonyl derivatives with benzofurazan oxide.[5] An alternative, more general, and potentially easier pathway should be the direct transfer of oxygen to the nitrogen atoms of quinoxaline derivatives in order to obtain the corresponding mono *N*-oxides and particularly quinoxaline *N*,*N*′-dioxides, which are hardly reported in the literature. The main reason for this "anomaly" is the second nitrogen of the ring system, which makes the diazines less reactive than pyridine toward electrophilic substitutions, including electrophilic oxygen transfer. Electron-withdrawing substituents, such as halogens, reduce the basicity of the ring nitrogens even further. Consequently, while it was difficult to make haloquinoxaline mono-*N*-oxides, it was practically impossible to form haloquinoxaline *N*,*N*′-dioxides by the orthodox oxygen transfer agents.[6] The reason for this failure is the first step that produces the mono-*N*-oxide moiety, which in turn deactivates almost completely the second nitrogen atom toward any further electrophilic attack.

SCHEME 1. Antibacterial Quinoxaline *N*,*N*′-Dioxides



We report here a general method for direct oxidation of quinoxaline derivatives using the HOF·CH_3CN complex. This oxygen transfer agent stands alone in its ability to oxidize azides and vicinal diamines into the corresponding nitro[7] and dinitro[8] derivatives. It was employed in the oxidation of C=N-containing compounds,[9] forming 1,10-phenanthroline *N*,*N*′-dioxide deriva-

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(2) (a) Chas Pfizer and Co. U.S. Patent **1968**, 3 371 090. (b) Research Corp. U.S. Patent **1968**, 3 398 141. (c) Haddadin, M. J.; Kattan, A. M. A.; Issidorides, C. H. *J. Org. Chem.* **1985**, *50*, 129.
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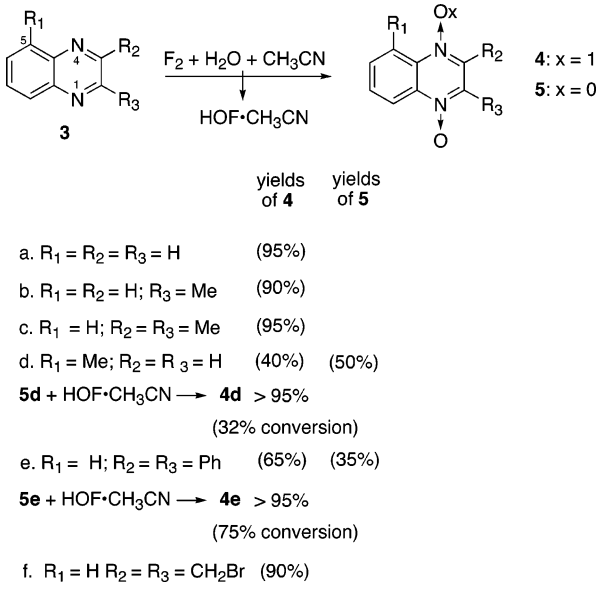
SCHEME 2. Oxygen Transfer to Some Quinoxaline Derivatives Using HOF·CH_3CN



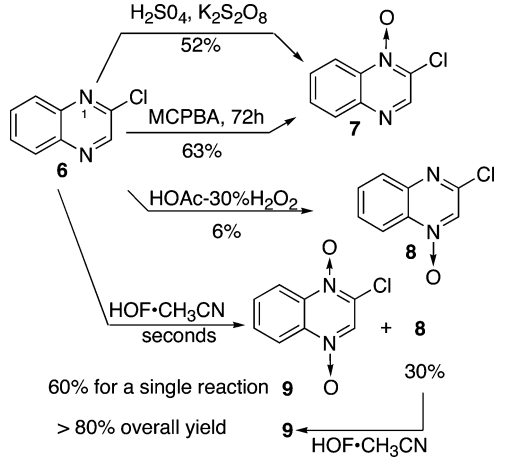
tives which eluded chemists for so many decades,[10] transferring oxygen atoms to sulfides, including electron-depleted ones,[11] to thiophenes,[12] polythiophenes,[13] and much more.[14]

Results and Discussion

Direct oxidation of quinoxaline with H_2O_2 is reported in the literature, but the yields never exceeded 50% and long reaction times were required.[15] It took less than 2 min for the HOF·CH_3CN complex to convert quinoxaline (**3a**) to quinoxaline *N*,*N*′-dioxide (**4a**) in 95% yield (Scheme 2). Although HOF·CH_3CN is known to react even with aromatic rings,[16] its reaction with both nitrogen atoms is faster and no difficulties were encountered with the more electron-rich aromatic ring of 2-methylquinoxaline (**3b**). This compound was transformed in 2 min to 2-methylquinoxaline *N*,*N*′-dioxide (**4b**) in 90% yield. It is noteworthy that compound **4b** has been previously obtained via the benzofurazane route by a multistep synthesis eventually resulting in less than 20% yield.[5b] Increased substitution on the quinoxaline skeleton was also tolerated, and when 2,3-dimethylquinoxaline (**3c**) was reacted with 2 equiv of HOF·CH_3CN, 2,3-dimethylquinoxaline *N*,*N*′-dioxide (**4c**) was obtained after 3 min in 95% yield.

It was of interest to see whether the HOF·CH_3CN could overcome steric hindrances, and 5-methylquinioxaline (**3d**) served as a test case. Using an excess of the oxidation agent provided a mixture of only 5-methylquinoxaline 1-*N*-oxide (**5d**) in 50% yield and 5-methylquinioxaline *N*,*N*′-dioxide (**4d**) in 40% yield. Adding more than 5 equiv of the reagent to the reaction mixture did not change the outcome. It seems that this result is related to the modest steric hindrance in an indirect way. Since the oxidation at the *N*-4 position is slower than that of *N*-1, the small amount of protons originating from the HF (formed simultaneously along the HOF) compete with the electrophilic oxygen and protonate the hindered nitrogen atom *N*-4. This protonation does not allow, of course, any further electrophilic oxygen transfer at that position. However, since the separation of **4d** and **5d** (after the appropriate workup that regenerates the free base) is easy, the latter can be brought once again in contact with HOF·CH_3CN forming **4d** in quantitative yield, but in 32% conversion. This process can be repeated until the original 40% yield of **4d** could be increased to higher than 90%.

SCHEME 3. Oxidation of 2-Chloroquinoxaline Using Various Popular Oxidation Reagents



Steric hindrance at the 2 and 3 positions did not cause any problem. Oxidation of 2,3-diphenylquinoxaline (**3e**) using 4 equiv of the oxidation agent for a few seconds resulted in a 35% yield of the 2,3-diphenylquinoxaline *N*-oxide (**5e**) and 65% yield of 2,3-diphenylquinoxaline *N*,*N*′-dioxide (**4e**). For comparison, oxidation of **3e** with either *m*-CPBA for 18 h or hydrogen peroxide in acetic acid resulted in 0.6% yield of the *N*,*N*′-dioxide (**4e**).[17,18] It should be noted that here again, separating **4e** from **5e** makes it possible to repeat the reaction with **5e** resulting in **4e** in higher than 95% yield (75% conversion). This brings the potential overall yield of **4e** to nearly quantitative.

Benzylic halogens, which are excellent synthetic entries, are also suitable substrates. Less than 1 min was needed for an excess of HOF·CH_3CN to transfer two oxygen atoms to 2,3-bis(bromoethyl)quinoxaline (**3f**) forming the corresponding 2,3-bis(bromoethyl)quinoxaline *N*,*N*′-dioxide (**4f**) in 90% yield (Scheme 2). To the best of our knowledge, no direct oxidation of **3f** has been achieved before.

Using HOF·CH_3CN for oxidation of 2-chloroquinoxaline (**6**) produced the unknown 2-chloroquinoxaline *N*,*N*′-dioxide (**9**) in 60% yield along with 30% of 2-chloroquinoxaline *N*-oxide (**8**), whose regioselectivity was controlled by the relative basicity of the quinoxaline nitrogens. Scheme 3 compares reactions of several peroxy reagents which are capable of transferring an oxygen atom to **6** (forming either **7** or **8**)[19] with HOF·CH_3CN.

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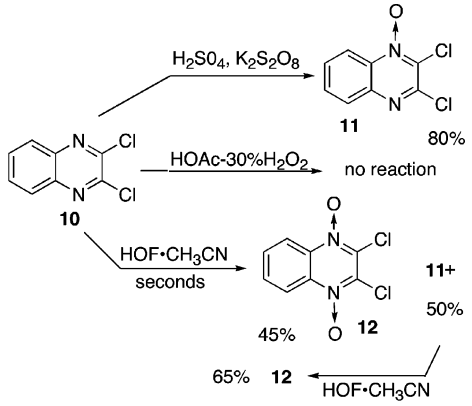
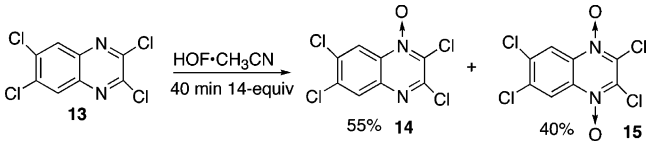
(19) Mixan, C. E.; Pews, R. G. *J. Org. Chem.* **1977**, *42*, 1869.

SCHEME 4. Oxidation of 2,3-Dichloroquinoxaline Using Various Oxidation Agents



SCHEME 5. Oxidation of Tetrachloroquinoxaline



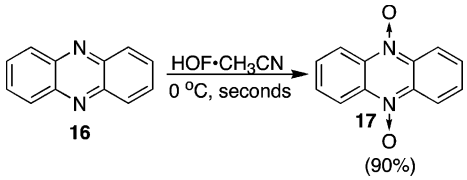
None of the former was able to produce the *N*,*N*′-dioxide **9**. As in the cases of **5d** and **5e**, adding large excess of the hypofluorous acid complex to **6** did not increase the **9**:**8** ratio apparently because both steric and electronic effects prioritize the protonation vs the oxygenation on *N*-1. During the workup, however, the *N*-1 in **8** regained its basicity, and since the separation between **9** and **8** is easy, the mono *N*-oxide **8** could be subjected once again to a very short reaction with HOF·CH_3CN increasing the overall yield of **9** to higher than 80%.

Dihalogenated quinoxalines are notoriously difficult to oxidize by direct oxidation, and the yields in the few successful cases are usually lower than 5%.[20] Oxidation of the electron-poor 2,3-dichloroquinoxaline (**10**) was attempted by several oxidation agents,[19] but once again only the HOF·CH_3CN complex was able to produce the desired *N*,*N*′-dioxide **12** in 45% yield and, as in the previous examples, after deprotonation of **11** and a second short reaction with HOF·CH_3CN, the overall yield of **12** could be increased to 65% (Scheme 4).

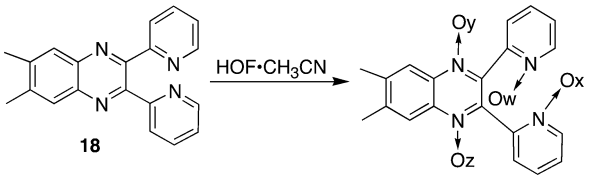
Polyhalogenated diazines were practically impossible to be converted to *N*,*N*′-dioxides. Systems such as peroxydichloromaleic acid,[21] 90% H_2O_2,[22] or 60% H_2O_2[23] were found to form exclusively the corresponding mono-*N*-oxides. Oxidation of 2,3,6,7-tetrachloroquinoxaline (**13**) was difficult even for the HOF·CH_3CN complex. It took a large excess of the oxidizing agent and 40 min to produce the two unknown derivatives 2,3,6,7-tetrachloroquinoxaline *N*-oxide (**14**) in 55% yield and 2,3,6,7-tetrachloroquinoxaline *N*,*N*′-dioxide in 40% yield (**15**) (Scheme 5).

Phenazine (**16**) was also reacted with the HOF·CH_3CN complex. The corresponding phenazine 5,10-*N*,*N*′-dioxide (**17**) was obtained in a few seconds using a 2-fold excess of the oxidizing agent. There are some reported methods for obtaining **17** using *tert*-amyl hydroperoxide, peracids, or hydrogen peroxide with various polluting heavy metal catalysts.[15b,24] The reaction with HOF·CH_3CN proceeds smoothly without any presence of catalysts and in 90% yield (Scheme 6).

SCHEME 6. Oxidation of Phenazine Using HOF·CH_3CN

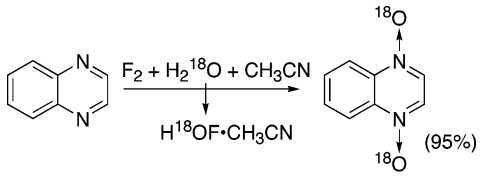


SCHEME 7. Oxidation of 6,7-Dimethyl-2,3-di(2-pyridyl)-quinoxaline



19 w = x = y = z = 1 (80%)
20 w = 1; x = y = z = 0 **21** w = x = 1; y = z = 0
22 w = x = y = 1; z = 0

SCHEME 8. Synthesis of Quinoxaline Di-*N*-oxide with [18]O Isotope



Oxidation of 6,7-dimethyl-2,3-di(2-pyridyl)quinoxaline **18** presented an additional challenge for the HOF·CH_3CN complex. This compound has never been fully oxidized previously. Reacting **18** at room temperature with an excess of 6 molar equiv of the reagent produced the 6,7-dimethyl-2,3-di(2-pyridyl)-quinoxaline *N*,*N*′,*N*″,*N*‴-tetraoxide (**19**) in 80% yield after only a few seconds (Scheme 7).

It was of interest to determine the oxygenation order of all of the nitrogen atoms in **18**. To answer this question, this compound was reacted with 1 equiv of HOF·CH_3CN. It was easy to conclude that one of the pyridine rings was first oxygenated forming **20**, followed by the oxygenation of the nitrogen atom in the second pyridine ring, **21**, as another molar equivalent of the reagent was added. Continuing addition of another 1.5 equiv of the acetonitrile complex of the hypofluorous acid resulted in another oxygen transfer, this time to one of the quinoxaline's nitrogens forming **22**, and finally, the last 2.5 equiv of the oxidizing agent afforded the tetra-*N*-oxide (**19**).

In many cases, especially when dealing with potential drugs, it is essential to have information on the metabolism of the studied compound. One of the techniques toward this end is to label the relevant molecule, or part of it, with some uncommon isotopes. One of the advantages of the HOF·CH_3CN complex is that its electrophilic oxygen originates from water, which is the best source for all oxygen isotopes. We passed fluorine through a solution of acetonitrile and $H_2{}^{18}O$, obtained as H^{18}-

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(21) Pollak, A.; Zupan, M.; Sket, B. *Synthesis* **1973**, 495.
(22) Chivers, G. E.; Suschitzky, H. *Chem. Commun*. **1971**, 28.
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OF·CH_3CN, which was then reacted with **3a**. The product's HRMS (CI) $m/z = 167.06193$ (M + 1) (calcd for $C_8H_6N_2{}^{18}O_2$, 167.059242) clearly showed that both oxygen atoms of **4a-[18]-O** are the ^{18}O isotope (Scheme 8).

Conclusion

HOF·CH_3CN is unique in its ability to oxidize quinoxaline derivatives, including sterically hindered and electron-depleted ones to the corresponding mono-*N*-oxides and *N*,*N*′-dioxides and if needed to transfer the former to the latter. Expanding this family of compounds and simplifying their synthesis may provide an easy tool for synthesis of new antibiotics and other antibacterial agents. Considering the commercial availability of premixed fluorine/nitrogen mixtures and the technical ease of the reaction, chemists should be encouraged to take advantage of the unique synthetic abilities of HOF·CH_3CN complex as a powerful oxygen transfer agent in organic chemistry.

Experimental Section

^1H NMR and ^{13}C NMR were obtained at 400 and 50 MHz, respectively, with $CDCl_3$ as a solvent and Me_4Si as an internal standard. MS spectra were measured under CI, EI, or FAB conditions. UV spectra were recorded in $CHCl_3$.

General Procedure for Working with Fluorine. This element is a strong oxidant and very corrosive material. It should be used only with an appropriate vacuum line.[25] For the occasional user, however, various premixed mixtures of F_2 in inert gases are commercially available, simplifying the process. If elementary precautions are taken, work with fluorine is relatively simple and we had no bad experiences working with it.

General Procedure for Producing HOF·CH_3CN. Mixtures of 10−20% F_2 with nitrogen were used in this work. The gas mixture was prepared in a secondary container before the reaction was started. It was then passed at a rate of about 400 mL per minute through a cold (−15 °C) mixture of 100 mL of CH_3CN and 10 mL of H_2O in regular glass reactor. The development of the oxidizing power was monitored by reacting aliquots with an acidic aqueous solution of KI. The liberated iodine was then titrated with thiosulfate. Typical concentrations of the oxidizing reagent were around 0.4−0.6 mol/L.

General Procedure for Working with HOF·CH_3CN. A quinoxaline derivative (usually 0.4−0.6 g) was dissolved in about 30 mL of $CHCl_3$, and the mixture was cooled to 0 °C. The oxidizing agent was then added in one portion to the reaction vessel (1 equiv means 1 molar equiv per each nitrogen). The excess of HOF·CH_3CN was quenched with saturated sodium bicarbonate, the solution extracted with $CHCl_3$, the organic layer dried over $MgSO_4$, and the solvent evaporated. The crude product was usually purified by vacuum flash chromatography using silica gel 60-H and increasing portions of EtOAc in PE as an eluent. Similar chromatography was used for separation of the mono- and *N*,*N*′-dioxides when obtained as a mixture. The spectral and physical properties of the known products thus obtained were compared with those reported in the literature. In every case, excellent agreement was obtained. All known compounds were referenced throughout this work. Data for the new compounds, or for those not well defined in the literature, is given below.

5-Methylquinoxaline *N*-oxide (5d) and 5-methylquinoxaline *N*,*N*′-dioxide (4d) were obtained from **3d** (0.62 g, 4.3 mmol), as described above, using 2.5 equiv of the oxidizing agent. The mixture was separated, and **5d** was obtained in 50% yield as a white solid: mp = 123−126 °C; UV−vis ($CHCl_3$) λ_{max} 240 ($\epsilon = 3.8 \times 10^4$), 330 ($\epsilon = 0.8 \times 10^4$); ^1H NMR 2.80 (3 H, s), 7.62−7.68 (2 H, m), 8.36 (1 H, d, $J = 1.8$ Hz) 8.44 (1 H, dd, $J_1 = 4.6$ Hz, $J_2 = 0.8$ Hz) 8.68 (1 H, d, $J = 1.8$ Hz); ^{13}C NMR 19.7, 118.7, 130.9, 131.8, 133.8, 139.7, 140.8, 146.4, 147.2; MS (CI) $m/z = 377.1$ (M + 1)$^+$. Anal. Calcd for $C_9H_8N_2O$: C, 67.49; H, 5.03; N, 17.49. Found: C, 67.20; H, 5.19; N, 17.34.

The *N*,*N*′-dioxide **4d** was obtained in 40% yield as a yellow solid: mp = 174−177 °C; UV−vis ($CHCl_3$) λ_{max} 240 ($\epsilon = 1.5 \times 10^4$), 375 ($\epsilon = 0.9 \times 10^4$), 390 ($\epsilon = 1 \times 10^4$); ^1H NMR 3.10 (3 H, s), 7.55 (1 H, d, $J = 3.8$ Hz), 7.69 (1 H, dd, $J_1 = 3.8$ Hz, $J_2 = 3.8$ Hz), 8.11 (1 H, d, $J = 2.8$ Hz) 8.16 (1 H, d, $J = 2.8$ Hz) 8.50 (1 H, d, $J = 3.8$ Hz); ^{13}C NMR 25.6, 120.7, 131.9, 133.4, 133.5, 136.7, 136.9, 139.9, 142; HRMS (CI) m/z = calcd 177.066403, found 177.066494 (M + 1)$^+$. Anal. Calcd for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.16; H, 4.85; N, 15.49. Compound **4d** could also be prepared by a similar procedure reacting 14 equiv of HOF·CH_3CN with **5d** forming **4d** in quantitative yield, but with 32% conversion raising the yield of this *N*,*N*′-dioxide to nearly 60%.

2,3-Diphenylquinoxaline *N*-oxide (5e) and 2,3-diphenylquinoxaline *N*,*N*′-dioxide (4e) were obtained from **3e** (0.6 g, 2.1 mmol), as described above, using 4 equiv of the oxidizing agent. The mixture was separated and **5e** obtained in 35% yield as a white solid: mp = 191 °C; UV−vis ($CHCl_3$) λ_{max} 249 ($\epsilon = 2.6 \times 10^4$), 270 ($\epsilon = 2.5 \times 10^4$), 334 ($\epsilon = 0.9 \times 10^4$); ^1H NMR 7.41−7.22 (10 H, m), 7.74 (1 H, ddd, $J_1 = 8$ Hz, $J_2 = 7.1$ Hz, $J_3 = 1.6$ Hz), 7.84 (1 H, ddd, $J_1 = 8$ Hz, $J_2 = 7.1$ Hz, $J_3 = 1.6$ Hz), 8.2 (1 H, ddd, $J_1 = 8$ Hz, $J_2 = 1.6$ Hz, $J_3 = 0.8$ Hz), 8.65 (1 H, ddd, $J_1 = 8$, Hz $J_2 = 1.6$ Hz, $J_3 = 0.8$ Hz); ^{13}C NMR 119.3, 127.9, 128.2, 128.9, 129.2, 129.5, 129.9, 130, 130.6, 131.4, 135.9, 137.9, 140, 143.8, 156.2; HRMS (CI) m/z = calcd 299.118438, found 299.117583 (M + 1)$^+$.

The *N*,*N*′-dioxide **4e** was obtained in 65% yield as a yellow solid: mp = 212−215 °C; UV−vis ($CHCl_3$) λ_{max} 240 ($\epsilon = 2.2 \times 10^4$), 290 ($\epsilon = 1.9 \times 10^4$), 395 ($\epsilon = 1.0 \times 10^4$); ^1H NMR 7.31−7.21 (10 H, m), 7.9 (2 H, dd, $J_1 = 6.7$ Hz, $J_2 = 3.2$ Hz), 8.7 (2 H, dd, $J_1 = 6.7$ Hz, $J_2 = 3.2$ Hz); ^{13}C NMR 119.1, 122.4, 126.6, 127.9, 128.7, 129.8, 130.1, 131, 132, 133.5, 137.8, 142.7; MS (FAB) m/z = 315 (M + 1)$^+$. Anal. Calcd for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.63; H, 4.58; N, 8.74. Compound **4e** could also be prepared by a similar procedure from **5e** in quantitative yield, but with 75% conversion using 12 equiv of the reagent.

2-Chloroquinoxaline *N*,*N*′-dioxide (9) was prepared from **6** (0.4 g, 2.43 mmol), as described above, using 2 equiv of the oxidizing agent resulting in the 65% yield of a yellow solid: mp = 198−199 °C; UV−vis ($CHCl_3$) λ_{max} 240 ($\epsilon = 1.3 \times 10^4$), 266 ($\epsilon = 1.8 \times 10^4$), 380 ($\epsilon = 0.98 \times 10^4$), 390 ($\epsilon = 0.99 \times 10^4$); ^1H NMR 7.87−7.95 (2 H, m), 8.47 (1 H, s), 8.58 (1 H, d, $J = 4.2$ Hz), 8.65 (1 H, d, $J = 4.2$ Hz); ^{13}C NMR 122.4, 122.5, 132.5, 133.8, 134.8, 136, 139.4, 139.9; MS (CI) $m/z = 197$ (M + 1)$^+$. Anal. Calcd for $C_8H_5N_2O_2Cl$: C, 48.88; H, 2.56; N, 14.25; Cl, 18.03. Found: C, 48.54; H, 2.79; N, 13.94; Cl, 18.23.

2,3-Dichloroquinoxaline mono-*N*-oxide (11) and 2,3-dichloroquinoxaline *N*,*N*′-dioxide (12) were prepared from **10** (0.5 g, 2.51 mmol), as described above, using 3 equiv of the oxidizing agent. The mixture was separated by chromatography to give **11** in 50% yield as a white solid: mp = 140−142 °C; UV−vis ($CHCl_3$) λ_{max} 250 ($\epsilon = 3.5 \times 10^4$), 325 ($\epsilon = 0.7 \times 10^4$); ^1H NMR 7.75−7.90 (2 H, m), 8.06 (1 H, ddd, $J_1 = 7.5$ Hz, $J_2 = 1.6$ Hz, $J_3 = 1.2$ Hz), 8.52 (1 H, ddd, $J_1 = 7.5$ Hz, $J_2 = 1.6$ Hz, $J_3 = 1.2$ Hz); ^{13}C NMR 118.9, 129.2, 130.7, 132.2, 136.9, 140.5, 146.4; MS (CI) m/z = 232 (M + 1)$^+$. Anal. Calcd for $C_8H_4N_2Cl_2O$: C, 44.68; H, 1.87; N, 13.03; Cl, 32.97. Found: C, 44.50; H, 2.01; N, 12.85; Cl, 33.30. The second component proved to be **12** obtained in 50% yield as a yellow solid: mp = 230−233 °C; UV−vis ($CHCl_3$) λ_{max} 240 ($\epsilon = 2.2 \times 10^4$), 270 ($\epsilon = 3.5 \times 10^4$), 370 ($\epsilon = 1.3 \times 10^4$), 385 ($\epsilon = 1.5 \times 10^4$); ^1H NMR 7.92 (2 H, dd, $J_1 = 3.3$ Hz, $J_2 = 1.7$ Hz) 8.65 (2 H, dd, $J_1 = 3.2$ Hz, $J_2 = 1.8$ Hz); ^{13}C NMR 120.3, 132.4, 135.4, 136.2; MS (CI) $m/z = 231$ (M)$^+$. Anal. Calcd for $C_8H_4N_2Cl_2O_2$: C, 41.59; H, 1.75; N, 12.13; Cl, 30.69. Found: C, 41.43; H, 1.86; N, 11.95; Cl, 30.21. Compound **12** could also be prepared by a

(25) Dayan, S.; Kol, M.; Rozen, S. *Synthesis* **1999**, 1427.

similar procedure from **11** in quantitative yield, but with 40% conversion using 8 molar equiv of the reagent bringing the overall yield of **12** to 65%.

2,3,6,7-Tetrachloroquinoxaline *N*-oxide (14) and 2,3,6,7-tetrachloroquinoxaline *N,N′*-dioxide (15) were obtained as a mixture from **13** (0.5 g, 1.87 mmol) as described above, using 7 equiv of the oxidizing agent. After separation by chromatography, compound **14** was obtained in 55% yield as a yellow solid: mp = 184 °C; UV−vis ($CHCl_3$) λ_{max} 260 ($\epsilon = 4.0 \times 10^4$), 330 ($\epsilon = 0.7 \times 10^4$), 365 ($\epsilon = 0.5 \times 10^4$); ^{1}H NMR 8.17 (1 H, s), 8.63 (1 H, s); ^{13}C NMR 120.2, 128.7, 130, 135.5, 136.3, 137.8, 139.2, 147.9; MS (CI) $m/z = 285$ $(M + 1)^+$. Anal. Calcd for $C_8H_2N_2Cl_4O$: C, 33.84; H, 0.71; N, 9.87; Cl, 49.95. Found: C, 34.21; H, 1.10; N, 9.78; Cl, 50.36. The second fraction proved to be the *N,N′*-dioxide **15** obtained in 40% yield as a yellow solid: mp = 188−189 °C; UV−vis ($CHCl_3$) λ_{max} 245 ($\epsilon = 1.4 \times 10^4$), 260 ($\epsilon = 1.2 \times 10^4$), 285 ($\epsilon = 1.4 \times 10^4$), 400 ($\epsilon = 0.3 \times 10^4$); ^{1}H NMR 8.74 (2 H, s); ^{13}C NMR 121.7, 117.6; MS (CI) $m/z = 301$ $(M + 1)^+$. Compound **15**, which could not be obtained in analytical purity, was also prepared from **14** by a similar procedure using 8 equiv of the reagent in quantitative yield, but with 10% conversion only.

6,7-Dimethyl-2,3-di(2-pyridyl)quinoxaline tetra-*N*-oxides (19) was prepared from **18** (0.6 g, 1.92 mmol), using altogether 6 equiv of the oxidizing agent as described above, resulting in 80% yield of a yellow solid which proved to be **19**: mp = 274 °C; UV−vis ($CHCl_3$) λ_{max} 240 ($\epsilon = 4.9 \times 10^4$), 270 ($\epsilon = 4.3 \times 10^4$), 375 ($\epsilon = 1.3 \times 10^4$), 395 ($\epsilon = 1.4 \times 10^4$); ^{1}H NMR 2.56 (6 H, s), 7.16−7.36 (4 H, m), 7.63 (2 H, dd, $J_1 = 7.5$ Hz, $J_2 = 1.7$ Hz), 8.24 (2 H, dd, $J_1 = 6.4$ Hz, $J_1 = 0.4$ Hz), 8.42 (2 H, s); ^{13}C NMR 20.4, 119.8, 125.4, 127.6, 129.1, 134.8, 136.7, 139.4, 139.9, 143.9 ppm; MS (FAB) $m/z = 377$ $(M + 1)^+$. Anal. Calcd. for $C_{20}H_{16}N_4O_4$: C, 63.83; H, 4.28; N, 14.89. Found: C, 63.83; H, 4.60; N, 14.51. As described in the Results and Discussion, it was possible to observe the formation of the mono-, di-, and trioxides **20**, **21**, and **22** with a recorded NMR spectrum of **21**: 2.53 (6 H, s), 7.22−7.39 (2 H, m), 7.85−7.91 (2 H, m), 7.95 (2 H, s), 8.01−8.07 (2 H, m), 8.44−8.47 (2 H, m).

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