Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.


# SUPPLYMENTARY INFORMATION

## Modification of oligonucleotides with weak basic residues via 2´-*O*-carbamoylethyl linker for improving nuclease resistance without loss of duplex stability and antisense activity

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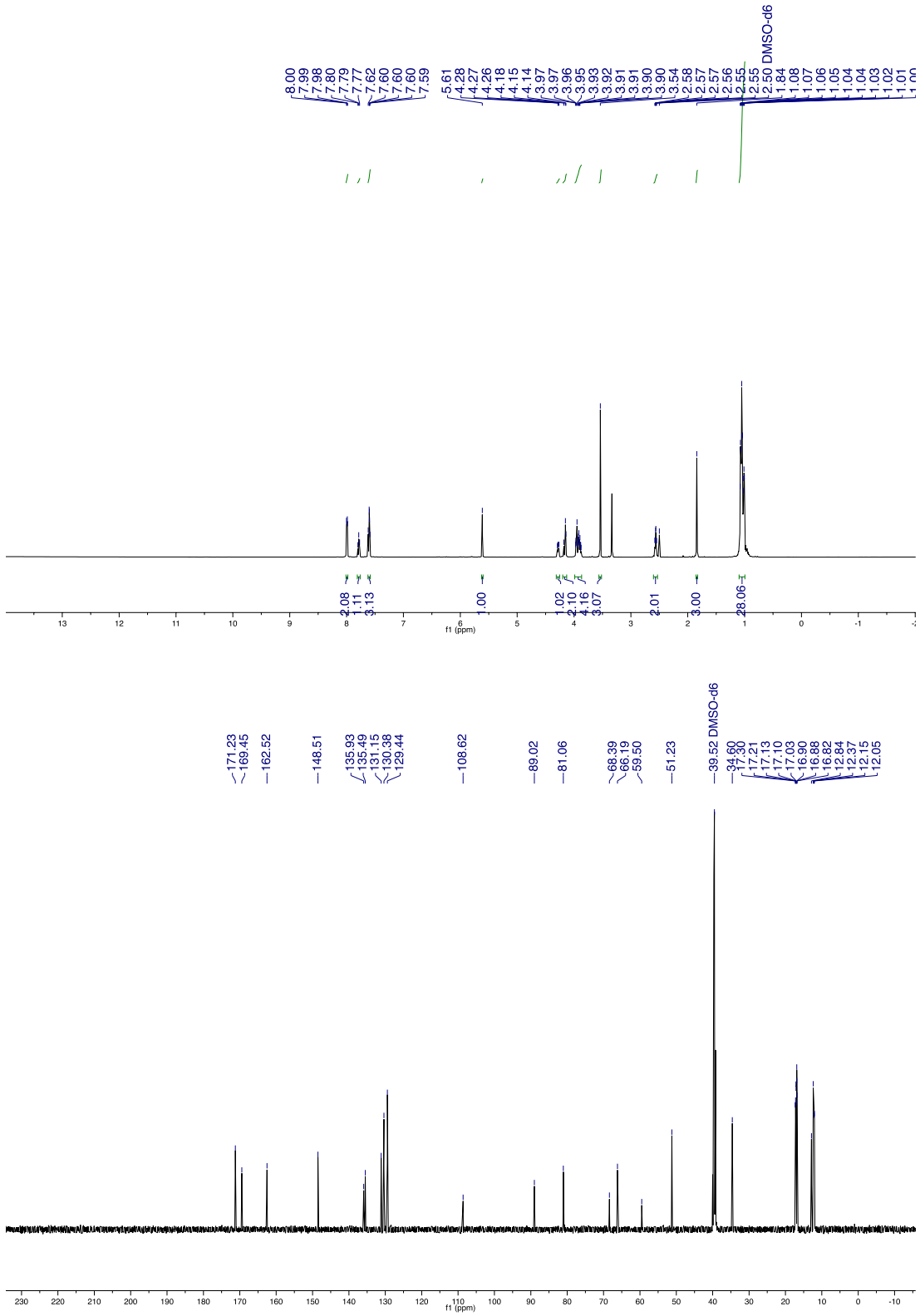
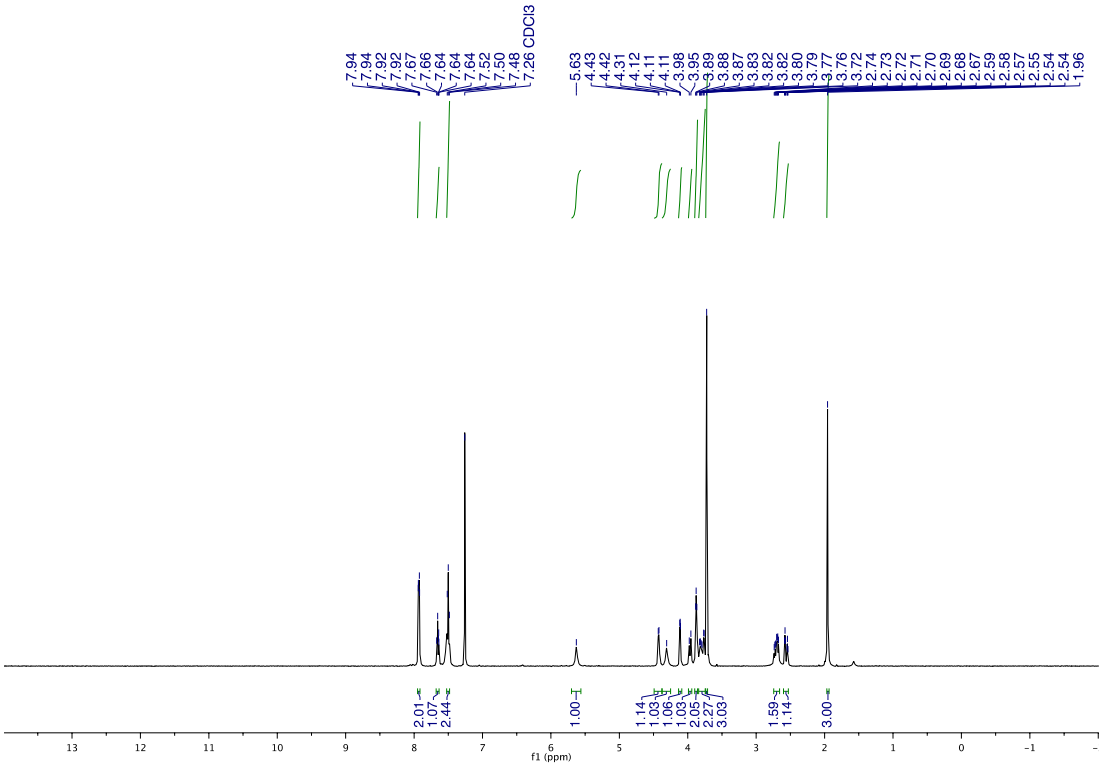
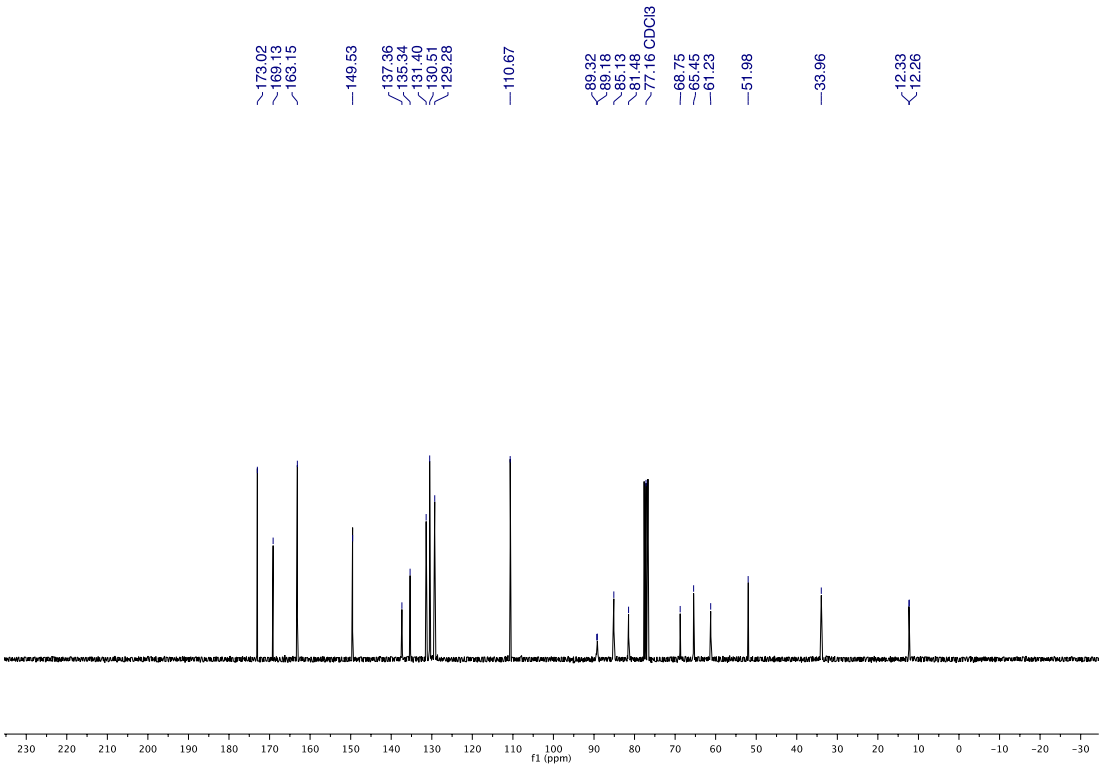
**$N^3$-benzoyl-2´-*O*-{2-(methoxycarbonyl)ethyl} 3´,5´-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl) 5-methyluridine (1')**

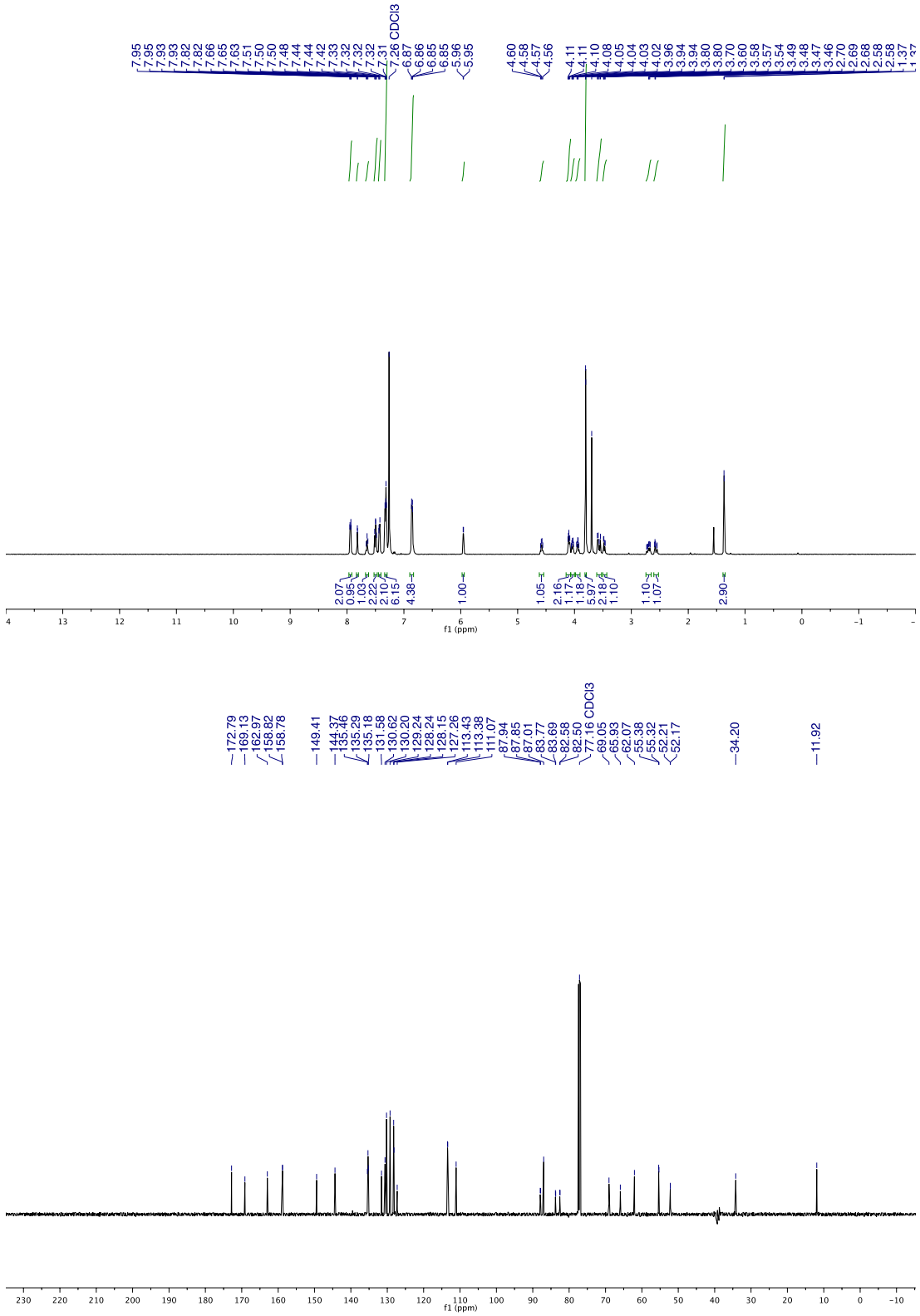


**$N^3$-benzoyl-2´-*O*-(2-methoxycarbonylethyl)-5-methyluridine (2)**

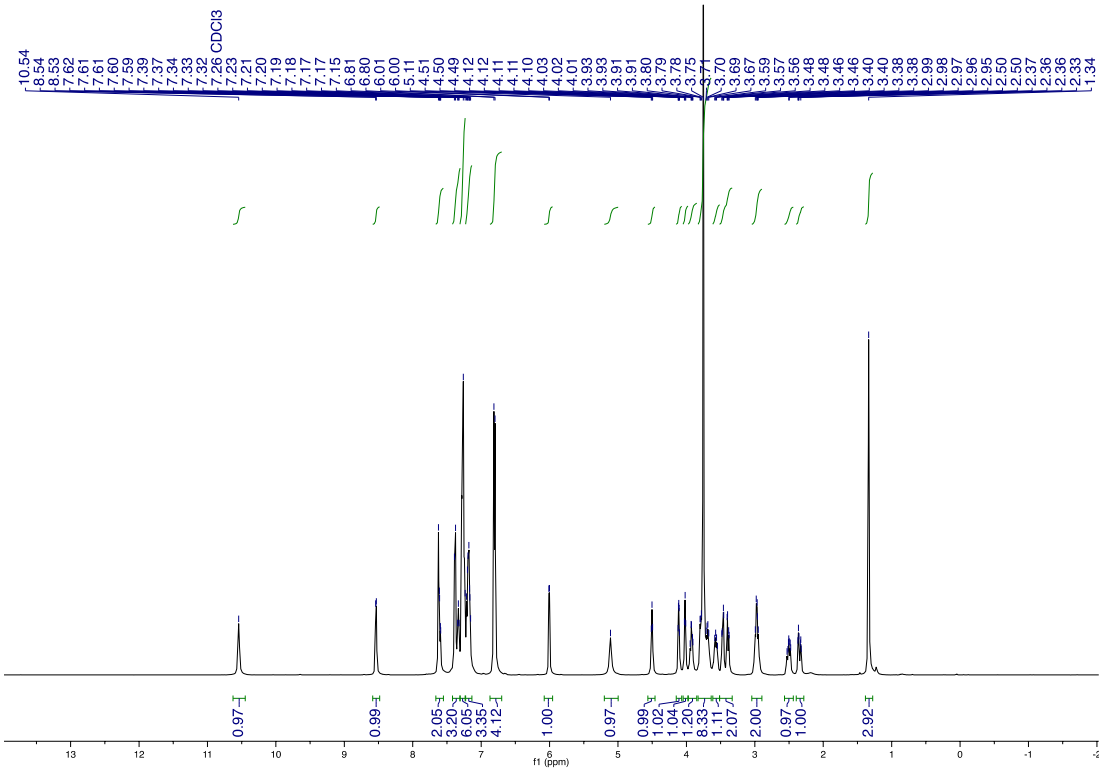


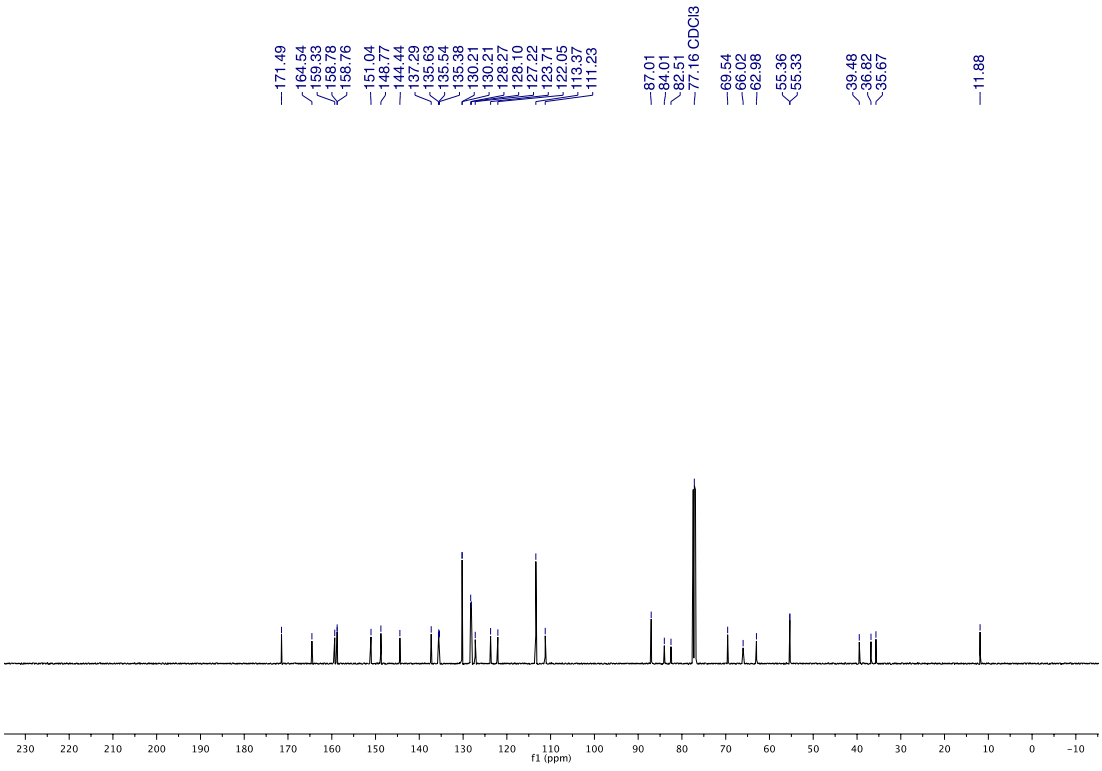
**$N^3$-benzoyl-2´-*O*-(2-methoxycarbonylethyl)-5´-*O*-(4,4´-dimethoxytrityl)-5-methyluridine (3)**



**$^{1}$H-NMR of compound 4a (PyECE)**




**$^{13}$C-NMR of compound 4a (PyECE)**



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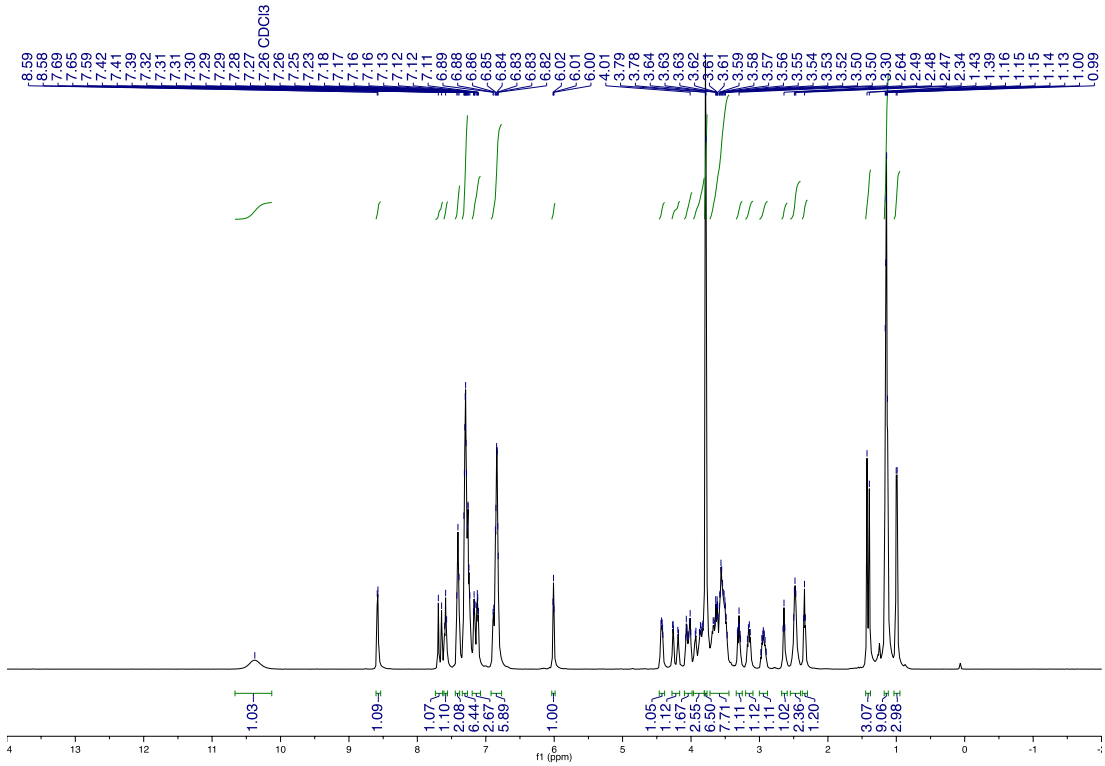
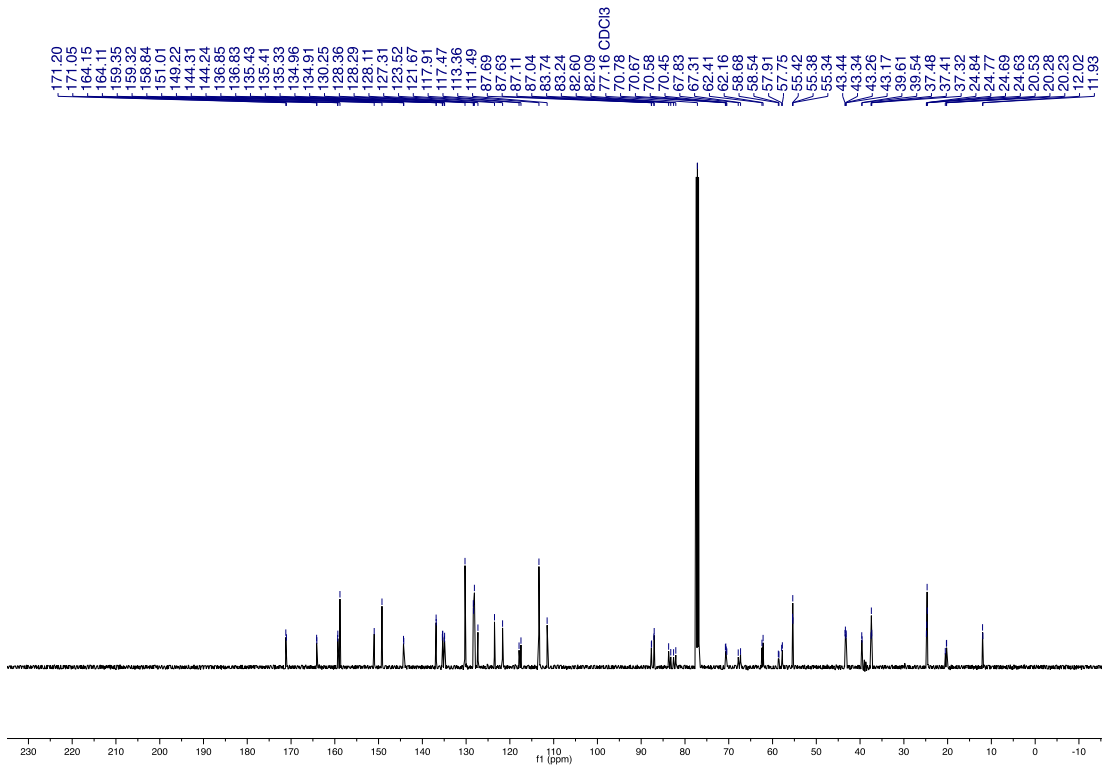



**$^{13}$C-NMR of compound 5a (PyECE)**



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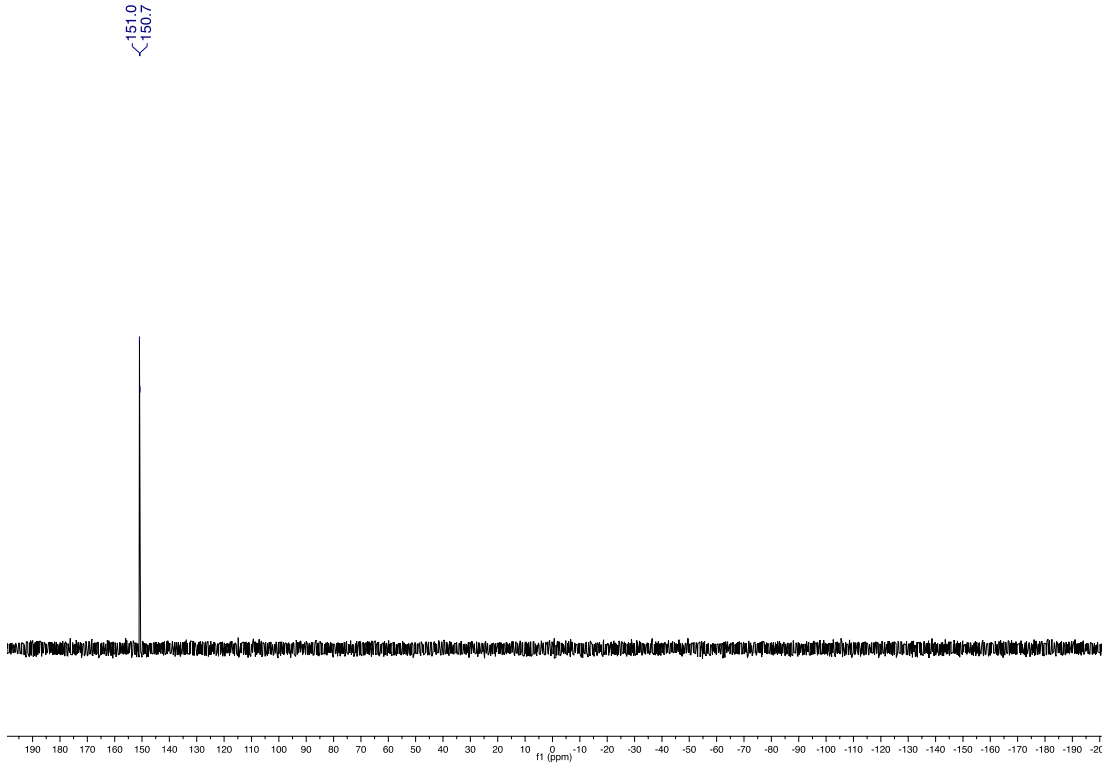

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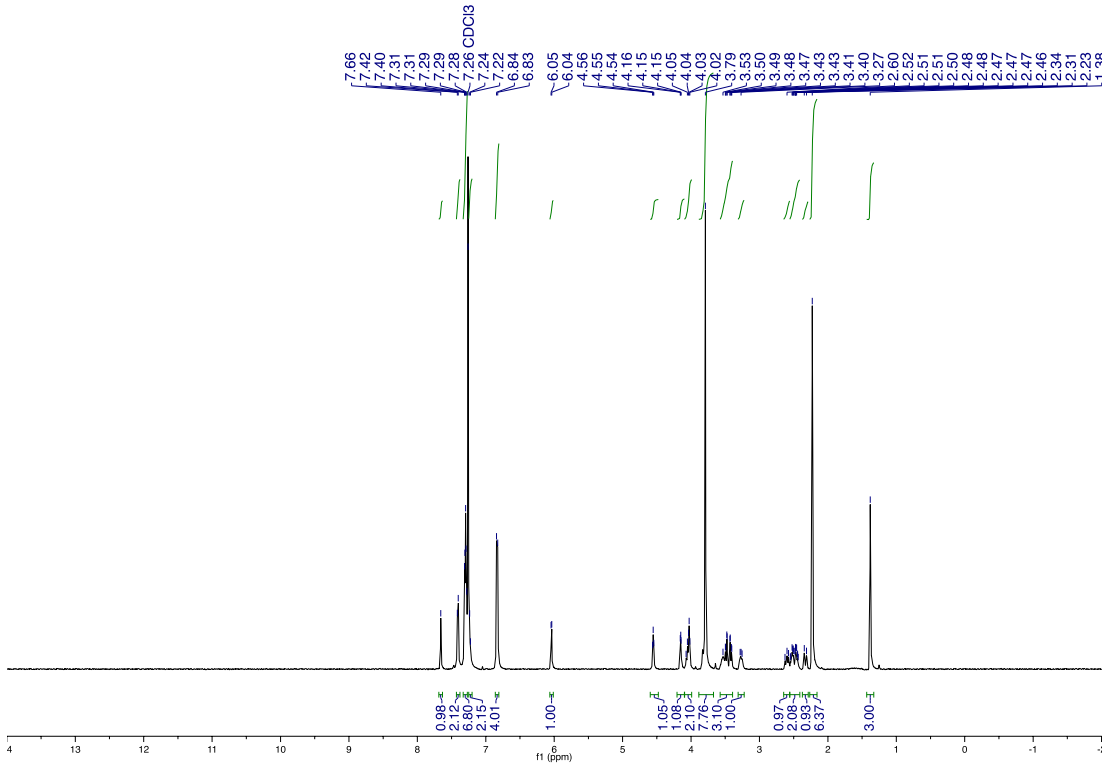


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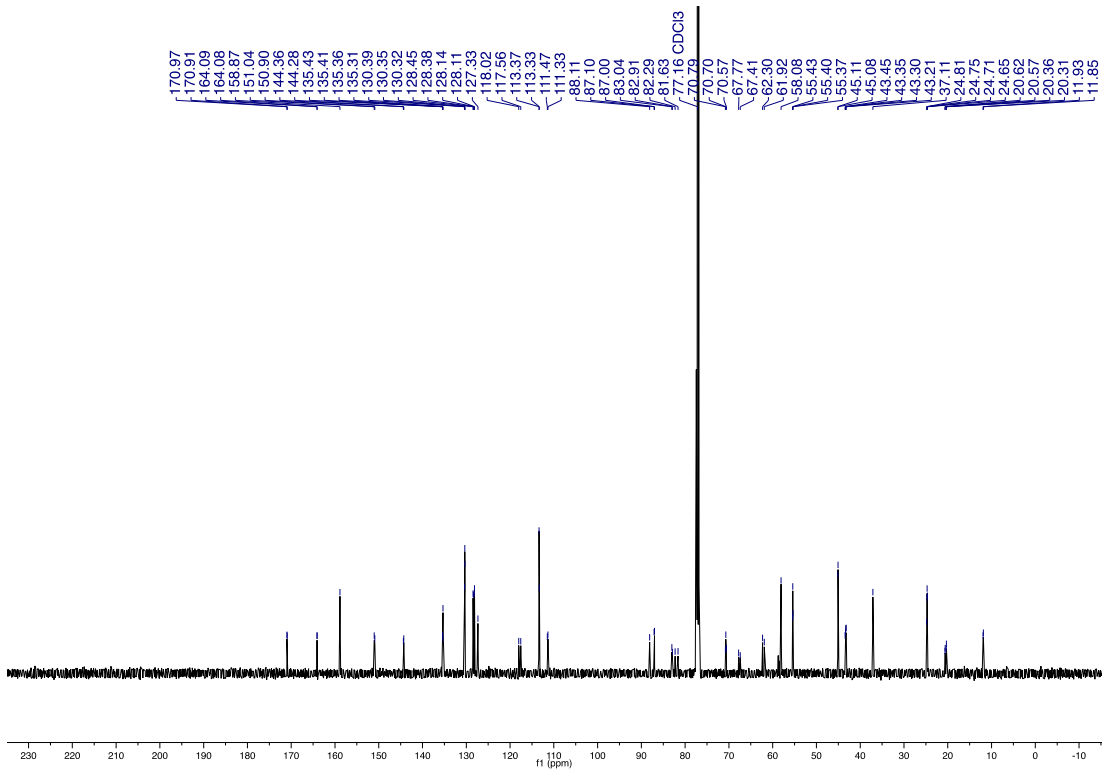

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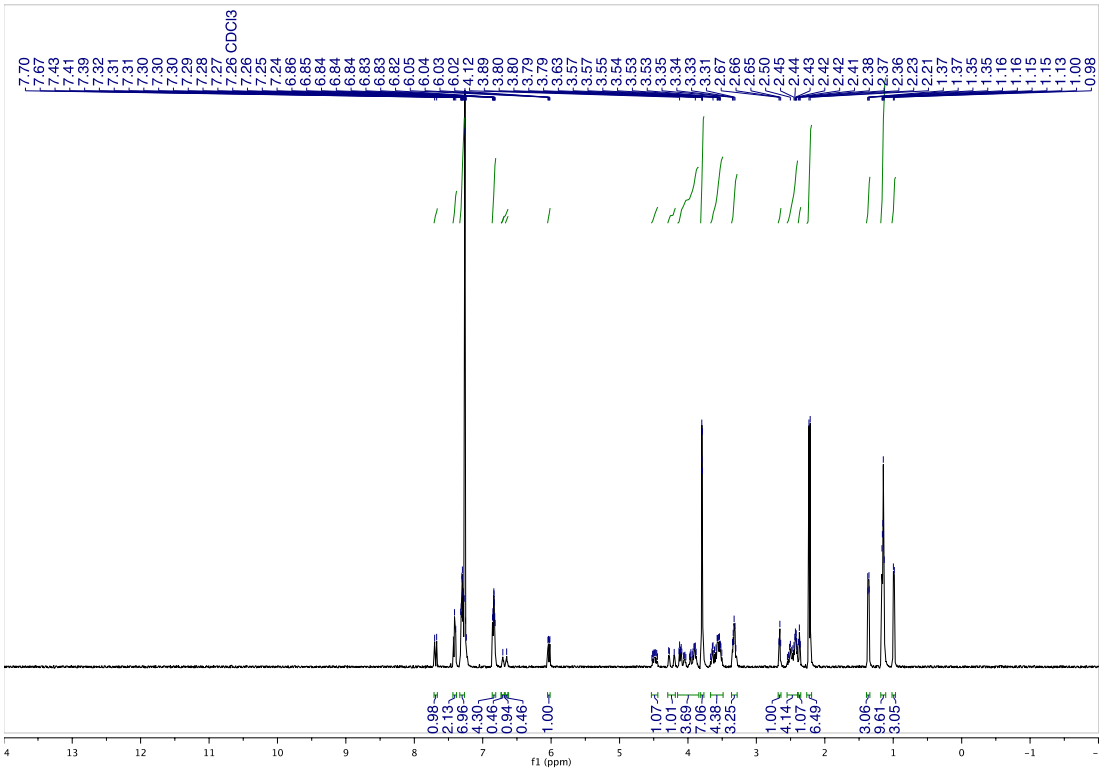


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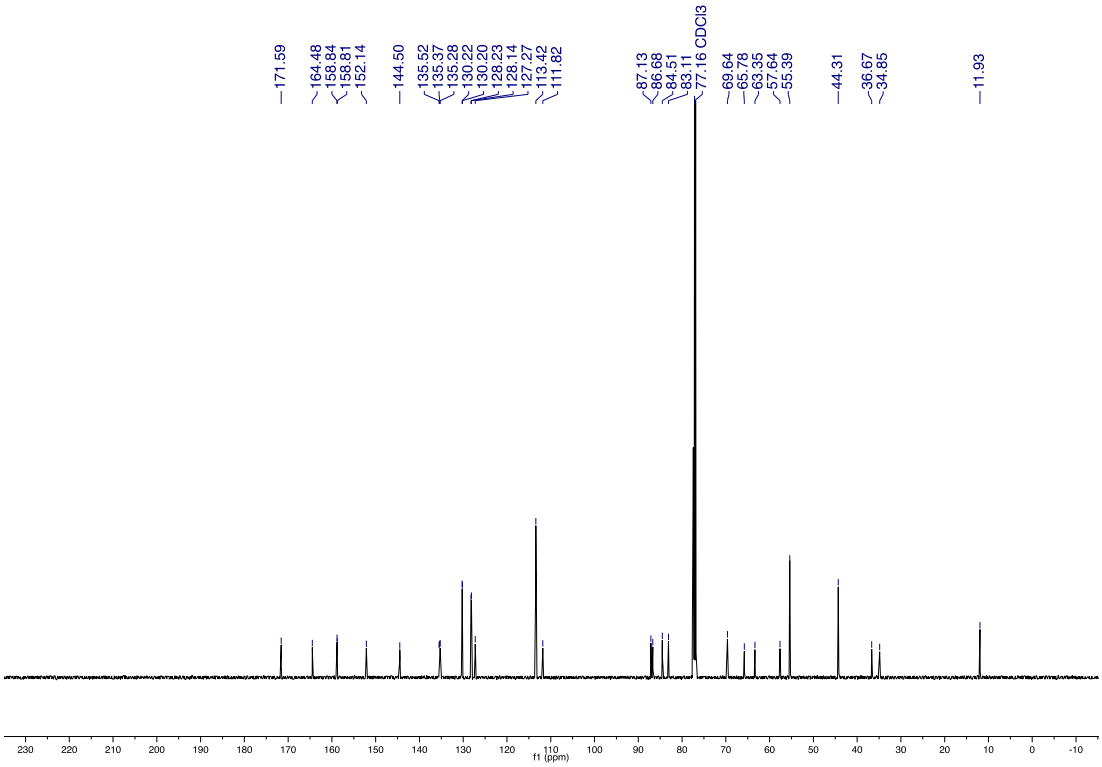
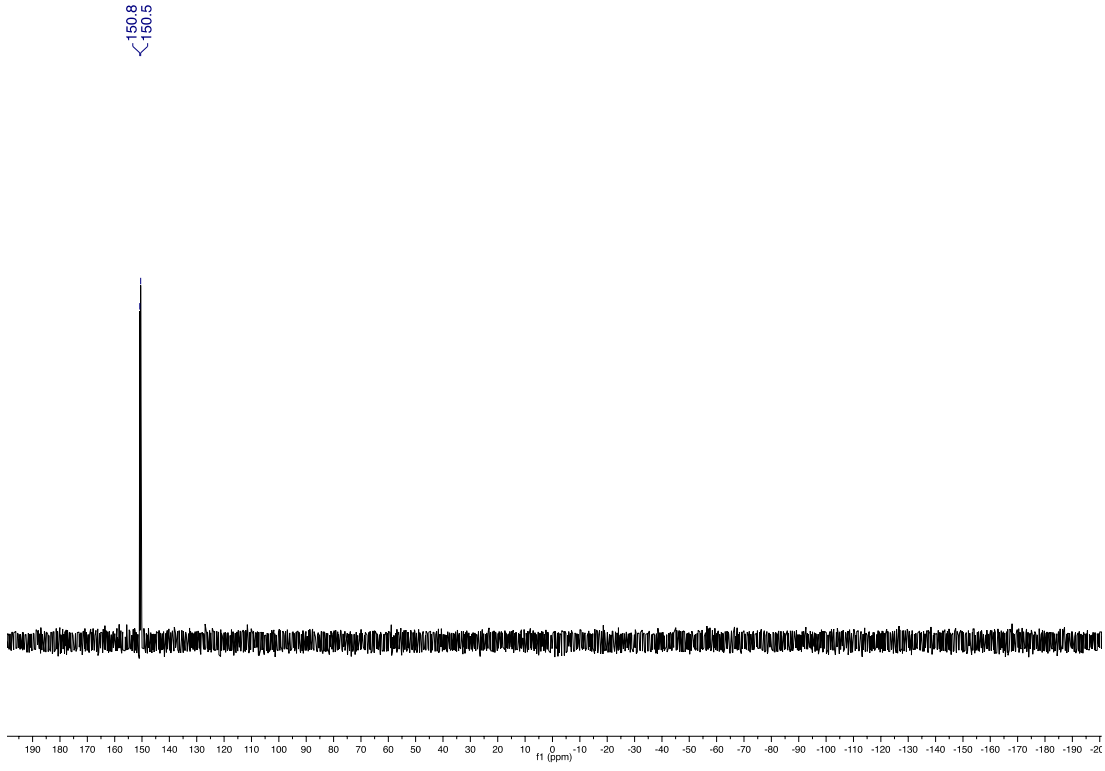
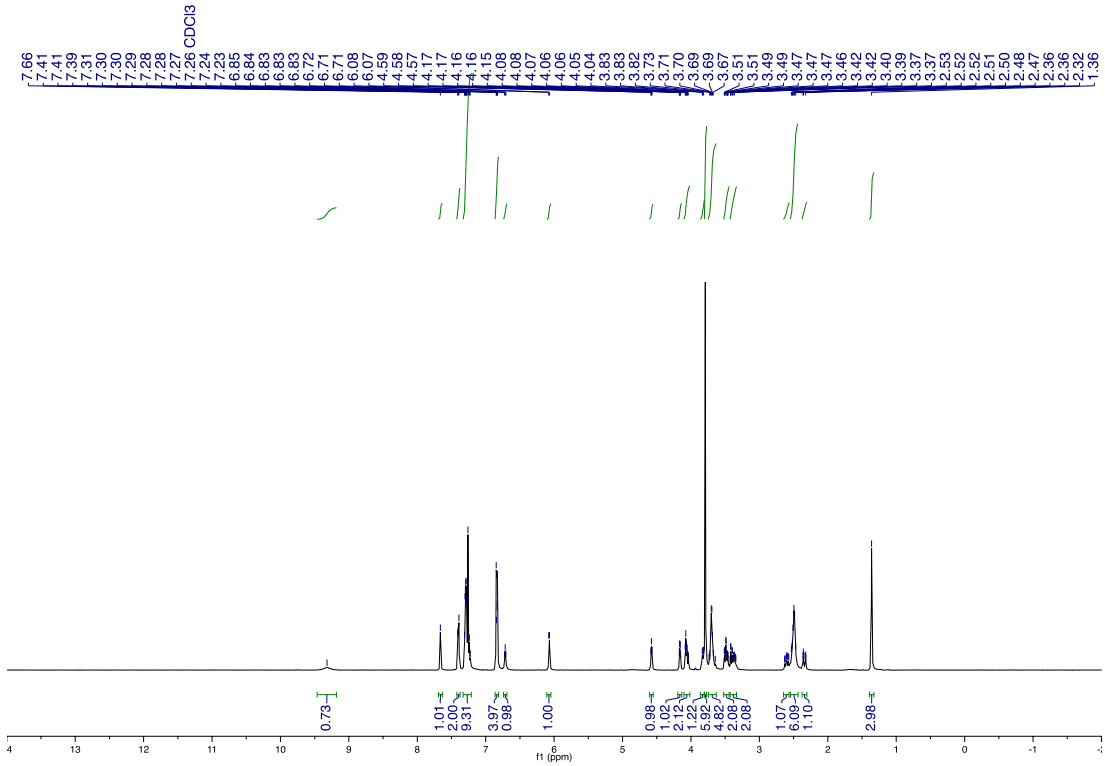


**$^{31}$P-NMR of compound 5b (DMAECE)**



**$^{1}$H-NMR of compound 4c (MorECE)**

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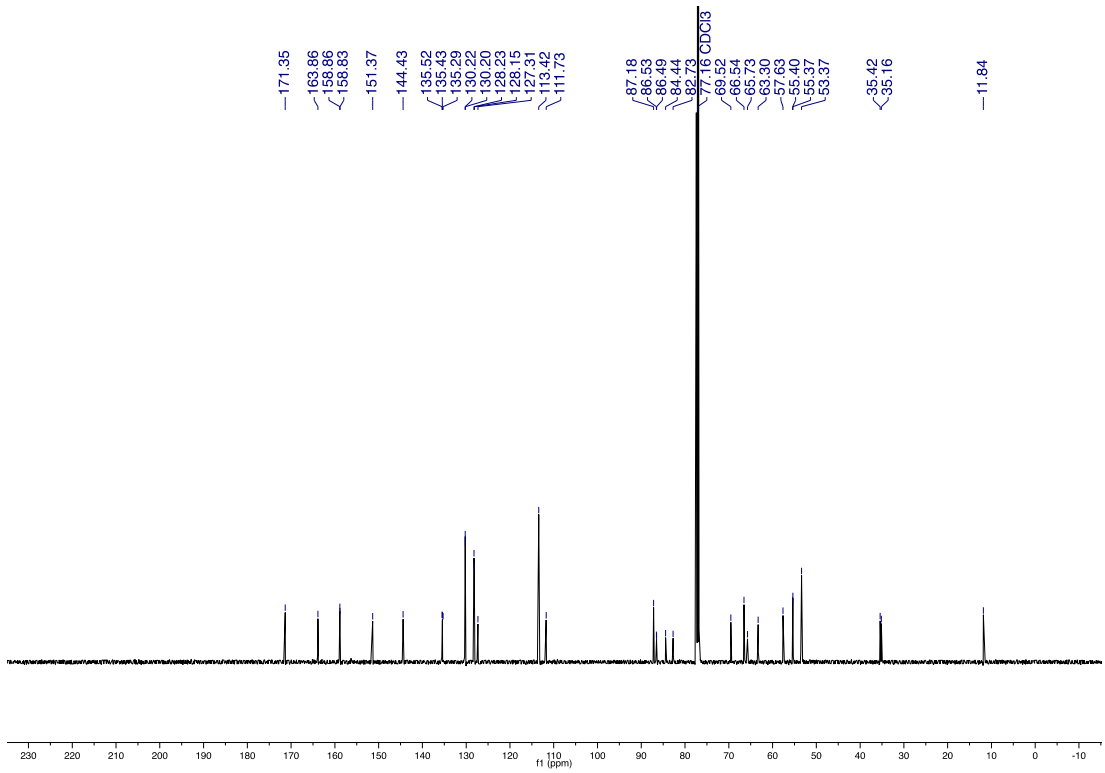

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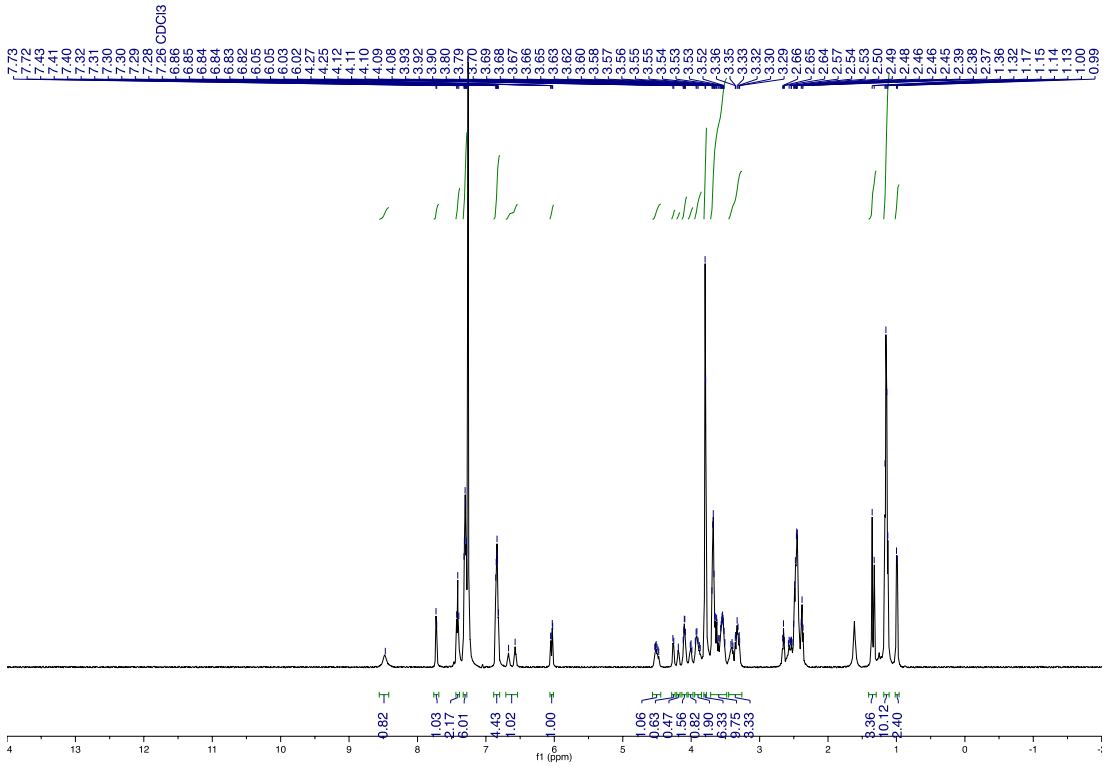

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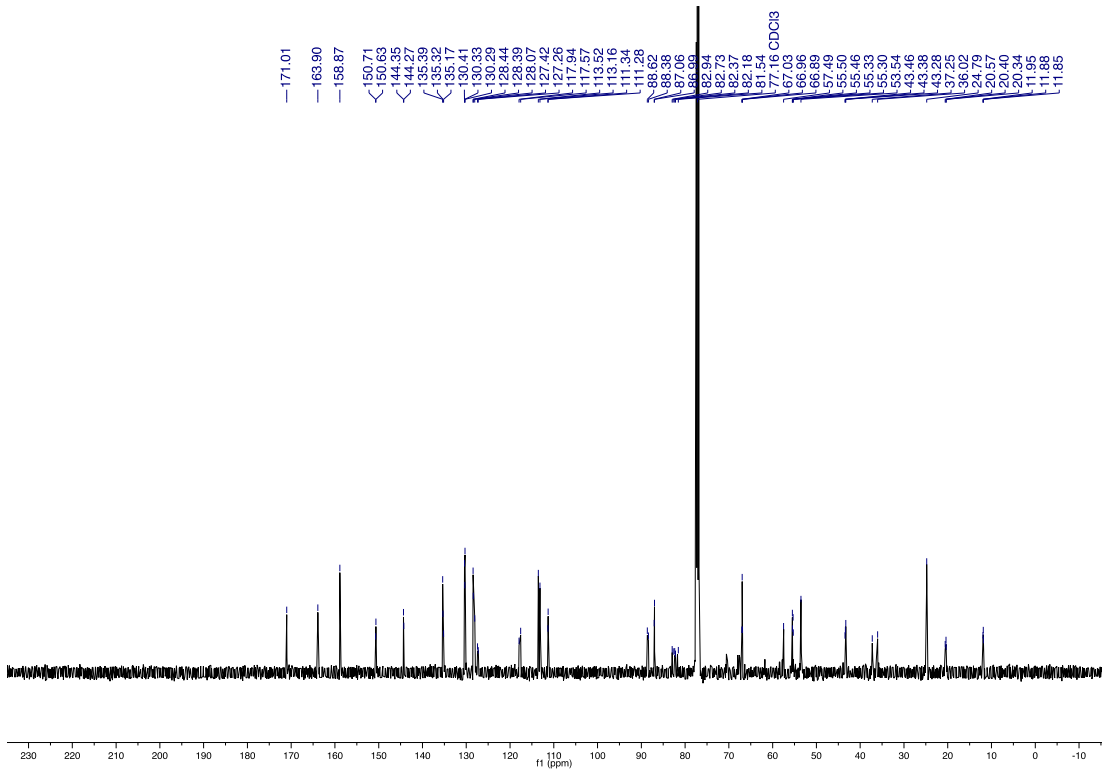
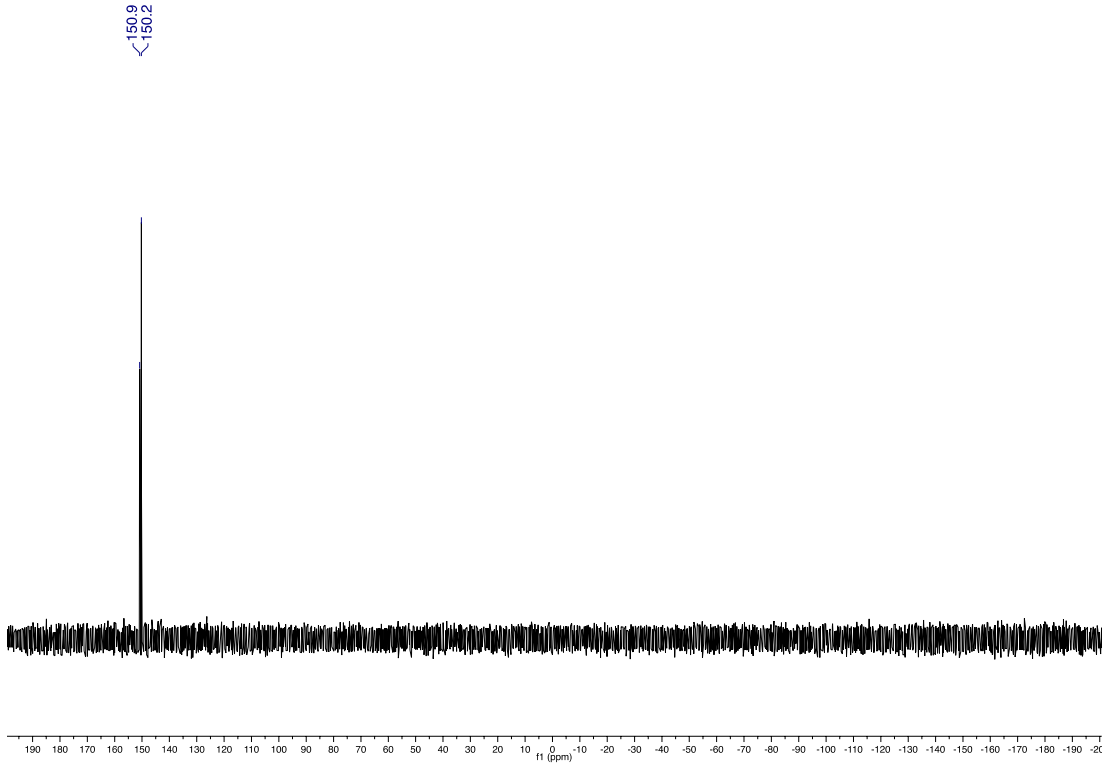
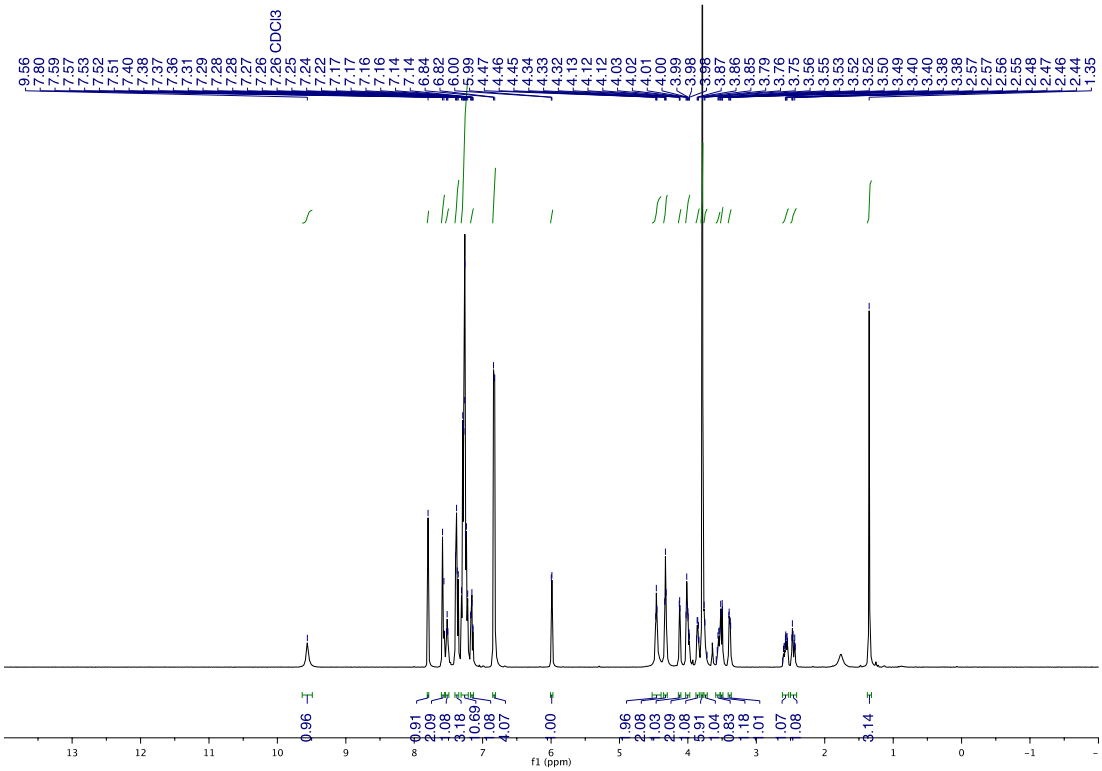


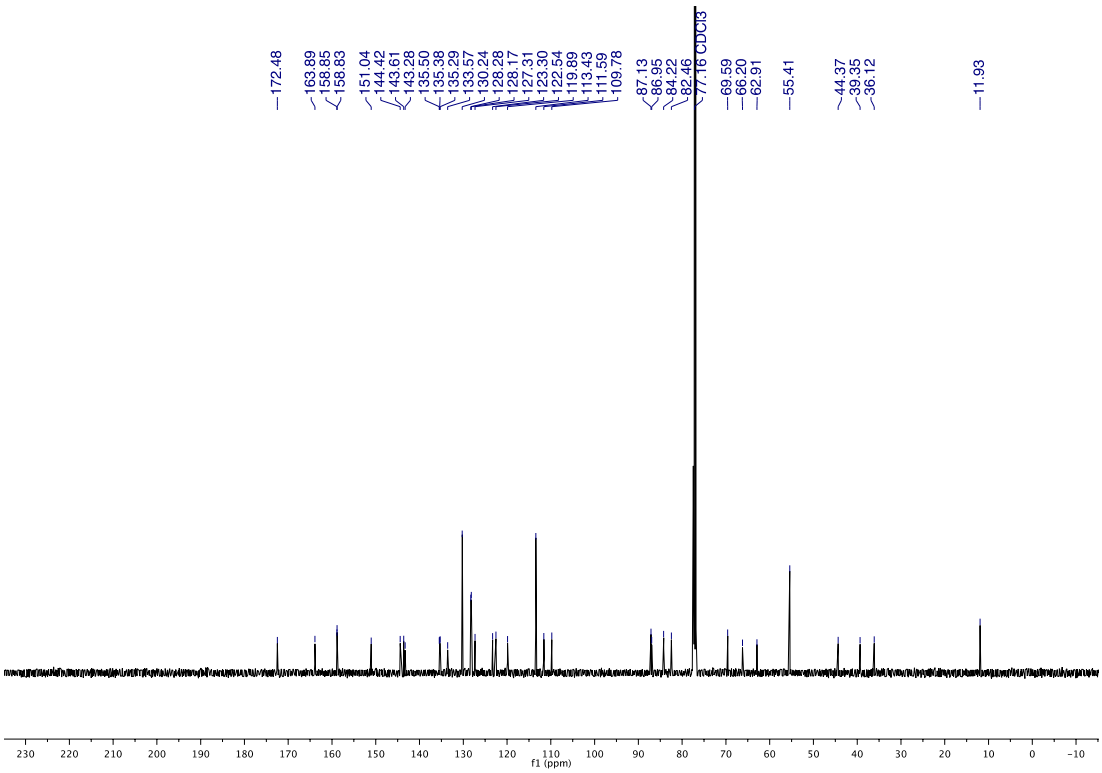
**$^{31}$P-NMR of compound 5c (MorECE)**



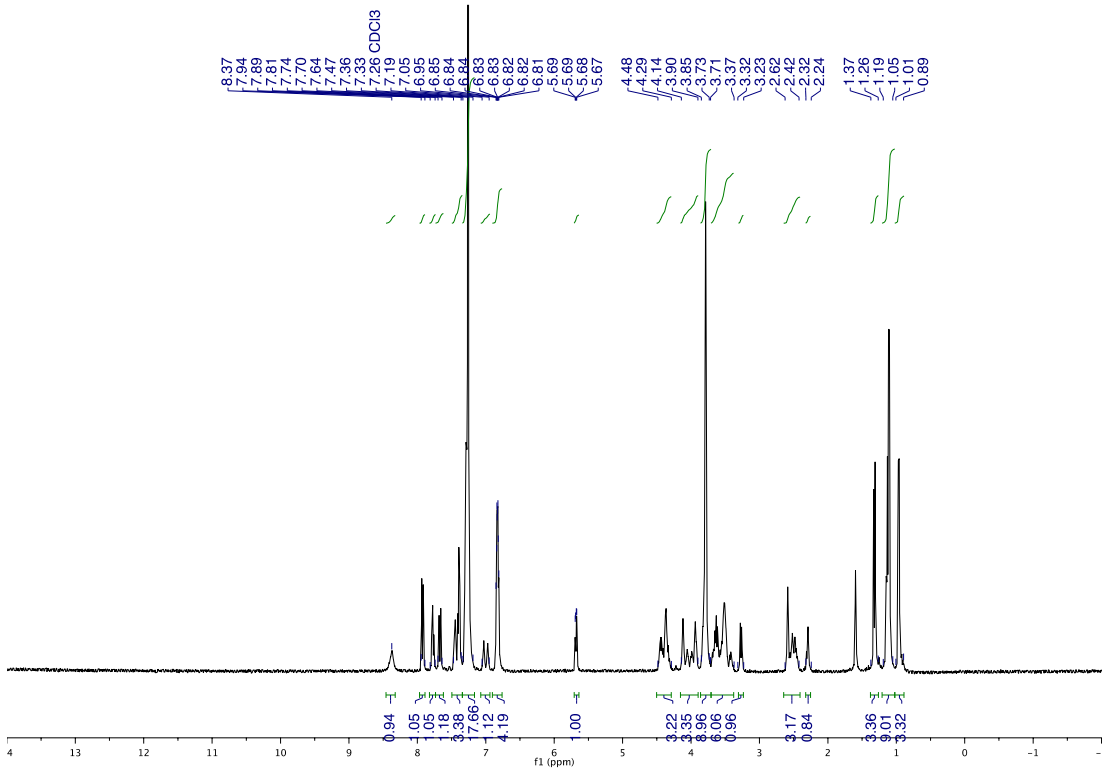
**$^{1}$H-NMR of compound 4d (BzimECE)**




**$^{13}$C-NMR of compound 4d (BzimECE)**



**$^{1}$H-NMR of compound 5d (BzimECE)**

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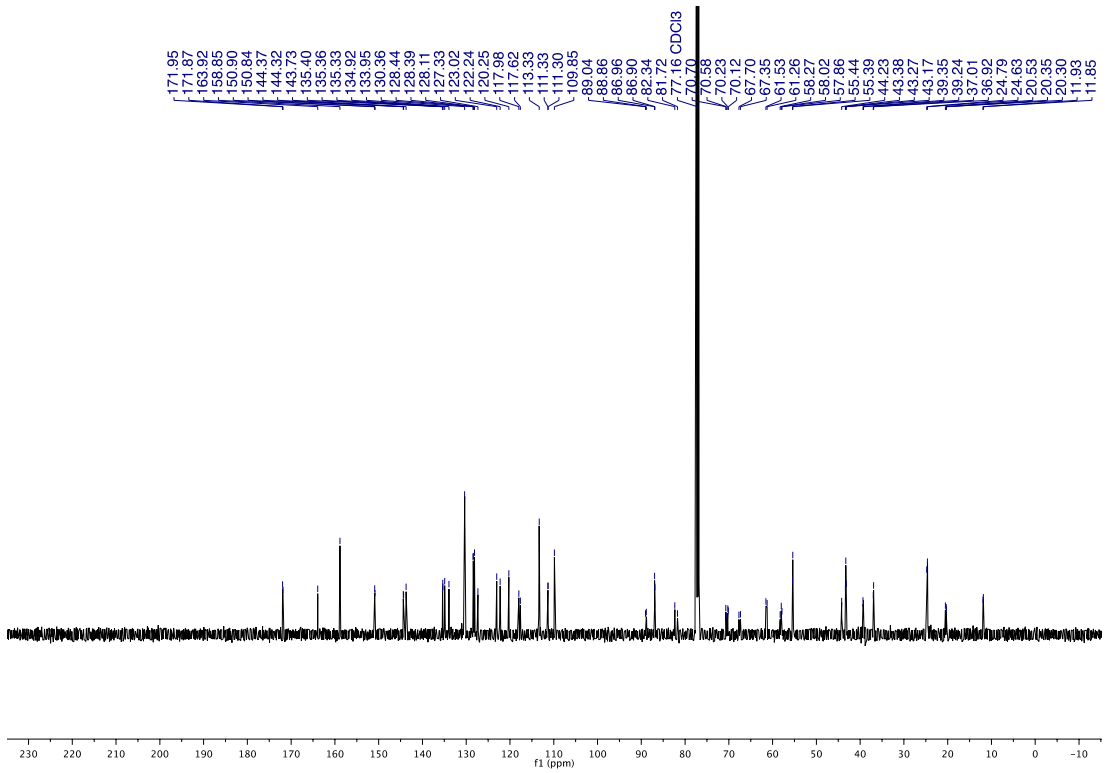
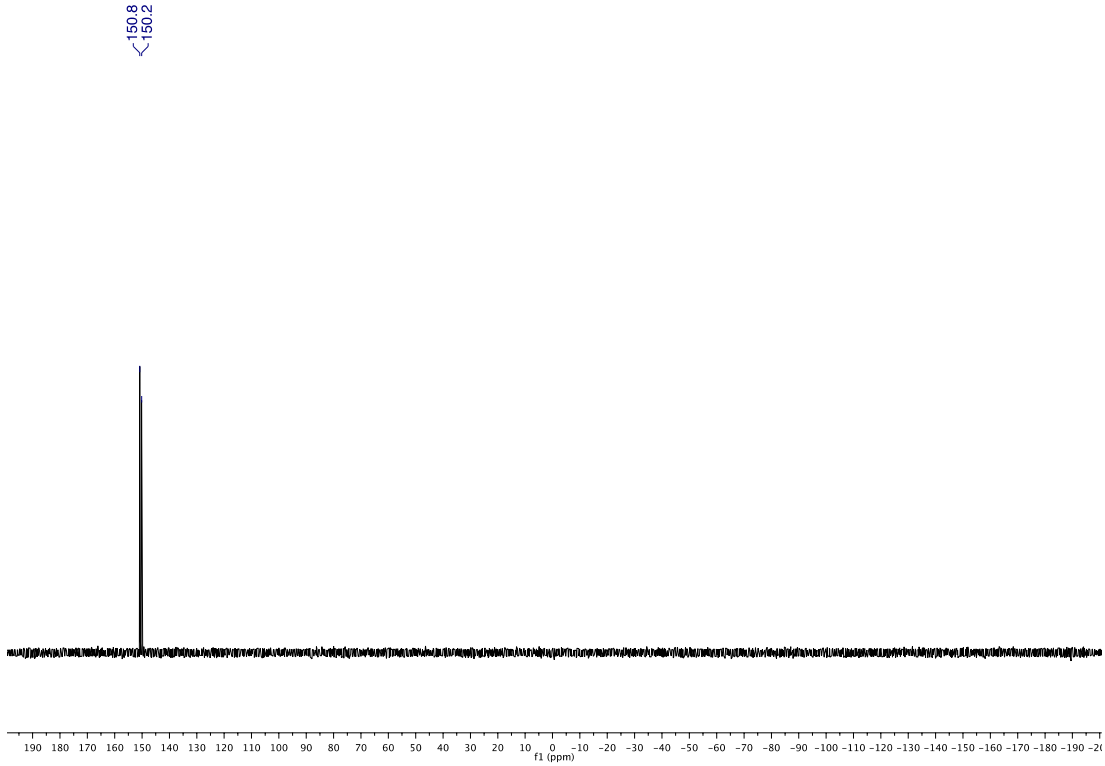


**$^{31}$P-NMR of compound 5d (BzimECE)**



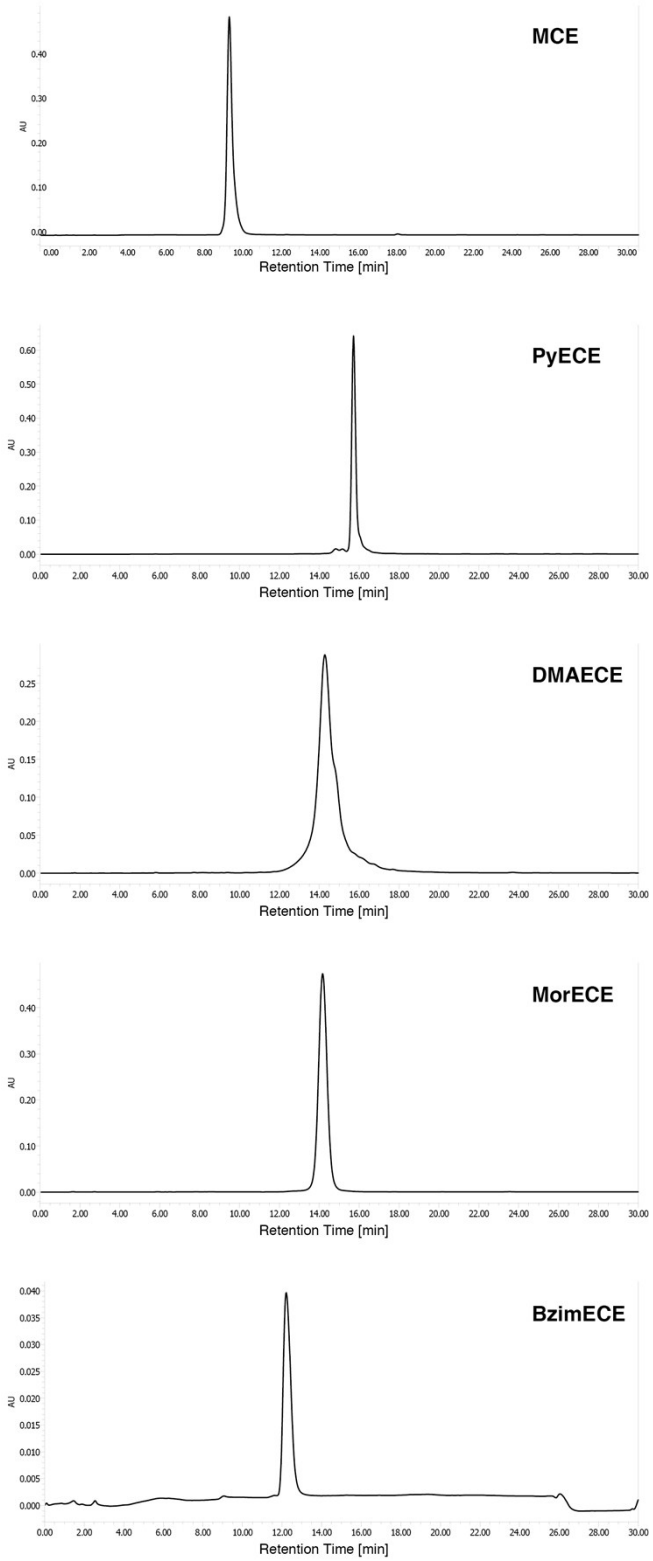



**Figure S1** HPLC chart of synthesized oligonucleotides for nuclease resistance. Mobile phase A: 30 mM $NH_4OAc$ buffer Mobile phase B: 100% MeCN, linear gradient from 0 to 40 minutes was 0% to 40% B.

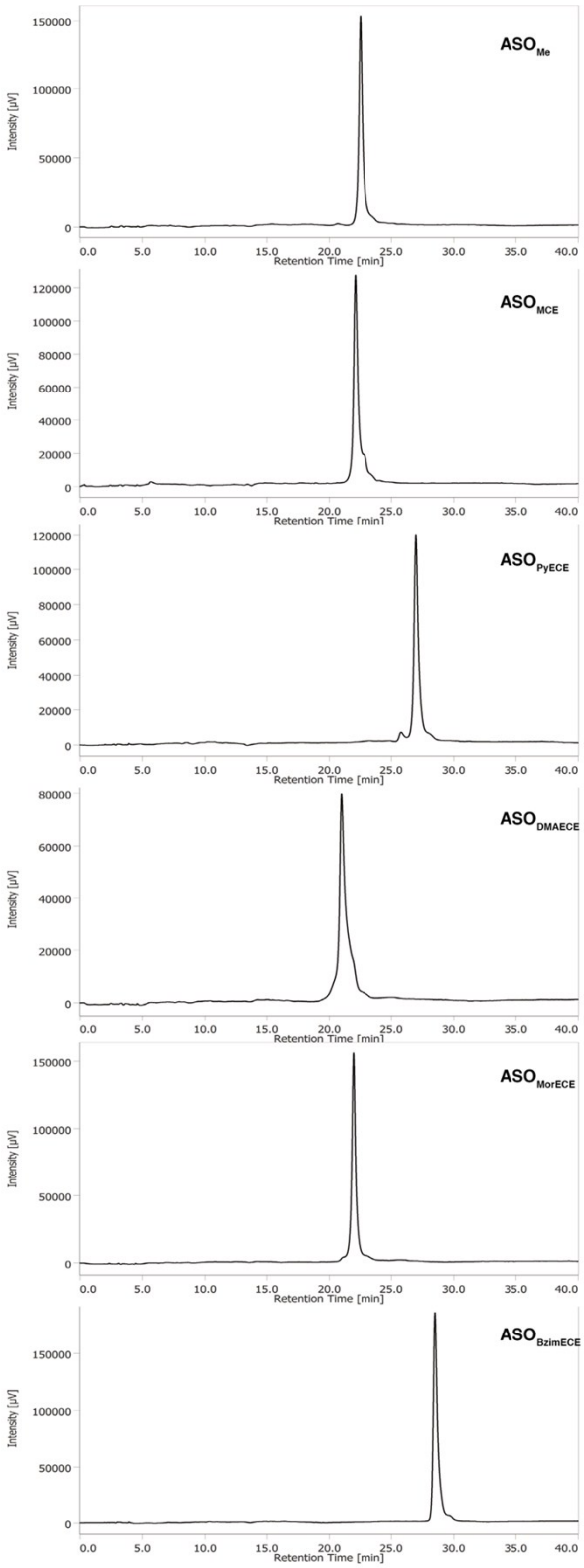



**Figure S2** HPLC chart of synthesized oligonucleotides for $T_m$ and antisense activity. Mobile phase A: 8 mM TEA, 100 mM HFIP buffer Mobile phase B: 100% MeOH, linear gradient from 0 to 40 minutes was 0% to 40% B.

**Table S1.** Summary of mass values of synthesized oligonucleotide (MALDI-TOF-Mass)

| oligonucleotide | calcd for [M+H] | found | purity (RP-HPLC) |
|---|---|---|---|
| **MCE** | 6123.2 | 6125.7 | 98 |
| **PyECE** | 6487.6 | 6489.2 | 92 |
| **DMAECE** | 6351.5 | 6353.6 | 89 |
| **MorECE** | 6519.7 | 6521.9 | 98 |
| **BzimECE** | 6643.8 | 6643.9 | 99 |
| | | | |
| **$ASO_{Me}$** | 6775.5 | 6776.6 | 92 |
| **$ASO_{MCE}$** | 7130.9 | 7132.7 | 89 |
| **$ASO_{PyECE}$** | 7585.5 | 7587.4 | 89 |
| **$ASO_{DMAECE}$** | 7416.4 | 7417.3 | 94 |
| **$ASO_{MorECE}$** | 7626.6 | 7627.4 | 92 |
| **$ASO_{BzimECE}$** | 7781.7 | 7782.7 | 95 |

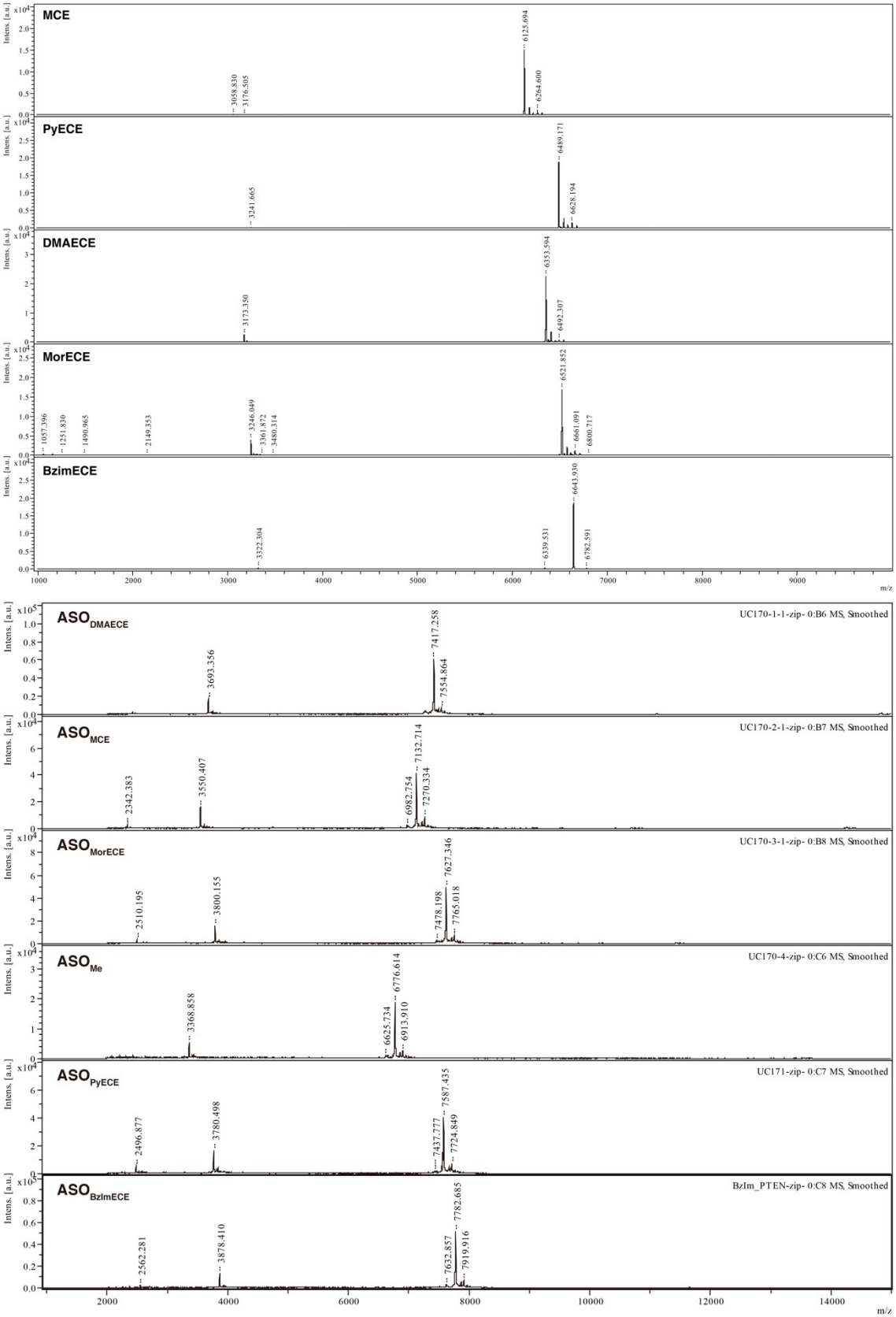



**Figure S3**. Observed MALDI-TOF-Mass spectrum of each oligonucleotide.

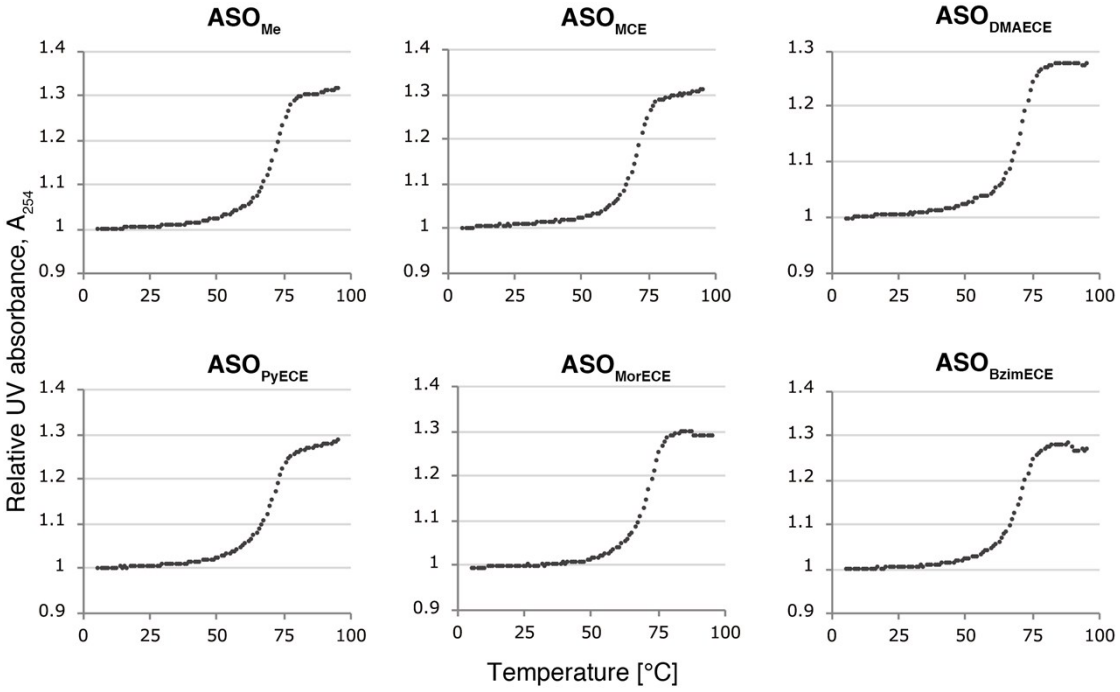



**Figure S4**. Observed melting curve of each duplex.