

Supporting Information

Total Synthesis of (±)-Galanthamine from GABA through Regioselective Aryne Insertion

Telugu Venkatesh,^{a,b} Prathama S. Mainkar,^{a,b} and Srivari Chandrasekhar^{*,a,b}

^a*Department of Organic Synthesis & Process Chemistry, CSIR-Indian Institute of Chemical Technology,
Hyderabad 500007, India*

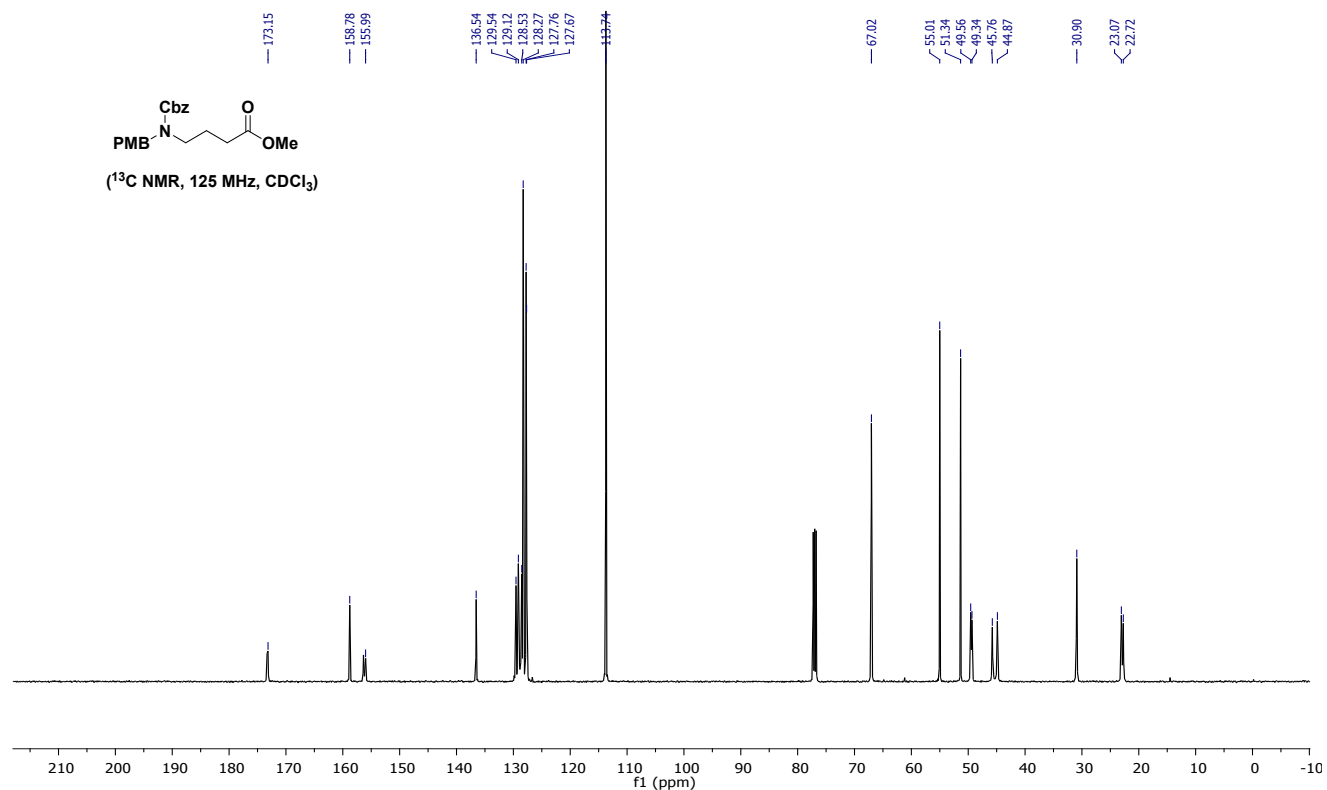
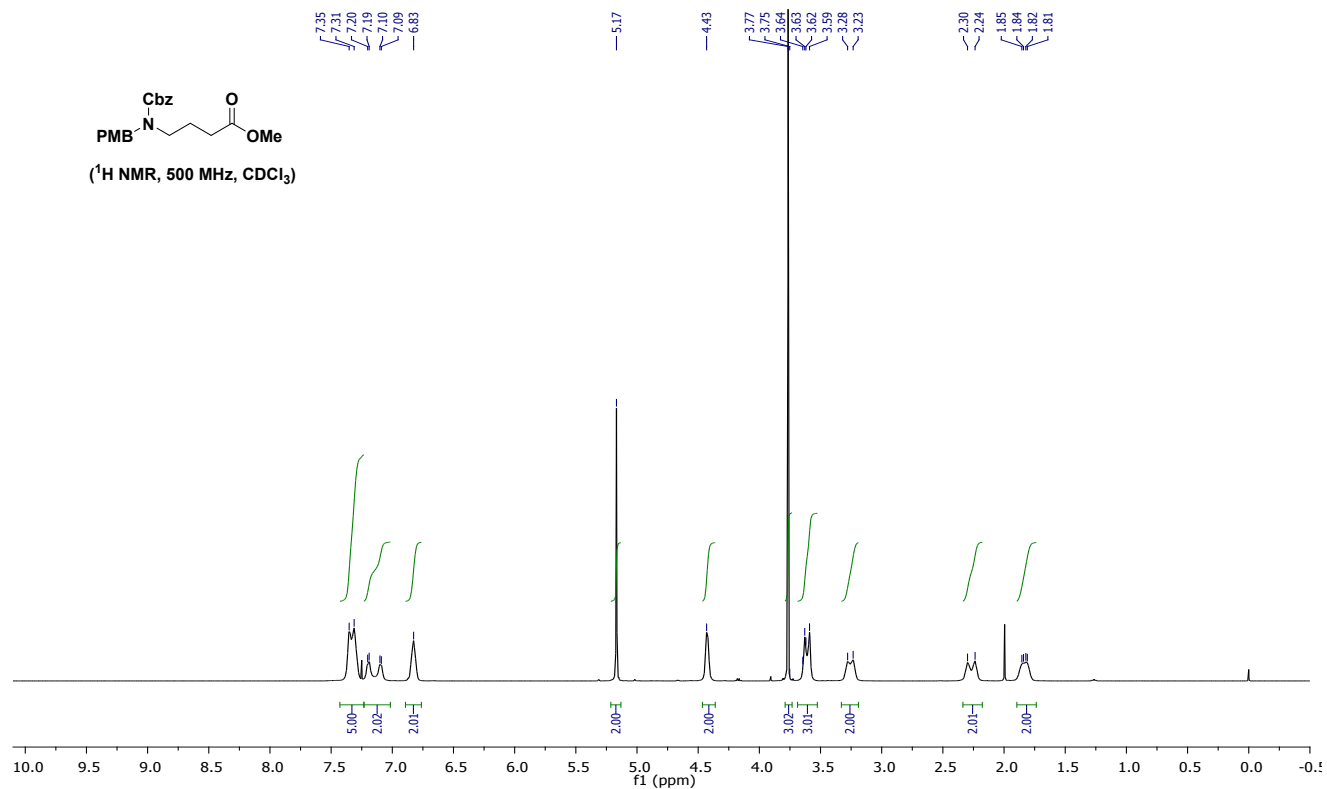
^b*Academy of Scientific & Innovative Research (AcSIR), New Delhi 110020, India*

Email: srivaric@iict.res.in

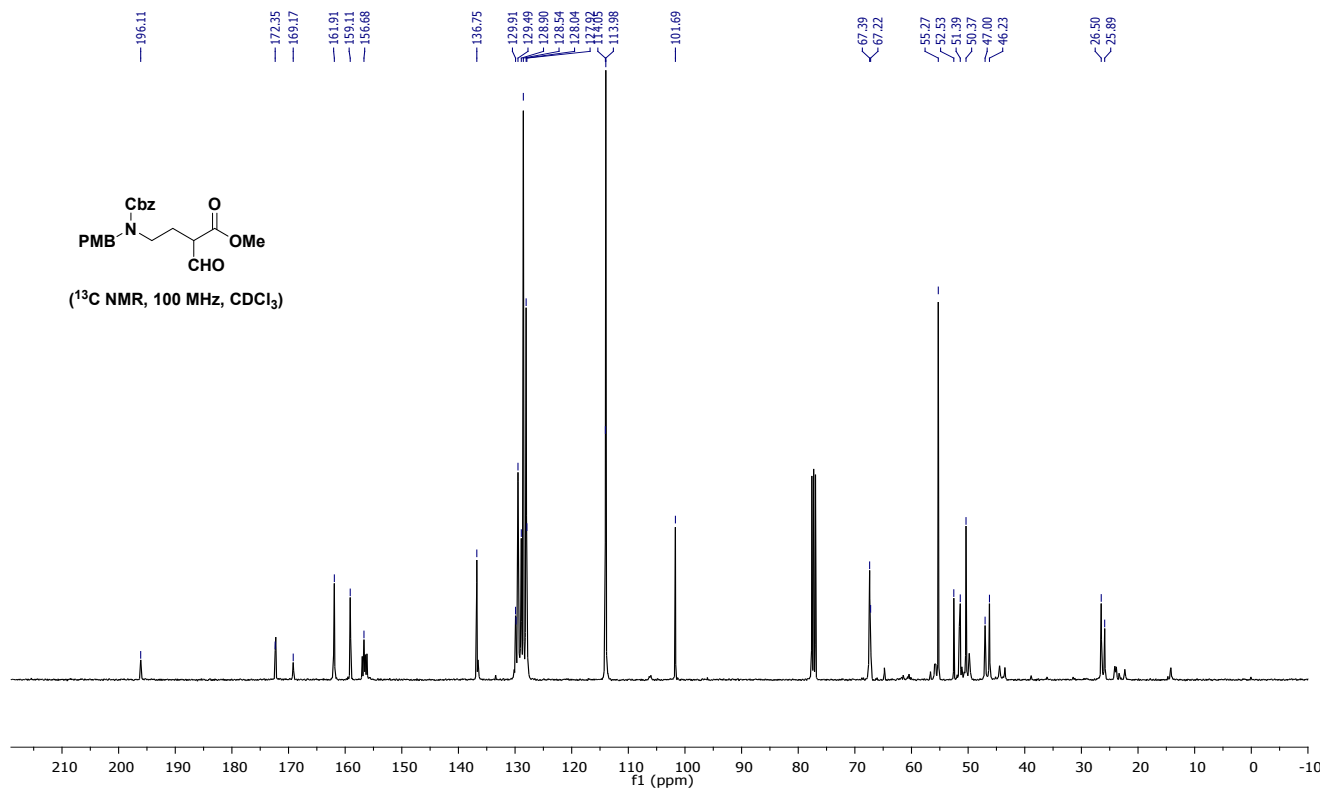
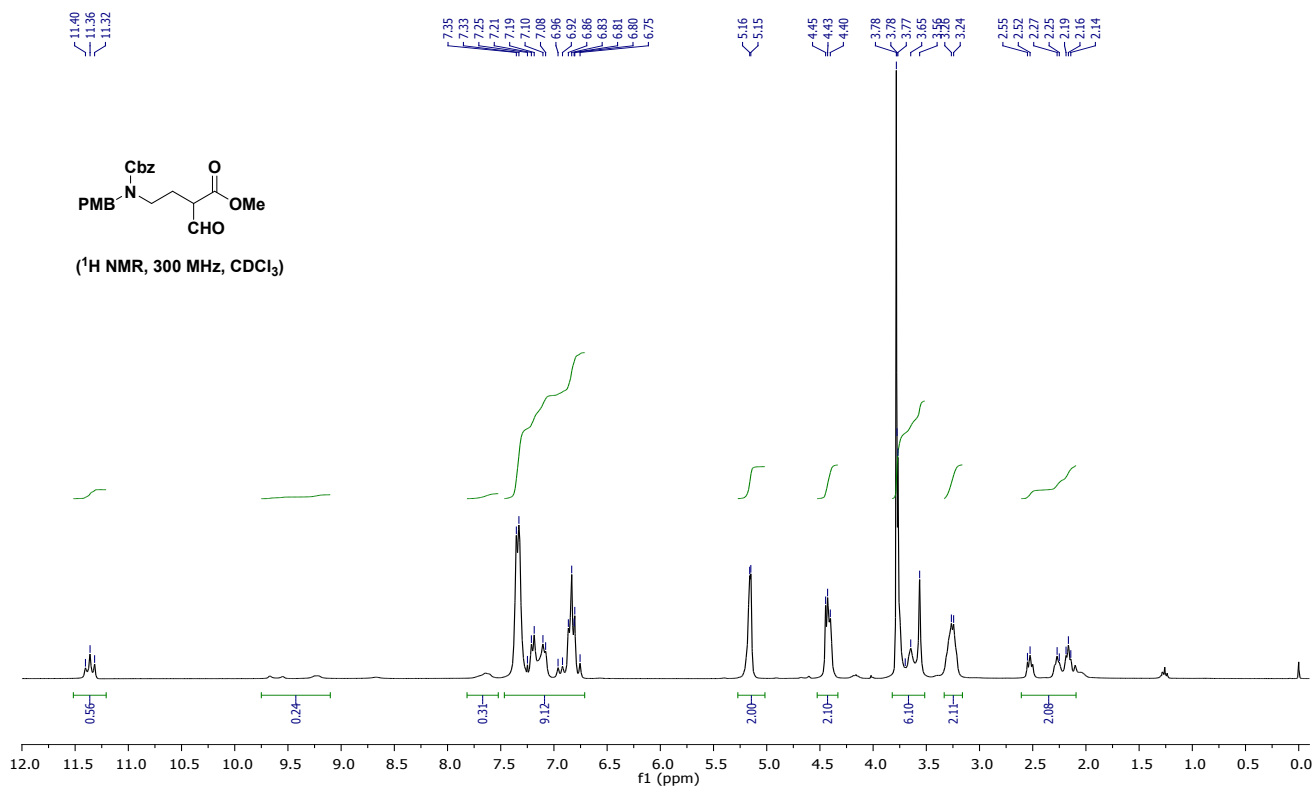
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3. ¹H & ¹³C NMR spectra:

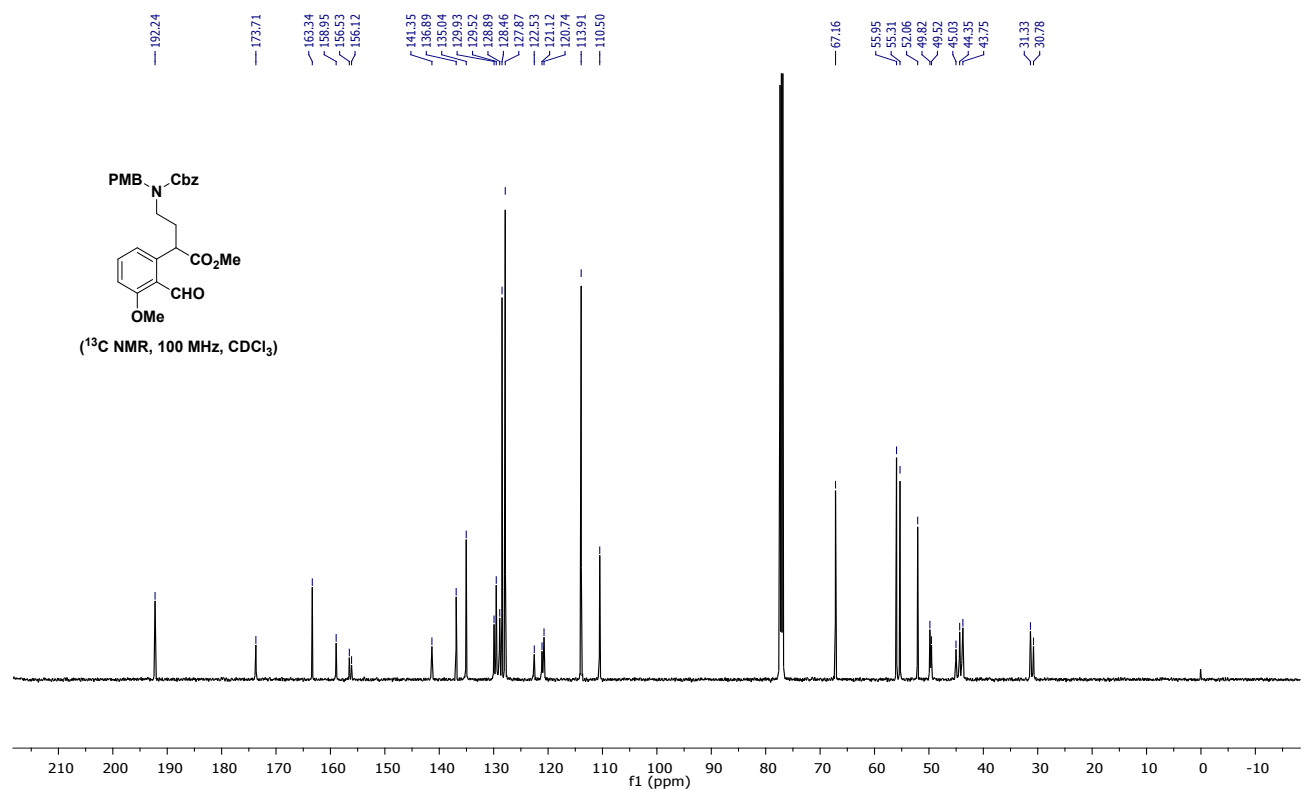
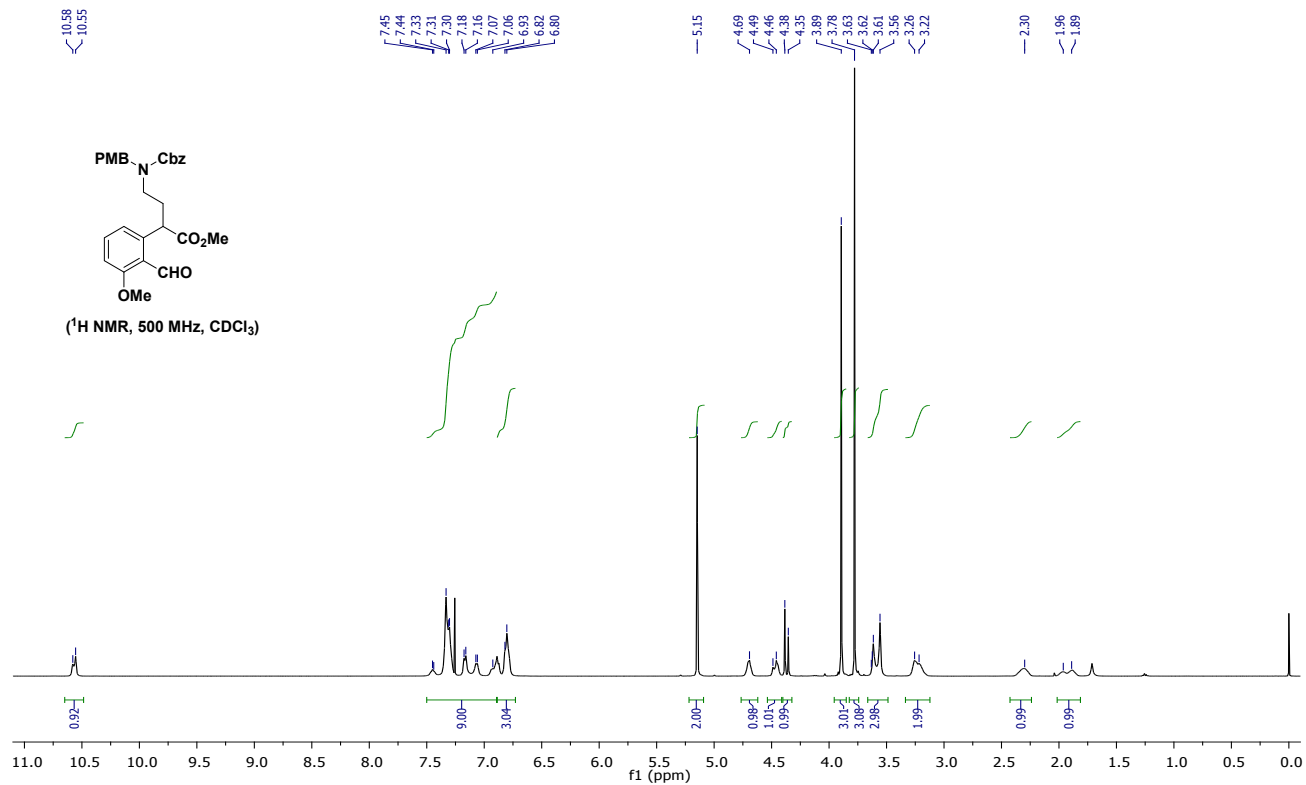
Methyl 4-(((benzyloxy)carbonyl)(4-methoxybenzyl)amino)butanoate (7):



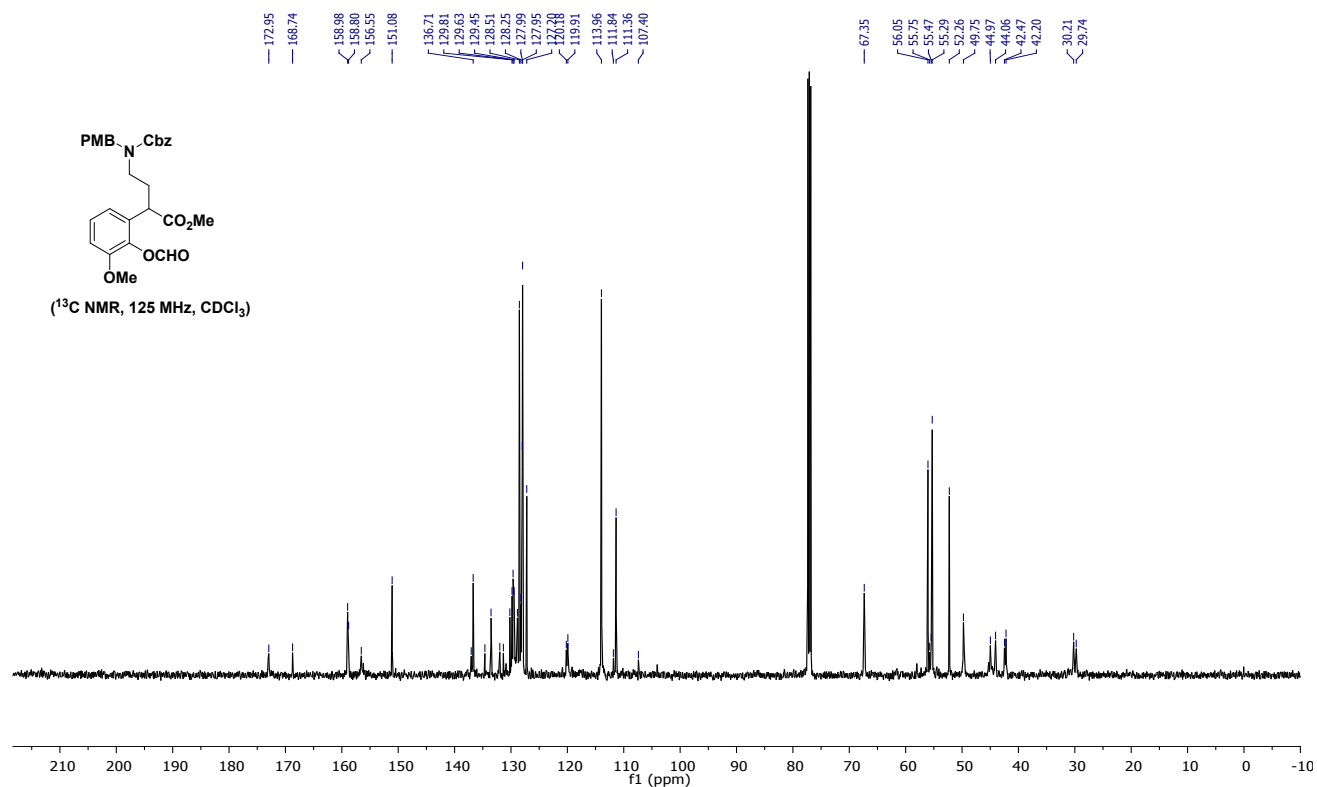
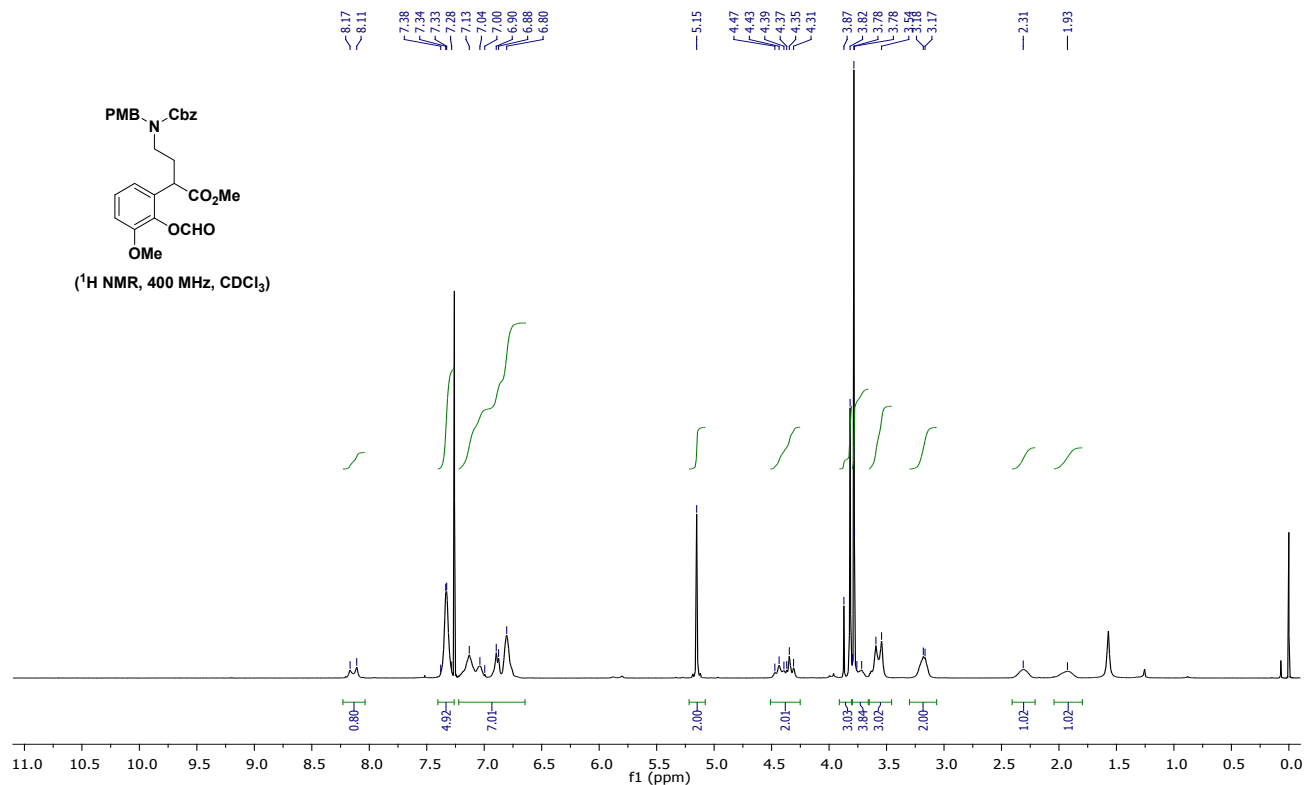
Methyl 4-(((benzyloxy)carbonyl)(4-methoxybenzyl)amino)-2-formylbutanoate (5):



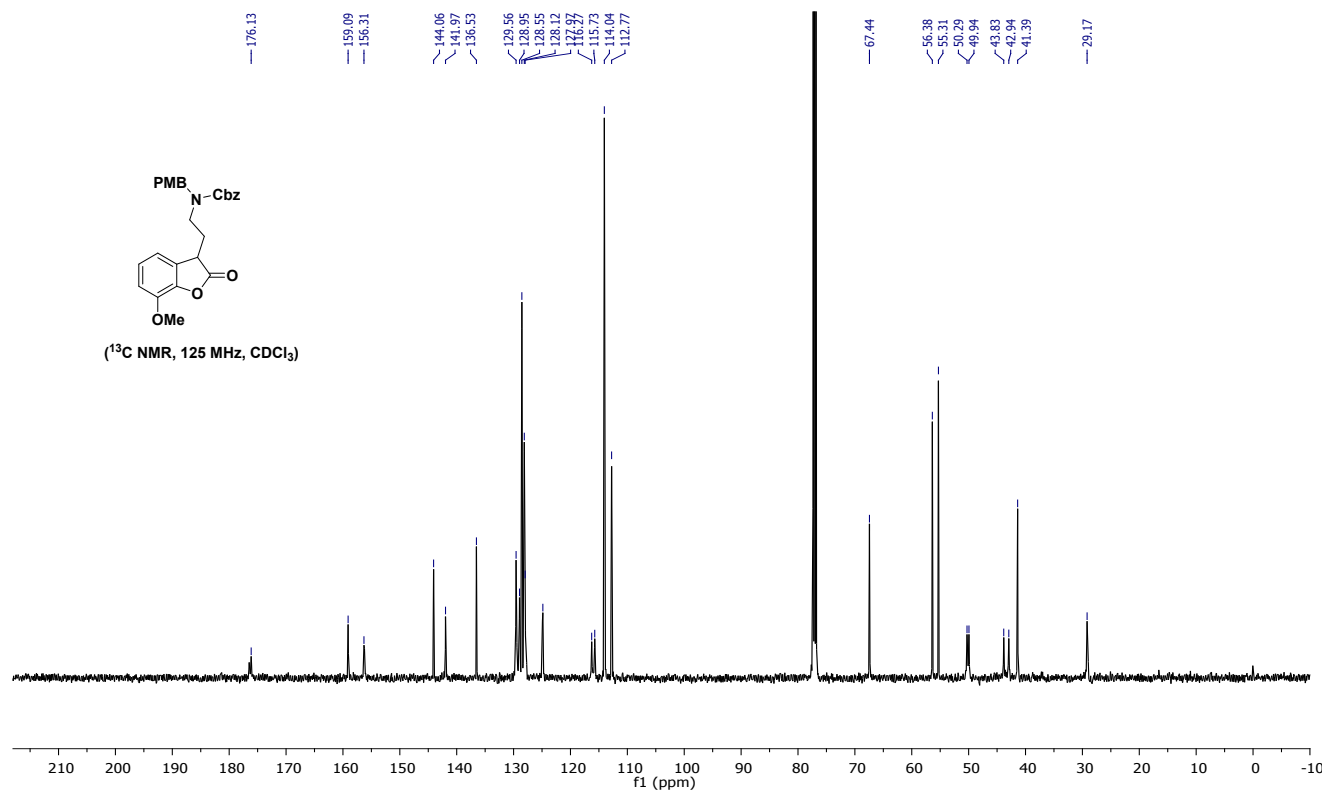
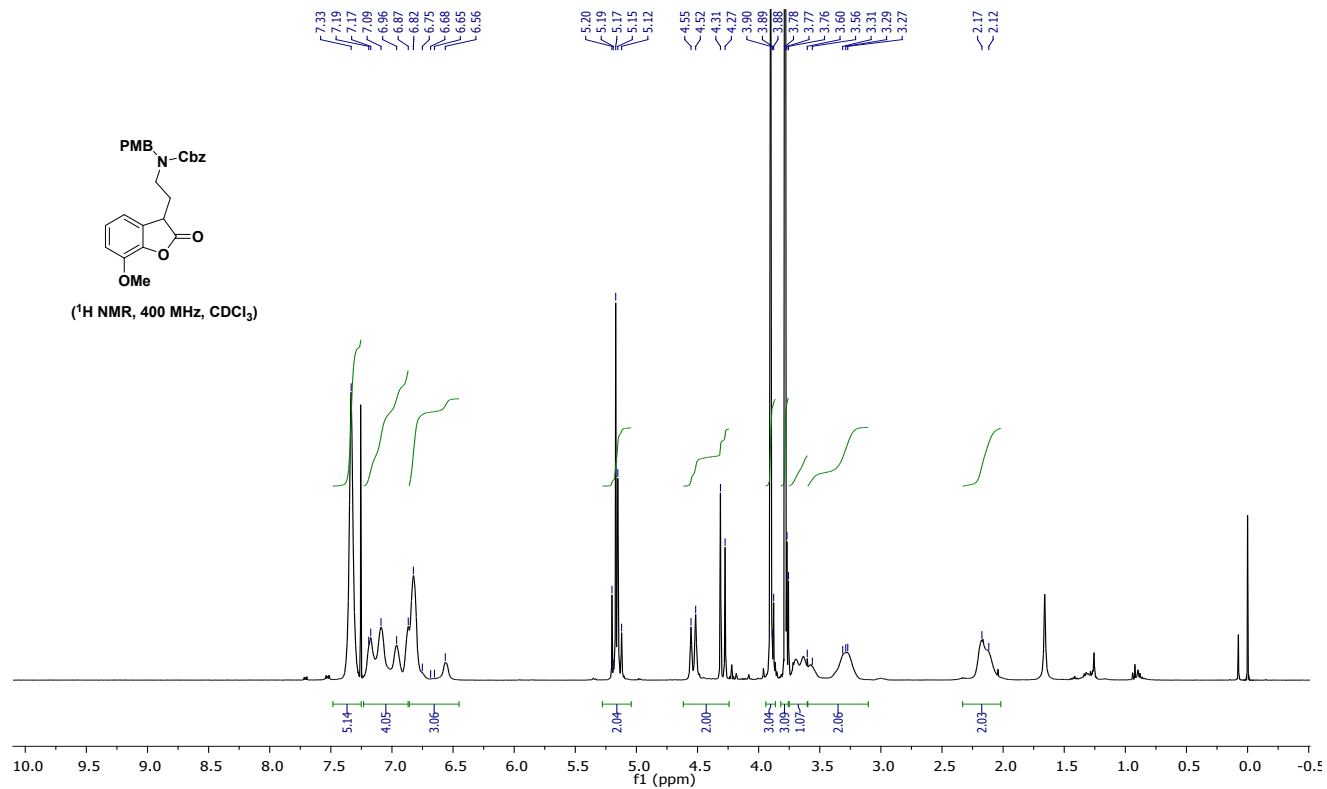
Methyl 4-(((benzyloxy)carbonyl)(4-methoxybenzyl)amino)-2-(2-formyl-3-methoxyphenyl)butanoate (3):



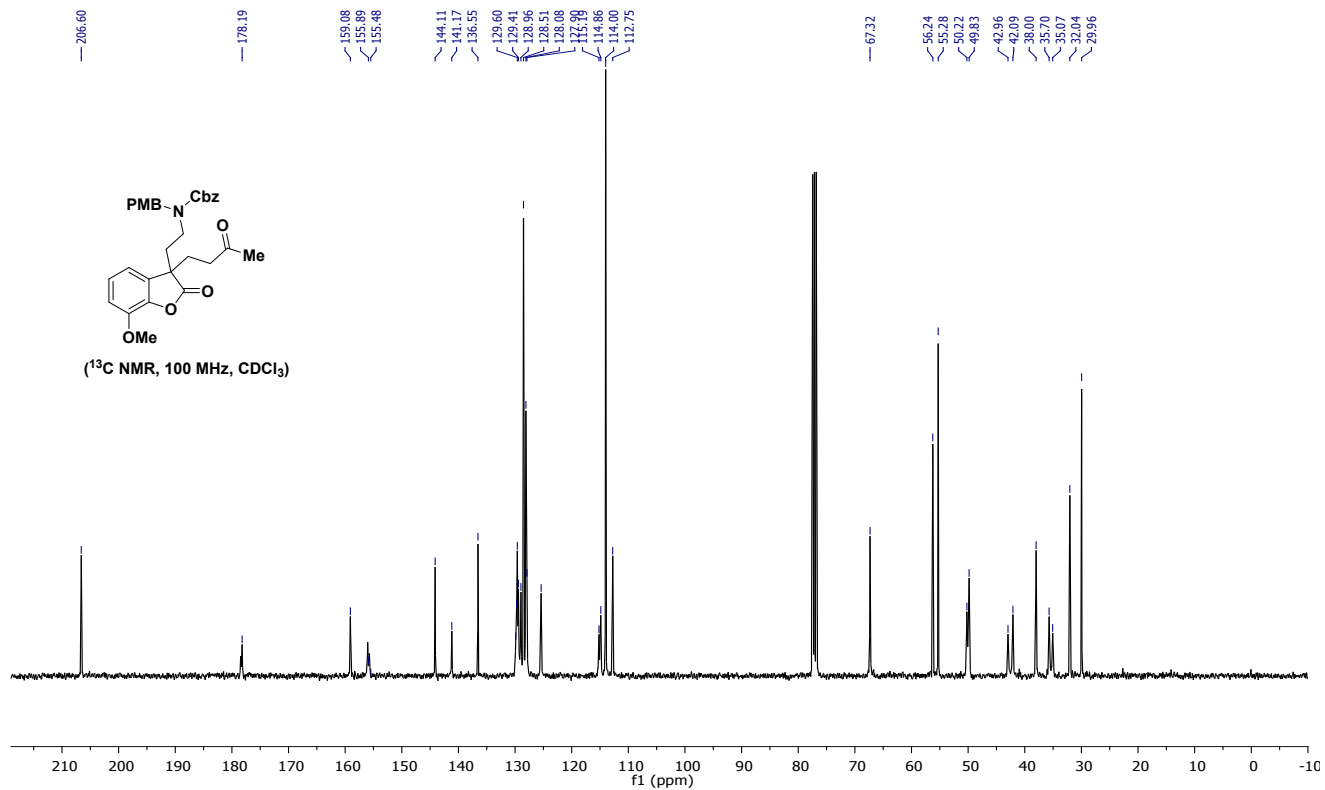
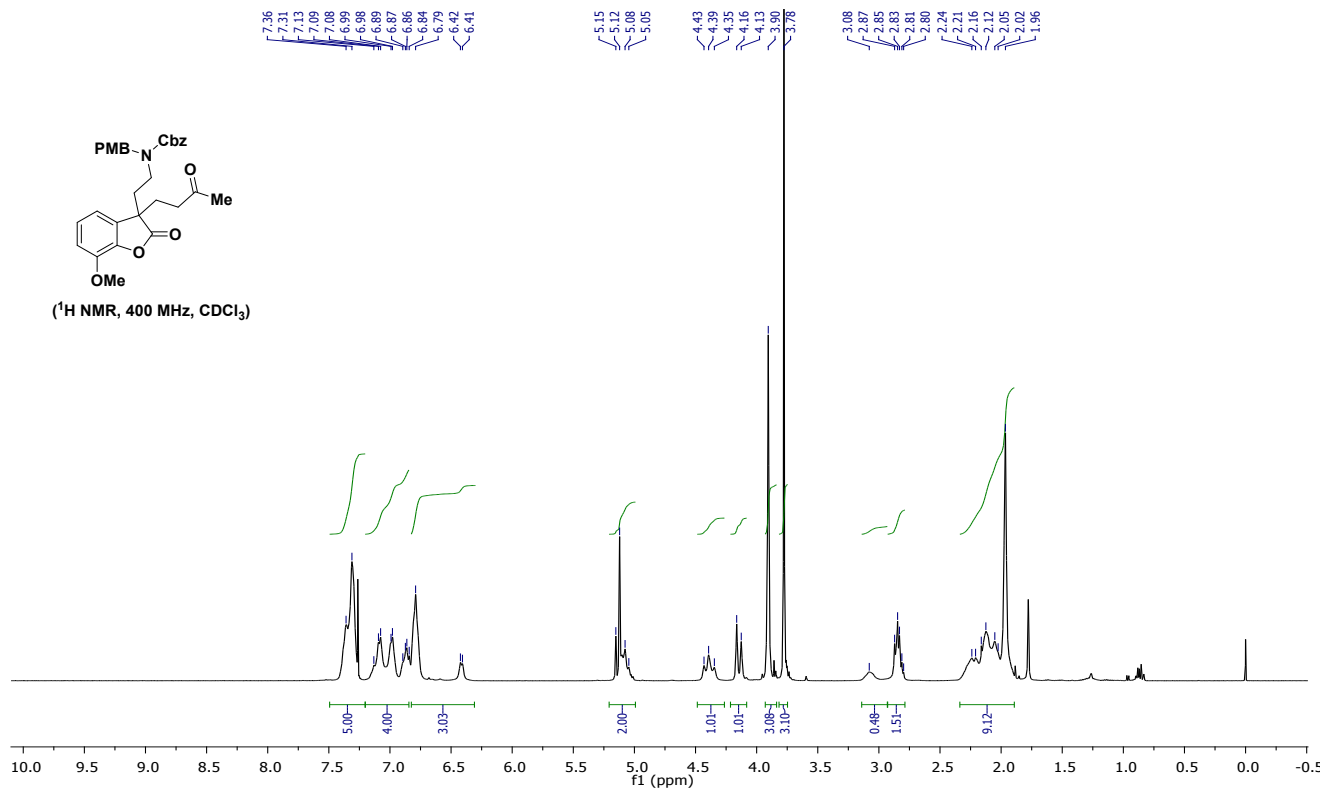
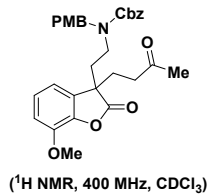
Methyl 4-(((benzyloxy)carbonyl)(4-methoxybenzyl)amino)-2-(2-(formyloxy)-3-methoxyphenyl)butanoate (8):



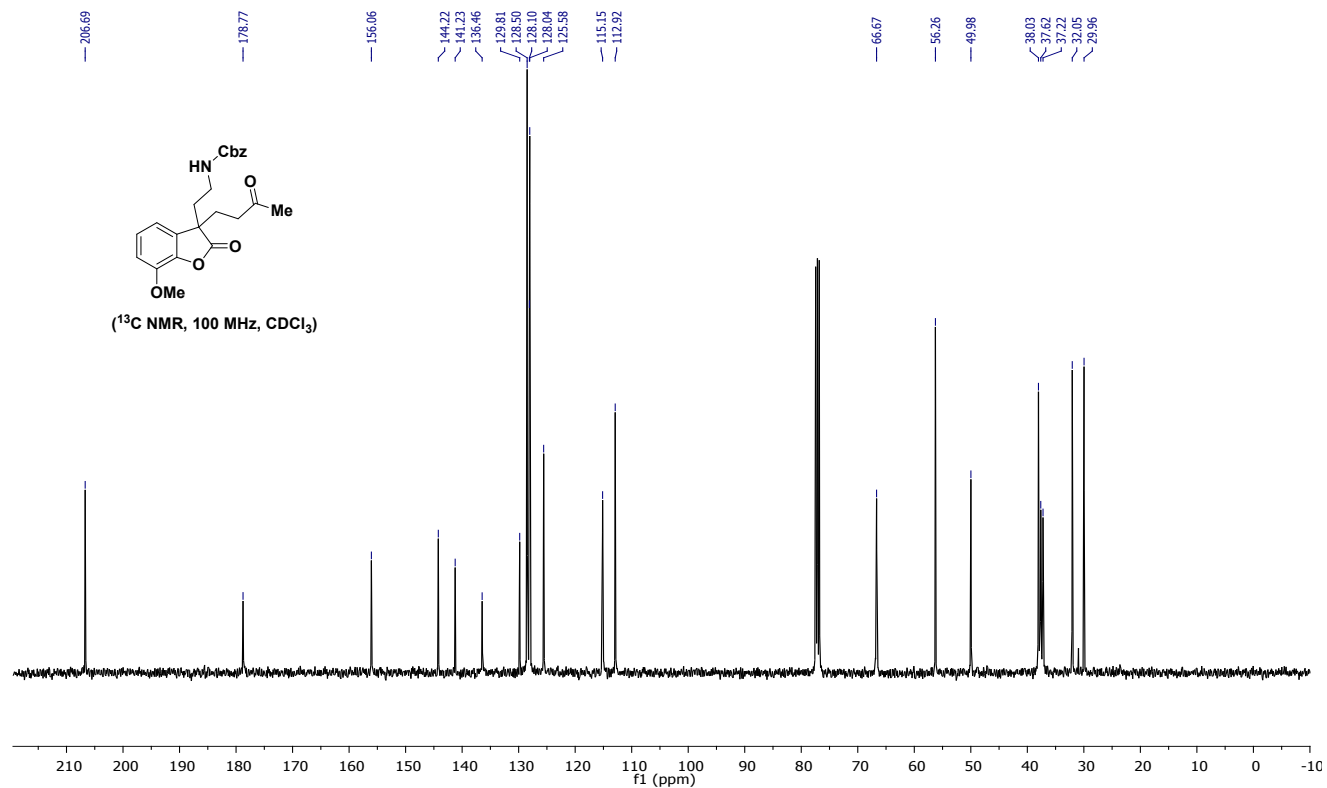
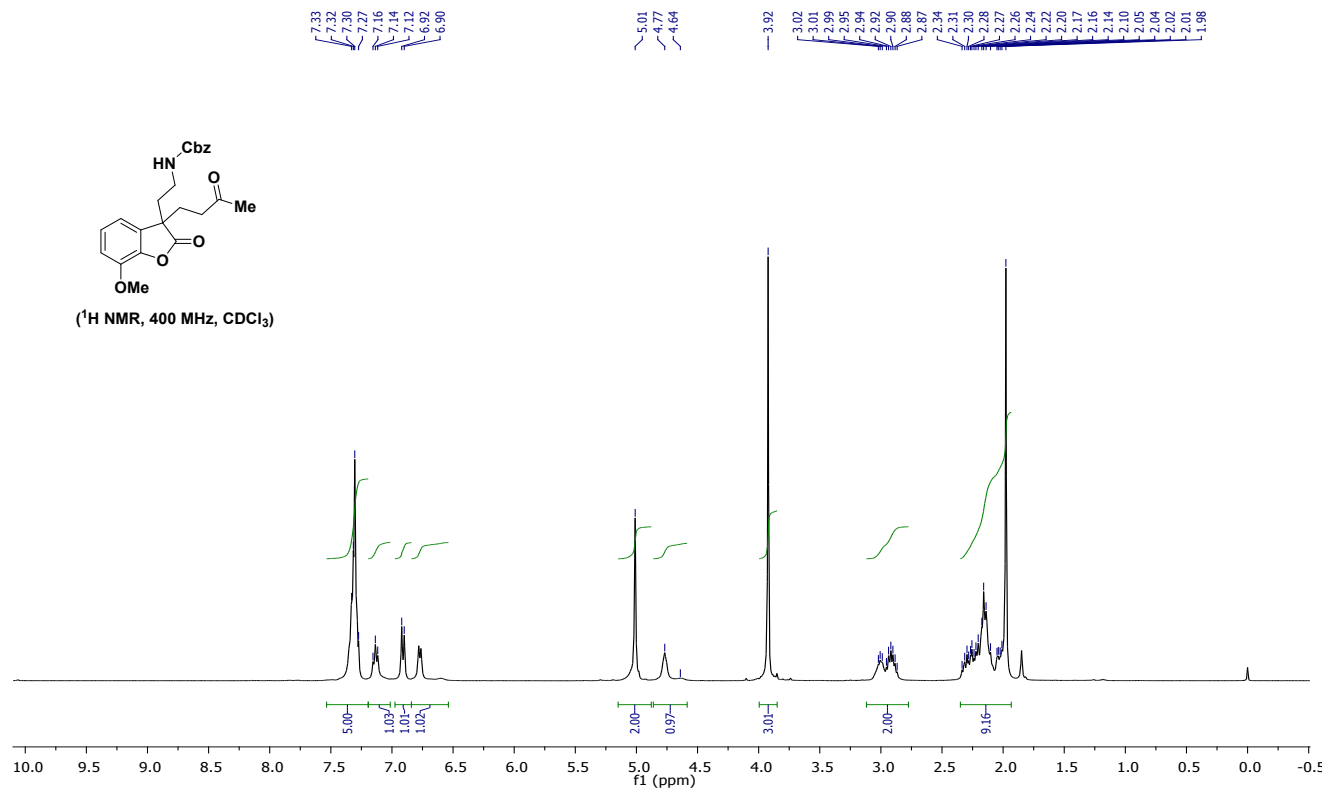
Benzyl (2-(7-methoxy-2-oxo-2,3-dihydrobenzofuran-3-yl)ethyl)(4-methoxybenzyl)carbamate (9):



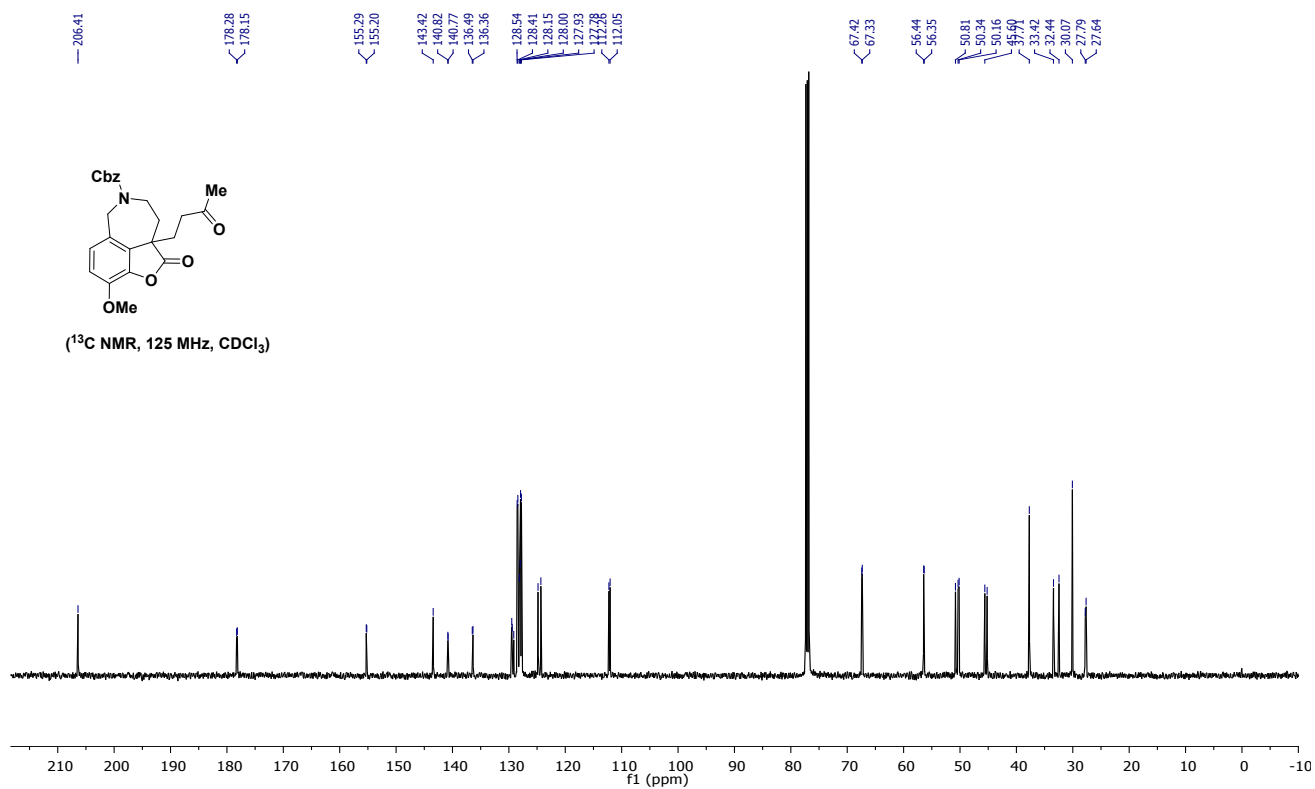
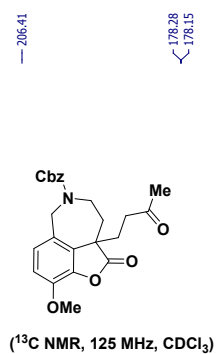
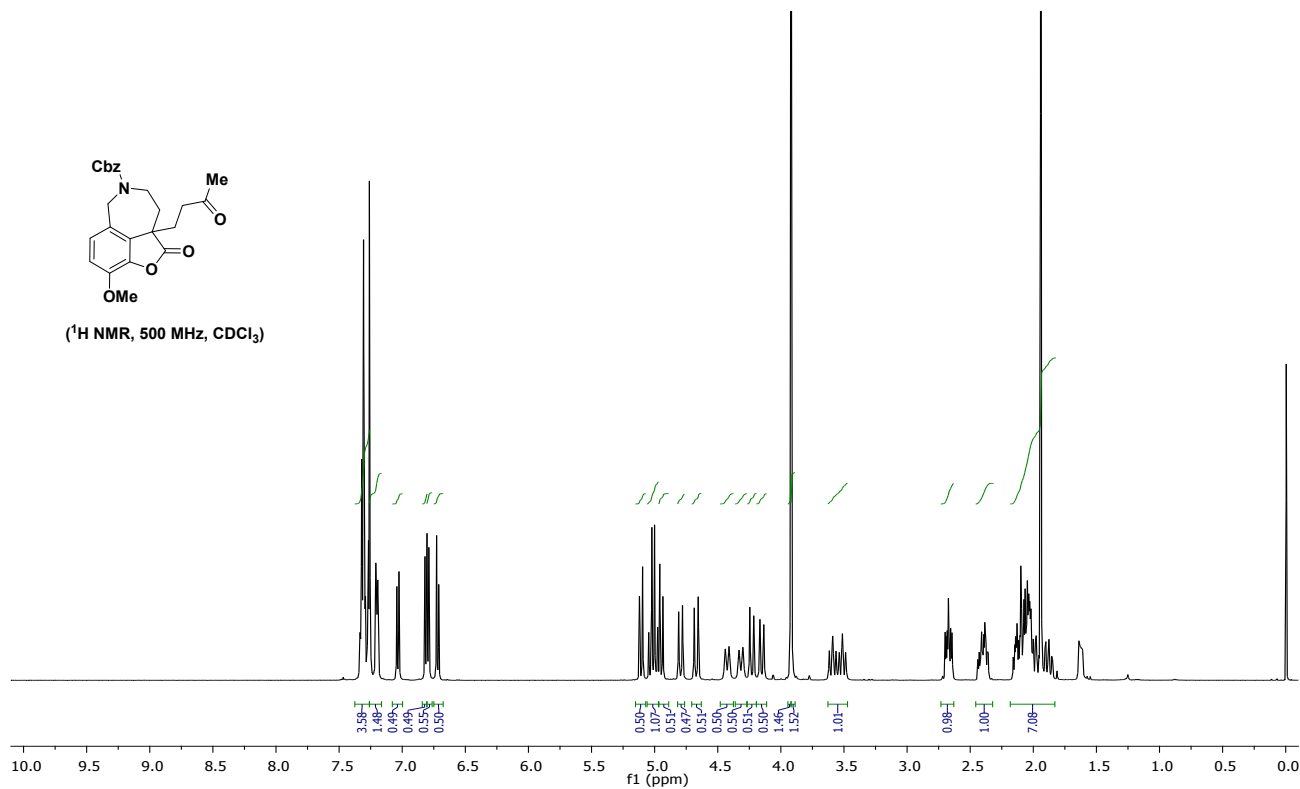
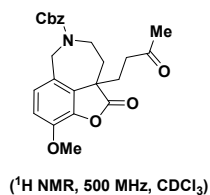
Benzyl (2-(7-methoxy-2-oxo-3-(3-oxobutyl)-2,3-dihydrobenzofuran-3-yl)ethyl)(4-methoxybenzyl)carbamate (2):



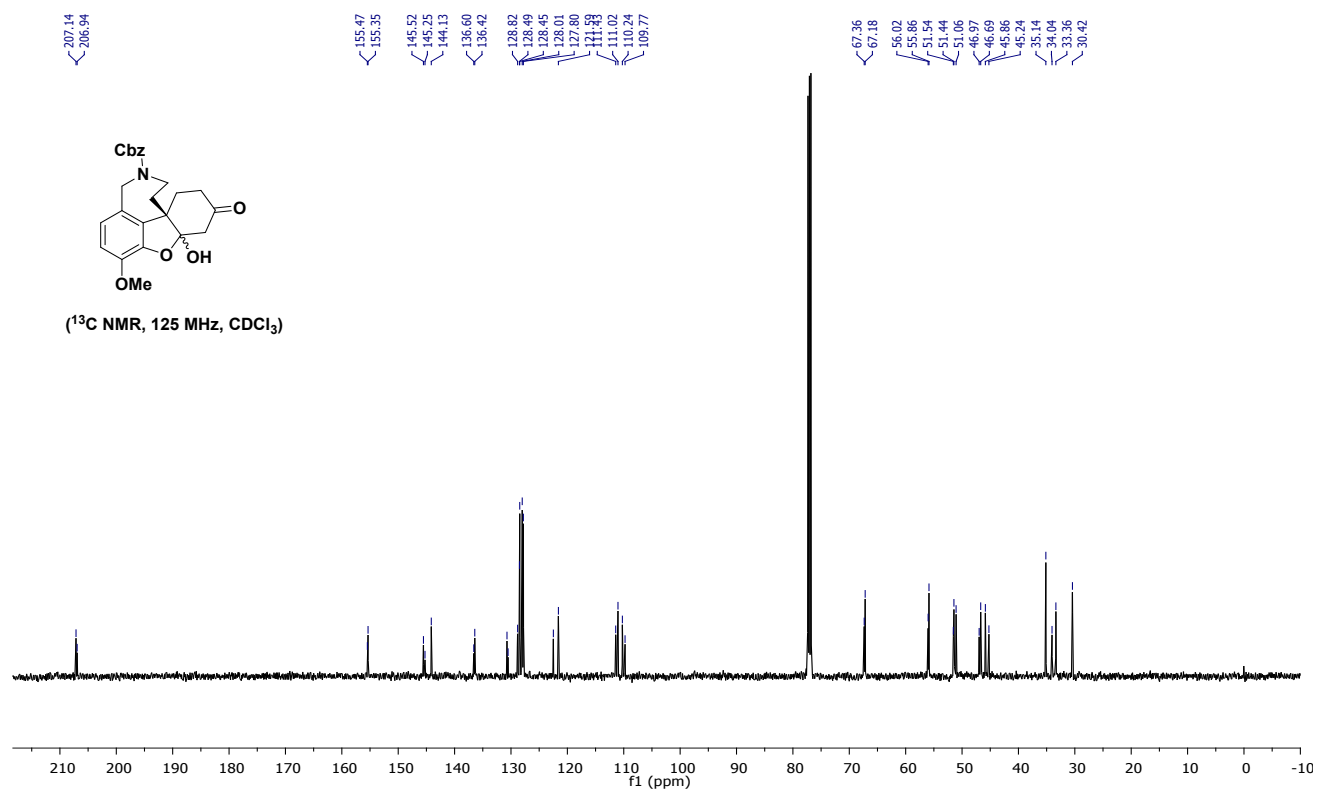
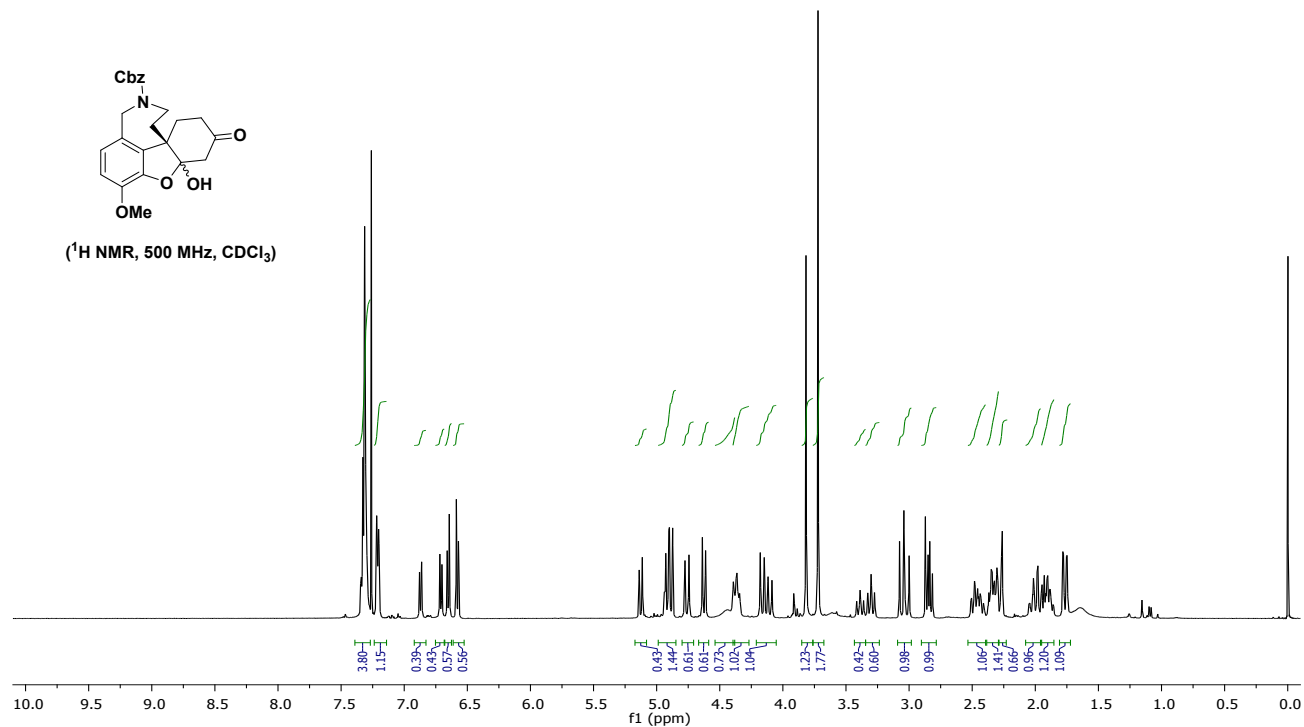
Benzyl (2-(7-methoxy-2-oxo-3-(3-oxobutyl)-2,3-dihydrobenzofuran-3-yl)ethyl)carbamate (10):



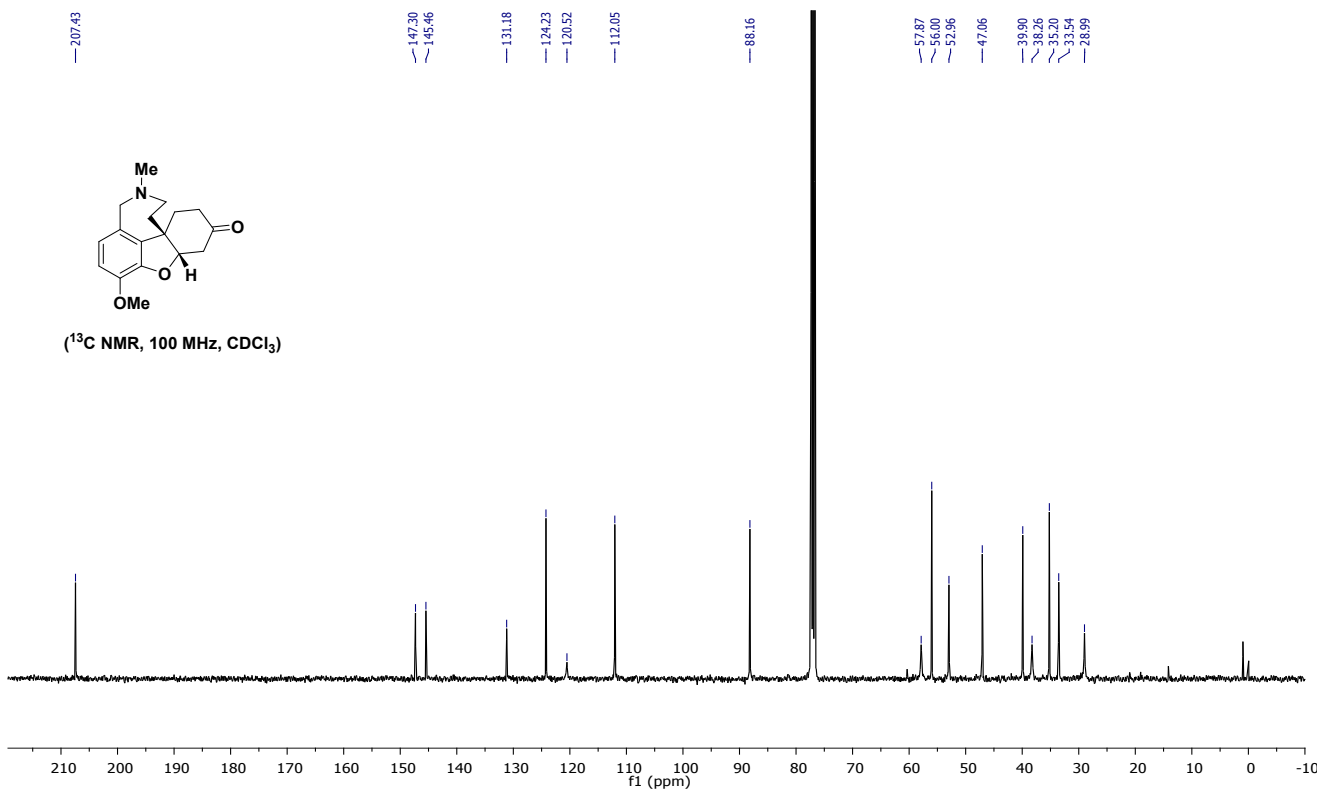
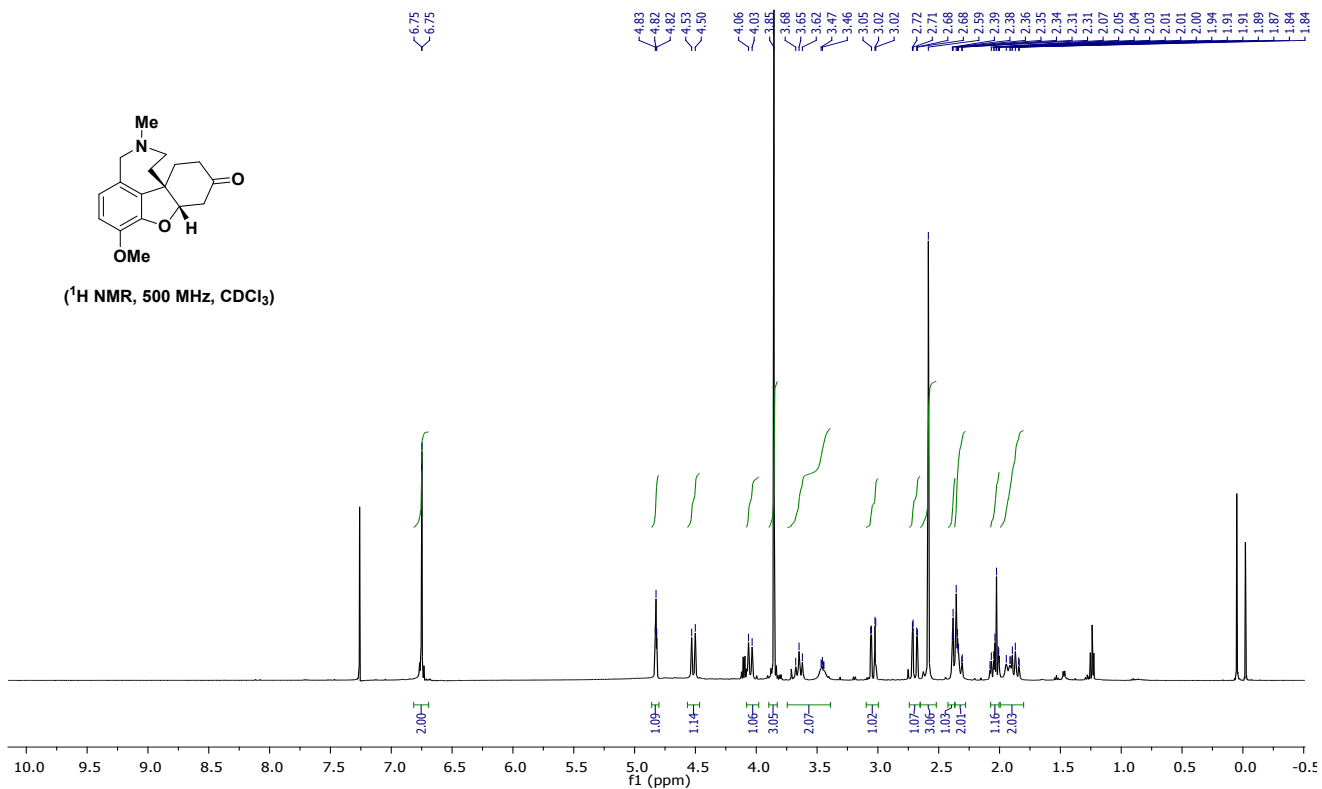
Benzyl 7-methoxy-5-oxo-4a-(3-oxobutyl)-3,4,4a,5-tetrahydrobenzofuro[4,3-cd]azepine-2(1-H)-carboxylate (11):



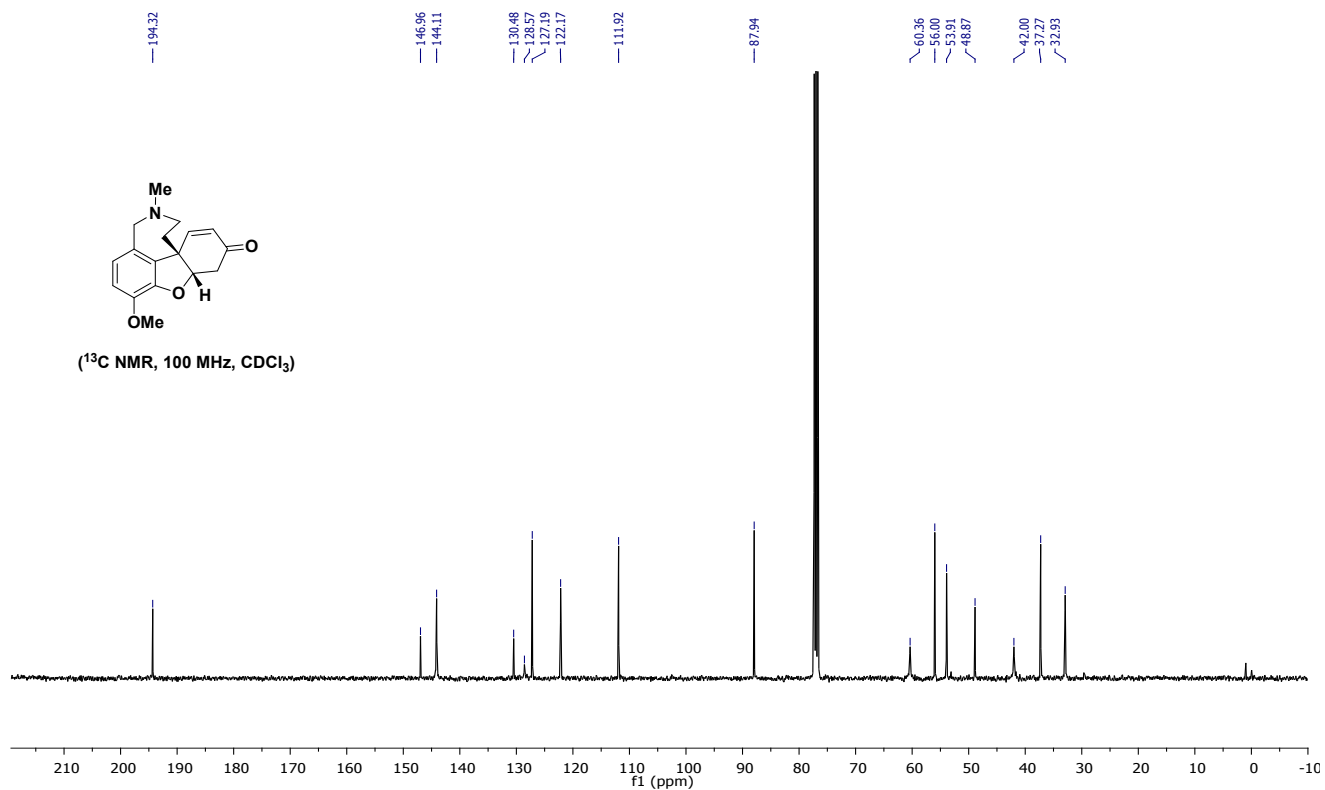
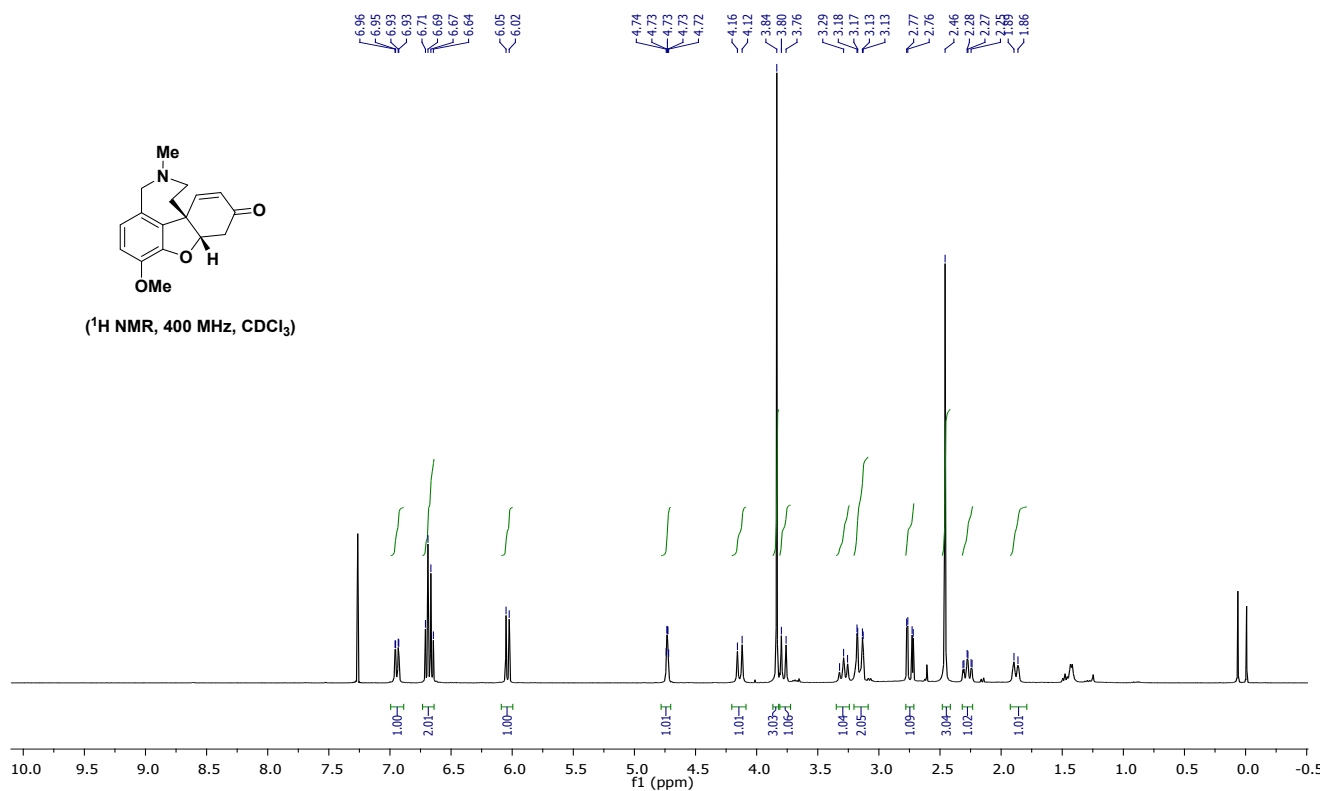
Benzyl 7-methoxy-5-oxo-4a-(3-oxobutyl)-3,4,4a,5-tetrahydrobenzofuro[4,3-*cd*]azepine-2(1*H*)-carboxylate (12):



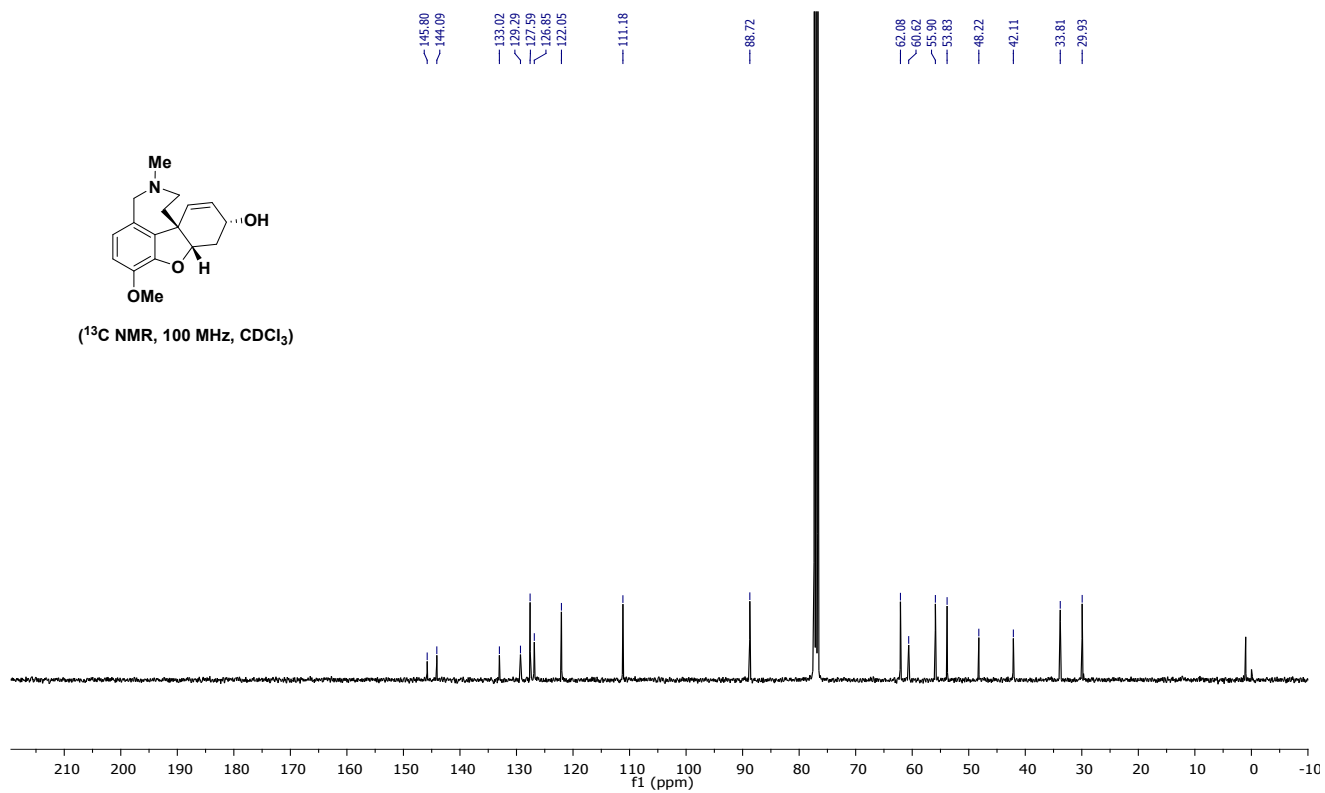
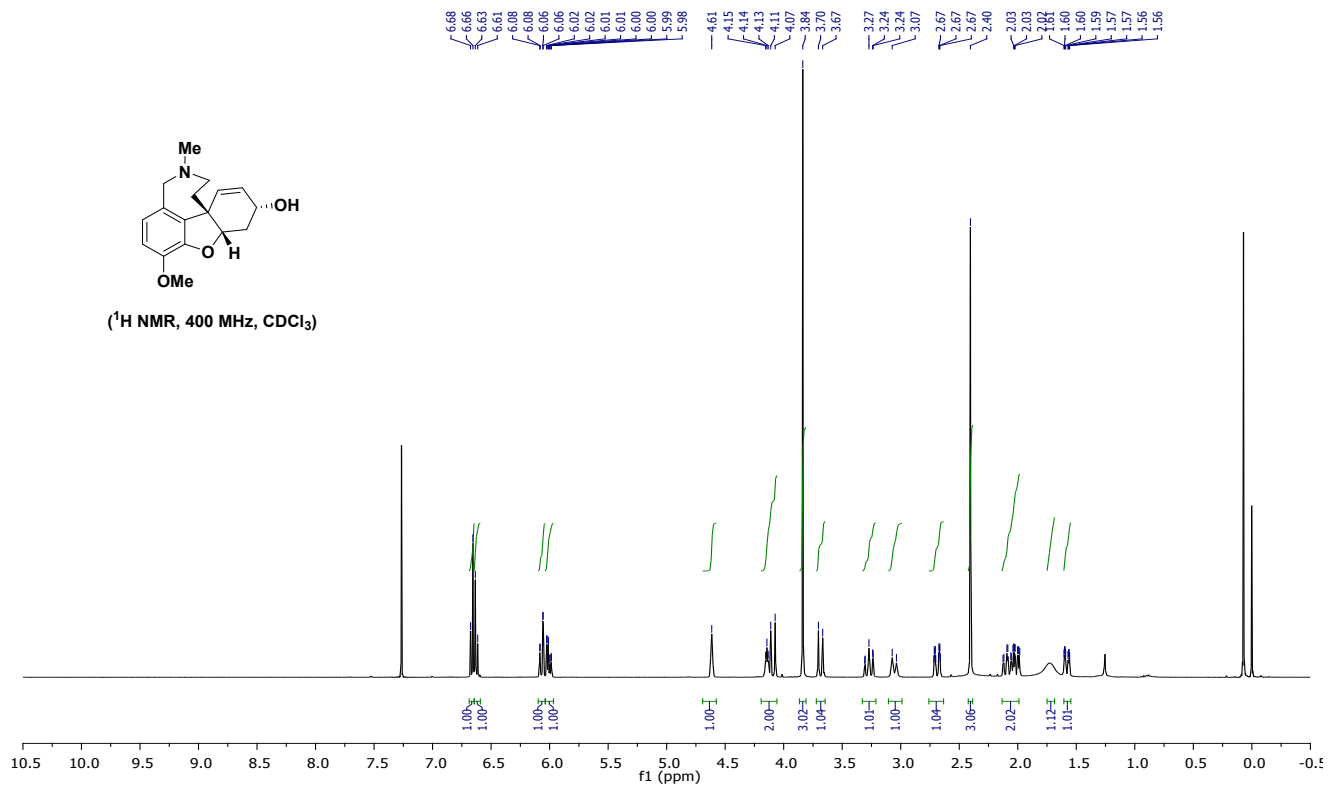
(4*aS*,8*aR*)-3-Methoxy-11-methyl-4*a*,5,7,8,9,10,11,12-octahydro-6*H*-benzo[2,3]benzofuro-[4,3-*cd*]azepin-6-one (14):



(4a*S*,8a*S*)-3-Methoxy-11-methyl-4a,5,9,10,11,12-hexahydro-6*H*-benzo[2,3]benzofuro[4,3-*cd*]azepin-6-one (or) Narwedine (15):



(±)-Galanthamine (1):



2. Comparison of ^1H and ^{13}C NMR spectral data of Galanthamine:

| Reported | | Synthetic | |
|---|-----------------|---|-----------------|
| ^1H | ^{13}C | ^1H | ^{13}C |
| 6.64 (d, $J = 8.3$ Hz, 1H) | 145.7 | 6.67 (d, $J = 8.2$ Hz, 1H) | 145.8 |
| 6.60 (d, $J = 8.3$ Hz, 1H) | 144.1 | 6.62 (d, $J = 8.2$ Hz, 1H) | 144.0 |
| 6.04 (d, $J = 10.2$ Hz, 1H) | 133.0 | 6.07 (dd, $J = 10.3, 1.1$ Hz, 1H) | 133.0 |
| 5.98 (ddd, $J = 10.2, 5.1, 1.0$ Hz, 1H) | 129.3 | 6.00 (ddd, $J = 10.2, 4.9, 1.0$ Hz, 1H) | 129.2 |
| 4.59 (s, 1H) | 127.6 | 4.61 (s, 1H) | 127.5 |
| 4.12 (br s, 1H), 4.07 (d, $J = 15.1$ Hz, 1H) | 126.8 | 4.19 – 4.06 (m, 2H) | 126.8 |
| 3.81 (s, 3H) | 122.0 | 3.84 (s, 3H) | 122.0 |
| 3.66 (d, $J = 15.1$ Hz, 1H) | 111.1 | 3.68 (d, $J = 14.6$ Hz, 1H) | 111.1 |
| 3.25 (t, $J = 13.0$ Hz, 1H) | 88.7 | 3.33 – 3.21 (m, 1H) | 88.7 |
| 3.03 (br d, $J = 13.9$ Hz, 1H) | 62.1 | 3.05 (d, $J = 14.4$ Hz, 1H) | 62.0 |
| 2.67 (ddt, $J = 15.9, 3.7, 1.2$ Hz, 1H) | 60.6, 55.9 | 2.69 (ddt, $J = 15.7, 3.1, 1.4$ Hz, 1H) | 60.6, 55.9 |
| 2.38 (s, 3H) | 53.8, 48.2 | 2.40 (s, 3H) | 53.8, 48.2 |
| 2.06 (td, $J = 13.2, 2.0$ Hz, 1H), 1.98 (ddd, $J = 15.9, 5.1, 2.4$ Hz, 1H), 1.67 (br s, 1H) | 42.1, 33.8 | 2.13 – 1.99 (m, 2H), 1.71 (br s, 1H) | 42.1, 33.8 |
| 1.55 (ddd, $J = 13.6, 3.6, 1.1$ Hz, 1H) | 29.9 | 1.58 (ddd, $J = 13.7, 3.9, 1.7$ Hz, 1H) | 29.9 |

Reference: B. M. Trost and F. D. Toste, *J. Am. Chem. Soc.* 2000, **122**, 11262-11263.