Supporting Information
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Supporting Information

Synthesis and hydrolysis of 4-chloro-PyMTA and 4-iodo-PyMTA esters and their oxidative degradation with Cu(I/II) and oxygen

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Preparation of iodo-dibromide 11

Scheme S1. Preparation of iodo-dibromide 11 via the treatment of iodo-diol 8 with PBr₃. (a) PBr₃, CHCl₃, 80 °C, 8h.

When following the reported procedure [1] for the preparation of iodo-dibromide 11 via treatment of iodo-diol 8 with PBr₃ in CHCl₃ at reflux for 8 h we obtained a mixture of iodo-dibromide 11 and halides 22 – 26 (Scheme S1). The yield of iodo-dibromide 11 was 31% and the overall yield of the halides 22 – 26 was 16%. A longer reaction time of 18 h decreased the yield of diodo-dibromide 11 to 7% and increased the overall yield of halides 22 – 26 to 44%. The compounds were identified with ¹H NMR spectroscopy and mass spectrometry of this mixture. In the ¹H NMR spectrum (Figure S1) the signals of all of the six compounds can clearly be seen. There are eight signals of aromatic protons, four singlets and four doublets. The singlets are assigned to compounds 11, 23, 24, and 26, and the doublets to compounds 22 and 25. In the spectral region for aliphatic protons eight singlets occur for the methylene protons. The EI-MS spectrum shows the signals of the molecular ions of all of the six compounds: m/z = 484.7 for [23]**; m/z = 436.7 for [22]** and [26]**; m/z = 388.7 for [11]** and [25]**; m/z = 340.8 for [24]**. These compounds are not separable, neither through crystallization nor through column chromatography.

Figure S1. ¹H NMR spectrum (500 MHz, acetone-d₆) of the mixture of iodo-dibromide 11 and halides 22 – 26.
Determination of the content of ligand in hydrolysis products

Basic hydrolysis of the 4-halo-PyMTA ethyl esters gave \{[4-halo-PyMTA - 4 H\(^+\)]\(^4\) • n H\(^+\) • n Na\(^+\)\}. Acidic hydrolysis of the 4-halo-PyMTA tert-butyl ester gave \{4-halo-PyMTA • n TFA\}. The content of the ligand was batch dependant. To quantify its content quantitative \(^1\)H NMR spectroscopy [2] was applied as follows. The material (ca. 5 mg) and maleic acid as the reference (mass fraction 99.99%, standard for quantitative NMR; ca. 2 mg) were weighed using a balance with an accuracy of 0.001 mg and dissolved in CD\(_2\)OD (0.6 mL) or D\(_2\)O (0.6 mL) in a NMR tube with 5 mm diameter. \(^1\)H NMR spectra were recorded on a Bruker DRX 500 spectrometer at 300 K using 30° pulses (Bruker zg30 pulse sequence) and a delay time of 30 s (for the samples in CD\(_2\)OD) or 40 s (for the samples in D\(_2\)O). 16 scans were averaged. The content in wt.% of the structural motive [4-halo-PyMTA - 4 H\(^+\)]\(^4\) in \{[4-halo-PyMTA - 4 H\(^+\)]\(^4\) • n H\(^+\) • n Na\(^+\)\} was calculated with the formula (1). The content of the structural motive 4-halo-PyMTA in \{4-halo-PyMTA • n TFA\} was calculated with the formula (2),

\[
P_{[4\text{-halo-PyMTA} - 4 \text{H}^+]^4} = \frac{I_{\text{PyMTA}}}{I_{\text{ref}}} \cdot \frac{N_{\text{ref}}}{N_{\text{PyMTA}}} \cdot \frac{M_{[4\text{-halo-PyMTA} - 4 \text{H}^+]^4}}{M_{\text{ref}}} \cdot \frac{m_{\text{ref}}}{m_{\text{material}}} \cdot P_{\text{ref}} \tag{1}
\]

\[
P_{\text{PyMTA}} = \frac{I_{\text{PyMTA}}}{I_{\text{ref}}} \cdot \frac{N_{\text{ref}}}{N_{\text{PyMTA}}} \cdot \frac{M_{\text{PyMTA}}}{M_{\text{ref}}} \cdot \frac{m_{\text{ref}}}{m_{\text{material}}} \cdot P_{\text{ref}} \tag{2}
\]

where \(P\) is the purity as mass fraction, \(I\) is the signal integral, \(N\) is the number of protons, \(M\) is the molar mass of the components, and \(m\) is the mass that had been dissolved. The index \(\text{ref}\) stands for reference. The index \(\text{material}\) stands for \{[4-halo-PyMTA - 4 H\(^+\)]\(^4\) • n H\(^+\) • n Na\(^+\)\} or \{4-halo-PyMTA • n TFA\} in equation (1) and equation (2), respectively. The signal of the aromatic protons of the ligand and the signal of the olefinic protons of maleic acid were taken for integration. The contents of the ligand in the materials are listed in Table S1.

**Table S1.** Ligand content of four representative samples as determined by quantitative \(^1\)H NMR spectroscopy.

<table>
<thead>
<tr>
<th>material</th>
<th>ligand content / wt.%</th>
</tr>
</thead>
<tbody>
<tr>
<td>{[4-chloro-PyMTA - 4 H(^+)](^4) • n H(^+) • n Na(^+)} (14)</td>
<td>[4-chloro-PyMTA - 4 H(^+)](^4) / 89.5 wt.%</td>
</tr>
<tr>
<td>{4-chloro-PyMTA • n TFA} (16)</td>
<td>4-chloro-PyMTA / 94.2 wt.%</td>
</tr>
<tr>
<td>{[4-iodo-PyMTA - 4 H(^+)](^4) • n H(^+) • n Na(^+)} (15)</td>
<td>[4-iodo-PyMTA - 4 H(^+)](^4) / 92.2 wt.%</td>
</tr>
<tr>
<td>{4-iodo-PyMTA • n TFA} (17)</td>
<td>4-iodo-PyMTA / 93.9 wt.%</td>
</tr>
</tbody>
</table>
Oxidative degradation of 4-iodo-PyMTA ethyl ester 10a to ester-aldehyde 21

\[
\begin{array}{c}
\text{CuI, air} \\
\text{THF, rt, 240 h}
\end{array}
\]

Figure S2. (1) \(^1\)H NMR spectrum (500 MHz, CDCl\(_3\)) of 4-iodo-PyMTA ethyl ester 10a. (2) \(^1\)H NMR spectrum (500 MHz, CDCl\(_3\)) of the mixture of 4-iodo-PyMTA ethyl ester 10a, ester-aldehyde 21, and diethyl iminodiacetate (5a).

The \(^1\)H NMR spectrum of 4-iodo-PyMTA ethyl ester 10a is shown in Figure S2 (1). After stirring a solution of this compound and CuI in CH\(_2\)Cl\(_2\) for 240 h in air, a \(^1\)H NMR spectrum of the material was recorded which is shown in Figure S2 (2). The latter spectrum shows six additional signals marked with the letters d-i with the intensity ratio of 1 : 1 : 1 : 2 : 4 : 4. The NMR data suggest the formation of ester-aldehyde 21 and diethyl iminodiacetate (5a). The singlet at 9.93 ppm clearly points to a formyl group. The two doublets at 8.29 ppm and 8.17 ppm with the same coupling constant of 1.53 Hz are assigned to the two aromatic protons and the singlets at 4.10 ppm and 3.60 ppm represent the diethyl nitrilodiacetate group of ester-aldehyde 21. The singlet at 3.45 ppm confirms the presence of diethyl iminodiacetate (5a) as the \(^1\)H NMR spectrum of diethyl iminodiacetate (5a) (Figure S12) shows a singlet at exactly the same position. The signals of the ethyl groups of 4-iodo-PyMTA ethyl ester 10a, ester-aldehyde 21 and diethyl iminodiacetate (5a) overlap. The ESI MS spectra of this material shows, in addition to the two signals at \(m/z\) 608.2 and 630.1 which are assigned to the ions [M + H]\(^+\) and [M + Na]\(^+\) of the 4-iodo-PyMTA ethyl ester 10a, signals at \(m/z\) 457.1, 212.0, and 190.0. These three signals
are assigned to the quasi molecular ions of ester-aldehyde 21 ([21 + Na]+) and of diethyl iminodiacetate (5a) ([5a + Na]+ and [5a + H]+), respectively.
Figure S3. $^1H$ NMR spectrum (500 MHz, CDCl$_3$) of dimethyl 4-chlorodipicolinate (2).
Figure S4. $^{13}$C NMR spectrum (125 MHz, CDCl$_3$) of dimethyl 4-chlorodipicolinate (2).
Figure S5. $^{13}$C DEPT 135 NMR spectrum (125 MHz, CDCl$_3$) of dimethyl 4-chlorodipicolinate (2).
Figure S6. $^1$H NMR spectrum (500 MHz, DMSO-$d_6$) of chloro-diol 3.
Figure S7. $^{13}$C NMR spectrum (125 MHz, DMSO-d$_6$) of chloro-diol 3.
Figure S8. $^{13}$C DEPT 135 NMR spectrum (125 MHz, DMSO-$d_6$) of chloro-diol 3.
Figure S9. $^1$H NMR spectrum (500 MHz, CDCl$_3$) of trichloride 4.
Figure S10. $^{13}$C NMR spectrum (125 MHz, CDCl$_3$) of trichloride 4.
**Figure S11.** $^{13}$C DEPT 135 NMR spectrum (125 MHz, CDCl$_3$) of trichloride 4.
Figure S12. $^1$H NMR spectrum (500 MHz, CDCl$_3$) of diethyl iminodiacetate (5a).
Figure S13. $^1$H NMR spectrum (500 MHz, CDCl$_3$) of 4-chloro-PyMTA ethyl ester 6a.
Figure S14. $^{13}$C NMR spectrum (125 MHz, CDCl$_3$) of 4-chloro-PyMTA ethyl ester 6a.
Figure S15. $^{13}$C DEPT 135 NMR spectrum (125 MHz, CDCl$_3$) of 4-chloro-PyMTA ethyl ester 6a.
Figure S16. HMQC NMR spectrum (500 MHz/125 MHz, CDCl₃) of 4-chloro-PyMTA ethyl ester 6a.
Figure S17. HMBC NMR spectrum (500 MHz/125 MHz, CDCl₃) of 4-chloro-PyMTA ethyl ester 6a.
Figure S18. $^1$H NMR spectrum (500 MHz, CDCl$_3$) of 4-chloro-PyMTA tert-butyl ester 6b.
Figure S19. $^{13}$C NMR spectrum (125 MHz, CDCl$_3$) of 4-chloro-PyMTA tert-butyl ester 6b.
Figure S20. $^{13}$C DEPT NMR spectrum (125 MHz, CDCl$_3$) of 4-chloro-PyMTA tert-butyl ester 6b.
Figure S21. HMBC NMR spectrum (500 MHz/125 MHz, CDCl₃) of 4-chloro-PyMTA tert-butyl ester 6b.
Figure S22. $^1$H NMR spectrum (500 MHz, CDCl$_3$) of dimethyl 4-iododipicolinate (7).
Figure S23. $^{13}$C NMR spectrum (125 MHz, CDCl$_3$) of dimethyl 4-iododipicolinate (7).
Figure S24. $^{13}$C DEPT 135 NMR spectrum (125 MHz, CDCl$_3$) of dimethyl 4-iododipicolinate (7).
Figure S25. $^1$H NMR spectrum (500 MHz, DMSO-d$_6$) of iodo-diol 8.
Figure S26. $^{13}$C NMR spectrum (125 MHz, DMSO-$d_6$) of iodo-diol 8.
Figure S27. $^{13}$C DEPT 135 NMR spectrum (125 MHz, DMSO-d$_6$) of iodo-diol 8.
**Figure S28.** $^1$H NMR spectrum (500 MHz, CDCl$_3$) of iodo-dimesylate 9.
Figure S29. $^1$H NMR spectrum (500 MHz, CD$_2$Cl$_2$) of iodo-dimesylate 9.
Figure S30. $^{13}$C NMR spectrum (125 MHz, CD$_2$Cl$_2$) of iodo-dimesylate 9.
Figure S31. $^{13}$C DEPT 135 NMR spectrum (125 MHz, CD$_2$Cl$_2$) of iodo-dimesylate 9.
Figure S32. HMBC spectrum (500 MHz/125 MHz, CD$_2$Cl$_2$) of iodo-dimesylate 9.
Figure S33. $^1$H NMR spectrum (500 MHz, CDCl$_3$) of 4-iodo-PyMTA ethyl ester 10a.
Figure S34. $^{13}$C NMR spectrum (125 MHz, CDCl$_3$) of 4-iodo-PyMTA ethyl ester 10a.
Figure S35. $^{13}$C NMR DEPT 135 spectrum (125 MHz, CDCl$_3$) of 4-iodo-PyMTA ethyl ester 10a.
Figure S36. HMQC NMR spectrum (500 MHz/125 MHz, CDCl$_3$) of 4-iodo-PyMTA ethyl ester 10a.
Figure S37. $^1$H NMR spectrum (500 MHz, CDCl$_3$) of 4-iodo-PyMTA tert-butyl ester 10b.
Figure S38. $^{13}$C NMR spectrum (125 MHz, CDCl$_3$) of 4-iodo-PyMTA tert-butyl ester 10b.
Figure S39. $^{13}$C DEPT 135 NMR spectrum (125 MHz, CDCl$_3$) of 4-ido-PyMTA tert-butyl ester 10b.
Figure S40. HMBC NMR spectrum (500 MHz/125 MHz, CDCl₃) of 4-iodo-PyMTA tert-butyl ester 10b.
**Figure S41.** $^1$H NMR spectrum (500 MHz, CDCl$_3$) of monochloride 12.
Figure S42. $^1$H NMR spectrum (500 MHz, CDCl$_3$) of iodo-dichloride 13.
Figure S43. $^1$H NMR spectrum (500 MHz, CD$_3$OD) of [(4-chloro-PyMTA - 4 H$^+$)• n H$^+$ • m Na$^+$] 14.
Figure S44. $^{13}$C NMR spectrum (125 MHz, CD$_3$OD) of $\{4$-chloro-PyMTA - 4 H$^+$\}$^4$ • n H$^+$ • m Na$^+$ 14.
Figure S45. $^{13}$C DEPT 135 NMR spectrum (125 MHz, CD$_3$OD) of ([4-chloro-PyMTA - 4 H$^+$]• n H$^+$ • m Na$^+$) 14.
Figure S46. HMBC NMR spectrum (500 MHz/125 MHz, CDCl₃) of [{[4-chloro-PyMTA - 4 H⁺]⁺ • n H⁺ • m Na⁺}].
Figure S47. $^1$H NMR spectrum (500 MHz, CD$_3$OD) of $\{4$-chloro-PyMTA • n TFA\} 16.
Figure S48. $^1$H NMR spectrum (500 MHz, D$_2$O) of (4-chloro-PyMTA $\cdot$ n TFA) 16.
Figure S49. $^{13}\text{C}$ NMR spectrum (125 MHz, CD$_3$OD) of {4-chloro-PyMTA • n TFA} 16.
Figure S50. $^{13}$C DEPT 135 NMR spectrum (125 MHz, CD$_3$OD) of (4-chloro-PyMTA • n TFA) 16.
Figure S51. $^{19}$F NMR spectrum (470 MHz, D$_2$O) of (4-chloro-PyMTA • n TFA) 16.
Figure S52. $^1$H NMR spectrum (500 MHz, CD$_3$OD) of {[4-iodo-PyMTA - 4 H$^+$]• n H$^+$ • m Na$^+$} 15.
Figure S3. $^{13}$C NMR spectrum (125 MHz, CD$_3$OD) of $\{[4$-iodo-PyMTA$]^{-}$ $\cdot$ n H$^+$ $\cdot$ m Na$^+$ $\}$ $\cdot$ n H$^+$ $\cdot$ m Na$^+$ 15.
Figure S54. $^{13}$C DEPT 135 NMR spectrum (125 MHz, CD$_3$OD) of \{[4-iodo-PyMTA - 4 H$^+$]$^{4-}$ • n H$^+$ • m Na$^+$} 15.
Figure S55. HMBC NMR spectrum (500 MHz/125 MHz, CD$_3$OD) of ([4-iodo-PyMTA - 4 H$^+$]$^n$ - n H$^+$ - m Na$^+$) 15.
Figure S56. $^1$H NMR spectrum (500 MHz, CD$_3$OD) of {4-iodo-PyMTA • n TFA} 17.
Figure S57. $^1$H NMR spectrum (500 MHz, D$_2$O) of {4-iodo-PyMTA • n TFA} 17.
Figure S58. $^{13}$C NMR spectrum (500 MHz, D$_2$O) of (4-iodo-PyMTA • n TFA) 17.
Figure S59. $^{13}$C DEPT 135 NMR spectrum (125 MHz, D$_2$O) of (4-iodo-PyMTA • n TFA) 17.
Figure S60. HMBC NMR spectrum (500 MHz/125 MHz, D$_2$O) of 4-ido-PyMTA • n TFA 17.
Figure S61. $^{19}$F NMR spectrum (470 MHz, D$_2$O) of \(\{4\text{-iodo-PyMTA} \cdot n \text{TFA}\} \) 17.
References
