

SUPPLEMENTARY MATERIAL

Improving the Yield of the Exhaustive Grignard Alkylation of *N*-Benzylphthalimide

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Synthetic Details Large Scale Reaction. (2-Benzyl-1,1,3,3-tetraethylisoindoline 8).....	S20

Figure S1. 2-Benzyl-3-ethyl-3-hydroxyisoindolin-1-one **5**, ^1H NMR spectrum (400 MHz, CDCl_3)

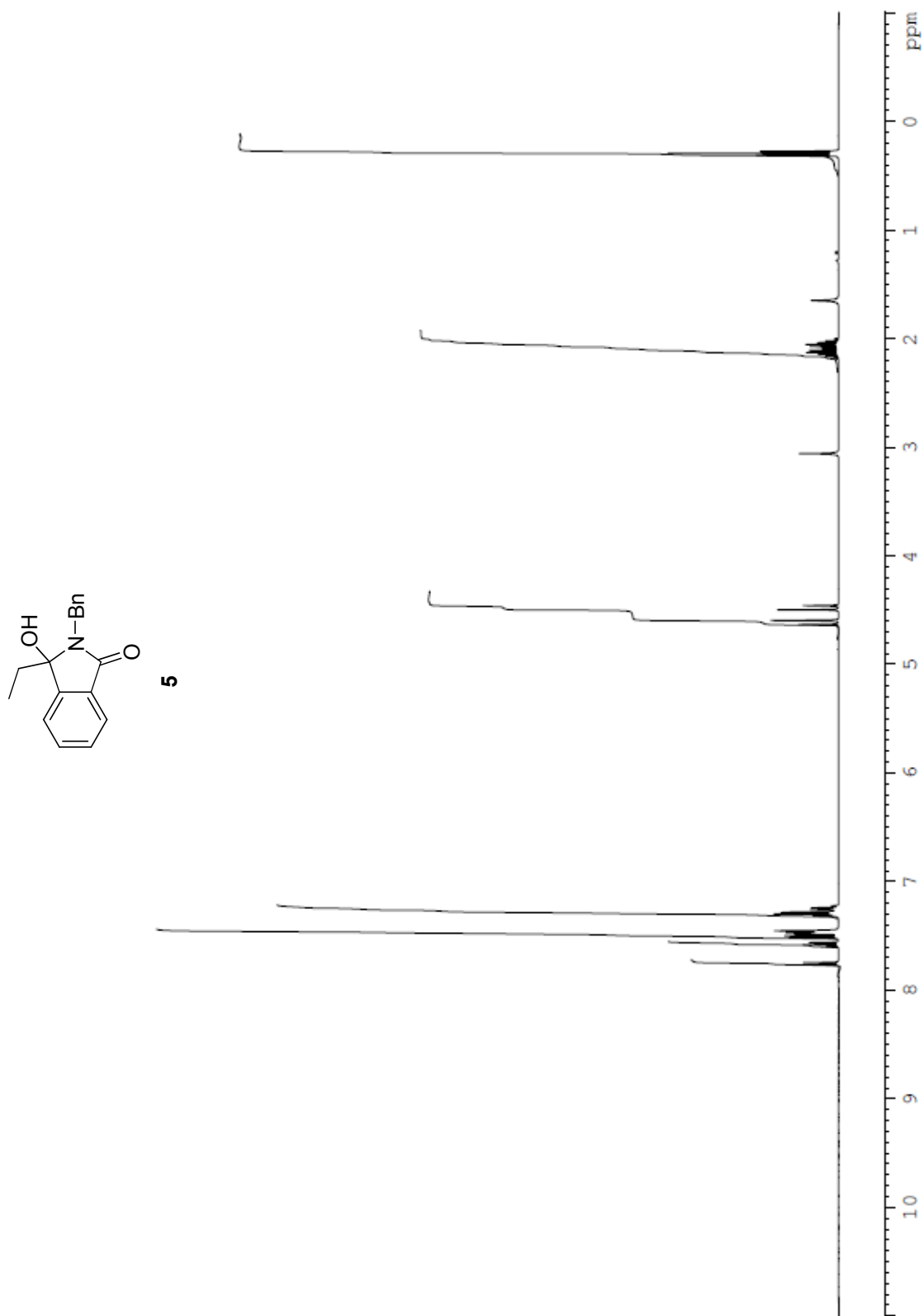


Figure S2. (*E*)-2-Benzyl-3-ethylideneisoindolin-1-one **6**, ^1H NMR spectrum (400 MHz, CDCl_3)

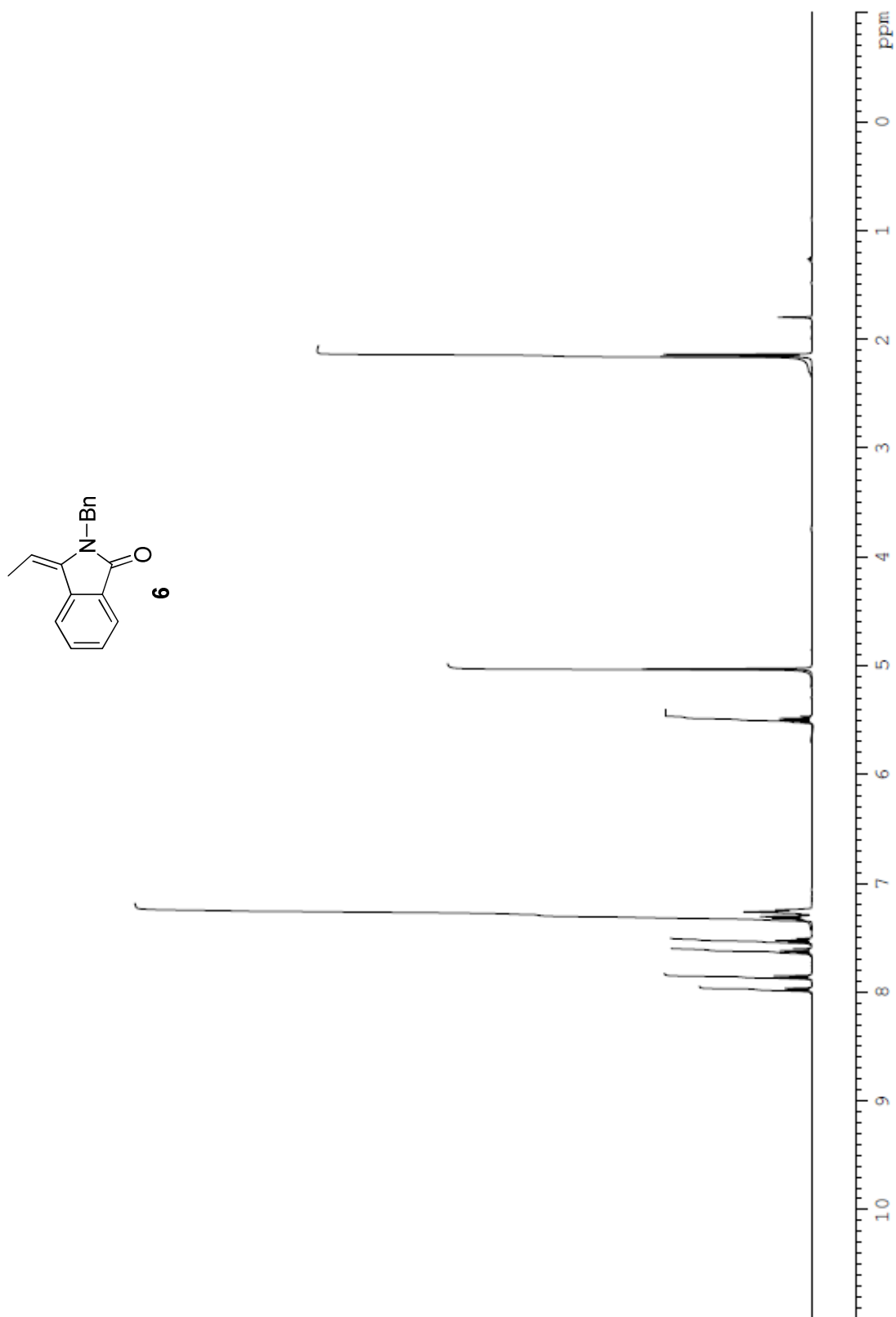


Figure S3. 2-Benzyl-3-ethyl-3-methoxyisoindolin-1-one **7**, ^1H NMR spectrum (400 MHz, CDCl_3)

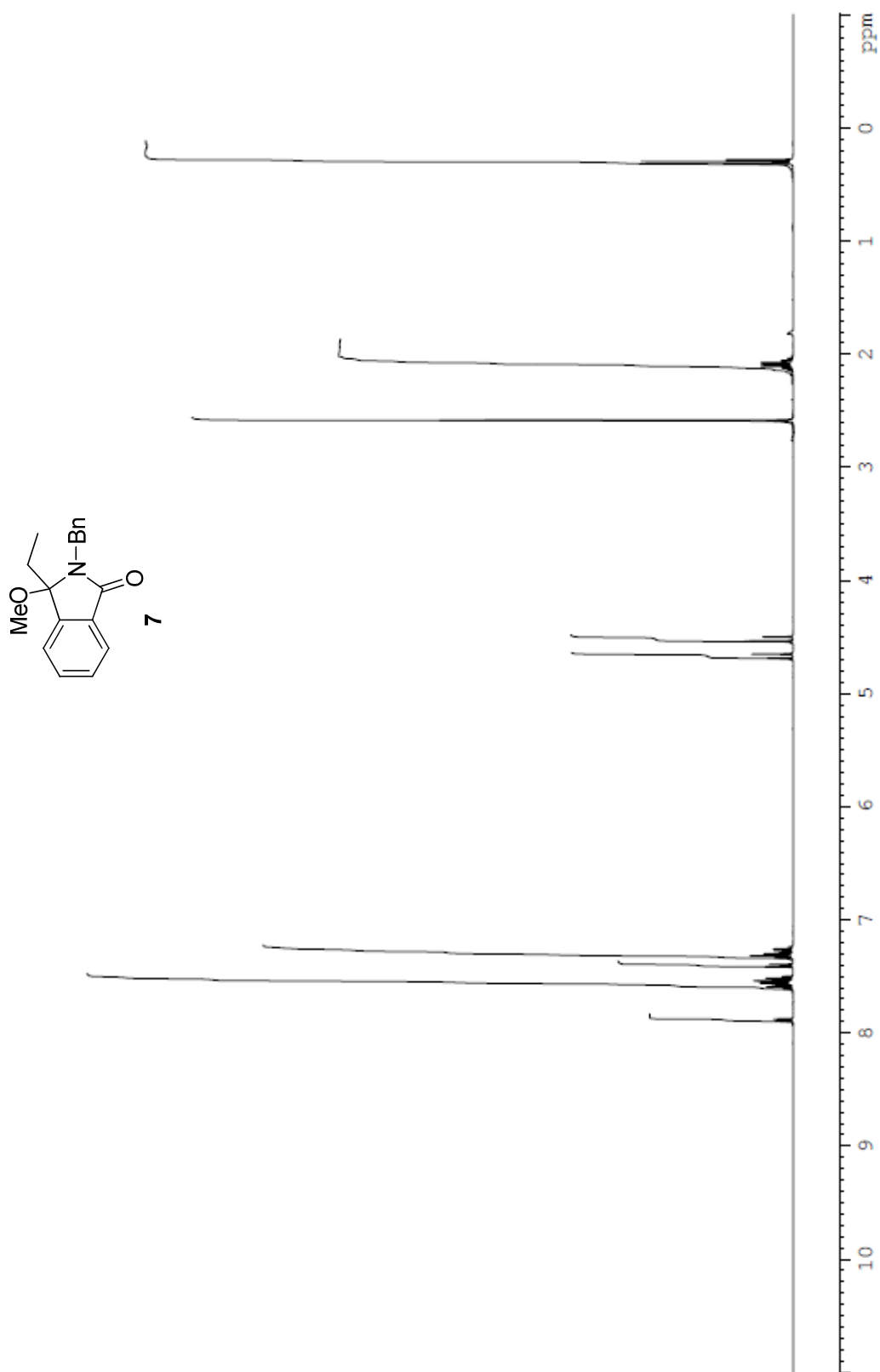


Figure S4. 2-Benzyl-1,1,3,3-tetraethylisoindoline **8**, ^1H NMR spectrum (400 MHz, CDCl_3)

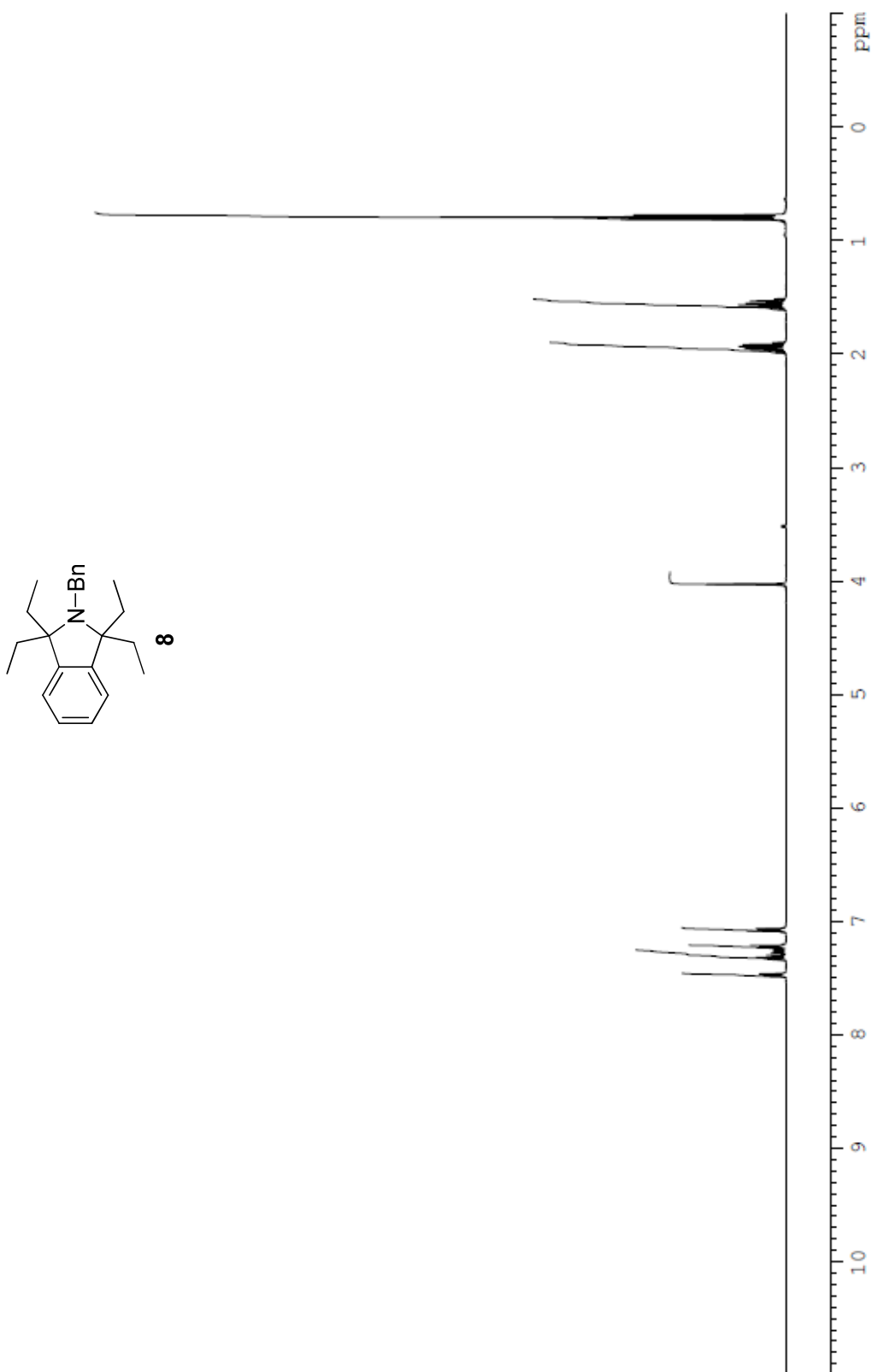


Figure S5. 2-Benzyl-3,3-diethylisoindolin-1-one **9**, ^1H NMR spectrum (400 MHz, CDCl_3)

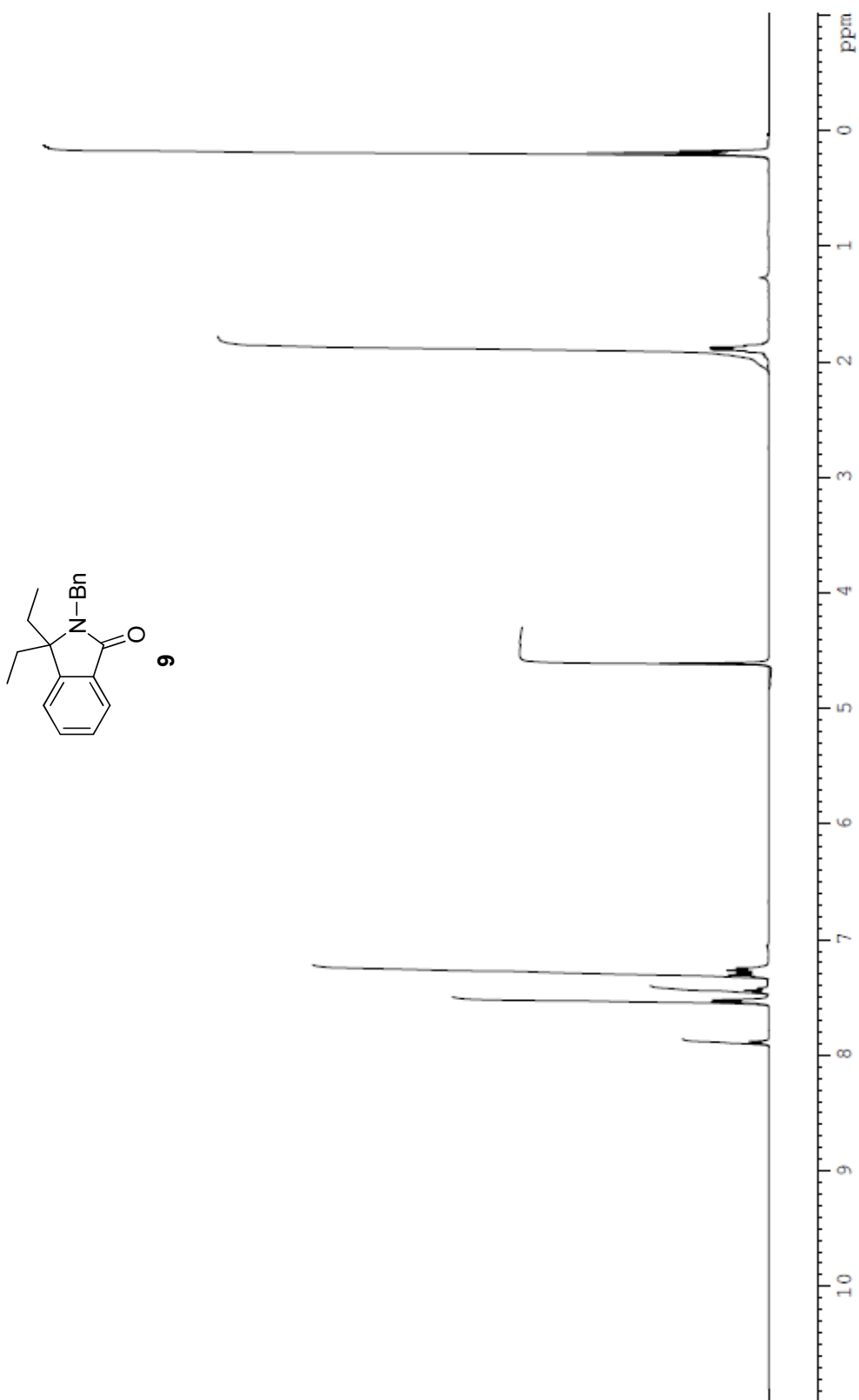


Figure S6. 2-Benzyl-3-ethylisoindolin-1-one **10**, ^1H NMR spectrum (400 MHz, CDCl_3)

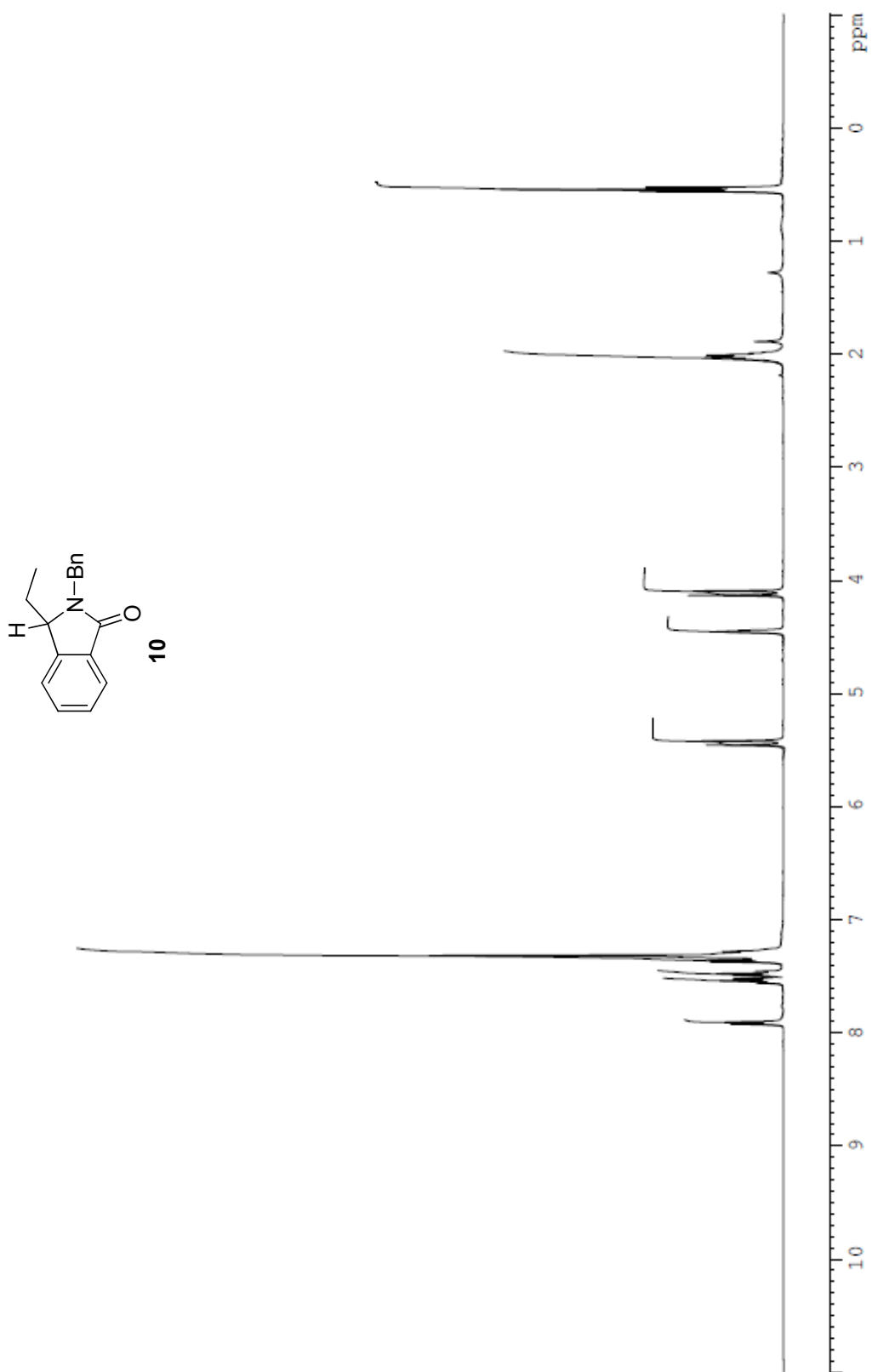


Figure S7. 2-Benzyl-3-ethyl-3-hydroxyisoindolin-1-one **5**, ^{13}C NMR spectrum (100 MHz, CDCl_3)

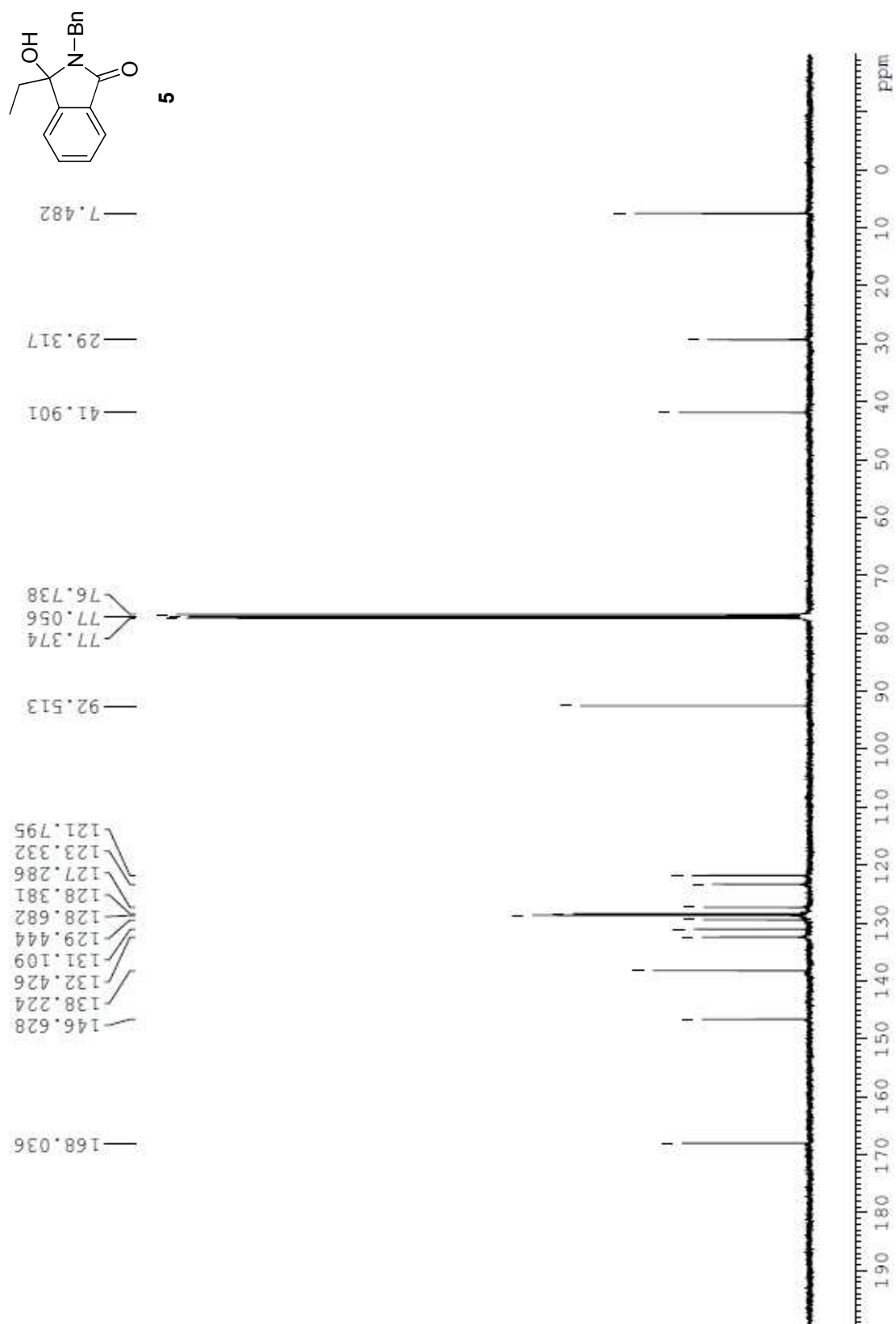


Figure S8. (*E*)-2-Benzyl-3-ethylideneisoindolin-1-one **6**, ^{13}C NMR spectrum (100 MHz, CDCl_3)

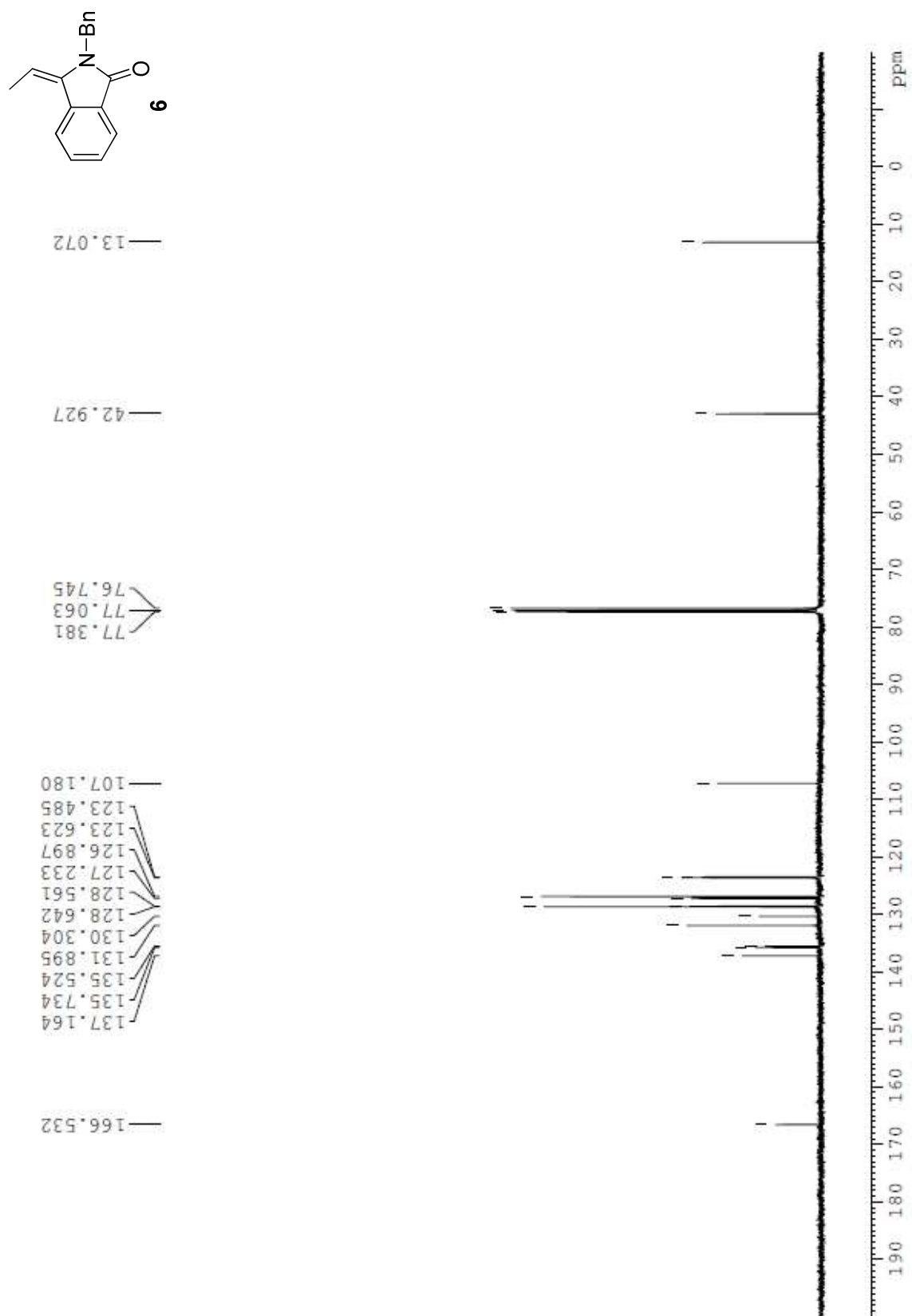


Figure S9. 2-Benzyl-3-ethyl-3-methoxyisoindolin-1-one **7**, ^{13}C NMR spectrum (100 MHz, CDCl_3)

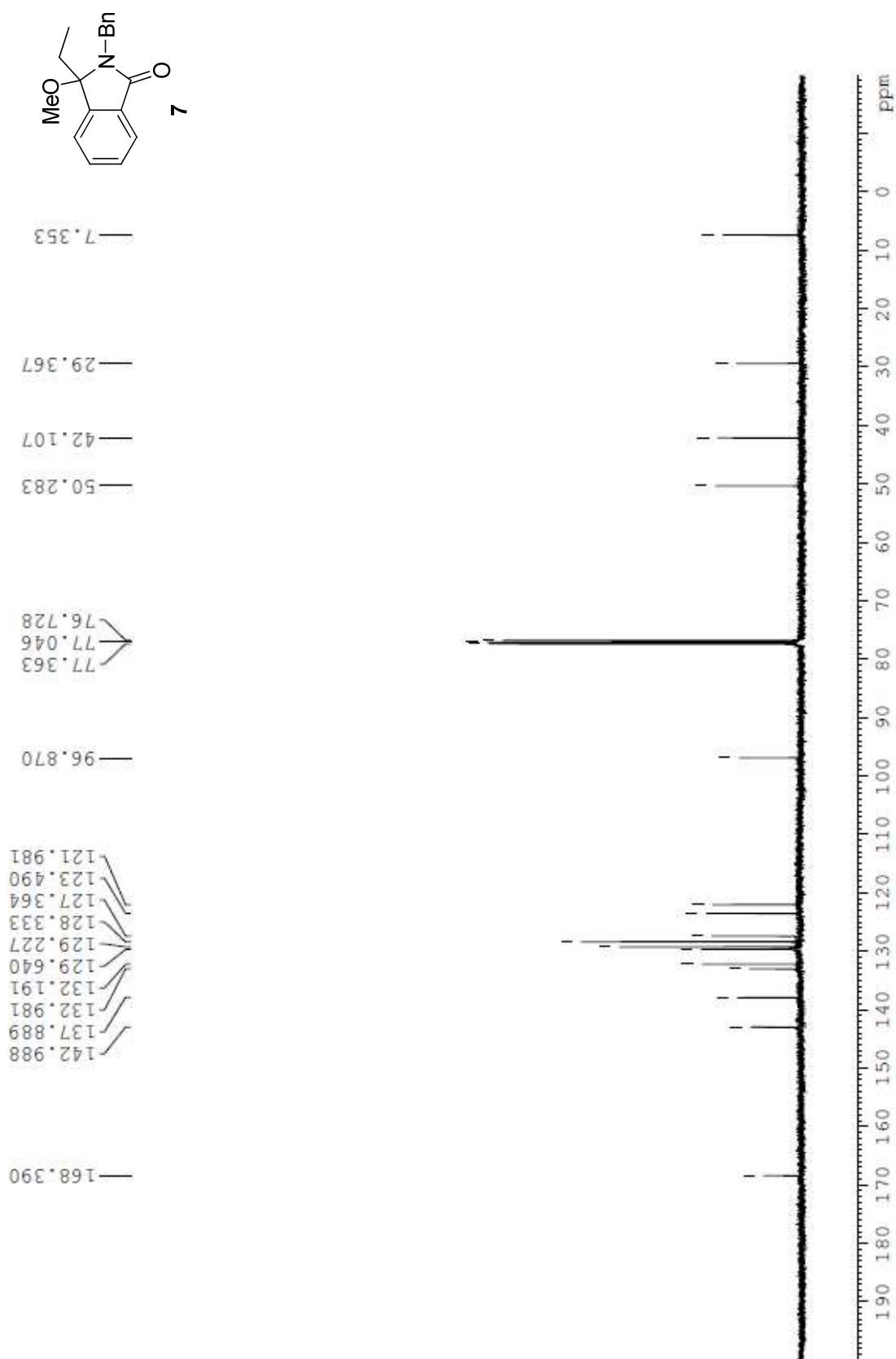


Figure S10. 2-Benzyl-1,1,3,3-tetraethylisoindoline **8**, ^{13}C NMR spectrum (100 MHz, CDCl_3)

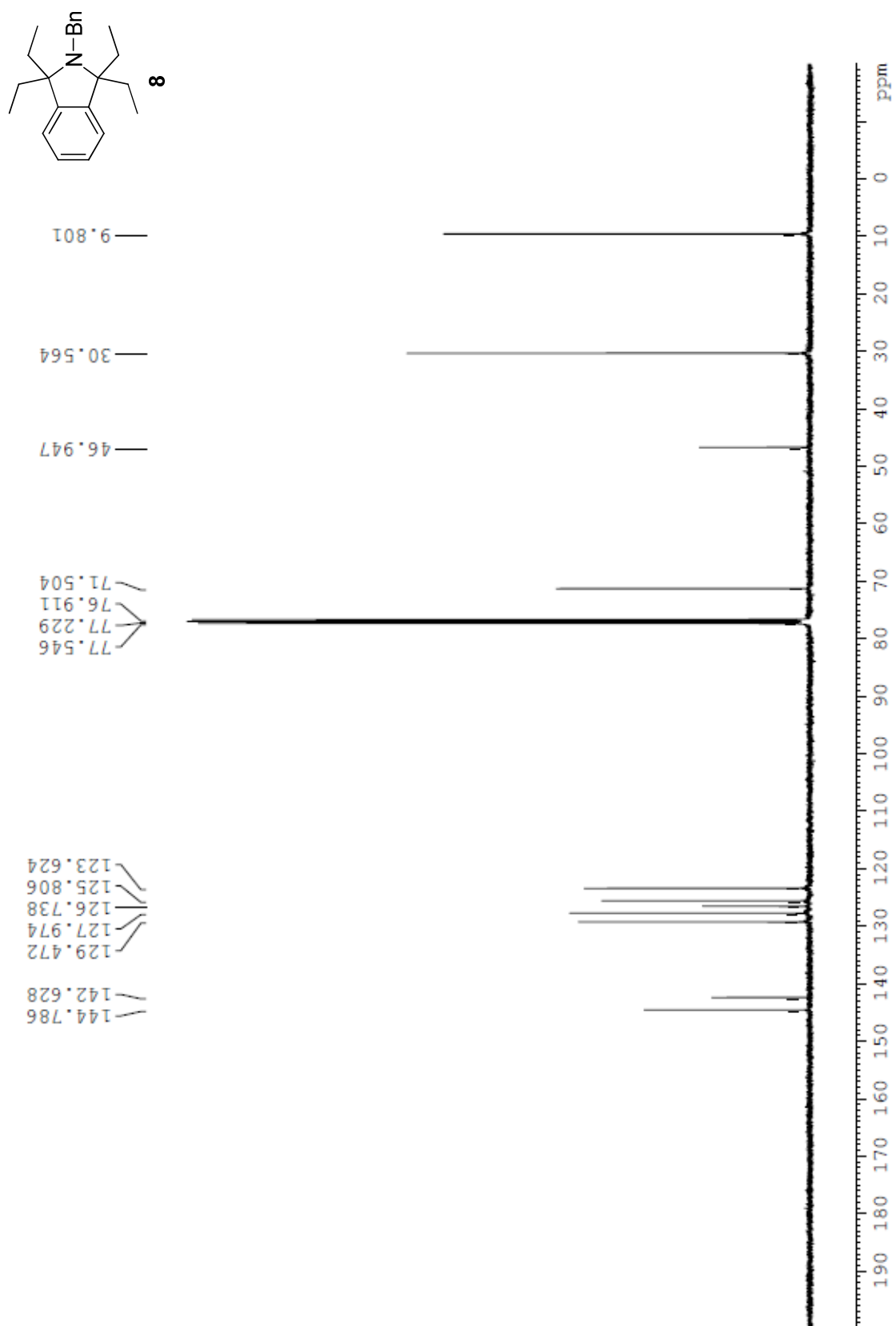


Figure S11. 2-Benzyl-3,3-diethylisoindolin-1-one **9**, ^{13}C NMR spectrum (100 MHz, CDCl_3)

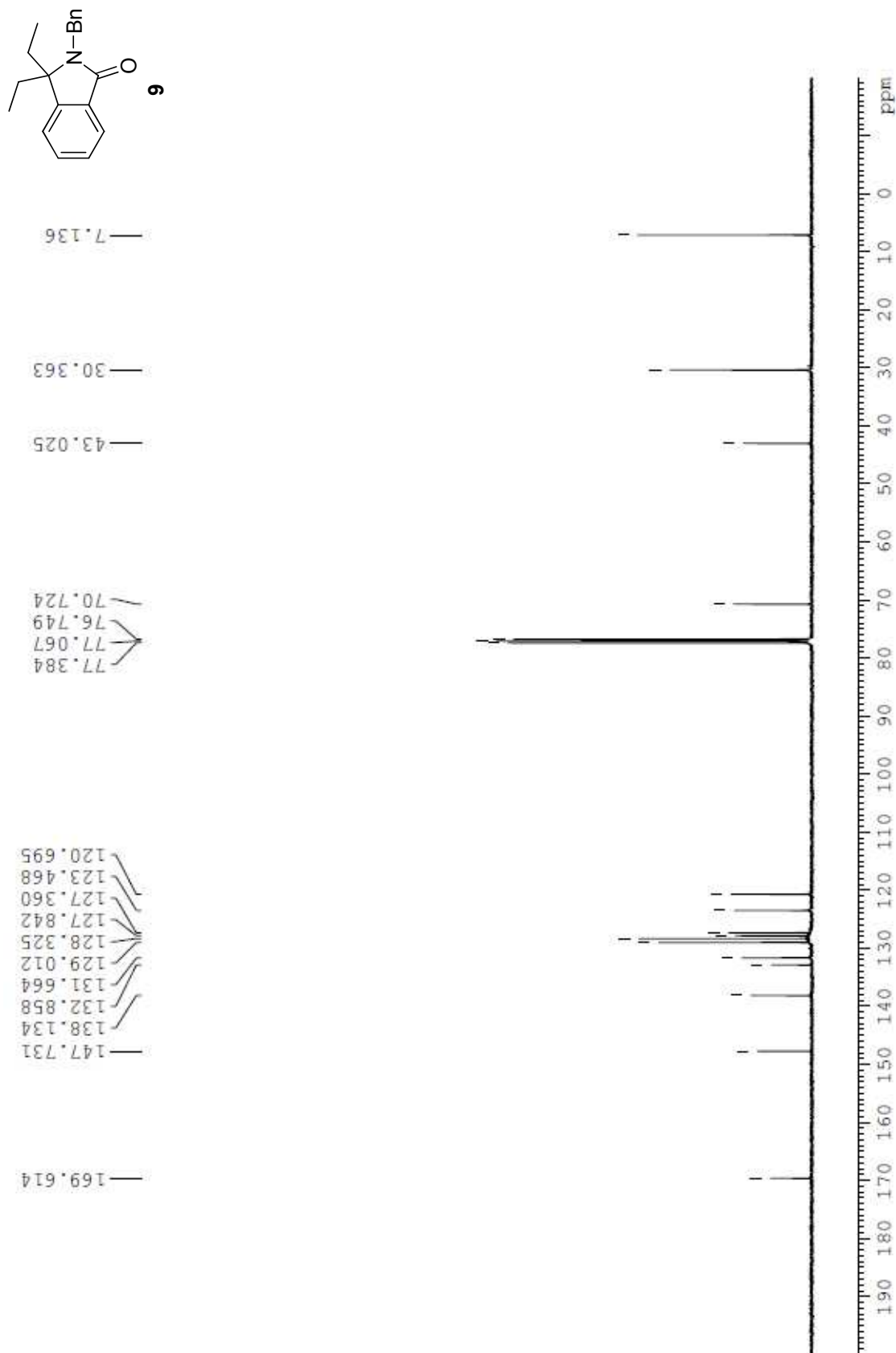


Figure S12. 2-Benzyl-3-ethylisoindolin-1-one **10**, ^{13}C NMR spectrum (100 MHz, CDCl_3)

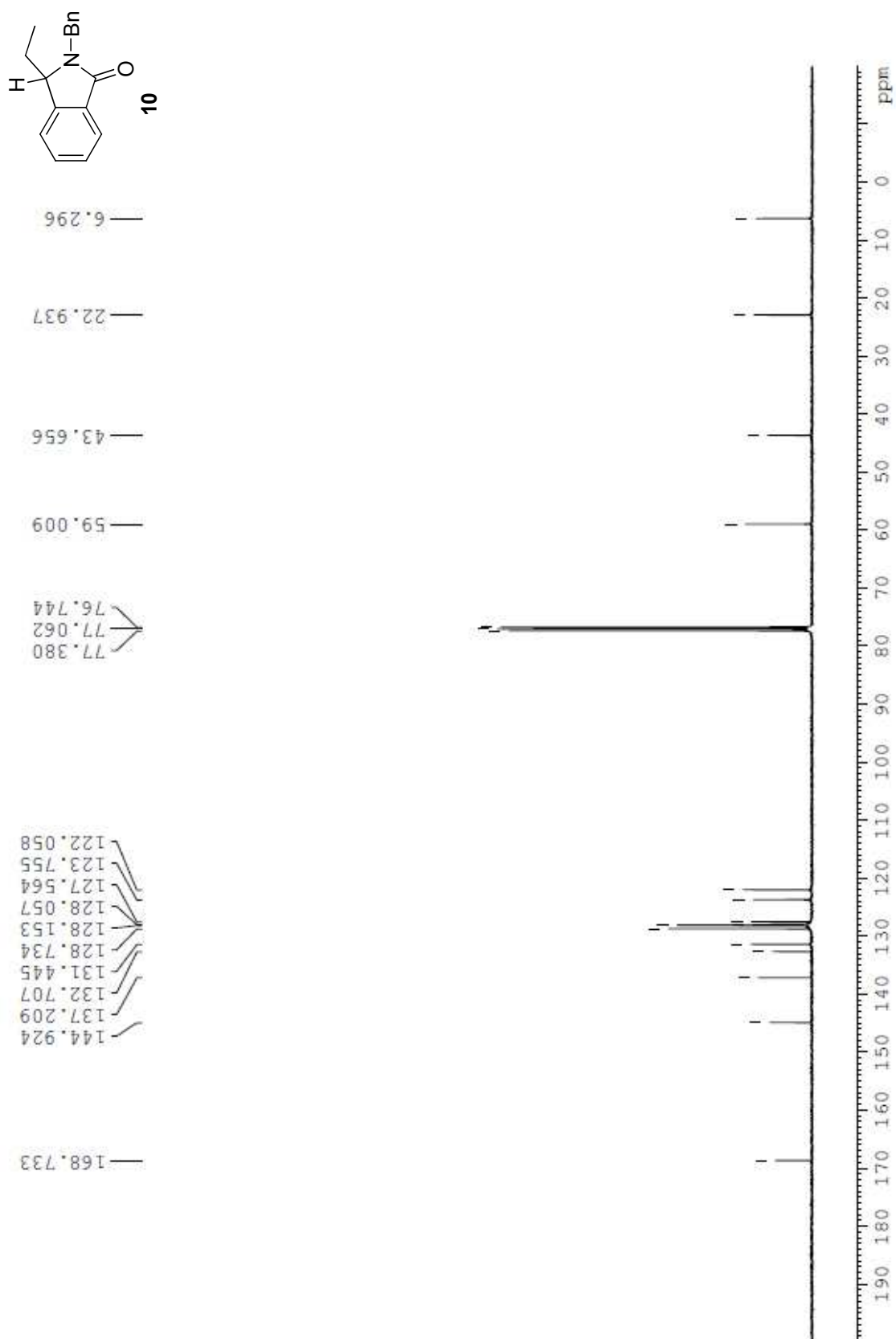


Figure S13. 2-Benzyl-3-ethyl-3-hydroxyisoindolin-1-one **5**, HPLC chromatogram (eluent 65% methanol/35% water).

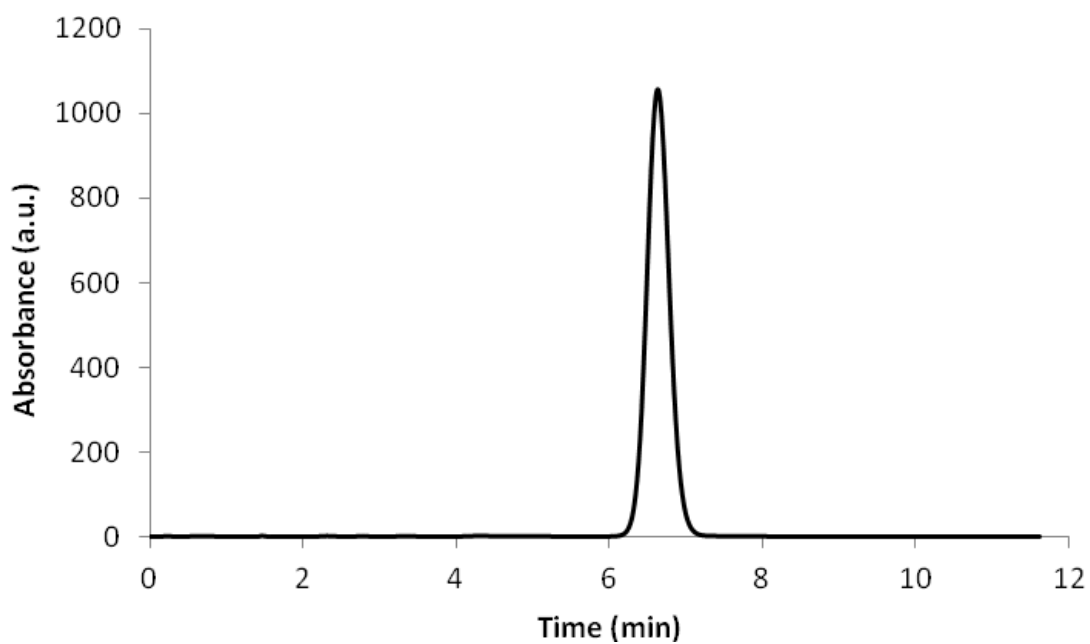


Figure S14. (*E*)-2-Benzyl-3-ethylideneisoindolin-1-one **6**, HPLC chromatogram (eluent 65% methanol/35% water).

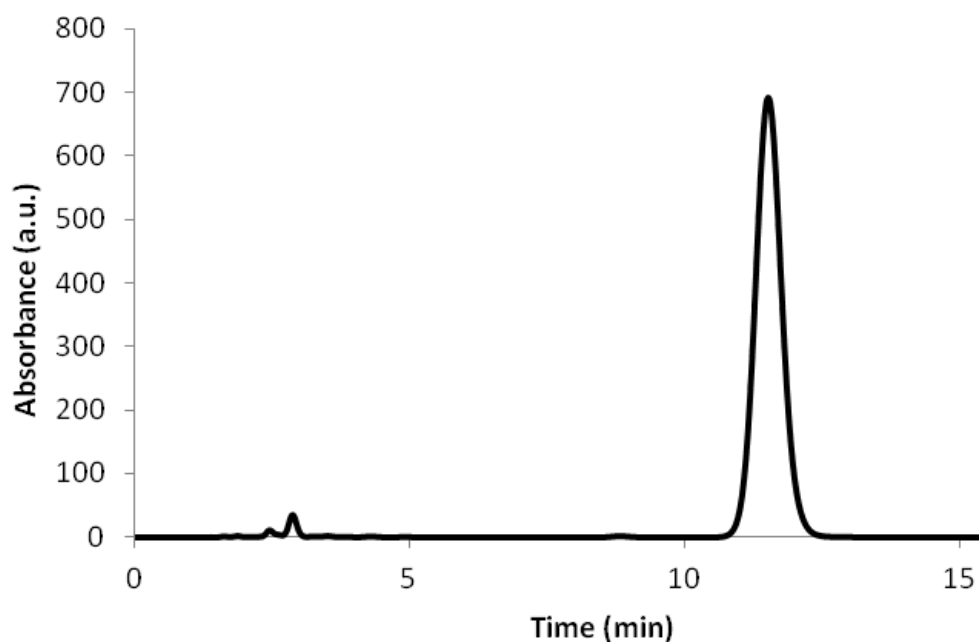


Figure S15. 2-Benzyl-3-ethyl-3-methoxyisoindolin-1-one **7**, HPLC chromatogram (eluent 65% methanol/35% water).

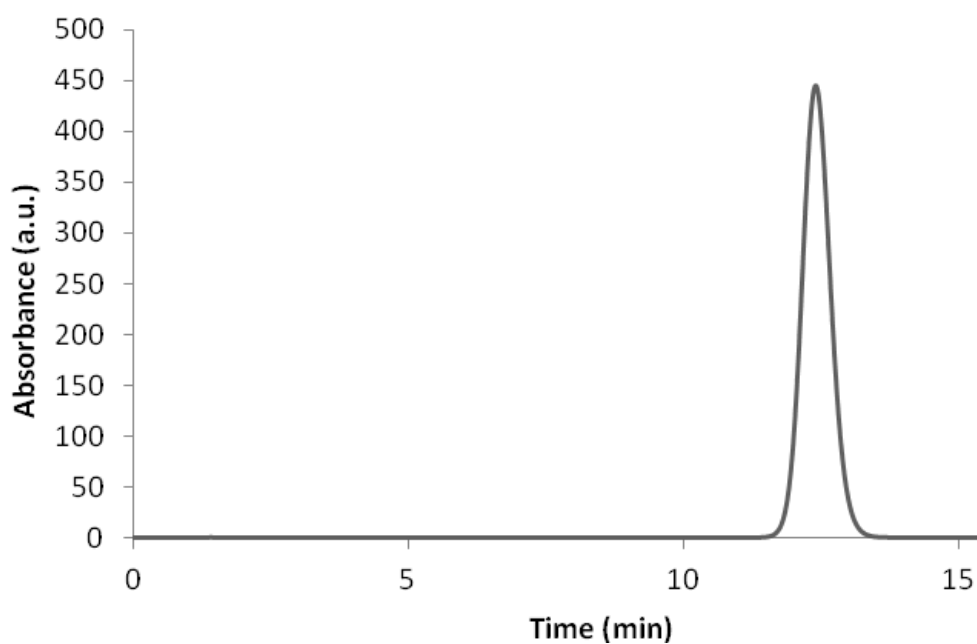


Figure S16. 2-Benzyl-1,1,3,3-tetraethylisoindoline **8**, HPLC chromatogram (eluent 65% methanol/35% water for 17 minutes, then ramped to 90% methanol/10% water over 10 minutes, then held at 90% methanol/10% water for 30 minutes)

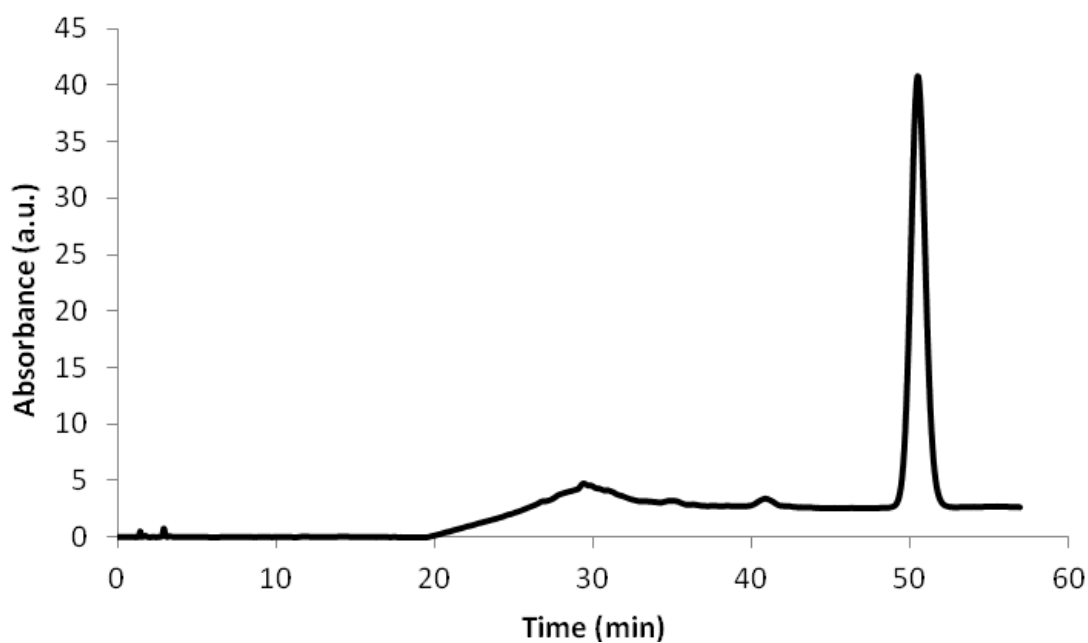


Figure S17. 2-Benzyl-3,3-diethylisoindolin-1-one **9**, HPLC chromatogram (eluent 65% methanol/35% water)

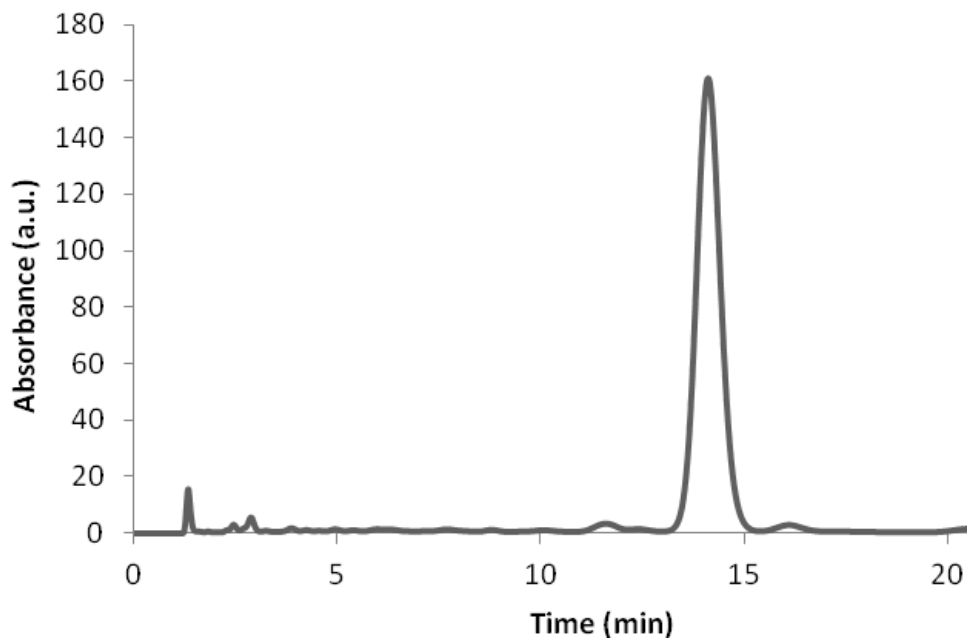


Figure S18. 2-Benzyl-3-ethylisoindolin-1-one **10**, HPLC chromatogram (eluent 65% methanol/35% water)

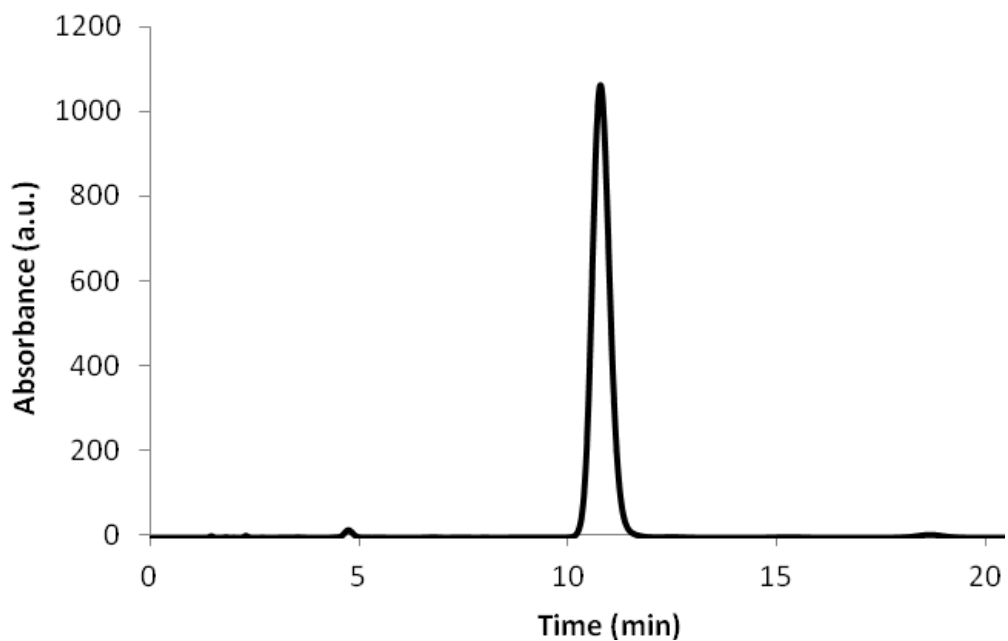


Figure S19. HPLC chromatogram for crude product from reaction of 2-benzyl-3-ethyl-3-methoxyisoindolin-1-one **7** with EtMgI (110°C, 72 hrs, Entry 7, Table 1) (eluent 65% methanol/35% water for 17 minutes, then ramped to 90% methanol/10% water over 10 minutes, then held at 90% methanol/10% water for 30 minutes).

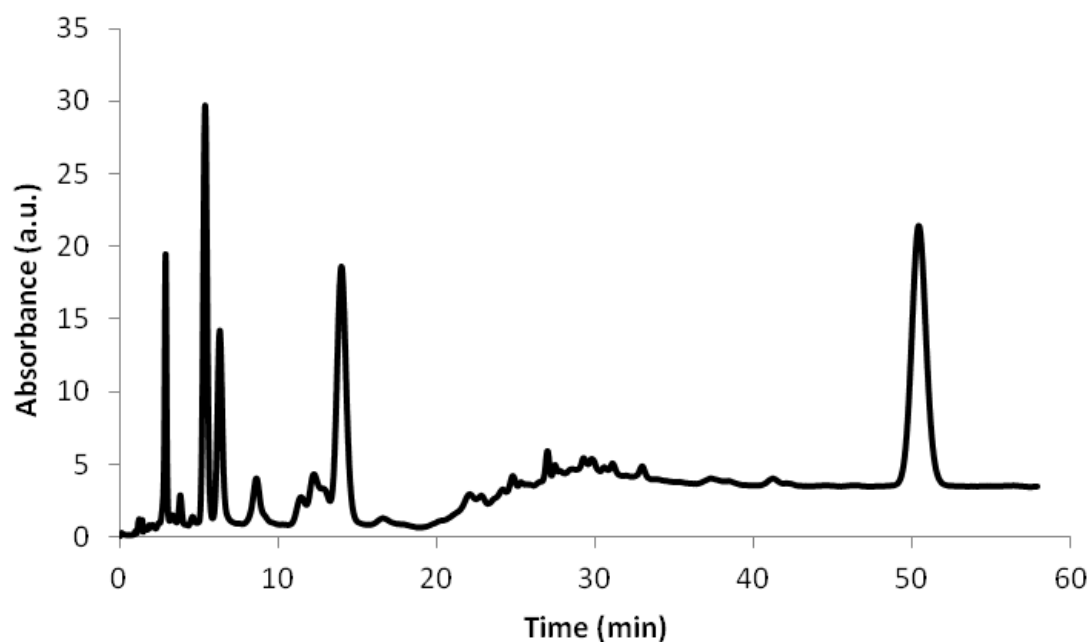
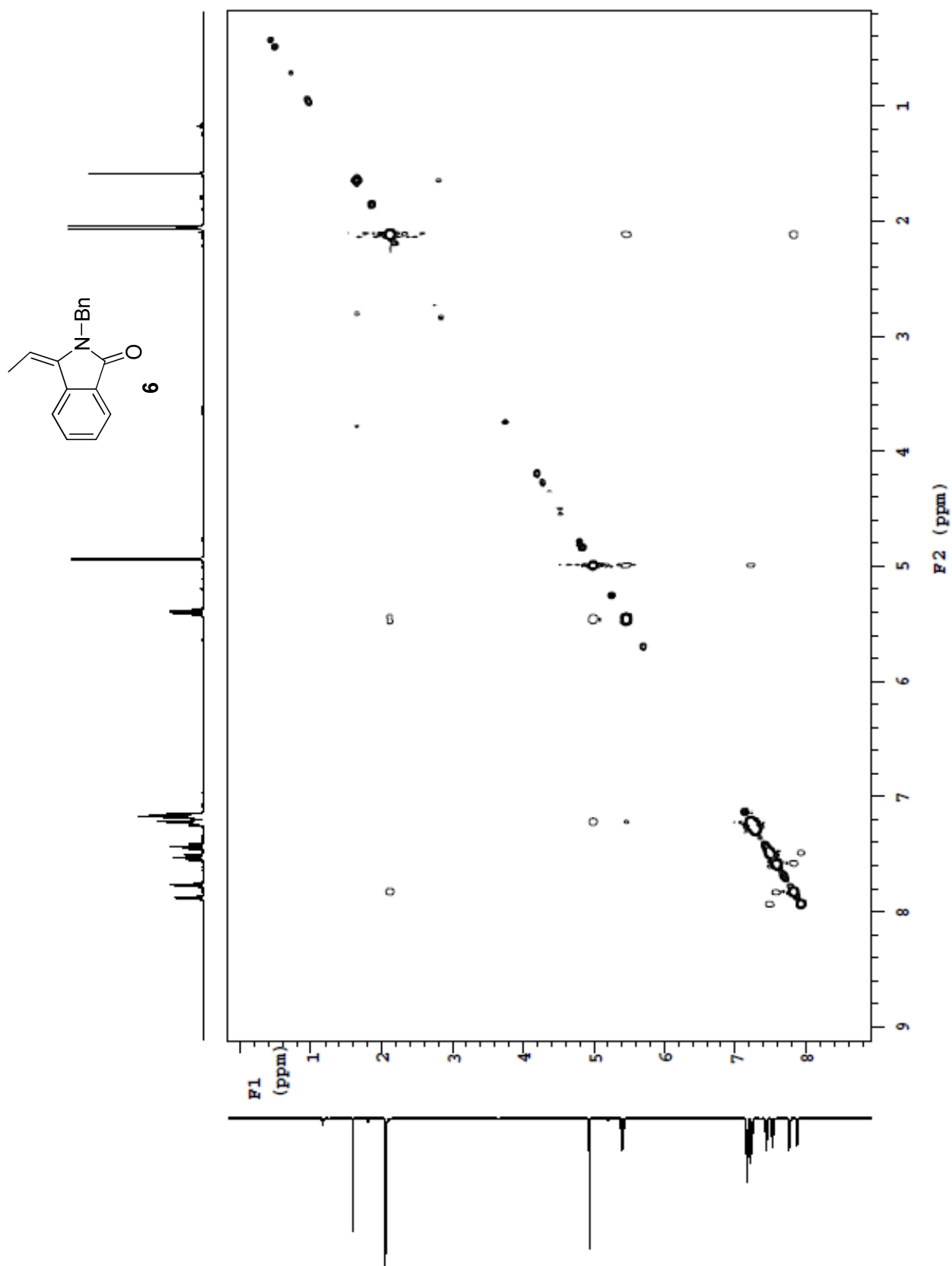


Figure S20. (*E*)-2-Benzyl-3-ethylideneisoindolin-1-one **6**, NOESY NMR spectrum



2-Benzyl-1,1,3,3-tetraethylisoindoline (8) – larger scale

Ethyl iodide (15.40 mL, 0.191 mol, 6 equiv.) was added dropwise to a suspension of pre-dried magnesium turnings (6.11 g, 0.255 mol, 8 equiv.) in anhydrous diethyl ether (60 mL). The mixture was stirred at room temperature for three hours and then concentrated by distillation until a temperature of 80 - 90 °C was reached. The reaction mixture was allowed to cool to 64 °C and a solution of 2-benzyl-3-ethyl-3-hydroxyisoindolin-1-one (**5**) (8.50 g, 0.032 mol) in dry toluene (50 mL) was added. Once the addition was completed, the mixture was refluxed at 110 °C for 3 days. Saturated ammonium chloride solution (80 mL) was then added and the mixture was stirred until all the solids had dissolved. The toluene layer was separated, dried over anhydrous Na₂SO₄ and evaporated to dryness. The dark brownish purple product obtained was run through a basic alumina column with hexane (2.50 L) to give **8** as a white solid (5.62 g, 55%). mp 72-74 °C (lit.[39] mp 76 °C); ¹H NMR (400 MHz, CDCl₃) δ 0.79 (t, *J* = 7.6 Hz, 12H), 1.53-1.59 (m, 4H), 1.92-1.97 (m, 4H), 4.03 (s, 2H), 7.06-7.09 (m, 2H), 7.21-7.23 (m, 2H), 7.26-7.34 (m, 3H), 7.47 (d, *J* = 6.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 9.8, 30.5, 46.9, 71.5, 123.6, 125.8, 126.7, 128.0, 129.5, 142.6, 144.8; HRMS: calcd for C₂₃H₃₂N [MH]⁺ 322.2589, found 322.2571. The obtained spectroscopic data was in agreement with that previously reported. ^[30]