# Supplementary data

**Investigation of porphyrin-forming reactions. Part 2. Examination of the reaction course in two-step, one-flask syntheses of meso-substituted porphyrins**

G. Richard Geier III and Jonathan S. Lindsey*

Department of Chemistry, North Carolina State University, Raleigh, North Carolina 27695-8204 USA

**Peak Assignments for Phenyl and *p*-Tolyl Containing Oligomers.** The molecular weights for oligomers possessing all of the possible combinations of phenyl and *p*-tolyl substituents are presented in Table S1. The left most column of masses are for oligomers with only phenyl substituents, and the right most column are for oligomers with only *p*-tolyl groups. The center columns show masses for oligomers containing a mixture of substituents, with the number of *p*-tolyl groups shown at the top of each column. The masses were calculated from the most dehydrogenated structure of each oligomer.

**Table S1.** Calculated masses for the possible oligomers from the condensation of pyrrole + benzaldehyde + *p*-tolualdehyde.

| | | all | phenyl and *p*-tolyl mixed oligomers | | | | | | | | | | | | | | | all |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Series | n | phenyl | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | *p*-tolyl |
| (PA)n | 1 | 155 | | | | | | | | | | | | | | | | 169 |
| | 2 | 308 | 322 | | | | | | | | | | | | | | | 336 |
| | 3 | 461 | 475 | 489 | | | | | | | | | | | | | | 503 |
| | 4 | 614 | 628 | 642 | 656 | | | | | | | | | | | | | 670 |
| | 5 | 767 | 781 | 795 | 809 | 823 | | | | | | | | | | | | 837 |
| | 6 | 920 | 934 | 948 | 962 | 976 | 990 | | | | | | | | | | | 1004 |
| | 7 | 1073 | 1087 | 1101 | 1115 | 1129 | 1143 | 1157 | | | | | | | | | | 1171 |
| | 8 | 1226 | 1240 | 1254 | 1268 | 1282 | 1296 | 1310 | 1324 | | | | | | | | | 1338 |
| | 9 | 1379 | 1393 | 1407 | 1421 | 1435 | 1449 | 1463 | 1477 | 1491 | | | | | | | | 1505 |
| | 10 | 1532 | 1546 | 1560 | 1574 | 1588 | 1602 | 1616 | 1630 | 1644 | 1658 | | | | | | | 1672 |
| | 11 | 1685 | 1699 | 1713 | 1727 | 1741 | 1755 | 1769 | 1783 | 1797 | 1811 | 1825 | | | | | | 1839 |
| | 12 | 1838 | 1852 | 1866 | 1880 | 1894 | 1908 | 1922 | 1936 | 1950 | 1964 | 1978 | 1992 | | | | | 2006 |
| | 13 | 1991 | 2005 | 2019 | 2033 | 2047 | 2061 | 2075 | 2089 | 2103 | 2117 | 2131 | 2145 | 2159 | | | | 2173 |
| | 14 | 2144 | 2158 | 2172 | 2186 | 2200 | 2214 | 2228 | 2242 | 2256 | 2270 | 2284 | 2298 | 2312 | 2326 | | | 2340 |
| | 15 | 2297 | 2311 | 2325 | 2339 | 2353 | 2367 | 2381 | 2395 | 2409 | 2423 | 2437 | 2451 | 2465 | 2479 | 2493 | | 2507 |
| A(PA)n | 1 | 245 | 259 | | | | | | | | | | | | | | | 273 |
| | 2 | 398 | 412 | 426 | | | | | | | | | | | | | | 440 |
| | 3 | 551 | 565 | 579 | 593 | | | | | | | | | | | | | 607 |
| | 4 | 704 | 718 | 732 | 746 | 760 | | | | | | | | | | | | 774 |
| | 5 | 857 | 871 | 885 | 899 | 913 | 927 | | | | | | | | | | | 941 |
| | 6 | 1010 | 1024 | 1038 | 1052 | 1066 | 1080 | 1094 | | | | | | | | | | 1108 |
| | 7 | 1163 | 1177 | 1191 | 1205 | 1219 | 1233 | 1247 | 1261 | | | | | | | | | 1275 |
| | 8 | 1316 | 1330 | 1344 | 1358 | 1372 | 1386 | 1400 | 1414 | 1428 | | | | | | | | 1442 |
| | 9 | 1469 | 1483 | 1497 | 1511 | 1525 | 1539 | 1553 | 1567 | 1581 | 1595 | | | | | | | 1609 |
| | 10 | 1622 | 1636 | 1650 | 1664 | 1678 | 1692 | 1706 | 1720 | 1734 | 1748 | 1762 | | | | | | 1776 |
| | 11 | 1775 | 1789 | 1803 | 1817 | 1831 | 1845 | 1859 | 1873 | 1887 | 1901 | 1915 | 1929 | | | | | 1943 |
| | 12 | 1928 | 1942 | 1956 | 1970 | 1984 | 1998 | 2012 | 2026 | 2040 | 2054 | 2068 | 2082 | 2096 | | | | 2110 |
| | 13 | 2081 | 2095 | 2109 | 2123 | 2137 | 2151 | 2165 | 2179 | 2193 | 2207 | 2221 | 2235 | 2249 | 2263 | | | 2277 |
| | 14 | 2234 | 2248 | 2262 | 2276 | 2290 | 2304 | 2318 | 2332 | 2346 | 2360 | 2374 | 2388 | 2402 | 2416 | 2430 | | 2444 |
| | 15 | 2387 | 2401 | 2415 | 2429 | 2443 | 2457 | 2471 | 2485 | 2499 | 2513 | 2527 | 2541 | 2555 | 2569 | 2583 | 2597 | 2611 |
| (PA)nP | 1 | 220 | | | | | | | | | | | | | | | | 234 |
| | 2 | 373 | 387 | | | | | | | | | | | | | | | 401 |
| | 3 | 526 | 540 | 554 | | | | | | | | | | | | | | 568 |
| | 4 | 679 | 693 | 707 | 721 | | | | | | | | | | | | | 735 |
| | 5 | 832 | 846 | 860 | 874 | 888 | | | | | | | | | | | | 902 |
| | 6 | 985 | 999 | 1013 | 1027 | 1041 | 1055 | | | | | | | | | | | 1069 |
| | 7 | 1138 | 1152 | 1166 | 1180 | 1194 | 1208 | 1222 | | | | | | | | | | 1236 |
| | 8 | 1291 | 1305 | 1319 | 1333 | 1347 | 1361 | 1375 | 1389 | | | | | | | | | 1403 |
| | 9 | 1444 | 1458 | 1472 | 1486 | 1500 | 1514 | 1528 | 1542 | 1556 | | | | | | | | 1570 |
| | 10 | 1597 | 1611 | 1625 | 1639 | 1653 | 1667 | 1681 | 1695 | 1709 | 1723 | | | | | | | 1737 |
| | 11 | 1750 | 1764 | 1778 | 1792 | 1806 | 1820 | 1834 | 1848 | 1862 | 1876 | 1890 | | | | | | 1904 |
| | 12 | 1903 | 1917 | 1931 | 1945 | 1959 | 1973 | 1987 | 2001 | 2015 | 2029 | 2043 | 2057 | | | | | 2071 |
| | 13 | 2056 | 2070 | 2084 | 2098 | 2112 | 2126 | 2140 | 2154 | 2168 | 2182 | 2196 | 2210 | 2224 | | | | 2238 |
| | 14 | 2209 | 2223 | 2237 | 2251 | 2265 | 2279 | 2293 | 2307 | 2321 | 2335 | 2349 | 2363 | 2377 | 2391 | | | 2405 |
| | 15 | 2362 | 2376 | 2390 | 2404 | 2418 | 2432 | 2446 | 2460 | 2474 | 2488 | 2502 | 2516 | 2530 | 2544 | 2558 | | 2572 |
| P(PA)nP | 1 | 285 | | | | | | | | | | | | | | | | 299 |
| | 2 | 438 | 452 | | | | | | | | | | | | | | | 466 |
| | 3 | 591 | 605 | 619 | | | | | | | | | | | | | | 633 |
| | 4 | 744 | 758 | 772 | 786 | | | | | | | | | | | | | 800 |
| | 5 | 897 | 911 | 925 | 939 | 953 | | | | | | | | | | | | 967 |

**Data from the Condensation of 5-Phenyldipyrromethane in the Absence of Aldehyde.** The yields of TPP and NC-TPP as a function of time are summarized for TFA catalysis and $BF_3$-etherate catalysis (Figure S1). LD-MS spectra for selected timepoints are shown for catalysis with TFA (Figure S2) or $BF_3$-etherate (Figure S3). The reaction conditions employed were as follows: 5 mM PDPM, 20 mM TFA or 1.0 mM $BF_3$-etherate, $CH_2Cl_2$, room temperature.

**Figure S1**. Yields of TPP and NC-TPP as a function of time from the reaction of PDPM in the absence of aldehyde under TFA catalysis or $BF_3$-etherate catalysis.

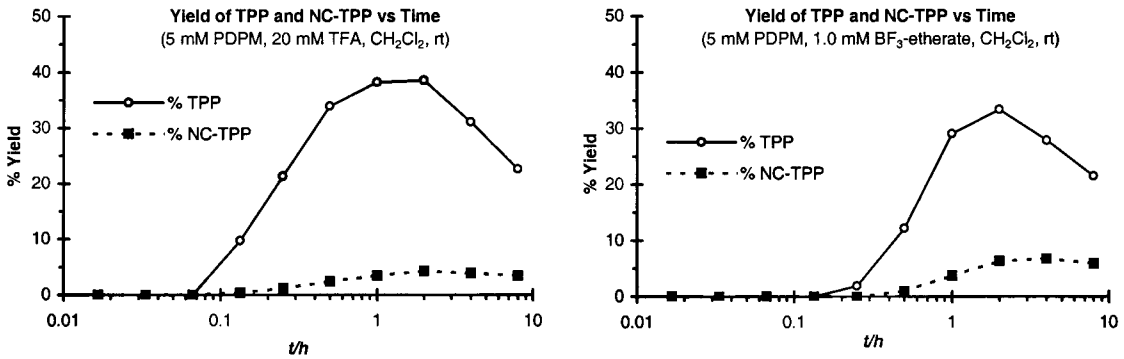


**Figure S2.** LD-MS spectra from selected timepoints from the reaction of PDPM in the absence of aldehyde (20 mM TFA). The peak corresponding to the *m/z* of TPP is marked with an asterisk.

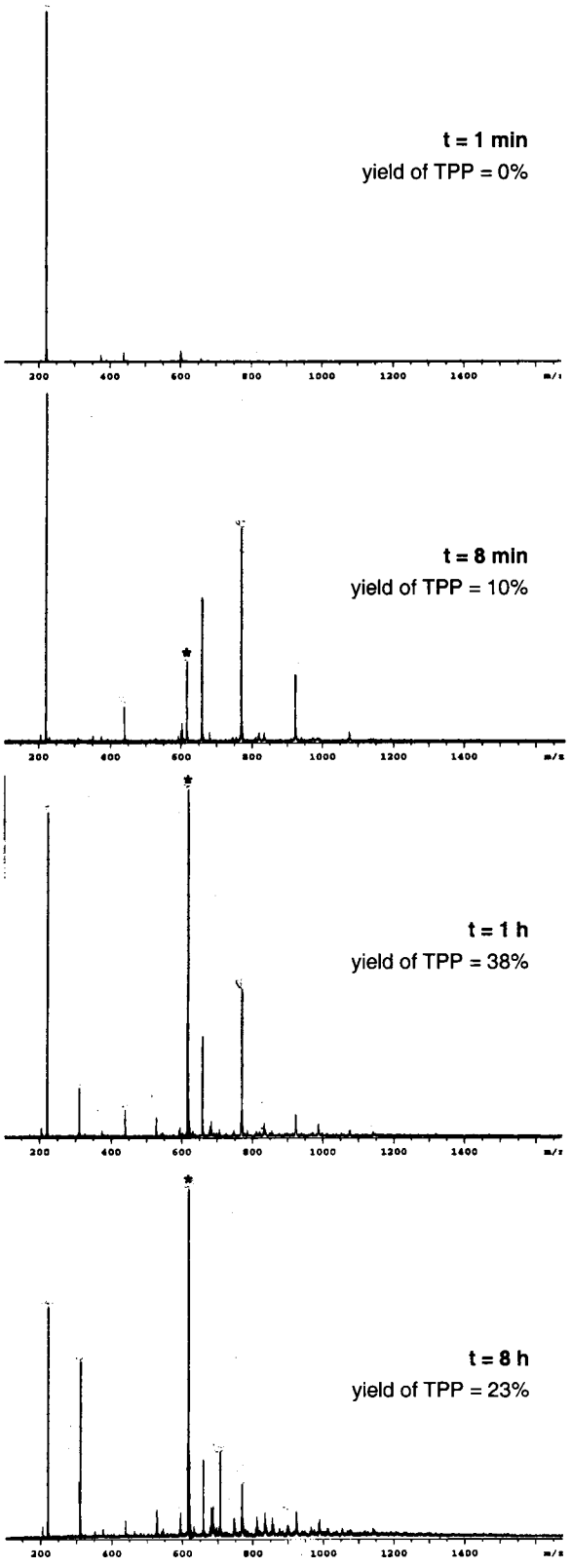
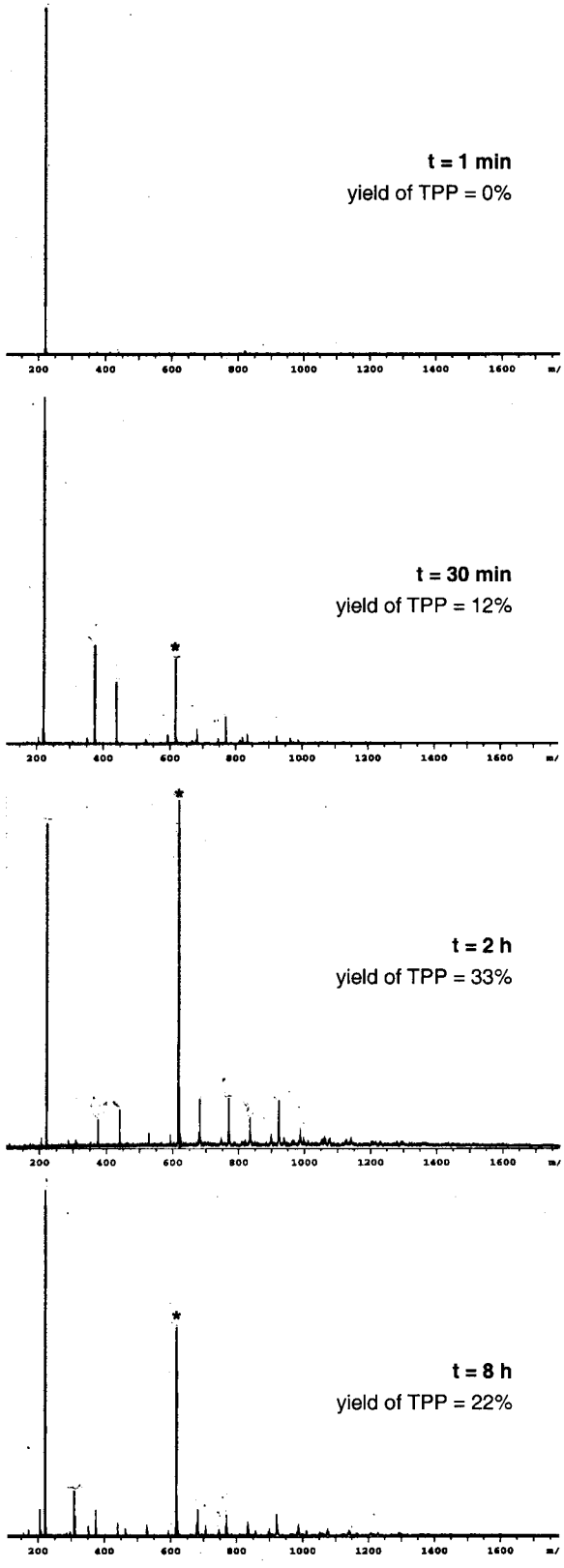


**Figure S3.** LD-MS spectra from selected timepoints from the reaction of PDPM in the absence of aldehyde (1.0 mM $BF_3$-etherate). The peak corresponding to the *m/z* of TPP is marked with an asterisk.



**Data from the Reaction of N-Confused-5-Phenyldipyrromethane in the Absence of Aldehyde.** LD-MS spectra for selected timepoints are shown for TFA catalysis (Figure S4) and $BF_3$-etherate catalysis (Figure S5). The reaction conditions employed were as follows: 5 mM PDPM, 20 mM TFA or 1.0 mM $BF_3$-etherate, $CH_2Cl_2$, room temperature.

**Figure S4.** LD-MS spectra from selected timepoints from the reaction of N-confused PDPM in the absence of aldehyde (20 mM TFA).

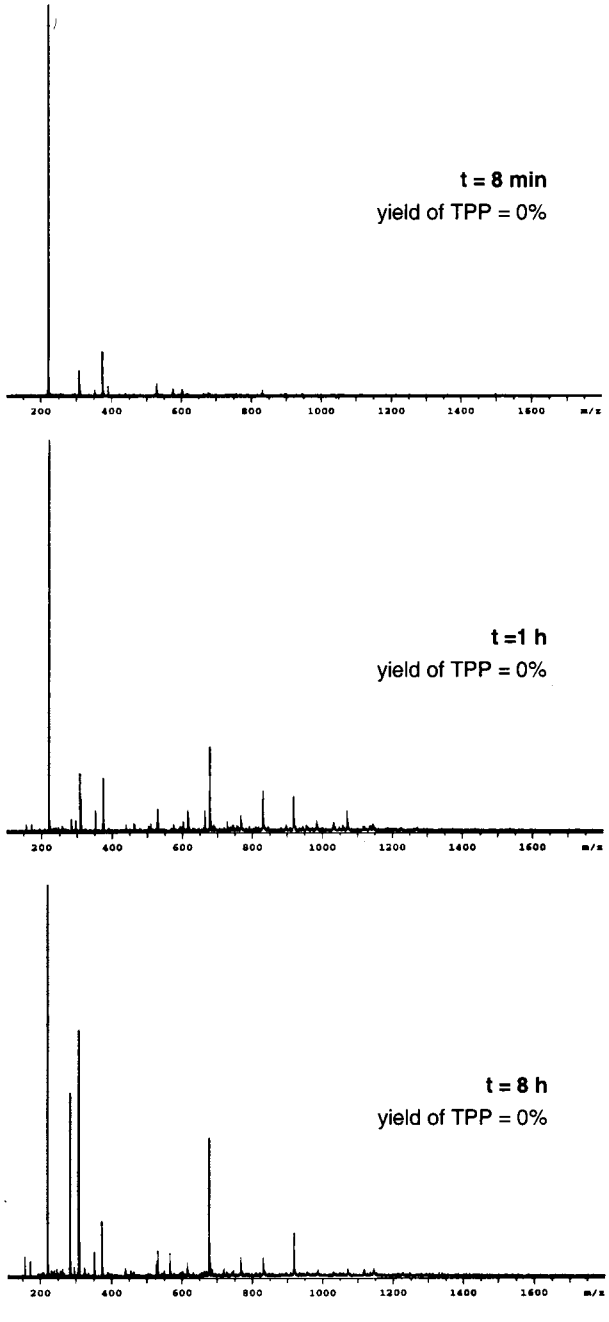
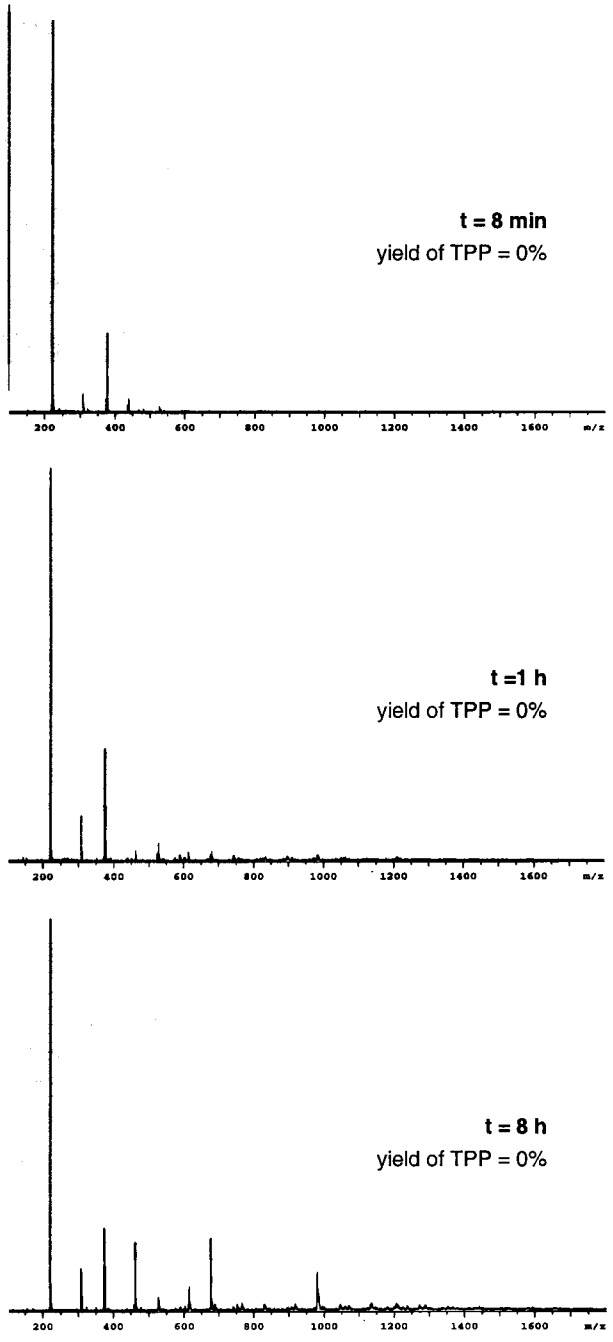


**Figure S5.** LD-MS spectra from selected timepoints from the reaction of N-confused PDPM in the absence of aldehyde (1.0 mM $BF_3$-etherate).



**Data from the Condensation of N-Confused-5-Phenyldipyrromethane + Benzaldehyde.** LD-MS spectra for selected timepoints are shown for TFA catalysis (Figure S6) and $BF_3$-etherate catalysis (Figure S7). The reaction conditions employed were as follows: 5 mM PDPM, 5 mM benzaldehyde, 20 mM TFA or 1.0 mM $BF_3$-etherate, $CH_2Cl_2$, room temperature.

**Figure S6.** LD-MS spectra from selected timepoints from the condensation of N-confused PDPM in the absence of aldehyde (20 mM TFA).

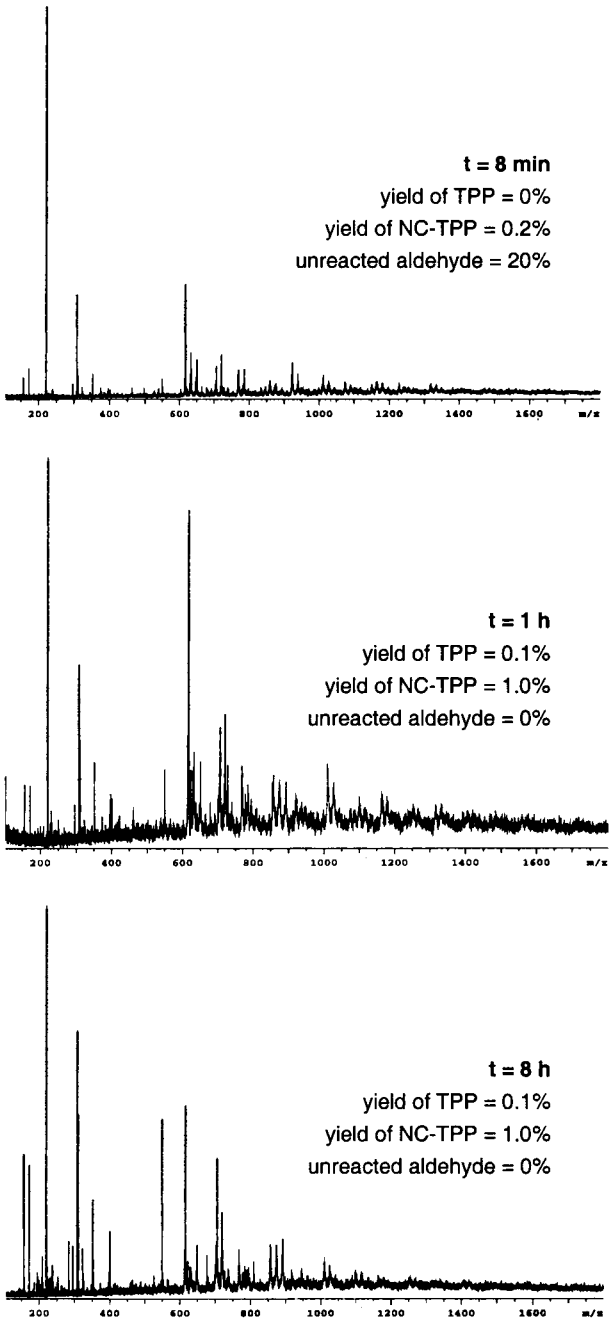
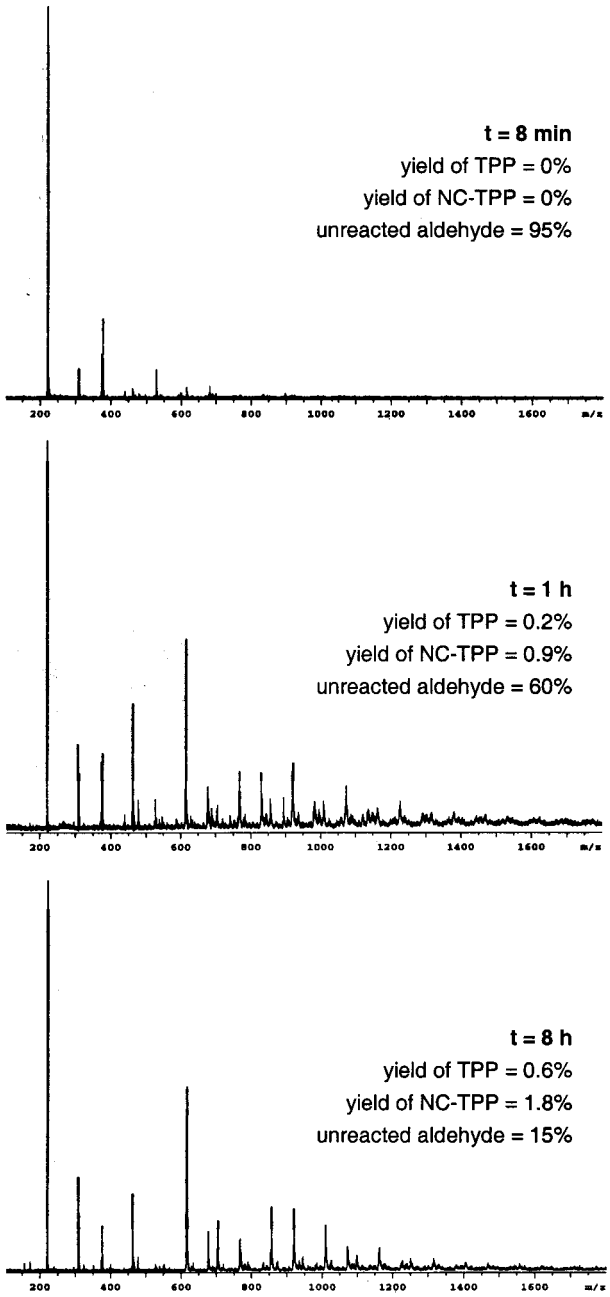


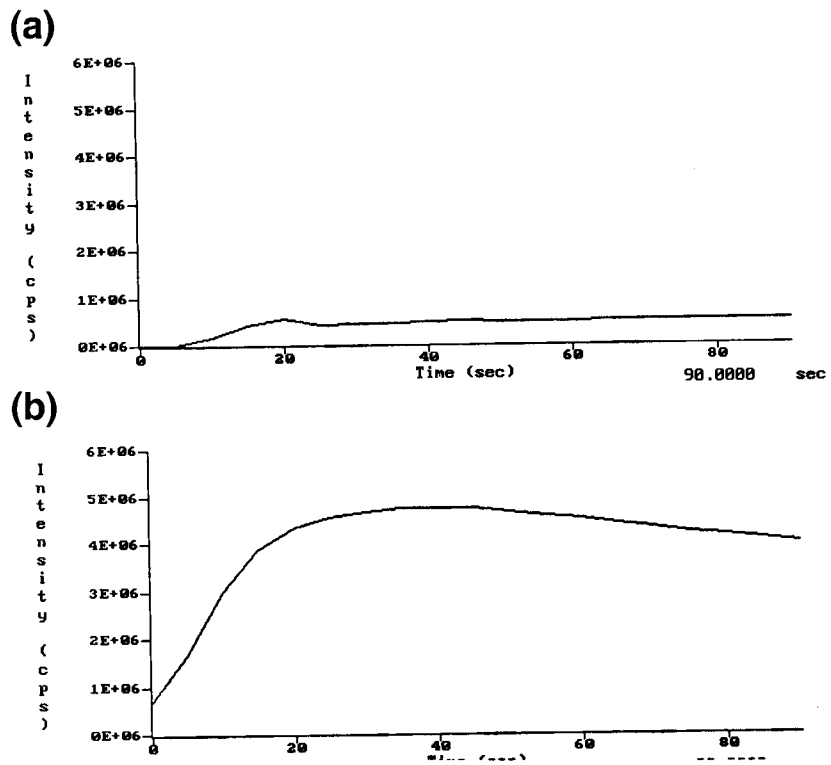
**Figure S7.** LD-MS spectra from selected timepoints from the condensation of N-confused PDPM in the absence of aldehyde (1.0 mM $BF_3$-etherate).



**Illustrative Light Scattering Data.** At 10 mM reactants, $BF_3$-etherate catalysis (1.0 mM) provided a clear, amber solution which showed no turbidity by light scattering spectroscopy or by visual inspection. Catalysis by TFA (20 mM) provided a very dark solution which likely interfered with light scattering measurements; however, turbidity was absent by visual inspection. With 100 mM reactants, TFA catalysis (64 mM) provided a solution so darkly colored that the absence of turbidity was difficult to determine visually. $BF_3$-etherate catalysis (10 mM) gave a low level of light scattering and the presence of turbidity was confirmed by visual inspection. The turbidity was detected within the first few seconds after addition of $BF_3$-etherate. Figure S8 shows a comparison of scattered light as a function of time for 100 mM reactants, 10 mM $BF_3$-etherate (Panel A) and a control reaction (100 mM reactants, 0.31 mM $Bu_3BzlNCl$, 10 mM $BF_3$-etherate) previously shown to provide extensive precipitate formation (Panel B).[1]

[1] Li, F.; Yang, K.; Tyhonas, J. S.; MacCrum, K. A.; Lindsey, J. S. *Tetrahedron* **1997**, *53*, 12339-12360.

**Figure S8.** Illustrative plots of scattered light as a function of reaction time showing the presence of precipitate. (a) 100 mM reactants, 10 mM $BF_3$-etherate. (b) 100 mM reactants, 0.31 mM $Bu_3BzlNCl$, 10 mM $BF_3$-etherate.




**Yield vs. Time and LD-MS Data for Condensations Involving Pyrrole-Carbinol (3), PDPM (1), PDPM-Monocarbinol (4) and PDPM-Dicarbinol (5).** Figure S9 presents yield vs. time plots for the four condensation reactions involving possible intermediates along the reaction pathway from pyrrole + aldehyde to porphyrinogen. Figures S10-S13 show LD-MS spectra from selected timepoints from each condensation reaction.

**Figure S9.** Yields of TPP and NC-TPP as a function of time for (a) 10 mM pyrrole-carbinol (**3**), 20 mM TFA; (b) 10 mM pyrrole-carbinol (**3**), 1.0 mM $BF_3$-etherate; (c) 5 mM PDPM (**1**), 5 mM benzaldehyde, 20 mM TFA; (d) 5 mM PDPM (**1**), 5 mM benzaldehyde, 1.0 mM $BF_3$-etherate; (e) 5 mM PDPM-monocarbinol (**4**), 20 mM TFA; (f) 5 mM PDPM-monocarbinol (**4**), 1.0 mM $BF_3$-etherate; (g) 2.5 mM PDPM-dicarbinol (**5**), 2.5 mM PDPM (**1**), 20 mM TFA; (h) 2.5 mM PDPM-dicarbinol (**5**), 2.5 mM PDPM (**1**), 1.0 mM $BF_3$-etherate.

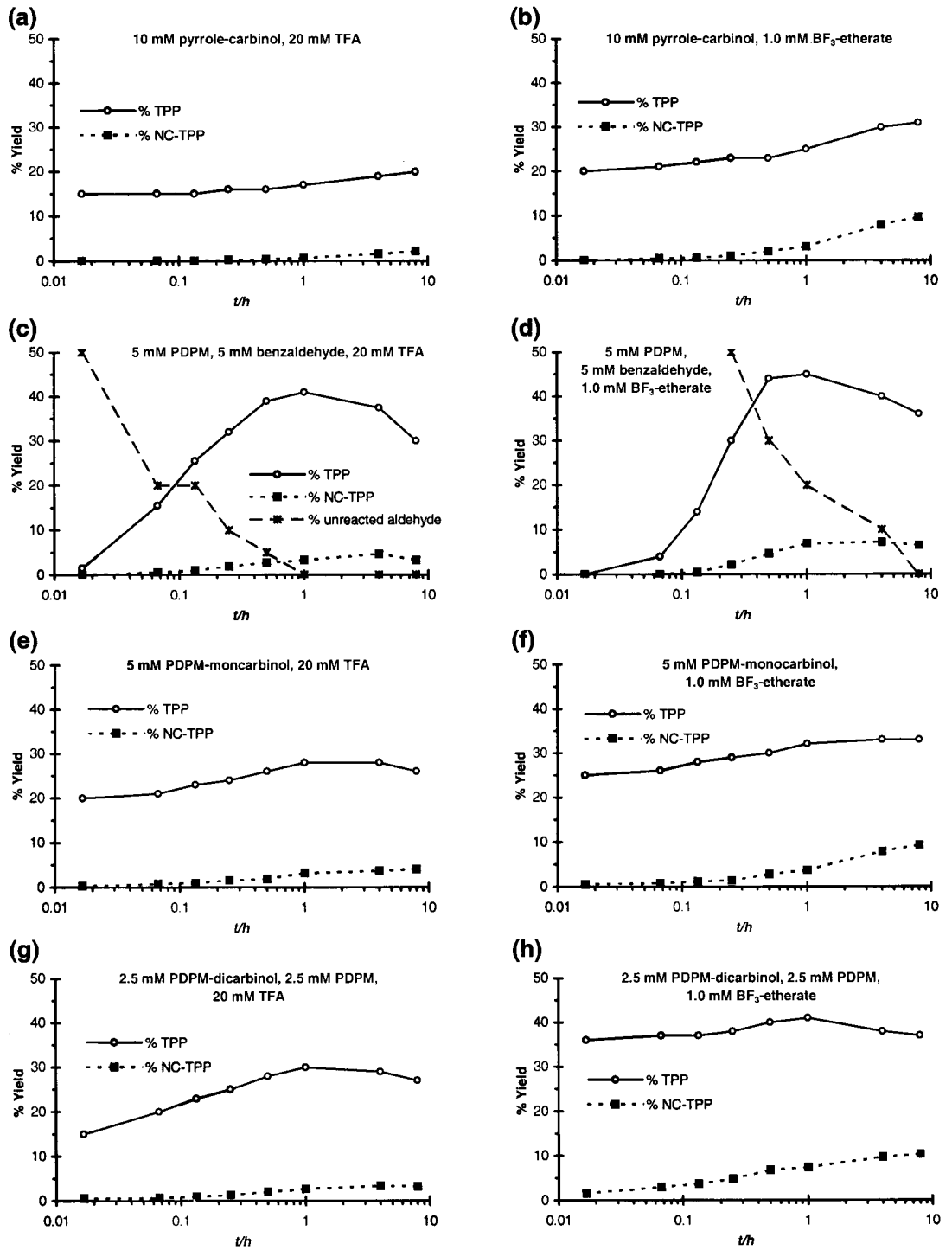


**Figure S10.** Selected LD-MS spectra from the condensation of pyrrole-carbinol (**3**, 10 mM) under (a) 20 mM TFA catalysis or (b) 1.0 mM $BF_3$-etherate catalysis. The peak with appropriate *m/z* for TPP is labeled with an asterisk.

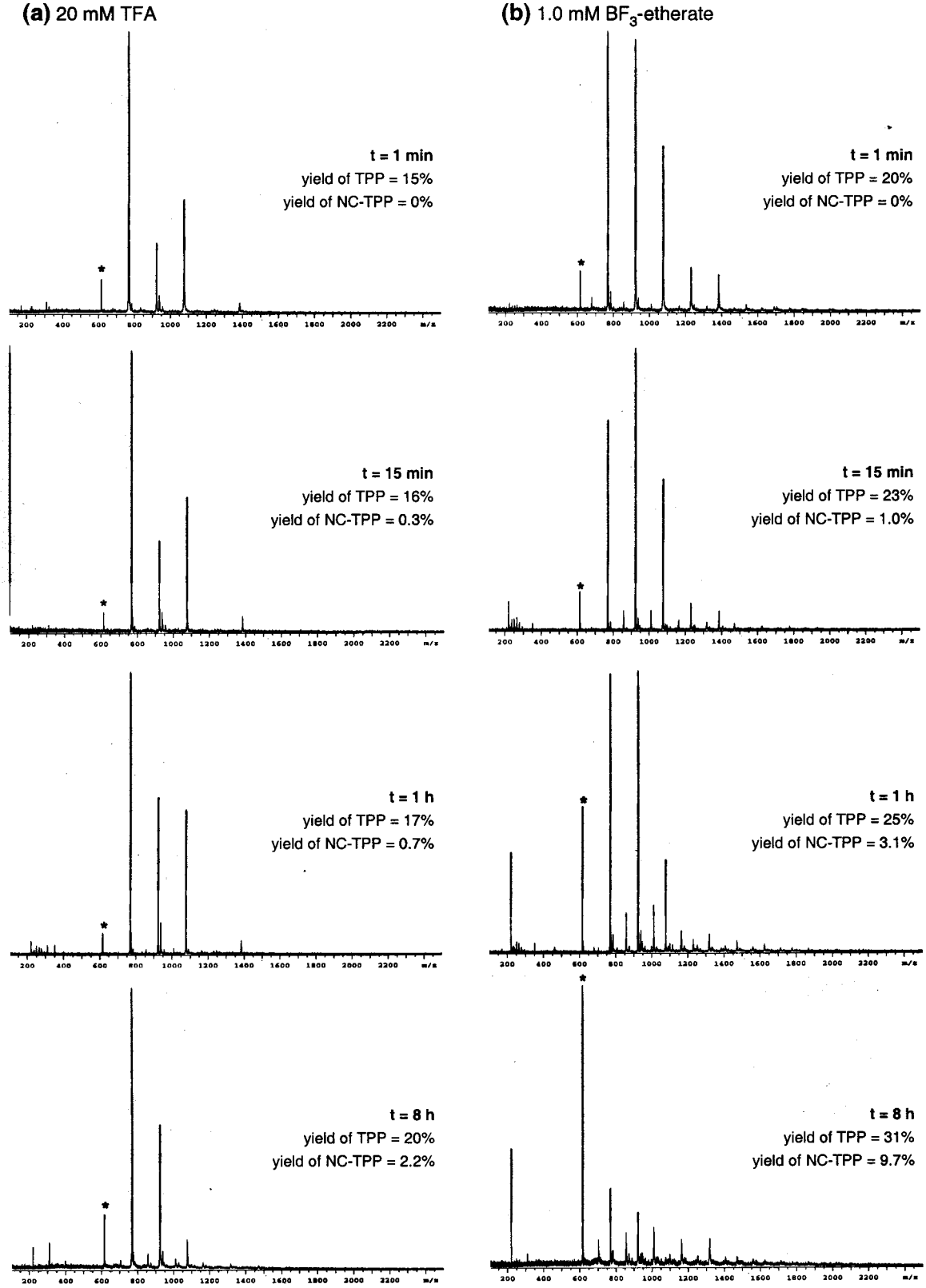


**Figure S11.** Selected LD-MS spectra from the condensation of PDPM (**1**, 5 mM) and benzaldehyde (5 mM) under (a) 20 mM TFA catalysis or (b) 1.0 mM $BF_3$-etherate catalysis. The peak with appropriate *m/z* for TPP is labeled with an asterisk.

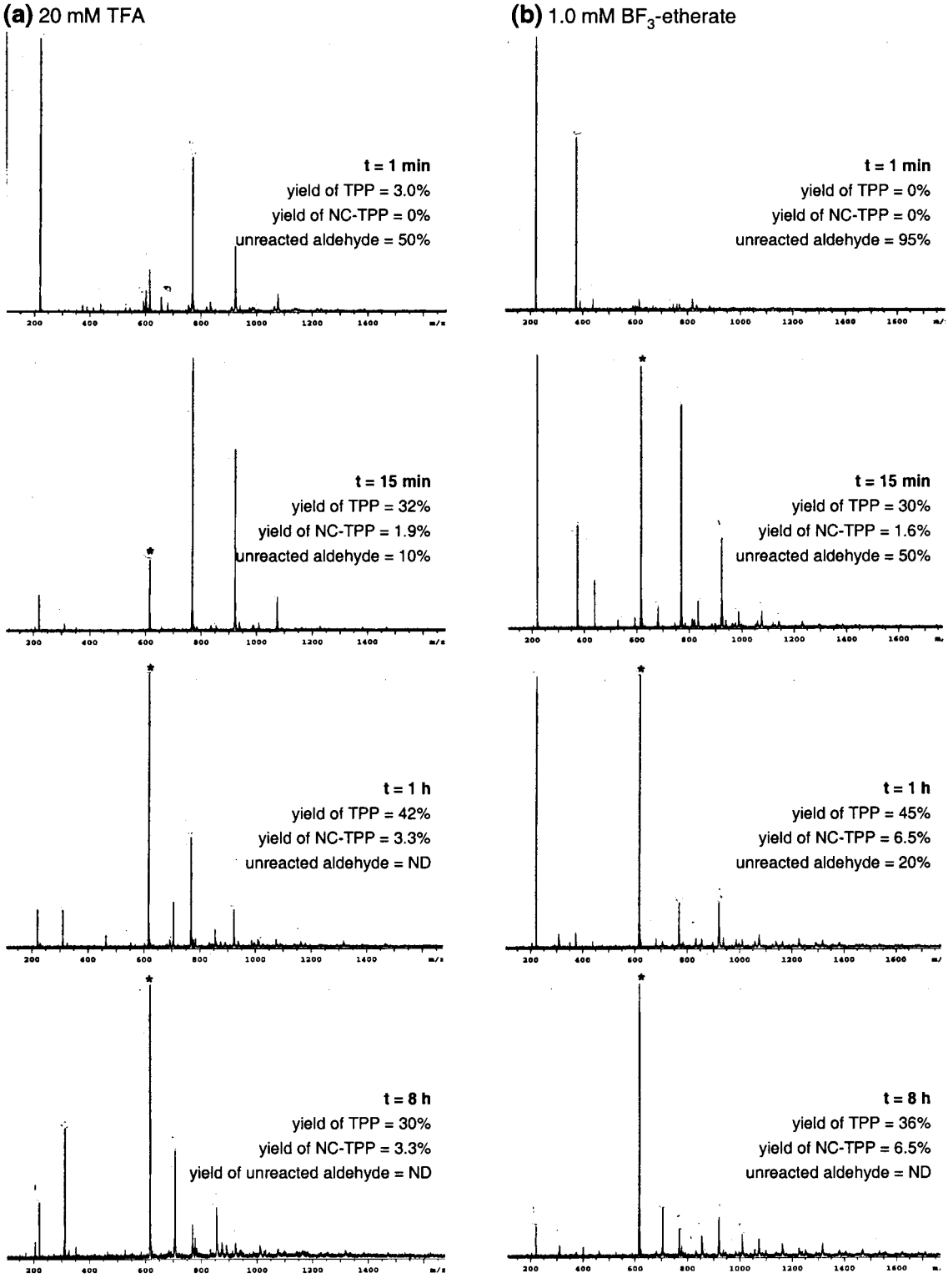


**Figure S12.** Selected LD-MS spectra from the condensation of PDPM-monocarbinol (**4**, 5 mM) under (a) 20 mM TFA catalysis or (b) 1.0 mM $BF_3$-etherate catalysis. The peak with appropriate *m/z* for TPP is labeled with an asterisk.

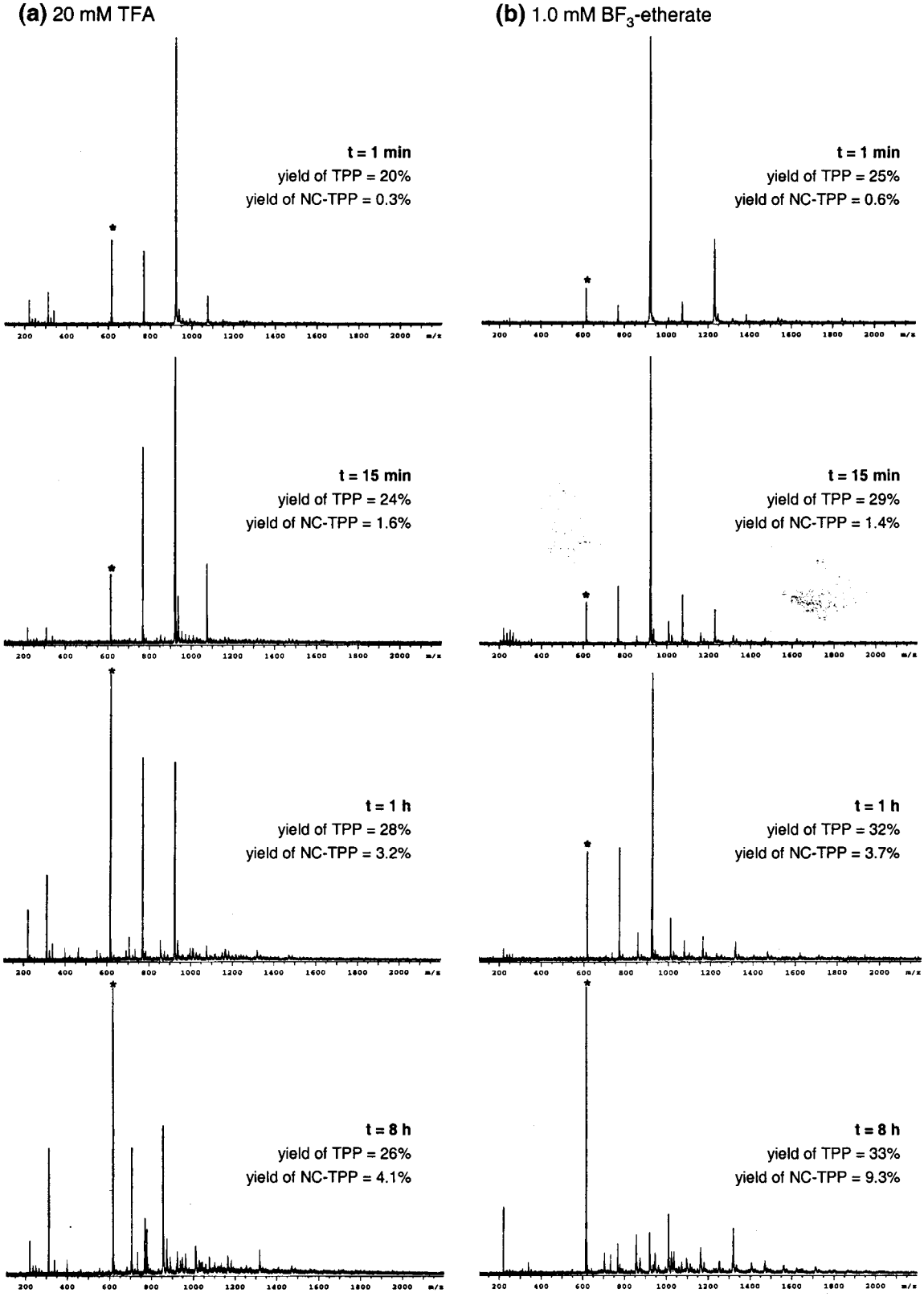
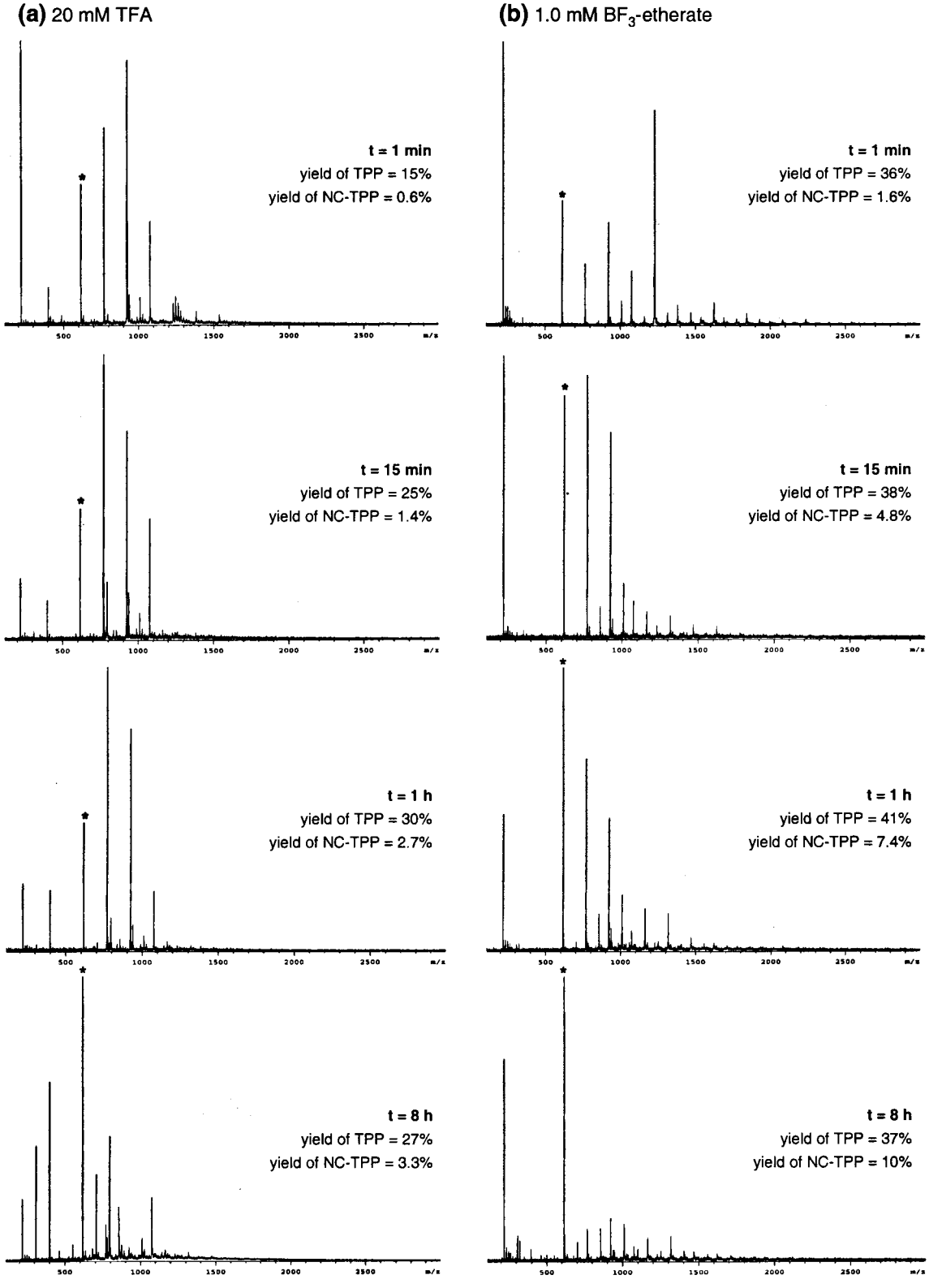


**Figure S13.** Selected LD-MS spectra from the condensation of PDPM-dicarbinol (**5**, 2.5 mM) and PDPM (**1**, 2.5 mM) under (a) 20 mM TFA catalysis or (b) 1.0 mM $BF_3$-etherate catalysis. The peak with appropriate *m/z* for TPP is labeled with an asterisk.



**Investigation of the Effect of Residual Methanol and THF in the Condensation of Carbinol-Containing Species.** The $NaBH_4$ reduction of acyl groups in this study involved the solvent system of THF/methanol (3:1). The resulting carbinol is isolated as an oil which very likely contains low levels of both THF and methanol.

Control experiments performed with pyrrole + benzaldehyde (10 mM) under TFA (20 mM) catalysis showed that the addition of methanol (50 mM) or THF (50 mM) sharply inhibited the condensation. At 1 h, the yield of TPP was 40% in the absence of methanol or THF, 2.3% in the presence of THF, and 6.9% in the presence of methanol. Under $BF_3$-etherate (1.0 mM) catalysis, the presence of THF (50 mM) decreased the yield of TPP at 1 h to 2.7% from the typical value of 26%, whereas methanol (50 mM) led to an increase in TPP yield to 43% at 1 h. Clearly, small quantities of methanol and THF affect the condensation of pyrrole + aldehyde.

Thus, experiments were performed to determine the impact of these residual solvents on condensations involving carbinol species. A sample of 2-benzoylpyrrole was reduced, affording pyrrole-carbinol **3**, then divided into five equal portions. Prior to condensation, sample A was placed under vacuum for 5 min, sample B was dissolved in toluene, evaporated to an oil, then placed under vacuum for 5 min; and samples C-E were placed under vacuum for 1.5 h. Samples A, B, and C were condensed on a 10 mL scale in $CH_2Cl_2$ with $BF_3$-etherate (1.0 mM) catalysis. Sample D had THF (50 mM) and sample E had methanol (50 mM) added to the reaction mixture prior to addition of $BF_3$-etherate. All five reactions were monitored from 1 min to 4 h. The yields of TPP from all five reactions were equivalent (all were ~20% with similar increase over time, Figure S14) and the yields of NC-TPP were also equivalent for all five reactions. Apparently, methanol and THF in small quantity do not significantly impact the condensation of the carbinols, perhaps due to the increased reactivity of the carbinol.

**Figure S14.** Yield of TPP as a function of time for experiments examining the impact of methanol and THF on pyrrole-carbinol condensations.