A direct method for oxidizing quinoxaline, tetraazaphenanthrene and hexaazatriphenylene moieties using hypervalent λ^3-iodinane compounds

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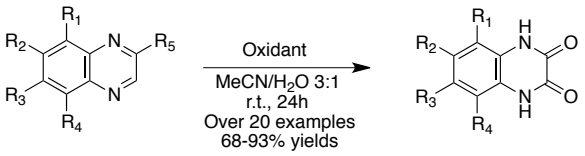


Abstract

An efficient oxidation reaction of various electron-poor quinoxaline-core containing compounds, such as quinoxalines, 1,4,5,8-tetraazaphenanthrenes and 1,4,5,8,9,12-hexaazatriphenylene using [bis(trifluoroacetoxy)iodo]benzene is reported. These compounds are converted into the corresponding quinoxaline-diones, with good to high yields, at room temperature, using a solvent mixture acetonitrile/water. This unprecedented reaction should enable the synthesis of a wide variety of compounds useful in several fields of chemistry.

Quinones and quinoxalinedione derivatives play an important role in organic chemistry, where they serve as building blocks for novel molecules,[1,2] coordination polymers,[3,4] or in coordination chemistry.[5] In medicinal chemistry[6] they are used for their antibacterial, anti-inflammatory, or antineoplastic effects as it is the case of tanshiones[7,8] which may be used against bone-resorptive diseases or β-lapachone which has significant antitumor activity against various forms of cancer.[9,10]

Even if quinoxalinediones may be synthesised by condensation of an *ortho*-phenylenediamine with oxalic acid,[11] there is currently no method to oxidize a quinoxaline moiety with good yields. Indeed, when a classical oxidant such as potassium permanganate is used with quinoxaline, the reaction only yields pyrazine-2,3-dicarboxylic acid.[12] Furthermore, when other oxidation reagents such as m-CPBA,[13] hydrogen peroxide,[14] potassium persulfate[15] or the efficient oxygen-transfer reagent $HOF{\cdot}CH_3CN$[16] are used on quinoxaline, the reaction only yields N-oxide or N,N'-dioxide, and no oxidation of the adjacent carbon atom is observed.

Finally, for more elaborated systems, such as 1,4,5,8-tetraazaphenanthrene (TAP)[17,18] and 1,4,5,8,9,12-hexaazatriphenylene, (HAT)[19,20] reactions are even more complicated, since these highly electron-withdrawing molecules are very reluctant towards oxidation.

In the course of our investigation of synthetic methodologies for the oxidation of electron-withdrawing molecules, we focused our research on well known hypervalent iodine derivatives,[21-23] namely (diacetoxyiodo)benzene (DIB)[24] and [bis(trifluoroacetoxy)iodo]benzene (BTI)[25,26] (Figure 1). These hypervalent λ^3 compounds have attracted great interest over the past decade due to their high versatility.[27-29]

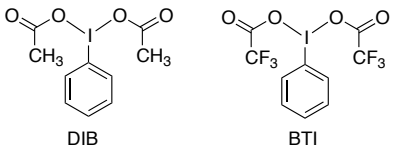
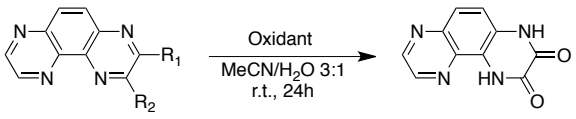


Figure 1: (diacetoxyiodo)benzene (DIB) and [bis(trifluoroacetoxy)iodo]benzene (BTI)

For instance, they are well known to oxidize a wide variety of compounds bearing a phenol group.[30-36] Furthermore, BTI is also used to convert methoxy derivatives into the corresponding quinones[37] via oxidative demethylation. These hypervalent iodine compounds present also the advantage of being commercially available, not expensive and rather easy to synthesise.[24-26] They have thus been widely used during the past decade and have allowed different groups to synthesise a wide variety of novel molecules.

In this paper, we report the use of [bis(trifluoroacetoxy)iodo]benzene as an oxidant for quinoxaline moieties. This oxidation reaction presents a unique character that has, to the best of our knowledge, never been reported in the literature for this type of structures. This novel oxidation strategy allowed us to convert substituted and unsubstituted quinoxalines, 1,4,5,8-tetraazaphenanthrenes and 1,4,5,8,9,12-hexaazatriphenylene into the corresponding "quinoxaline-diones" with high yields and at ambient temperature. The efficiency of this reaction is particularly remarkable because oxidation of these electron-poor polyazaaromatic compounds is generally unfeasible.

The study was initiated with attempts for oxidising two hydroxy-1,4,5,8-tetraazaphenanthrene derivatives **1a** and **2a**. Using DIB or BTI, we managed to convert both isomers **1a** and **2a** into the corresponding quinoxalinedione **1b** with high yields (Figure 2).

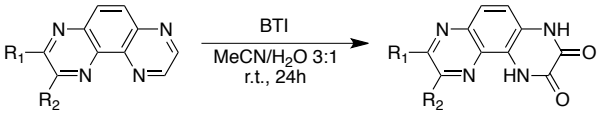


Compound	Substituent	Oxidant	Product	yield
1a	R1 = OH, R2 = H	BTI	1b	89%
2a	R1 = H, R2 = OH	BTI	1b	89%
1a	R1 = OH, R2 = H	DIB	1b	86%
2a	R1 = H, R2 = OH	DIB	1b	84%

Figure 2: Oxidation of 1,4,5,8-tetraazaphenanthrene hydroxy derivatives using DIB and BTI

The structure of these reaction products is in perfect agreement with the reported literature on phenolic oxidation using the λ^3 hypervalent iodine compounds, where the phenol compounds yield the corresponding quinones. In contrast, when BTI is used on the methoxy derivatives **3a** and **4a**, the product obtained after reaction corresponds surprisingly to an oxidation of the unsubstituted quinoxaline core (Figure 3).

This result suggests that the moiety sensitive towards BTI oxidation is the quinoxaline one, and not the methoxy substituent as already reported in the literature for other methoxy derivatives.[37] Comparatively, no reaction occurred when DIB was used instead of BTI.



Compound	Substituent	Product	yield
3a	R1 = OMe, R2 = H	3b	69%
4a	R1 = H, R2 = OMe	4b	76%

Figure 3: Oxidation of 1,4,5,8-tetraazaphenanthrene methoxy derivatives using BTI

In order to verify this hypothesis, we investigated the action of BTI and DIB on various unsubstituted quinoxaline-core containing compounds (Figure 4), such as quinoxaline **5a**, 1,4,5,8-

tetraazaphenanthrene **6a** (TAP) and 1,4,5,8,9,12-hexaazatriphenylene **7a** (HAT). Although DIB was in all cases unable to oxidise these molecules, BTI always yielded the corresponding quinoxaline-diones with good to high yields, showing that the quinoxaline core is the reactive moiety, and that no particular functional group is required for the oxidation to occur. This result is particularly remarkable as these highly electron-poor heterocycles are generally inert toward oxidation. We managed to upscale the reaction up to one gram of compounds **5a**, **6a**, and **7a** with no significant change in the reaction yield.

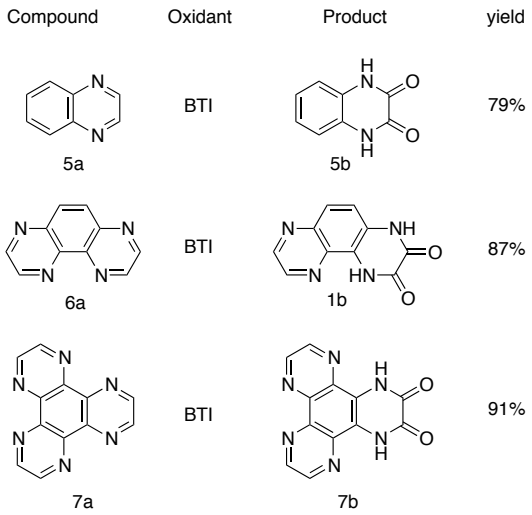
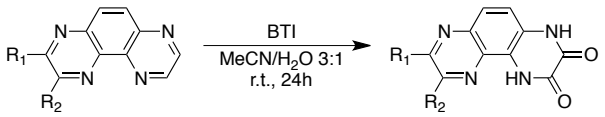


Figure 4: Oxidation of unsubstituted quinoxaline-core containing compounds using BTI

To further extend the scope of this reaction, we used BTI on various quinoxaline and 1,4,5,8-tetraazaphenanthrene compounds. Electron-poor 1,4,5,8- tetraazaphenanthrene was substituted on the position 2 or 3 by several functional groups, such as methoxy **3a**, **4a**, **8a**, chloride **9a**, **10a**, formyl **11a**, ethanoloxy **12a** and methyl **13a** groups (Figure 5). Results show that in all cases, the product that is formed is the one where the unsubstituted quinoxaline core is oxidized.



Compound	Substituent	Product	yield
8a	R1 = R2 = OMe	8b	83%
9a	R1 = Cl, R2 = H	9b	82%
10a	R1 = H, R2 = Cl	10b	68%
11a	R1 = CHO, R2 = H	11b	92%
12a	R1 = OCH_2CH_2OH, R2 = H	12b	75%
13a	R1 = CH_3, R2 = H	13b	73%

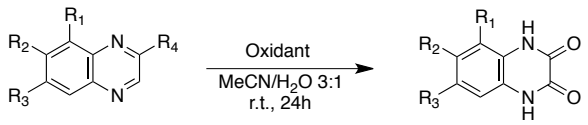
Figure 5: Oxidation of various 1,4,5,8-tetraazaphenanthrene derivatives using BTI

Regarding quinoxalines, these molecules were substituted on various positions by numerous functional groups, such as halogen (chloride **14a**, **15a**, **16a**, bromide **17a**, iodide **18a**), nitro (**19a**, **20a**, **21a**, **22a, 23a**), hydroxyl (**24a**, **25a**), methoxy (**26a**, **27a**) or methyl (**28a**). Once again, results show that in all cases, the oxidation occurs on the quinoxaline core (Figure 6). These results indicate that the BTI-quinoxaline oxidation is very selective towards the quinoxaline core, and does not react with the variety of substituents that were used. Nevertheless, if the quinoxaline is substituted by a hydroxyl group on the benzene ring, only phenolic oxidation occurs.[33,38]

In view of determining the key parameters required for the oxidation, we investigated the reaction of BTI with several types of system, namely pyrazine, pyridine, pyridine derivatives and quinoline. The comparison between pyrazine and pyridine moieties should allow to determine if the reactive subunit is the pyridinic one or if two nitrogen atoms are required for the oxidation to occur. Comparison of pyrazine/quinoxaline and pyridine/quinoline derivatives should indicate if the presence of a second fused aromatic ring is necessary to isolate the reported oxidation products.

Despite our efforts, the reaction of BTI with pyridine and quinoline derivatives never gave rise to the formation of the expected oxidation products, nor did the reaction on pyrazine. This strongly

suggests that the presence of two nitrogen atoms, and a second conjugated aromatic ring are required for the reaction to occur.



Compound	Substituent	Oxidant	Product	yield
14a	R1 = H, R2 = Cl, R3 = R4 = H	BTI	14b	82%
15a	R1 = Cl, R2 = R3 = R4 = H	BTI	15b	88%
16a	R1 = H, R2 = R3 = Cl, R4 = H	BTI	16b	82%
17a	R1 = H, R2 = Br, R3 = R4 = H	BTI	17b	79%
18a	R1 = H, R2 = I, R3 = R4 = H	BTI	18b	86%
19a	R1 = H, R2 = Cl, R3 = NO_2, R4 = H	BTI	19b	86%
20a	R1 = H, R2 = Br, R3 = NO_2, R4 = H	BTI	20b	87%
21a	R1 = H, R2 = I, R3 = NO_2, R4 = H	BTI	21b	93%
22a	R1 = H, R2 = NO_2, R3 = R4 = H	BTI	22b	77%
23a	R1 = Cl, R2 = NO_2, R3 = R4 = H	BTI	23b	85%
24a	R1 = R2 = R3 = H R4= OH	BTI	5b	81%
24a	R1 = R2 = R3 = H R4= OH	DIB	5b	84%
25a	R1 = R2 = H, R3 = NO_2, R4 = OH	BTI	22b	80%
25a	R1 = R2 = H, R3 = NO_2, R4 = OH	DIB	22b	82%
26a	R_1 = H, R_2 = MeO, R_3 = NO_2, R_4 = H	BTI	26b	89%
27a	R1 = MeO, R2 = NO_2, R3 = R4 = H	BTI	27b	85%
28a	R1 = Me, R2 = R3 = R4 = H	BTI	28b	90%

Figure 6: Oxidation of substituted quinoxalines using BTI

In the cases of pyridine derivatives, quinoline derivatives and pyrazine, the product isolated after reaction corresponds to iodylbenzene $PhIO_2$, resulting from the hydrolysis of the trifluoroacetate groups or from the disproportionation of BTI (Figure 7). Even if it is commonly accepted that the hydrolysis of BTI produces PhIO, this hydrolysis is generally carried out under alkali condition.[39] Disproportionation or hydrolysis of BTI leading to $PhIO_2$ was confirmed by high-resolution mass spectrometry, infrared spectroscopy and ^{1}H and ^{13}C NMR which are in agreement with the reported chemical shifts.[40] Furthermore, we have also verified that this hydrolysis product was not the oxidative species, confirming therefore that BTI is the real oxidative species in the BTI-mediated quinoxaline oxidation.

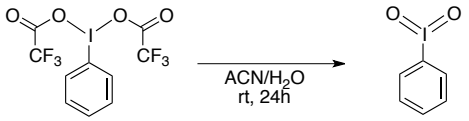


Figure 7: Hydrolysis reaction of BTI

Thus, comparison of the results obtained with pyrazine and quinoxaline derivatives indicates that, even if two nitrogen atoms are required for this particular oxidation, only compounds containing at least one supplementary fused aromatic ring allow isolation of the expected oxidised products.

Based on our results, we could propose the following mechanism (Figure 9). First, a nucleophilic attack of one of the nitrogen atom from the quinoxaline core on the iodine atom would take place. This attack would be followed by the addition of water, leading to the hydroxy derivative. This nucleophilic attack by water is most likely favoured by the presence of the second nitrogen atom, which decreases even more the electron density on the carbon atom as compared to that of the pyridinic core. The second aromatic ring might also stabilize the intermediate. Once the first hydroxy group is present on the molecule, the standard mechanism that is proposed in the literature for phenolic derivatives would take place.[30]

The hypothesis concerning this second step is strengthened by the fact that 2- and 3-hydroxy-1,4,5,8-tetraazaphenanthrene **1a** and **2a** yield the same product **1b**, where only phenolic oxidation occurred, and where no oxidation of the unsubstituted quinoxaline core is observed. If this hypothesis were not correct, we should observe oxidation also in the unsubstituted quinoxaline subunit. In order to confirm the mechanism involving a nucleophilic attack by water, an experiment was conducted using $H_2{}^{18}O$ instead of H_2O. This experiment allowed us to isolate the desired ^{18}O-enriched quinoxalinedione.

In summary, we have reported the unprecedented use of [bis(trifluoroacetoxy)iodo]benzene as an oxidant towards quinoxaline-core containing molecules. Oxidation using [bis(trifluoroacetoxy)iodo]benzene was investigated on a wide variety of compounds, such as substituted and unsubstituted quinoxalines, 1,4,5,8-tetraazaphenanthrenes and 1,4,5,8,9,12-hexaazatriphenylene. This reaction, carried out at room temperature, always yielded the desired quinoxaline-dione with good to high yields. When hydroxyl-derivatives are used, it is always the phenolic moiety that is oxidized, which is in agreement with literature. The phenolic group is more nucleophilic than the nitrogen atom in the quinoxaline, which probably explains this behaviour. This reaction can be upscaled to a gram of compounds with no significant loss in the reaction yield.

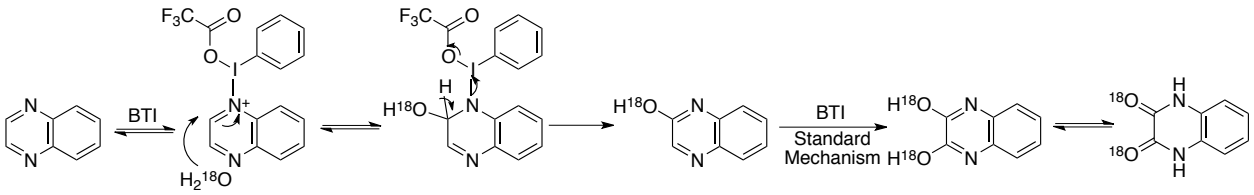


Figure 8: Proposed mechanism for the quinoxaline-core containing compounds using BTI

Experimental Section

General

^{1}H NMR and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer, using DMSO-d_6 as solvent. Chemical shifts are reported in ppm using the relative solvent peak as a reference standard. The mass spectrometric experiments were performed on a large scale tandem mass spectrometer having an E1B1E2E3B2E4 geometry, where E stands for electrostatic sector and B for magnetic sector. The electron ionization mass spectra (EI-MS) were recorded by scanning the field of the first magnetic field (B1). The mass-separated ions were counted using an off-axis photomultiplier located after the second electrostatic sector. The accurate mass measurements were recorded using perfluorokerosene (PFK) as the internal calibrant by scanning the accelerating voltage (voltage scan) and increasing the resolution of the mass spectrometer to R = 10.000 at 5% of the peak intensity. The ESI measurements were performed on a QToF2 mass spectrometer. The HRMS measurement was performed at 10000 resolution using m/z 322.7782 ions from a NaI solution (10 mg/ml isopropanol/water) as the lock mass. Infrared spectra were recorded in ATR mode on a Germanium crystal.

General procedure for the oxidation using (bisacetoxy)iodobenzene or bis(trifluoroacetoxy)iodobenzene:

The starting material (0.5 mmol) is dissolved in 15 mL of a mixture acetonitrile/water 3 :1. The mixture is stirred at room temperature and bis(trifluoroacetoxy)iodobenzene (1.1 mmol) or (bisacetoxy)iodobenzène (1.1 mmol) is then added. The reaction mixture is stirred at room temperature for a period of 24 hours. The reaction is monitored using TLC (alumina. $CHCl_3$/Acetone 8 :2). If needed, another equivalent of bis(trifluoroacetoxy)iodobenzene is added during the reaction. After completion, the reaction is concentrated under vaccum and the product

is collected by filtration, washed with water, acetonitrile and diethylether. The product is finally dried in a dessicator overnight at room temperature.

Pyrazino[2,3-*f*]quinoxaline-2,3(1*H*,4*H*)-dione (1b)

Product **1b** is obtained starting from different starting materials. When hydroxy derivatives **1a** and **2a** are used, the conversion is achieved using BTI or DIB as the oxidant. When the unsubstituted derivative **6a** is used, only BTI allowed the oxidation to occur. The product is obtained as a white solid with yields ranging from 84 to 89% depending on the starting material (**1a**, **2a** or **6a** (89.5-96 mg)). RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.67 (d, J = 9.0Hz, 1H), 7.83 (d, J = 9.0Hz, 1H), 8.93 (dd, J = 1.8Hz, 2H), 12.05 (bs, 1H), 12.35 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.7 ; 177.1 ; 144.4 ; 138.7 ; 131.5 ; 124.5 ; 123.3 ; 119.9 ; 119.7. EI(+)-MS : m/z (%) = 186 (100) (M^+ - CO), 214 (58) (M^+), 158 (58) (M^+ - 2CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{10}H_6N_4O_2$ 214.0491; Found 214.0498. IR (neat. ν_{max}/cm^{-1}): 1680.8, 1360.8.

8-Methoxypyrazino[2,3-*f*]quinoxaline-2.3(1*H*,4*H*)-dione (3b)

The product is obtained as a white solid with a yield of 69% (84.6 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 4.04 (s, 3H), 7.57 (AB, 2H, J= 9.0Hz), 8.60 (s, 1H) 12,07 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.5 ; 138.6 ; 136.2 ; 122.7 ; 121.2 ; 120.7 ; 119.7 ; 54.0. EI(+)-MS :

m/z (%) = 216 (100) (M^+ - CO), 244 (86) (M^+). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{11}H_8N_4O_3$ 244.0596; Found 244.0589. IR (neat. ν_{max}/cm^{-1}): 1693.4, 1378.6, 1327.5.

9-Methoxypyrazino[2,3-*f*]quinoxaline-2.3(1*H*,4*H*)-dione (4b)

The product is obtained as a white solid with a yield of 76% (92.6 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^1H (300.1 MHz. δ-DMSO-*d_6*): 4.19 (s, 3H), 7.41 (d, 1H, J=9.0Hz), 7.73 (d, 1H, J = 9.0Hz), 8.53 (s, 1H), 11.96 (bs, 1H), 12.26 (bs, 1H). ^{13}C spectra for compound 4b could not be obtained due to extremely low solubility of this compounds in conventional organic solvents. EI(+)-MS : m/z (%) = 216 (100) (M^+ - CO), 244 (70) (M^+). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{11}H_8N_4O_3$ 244.0596; Found 244.0589. IR (neat. ν_{max}/cm^{-1}): 1713.1, 1682.17, 1578.0, 1346.8.

Quinoxaline-2,3(1*H*,4*H*)-dione (5b)

Product **5b** is obtained from different starting materials. When hydroxy derivative **24a** is used, the conversion is achieved using BTI or DIB as the oxidant. When the unsubstituted derivative **5a** is used, only BTI allowed the oxidation to occur. The product is obtained as a white solid with yields ranging from 79 to 84% depending on the starting material (**5a** (64.1 mg) or **24a** (68.1 mg)). RMN ^1H (300.1 MHz. δ-DMSO-*d_6*): 7.10 (m, 4H), 11.90 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d_6*): 155.1 ; 125.6 ; 123.0 ; 115.1. EI(+)-MS : m/z (%) = 162 (100) (M^+), 134 (60) (M^+ - CO), 106 (56) (M^+ - 2CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_6N_2O_2$ 162.0429; Found 162.0435. IR (neat. ν_{max}/cm^{-1}): 1675.0.

Dipyrazino[2,3-*f*:2',3'-*h*]quinoxaline-2,3(1*H*,4*H*)-dione (7b)

The product is obtained as a beige solid with a yield of 91% (121.2 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-d_6): 9.16 (d, 2H, J = 1.8Hz), 9.17 (d, 2H, J = 1.8Hz), 12.25 (bs, 2H). RMN ^{13}C (75.5 MHz. δ-DMSO-d_6): 166.8 ; 1565 ; 146.6 ; 145.3 ; 127.7 ; 135.6. EI(+)-MS : m/z (%) = 238 (100) (M^+ - CO), 266 (66) (M^+), 210 (42) (M^+ - 2CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{12}H_6N_6O_2$ 266.0552; Found 266.0553. IR (neat. ν_{max}/cm^{-1}): 1690.6 ; 1627.4 ; 1375.8.

8,9-dimethoxypyrazino[2,3-f]quinoxaline-2,3(1H,4H)-dione (8b)

The product is obtained as a white solid with a yield of 83% (113.7 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-d_6): 4.02 (s, 3H), 4.20 (s, 3H), 7.31 (d, 1H, J = 9Hz), 7.48 (d, 1H, J = 9Hz), 11,85 (bs, 1H), 11.15 (bs, 1H). ^{13}C spectra for compound 8b could not be obtained due to extremely low solubility of this compounds in conventional organic solvents. EI(+)-MS : m/z (%) = 246 (100) (M^+ - CO), 274 (100) (M^+). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{12}H_{10}N_4O_4$ 274.0702; Found 274.0714. IR (neat. ν_{max}/cm^{-1}): 1720.4 ; 1677.1 ; 1352.3.

8-Chloropyrazino[2,3-*f*]quinoxaline-2,3(1*H*,4*H*)-dione (9b)

The product is obtained as a pale yellow solid with a yield of 82% (102.2 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.70 (d, 1H, J=9.0Hz), 7.77 (d, 1H, J = 9.0Hz), 8.97 (s, 1H), 12.30 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.6 ; 155.1 ; 145.6 ; 144.0 ; 137.7 ; 129.8 ; 125.0 ; 122.1 ; 121.1 ; 120.1. EI(+)-MS : m/z (%) = 220 (100) (M^+ - CO), 248 (62) (M^+), 192 (46) (M^+ - 2CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{10}H_5N_4O_2Cl$ 248.0101; Found 248.0093. IR (neat. ν_{max}/cm^{-1}): 1682.6, 1379.3, 1141.5.

9-Chloropyrazino[2,3-*f*]quinoxaline-2,3(1*H*,4*H*)-dione (10b)

The product is obtained as a yellow solid with a yield of 68% (84.4 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.67 (d, 1H, J=9Hz), 7.86 (d, 1H, J = 9Hz), 8.94 (s, 1H), 12.07 (bs, 1H), 12.40 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.9 ; 155.3 ; 146.5 ; 144.1 ; 137.2 ; 126.1 ; 123.4 ; 120.2 ; 119.5. EI(+)-MS : m/z (%) = 220 (100) (M^+ - CO), 248 (58) (M^+), 192 (42) (M^+ - 2CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{10}H_5N_4O_2Cl$ 248.0101; Found 248.0093. IR (neat. ν_{max}/cm^{-1}): 1730.9, 1369.2, 1128.7.

8-formylpyrazino[2,3-*f*]quinoxaline-2,3(1*H*,4*H*)-dione (11b)

The product is obtained as a pale yellow solid with a yield of 92% (111.1 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.80 (d, 1H, J=9.0Hz), 8.02 (d, 1H, J = 9.0Hz), 9.29 (s, 1H), 10.17 (s,

1H), 12.26 (bs, 1H), 12.50 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 192.5 ; 155.8 ; 154.9 ; 145.1 ; 141.5 ; 137.5; 132.6 ; 127.0 ; 124.4 ; 121.3 ; 119.9. EI(+)-MS : m/z (%) = 214 (100) (M^+ - CO), 242 (52) (M^+), 158 (48) (M^+ - 3CO), 186 (46) (M^+ - 2CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{11}H_6N_4O_3$ 242.04399; Found 242.0435. IR (neat. ν_{max}/cm^{-1}): 1694.8; 1590.6; 1383.1; 875.5.

8-(2-hydroxyethoxy)pyrazino[2,3-*f*]quinoxaline-2,3(1*H*,4*H*)-dione (12b)

The product is obtained as a white solid with a yield of 75% (102.6 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 3.80 (m, 2H), 4.72 (m, 2H), 4.88 (t, 1H, J=5.4Hz), 7.40 (d, 1H, J=9.0Hz), 7.71 (d, 1H, J = 9.0Hz), 8.51 (s, 1H sector instrument), 11.95 (bs, 1H), 12.26 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 156.9 ; 155.7 ; 155.2 ; 138.2 ; 135.2 ; 128.5 ; 125.2 ; 122.9 ; 118.5 ; 115.3 ; 68.8 ; 59.4. HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{12}H_{10}N_4O_4$ 274.0702; Found 274.0703. IR (neat. ν_{max}/cm^{-1}): 3091.6; 1695.0; 1320.8; 833.4.

8-methylpyrazino[2,3-*f*]quinoxaline-2,3(1*H*,4*H*)-dione (13b)

The product is obtained as a white solid with a yield of 73% (83.1 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 2.71 (s, 3H), 7.61 (d, 1H, J=9.0Hz), 7.73 (d, 1H, J = 9.0Hz), 8.85 (s, 1H), 12.05 (bs, 1H), 12.24 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.6 ; 155.1 ; 153.2 ; 145.2 ;

123.6 ; 122.5 ; 119.8 ; 119.5 ; 106.8 ; 21.9. HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_{11}H_8N_4O_2$ 228.0647; Found 228.0651. IR (neat. ν_{max}/cm^{-1}): 1675.6; 1387.9; 861.2.

6-Cl-Quinoxaline-2,3(1*H*,4*H*)-dione (14b)

The product is obtained as a white solid with a yield of 82% (80.7 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.11 (m, 3H), 11.97 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.0 ; 154.8 ; 126.9 ; 126.5 ; 124.8 ; 122.6 ; 116.6 ; 114.4. EI(+)-MS : m/z (%) = 196 (100) (M^+), 168 (48) (M^+ - CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_5N_2O_2Cl$ 196.0039; Found 196.0032. IR (neat. ν_{max}/cm^{-1}): 1691.4; 1392.4.

5-Cl-Quinoxaline-2,3(1*H*,4*H*)-dione (15b)

Product is obtained as a beige solid with a yield of 88% (85.9 mg). RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.07 (m, 2H), 7.17 (m, 1H,), 11.35 (bs, 1H), 12.06 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.4 ; 154.8 ; 127.1 ; 123.7 ; 123.4 ; 122.9 ; 118.6 ; 114.2. HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_5N_2O_2Cl$ 196.0039; Found 196.0031. IR (neat. ν_{max}/cm^{-1}): 1674.2; 1394.9.

6,7-diCl-Quinoxaline-2,3(1*H*,4*H*)-dione (16b)

The product is obtained as a white solid with a yield of 82% (94.4 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.25 (s, 2H), 12.01 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 154.7 ; 126.1 ; 124.3 ; 116.0. HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_4N_2O_2Cl_2$ 229.9650; Found 229.9652. IR (neat. ν_{max}/cm^{-1}): 1686.9; 1396.9; 873.1.

6-Br-Quinoxaline-2,3(1*H*,4*H*)-dione (17b)

The product is obtained as a white solid with a yield of 79% (95.0 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.05 (m, 1H), 7.25 (m, 2H), 11.97 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.0 ; 154.8 ; 127.2 ; 125.4 ; 125.2 ; 117.2 ; 116.9 ; 114.2. EI(+)-MS : m/z (%) = 240 (100) (M^+), 212 (34) (M^+ - CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_5N_2O_2Br$ 239.9534; Found 239.9539. IR (neat. ν_{max}/cm^{-1}): 1693.7; 1389.2.

6-I-Quinoxaline-2,3(1*H*,4*H*)-dione (18b)

The product is obtained as a white solid with a yield of 86% (123.5 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 6.91 (d, 1H, H = 8.1Hz), 7.40 (m, 2H), 11.90 (bs, 1H), 11.95 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 154.9 ; 154.9 ; 131.2 ; 127.3 ; 125.5 ; 122.9 ; 117.1 ; 85.8. EI(+)-MS : m/z (%) = 288 (100) (M^+), 260 (22) (M^+ - CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_5N_2O_2I$ 287.9396; Found 287.9401. IR (neat. ν_{max}/cm^{-1}): 1693.9; 1383.2.

6-Cl-7-NO_2- Quinoxaline-2,3(1*H*,4*H*)-dione (19b)

The product is obtained as a white solid with a yield of 86% (103.5 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.26 (s, 1H), 7.82 (s, 1H), 12.24 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.0 ; 154.5 ; 130.9 ; 125.3 ; 119.8 ; 116.7 ; 112.9. EI(+)-MS : m/z (%) = 241 (100) (M^+). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_4N_3O_4Cl$ 240.9890; Found 240.9882. IR (neat. ν_{max}/cm^{-1}): 1695.4; 1397.7; 881.5.

6-Br-7-NO_2- Quinoxaline-2,3(1*H*,4*H*)-dione (20b)

The product is obtained as a white solid with a yield of 87% (124.2 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.43 (s, 1H), 7.79 (s, 1H), 12.22 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.0 ; 154.6 ; 142.6 ; 130.9 ; 125.7 ; 119.8 ; 112.8 ; 106.9. EI(+)-MS : m/z (%) = 285 (20) (M^+), 253 (100) (M^+ - CO), 207 (42) (M^+ - CO - NO_2). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_4N_3O_4Br$ 284.9385; Found 284.9376. IR (neat. ν_{max}/cm^{-1}): 1694.6; 1396.9; 881.3.

6-I-7-NO_2- Quinoxaline-2,3(1*H*,4*H*)-dione (21b)

The product is obtained as a pale yellow solid with a yield of 93% (154.5 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.68 (s, 1H), 7.75 (s, 1H), 12.17 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.0 ; 154.6 ; 146.0 ; 130.9 ; 126.4 ; 126.1 ; 112.3 ; 80.2. EI(+)-MS : m/z (%) = 333 (10) (M^+), 301 (100) (M^+ - O_2), 255 (36) (M^+ - CO - NO_2). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_4N_3O_4I$ 332.9247; Found 332.9233. IR (neat. ν_{max}/cm^{-1}): 1691.9; 1395.1.

6-NO_2-Quinoxaline-2,3(1*H*,4*H*)-dione (22b)

Product **22b** is obtained from different starting materials. When hydroxy derivative **25a** is used, the conversion is achieved using BTI or DIB as the oxidant. When the unsubstituted derivative **22a** is used, only BTI allowed the oxidation to occur. The product is obtained as a pale yellow solid with yields ranging from 77 to 82% depending on the starting material (**22a** (80.6 mg) or **25a** (85.1 mg)). RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 7.26 (d, 1H, J = 8.7 Hz), 7.97 (m, 2H), 12.26 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.1 ; 154.7 ; 142.1 ; 131.7 ; 126.1 ; 118.6 ; 115.5 ; 110.3. EI(+)-MS : m/z (%) = 207 (100) (M^+), 179 (16) (M^+ - CO). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_5N_3O_4$ 207.0280; Found 207.0270. IR (neat. ν_{max}/cm^{-1}): 1693.3; 1337.7.

5-Cl-6-NO_2-Quinoxaline-2,3(1*H*,4*H*)-dione (23b)

The product is obtained as a pale yellow solid with a yield of 85% (101.9 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H

(300.1 MHz. δ-DMSO-*d*$_6$): 7.19 (d, 1H, J = 9.0 Hz), 7.82 (d, 1H, J = 9.0 Hz), 11.70 (bs, 1H), 12.39 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.2 ; 154.5 ; 142.3 ; 130.6 ; 124.6 ; 120.1 ; 113.7 ; 112.0. HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_8H_4N_3O_4Cl$ 240.9890; Found 240.9891. IR (neat. ν_{max}/cm^{-1}): 1720.6; 1535.6 ; 1396.6.

6-MeO-7-NO$_2$-Quinoxaline-2,3(1*H*,4*H*)-dione (26b)

The product is obtained as a yellow solid with a yield of 89% (105.1 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 6.91 (s, 1H), 7.72 (s, 1H), 12.04 (bs, 2H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.3 ; 154.2 ; 149.6 ; 132.8 ; 131.8 ; 118.9 ; 112.5 ; 99.9 ; 56.7. EI(+)-MS : m/z (%) = 237 (20) (M^+). HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_9H_7N_3O_5$ 237.0386; Found 237.0391. IR (neat. ν_{max}/cm^{-1}): 1709.3; 1311.0.

5-MeO-6-NO$_2$-Quinoxaline-2,3(1*H*,4*H*)-dione (27b)

Product is obtained as a white solid with a yield of 85% (101.2 mg). RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 6.99 (d, 1H, J=9.0Hz), 7.76 (d, 1H, J = 9.0Hz), 11.87 (bs, 1H), 12.28 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.0 ; 154.9 ; 141.4 ; 137.2 ; 131.4 ; 121.0 ; 119.9 ; 110.4 ; 62.8. HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_9H_7N_3O_5$ 237.0386; Found 237.0394. IR (neat. ν_{max}/cm^{-1}): 1726.6; 1538.8 ; 1387.8.

5-Me-Quinoxaline-2,3(1*H*,4*H*)-dione (28b)

The product is obtained as a white solid with a yield of 90% (79.4 mg) following the general procedure described for the oxidation using bis(trifluoroacetoxy)iodobenzene. RMN ^{1}H (300.1 MHz. δ-DMSO-*d*$_6$): 2.34 (s, 3H), 6.93 (m, 1H), 6.99 (m, 2H), 11.22 (bs, 1H), 11.90 (bs, 1H). RMN ^{13}C (75.5 MHz, δ-DMSO-*d*$_6$): 155.7 ; 154.8 ; 125.5 ; 124.7 ; 124.0 ; 123.9 ; 122.8 ; 113.2 ; 17.2. HRMS (EI, sector instrument) m/z: [M^+] calcd for $C_9H_8N_2O_2$ 176.0586; Found 176.0592. IR (neat. ν_{max}/cm^{-1}): 1679.8; 1396.9.

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Supporting Information Available: General informations about spectroscopic apparatus and copies of ^{1}H, ^{13}C, IR, MS, HRMS spectra for the different compounds when available. This material is available free of charge via the internet at http://pubs.acs.org.

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