Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Synthesis of (–)-mesembrine using the quaternary carbon-constructing allylic substitution

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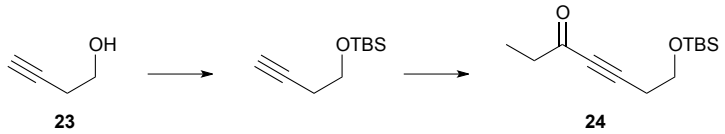
General Methods. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured in $CDCl_3$ using $SiMe_4$ (δ = 0 ppm), residual $CHCl_3$ (δ = 7.26 ppm), and the center line of $CDCl_3$ triplet (δ = 77.1 ppm) as internal standards, respectively.

7-[(*tert*-Butyldimethylsilyloxy)oxy]hept-4-yn-3-one (24)



23 **24**

To an ice-cold solution of 3-butyn-1-ol (**23**) (1.40 g, 20.0 mmol) in DMF (40 mL) were added imidazole (1.64 g, 24.0 mmol) and TBSCl (3.38 g, 22.4 mmol). The mixture was stirred at rt overnight, and diluted with saturated NH_4Cl and EtOAc with vigorous stirring. The layers were separated and the aqueous layer was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford silyl ether (3.57 g, 97%) as a colorless oil: R_f = 0.78 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 6 H), 0.90 (s, 9 H), 1.96 (t, J = 2.7 Hz, 1 H), 2.41 (dt, J = 7.2, 2.7 Hz, 2 H), 3.75 (t, J = 7.2 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –5.2 (CH_3, +), 18.4 (C, –), 22.9 (CH_2, –), 25.9 (CH_3, +), 61.8 (CH_2, –), 69.4 (CH (propagyl), −), 81.6 (C, –). The ^{1}H and ^{13}C NMR spectra were consistent with those reported.[S1]

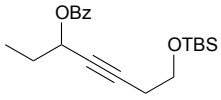
To a solution of silyl ether (875 mg, 4.75 mmol) in THF (40 mL) was added *n*-BuLi (1.55 M in hexane, 4.30 mL, 6.67 mmol) dropwise at –78 ºC. After 1 h at –78 ºC, *N*-methoxy-*N*-methylpropionamide (848 mg, 7.24 mmol) in THF (3 mL) was added to it dropwise. The mixture was stirred at –78 ºC to –30 ºC overnight, and diluted with saturated NH_4Cl and EtOAc with vigorous stirring. The layers were separated and the aqueous layer was extracted with EtOAc three times. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford ynone **24** (1.07 g, 94%) as a colorless oil: R_f = 0.72 (hexane/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 6 H), 0.90 (s, 9 H), 1.14 (t, J = 7.4 Hz, 3 H), 2.56 (q, J = 7.4 Hz, 2 H), 2.58 (t, J = 6.9 Hz, 2 H), 3.78 (t, J = 6.9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –5.3 (CH_3, +), 8.1 (CH_3, +), 18.3 (C,

–), 23.4 (CH_2, –), 25.9 (CH_3, +), 38.8 (CH_2, –), 60.9 (CH_2, –), 81.4 (C, –), 91.1 (C, –), 188.7 (CO, –). The ^{1}H and ^{13}C NMR spectra were consistent with those reported.[S2]

References

S1 (*a*) T. Jensen, H. Pedersen, B. Bang-Andersen, R. Madsen and M. Jørgensen, *Angew. Chem. Int. Ed*., 2008, **47**, 888–890; (*b*) C. Z. Rotsides, C. Hu and K. A. Woerpel, *Angew. Chem. Int. Ed*., 2013, **52**, 13033–13036.

S2 T. E. Nielsen, M. A. C. de Dios and D. Tanner, *J. Org. Chem*., 2002, **67**, 7309–7313.



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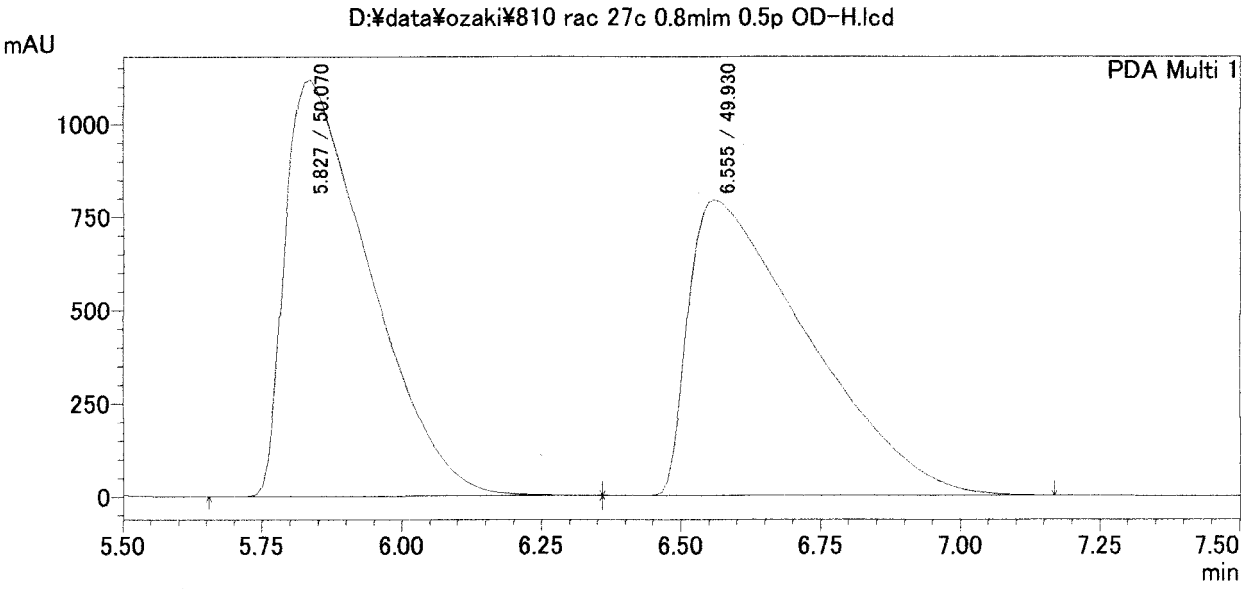

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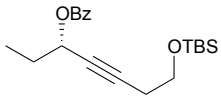

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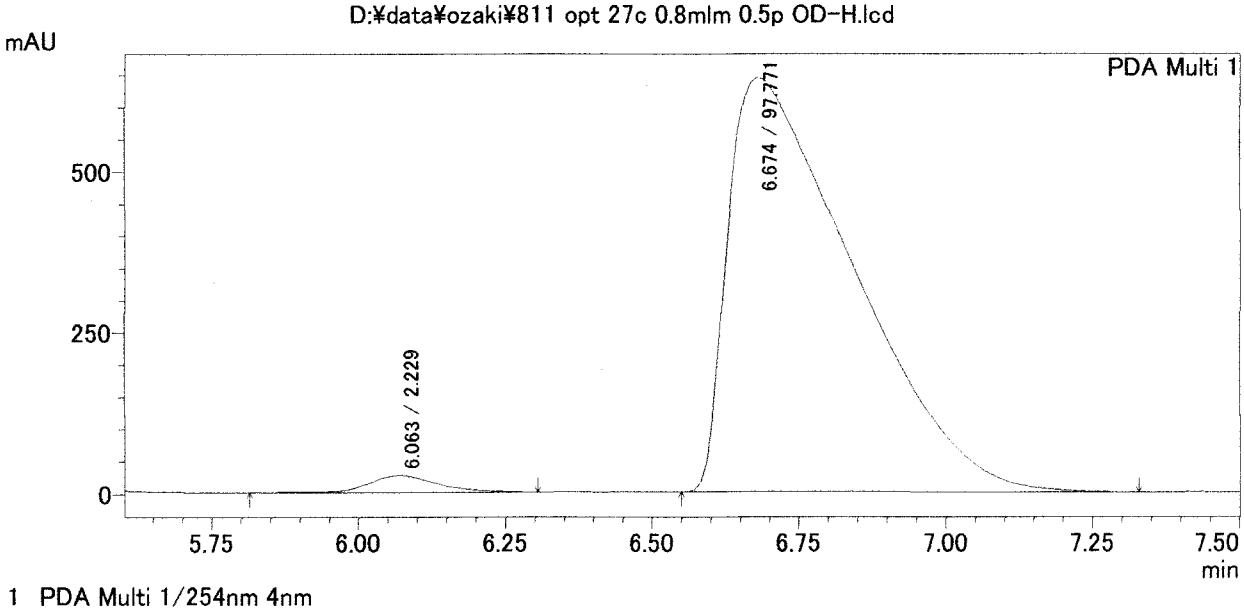

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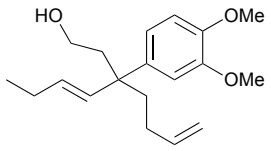

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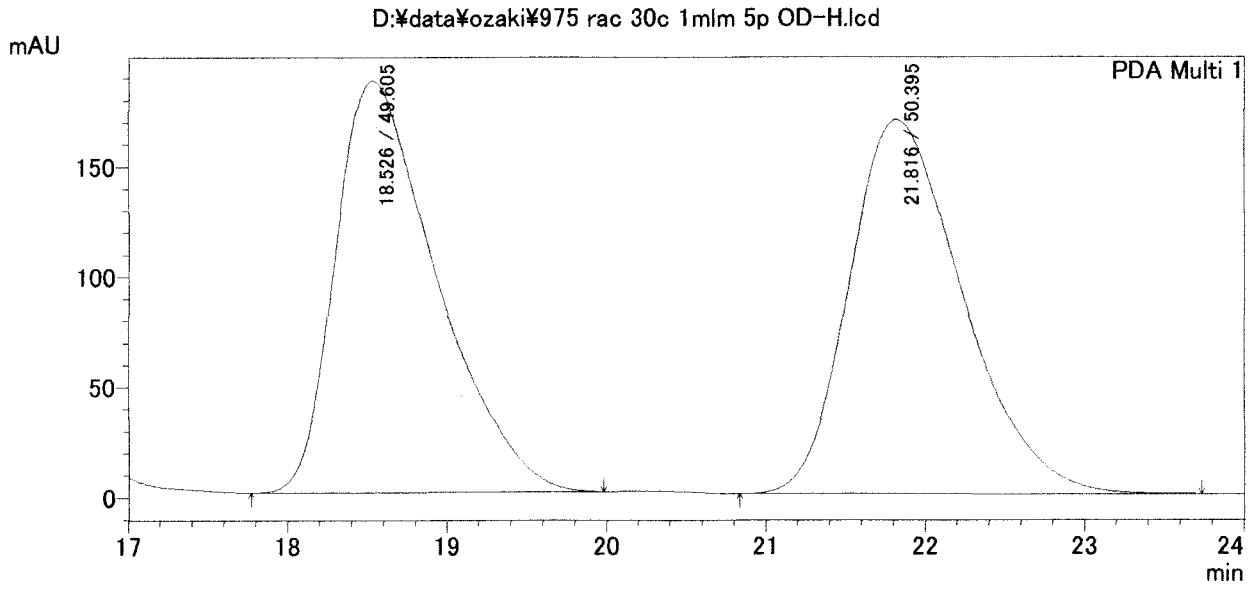

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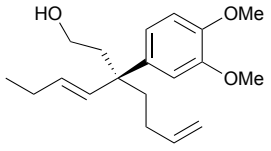

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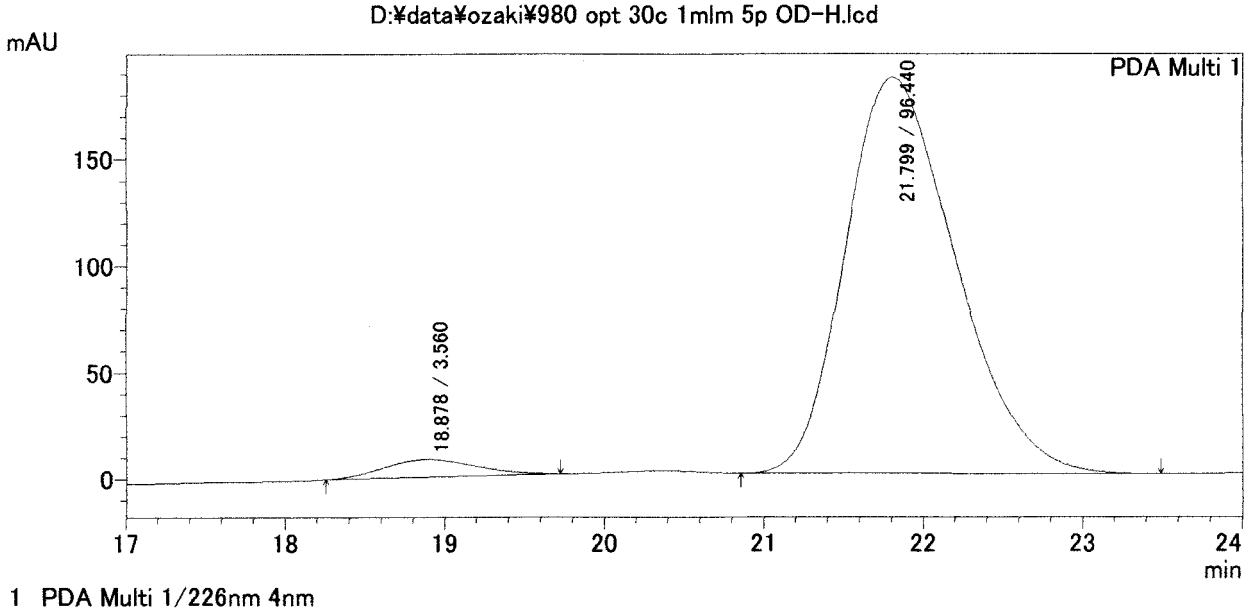

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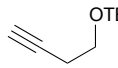

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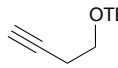
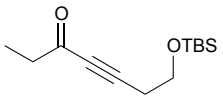


APT, $CDCl_3$, 75 MHz



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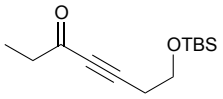

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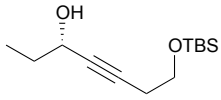

(*S*)-**13**

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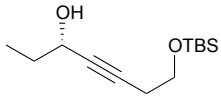
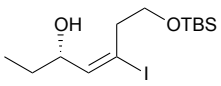


(*S*)-**13**

APT, $CDCl_3$, 75 MHz



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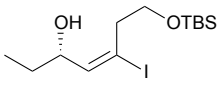

(*S*)-**14**

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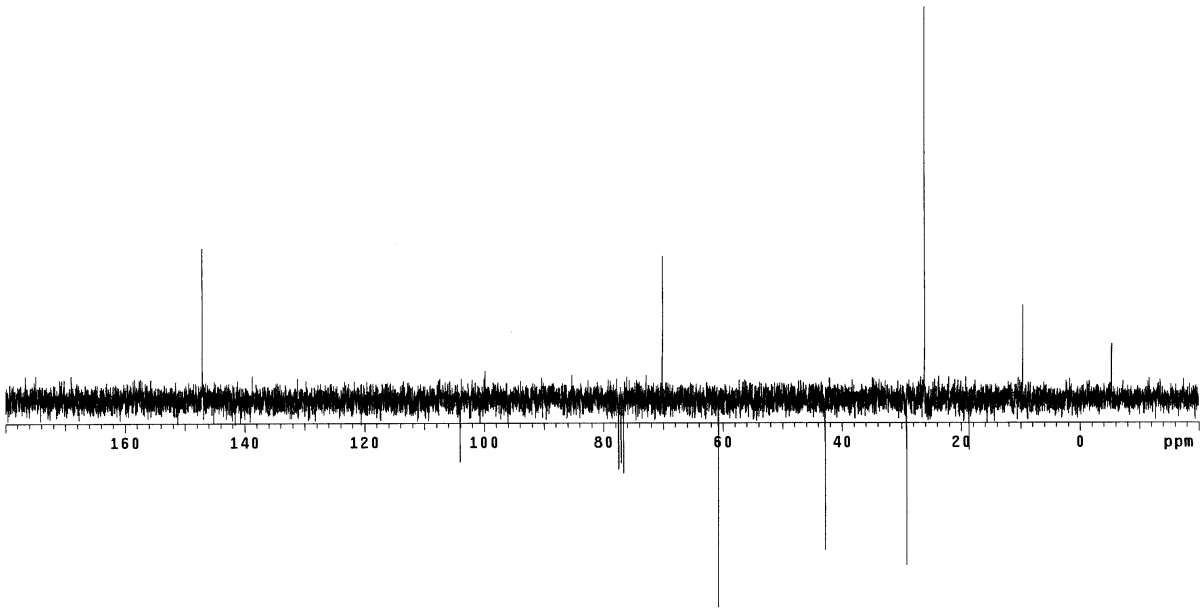

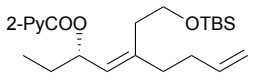

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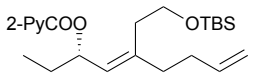

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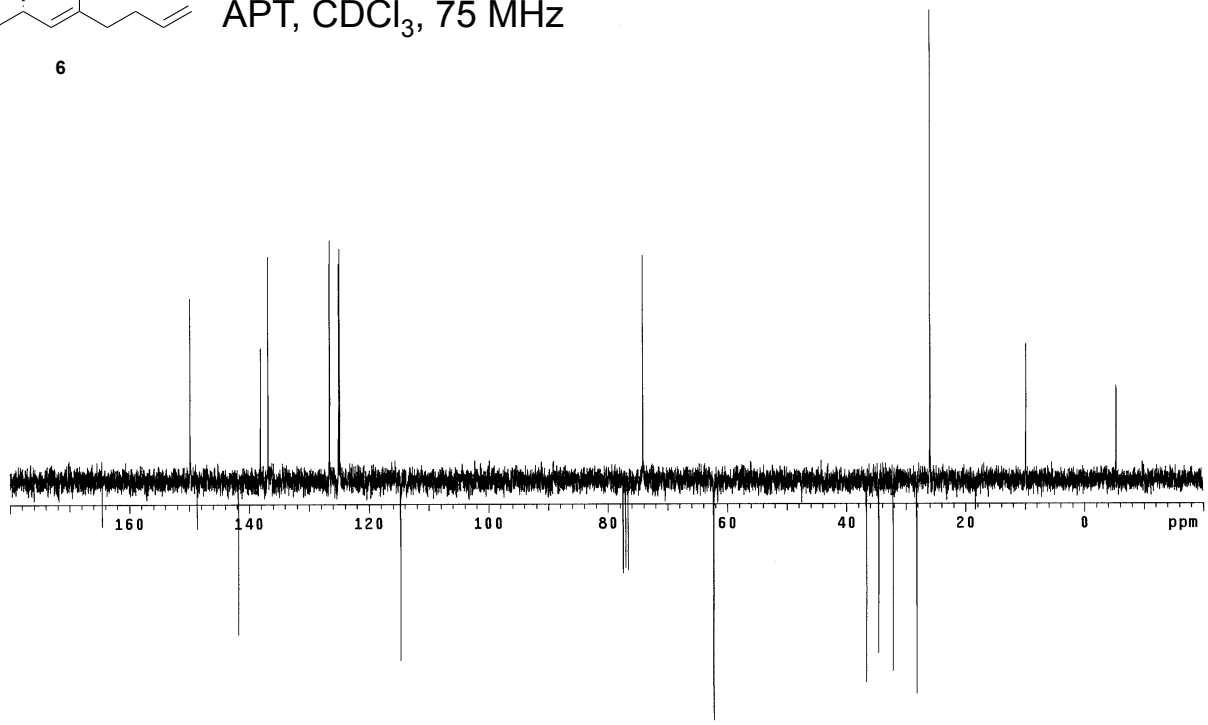

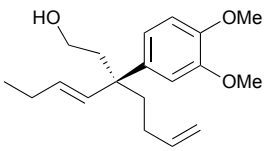

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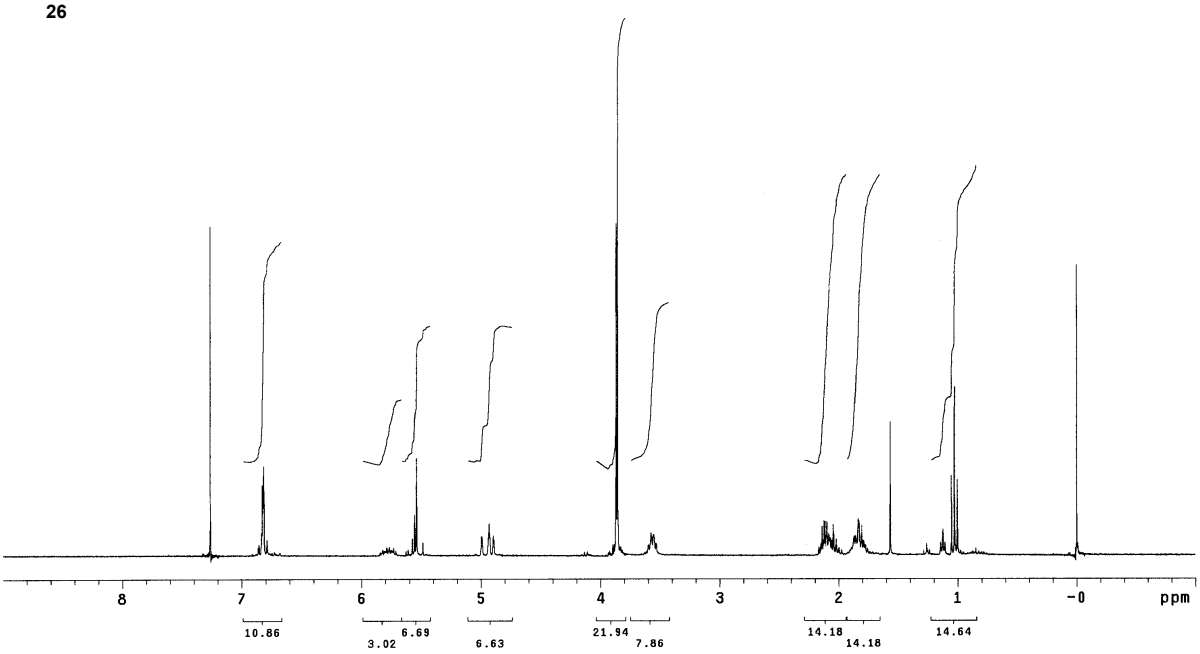

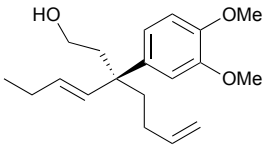

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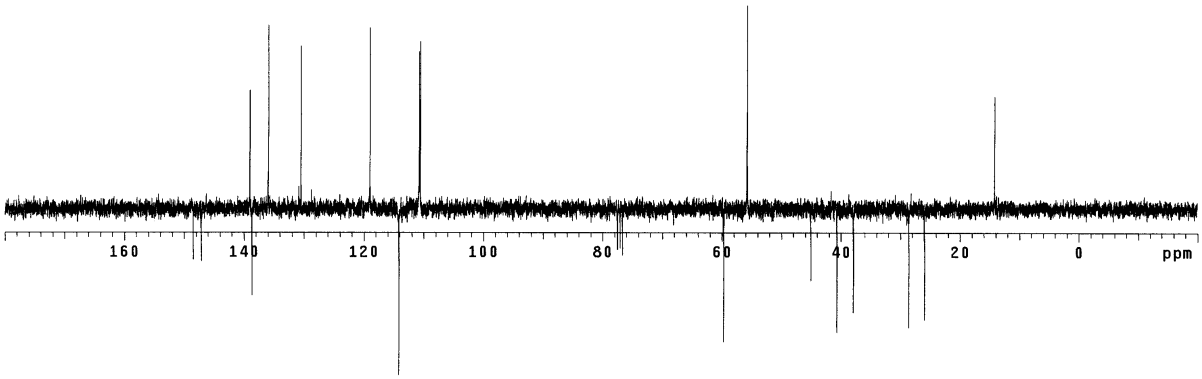

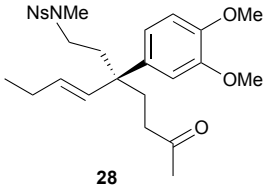

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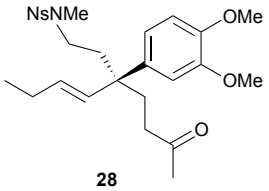

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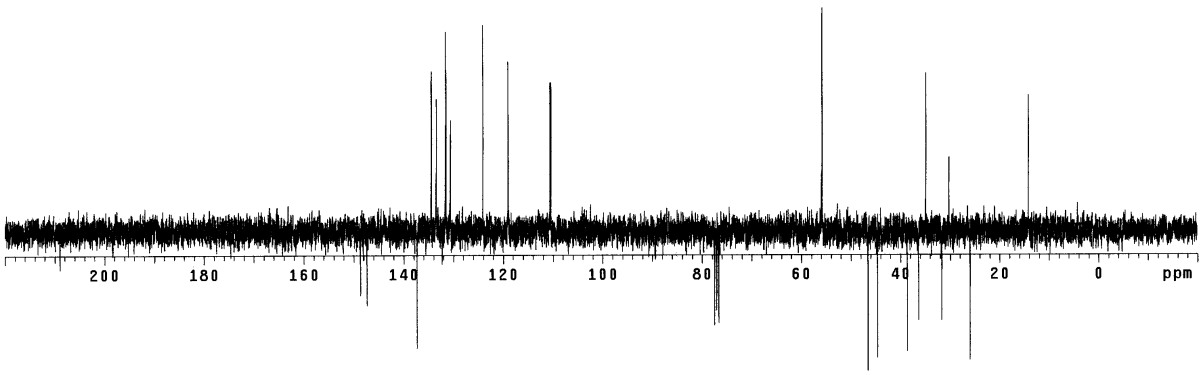

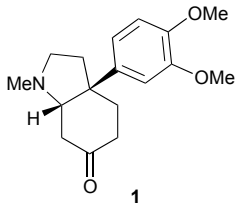

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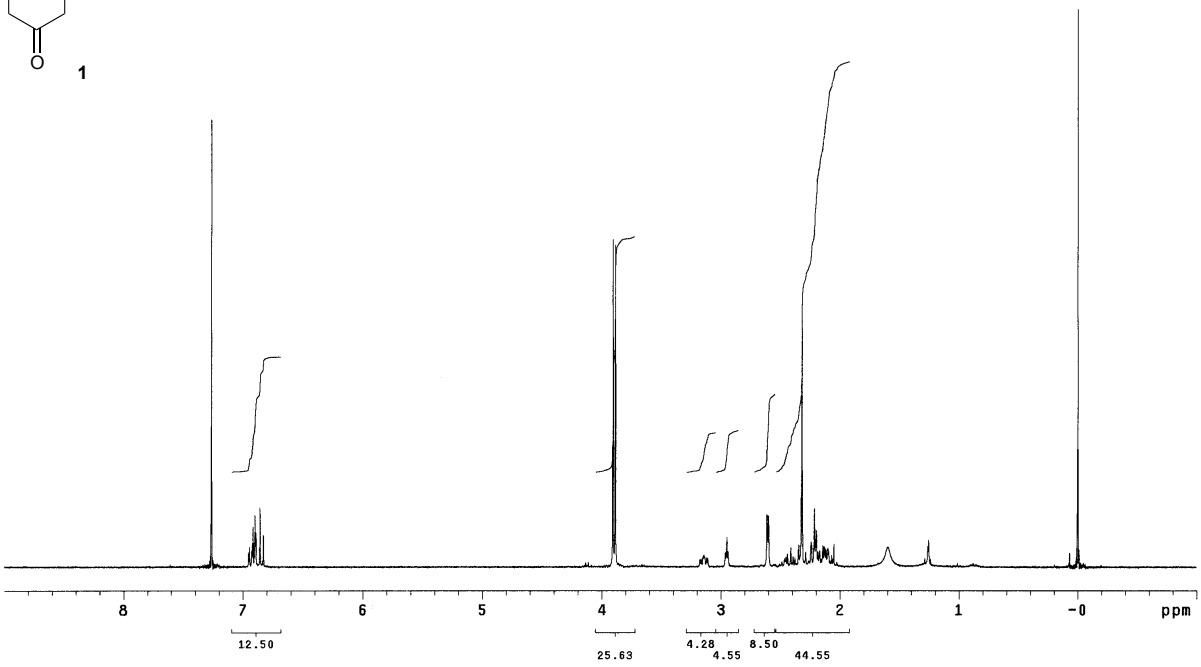

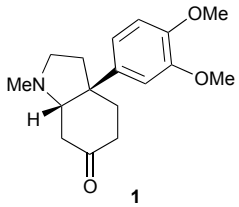

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