Rhodium-Catalyzed Novel Trifluoromethylation at α-Position of α,β-Unsaturated Ketones

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Supporting Information

General Information.

^{1}H-NMR and ^{13}C-NMR spectra were recorded on JNM-GX400 spectrometers and tetramethylsilane (TMS) was used as an internal standard. ^{19}F-NMR spectra were recorded on Hitachi FT-NMR R-1500 and benzotrifluoride (BTF) was used as an internal standard. Mass spectra were obtained on JEOL JMS-700T spectrometers. IR spectra were recorded on Hitachi 270-30 Infrared spectrophotometer. Gas-liquid chromatography (GLC) was carried out on a Hitachi 263-50 gas chromatograph (column, 5% SE-30 3 mm x 2 m, carrier, N_2 at 30 ml/min). Peak areas were calculated on a Hitachi D-2000 Chromato-Integrator. All commercially available reagents were used without further purification.

Experimental Section.

Methyl 4-(3-oxo-1-butenyl)benzoate (**2g**) and 4-(4-methoxyphenyl)-3-buten-2-one (**2h**) were synthesized according to the literatures 1 and 2.

General Procedure

4-Phenyl-3-trifluoromethyl-2-butanone (7a)

Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2a** (292 mg, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7a** (332 mg, 77%). **7a**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.07 (s, 3H), 3.06 (dd, 1H, *J* = 13.9, 4.2 Hz), 3.18 (dd, 1H, *J* = 13.9, 10.9 Hz), 3.56 (ddd, 1H, *J* = 10.9, 8.3, 4.2 Hz), 7.12-7.32 (m, 5H); ^{13}C NMR ($CDCl_3$) δ: 31.8 (q, *J* = 1.6 Hz), 31.9 (q, *J* = 2.7 Hz), 57.6 (q, *J* = 24.9 Hz), 124.4 (q, *J* = 280.3 Hz), 127.1, 128.7, 128.8, 136.4, 201.3 (q, *J* = 1.9 Hz); ^{19}F NMR ($CDCl_3$) δ: -4.42 (d, 3F, *J* = 8.3 Hz); MS *m*/*z*: 216 (M^+); HRMS Calc. $C_{11}H_{11}OF_3$: 216.08 (M^+), Found: 216.08; IR (neat) cm^{-1}: 1734, 1264.

1,3-Diphenyl-2-trifluoromethyl-1-propanone (7b)

Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2b** (417 mg, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7b** (171 mg, 31%). **7b**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 3.20 (dd, 1H, *J* = 13.8, 4.1 Hz), 3.43 (dd, 1H, *J* = 13.8, 10.7 Hz), 4.48 (m, 1H), 7.18 (m, 5H), 7.39 (m, 2H),

7.53 (m, 1H), 7.74 (m, 2H); ^{13}C NMR ($CDCl_3$) δ: 32.7 (q, *J* = 2.6 Hz), 51.4 (q, *J* = 25.1 Hz), 124.5 (q, *J* = 280.8 Hz), 126.9, 128.4, 128.6, 128.6, 128.8, 133.7, 136.6, 136.8, 193.9 (q, *J* = 1.8 Hz); ^{19}F NMR ($CDCl_3$) δ: -3.63 (d, 3F, *J* = 7.6 Hz); MS *m*/*z*: 278 (M^+); HRMS Calc. $C_{16}H_{13}OF_3$: 278.09 (M^+), Found: 278.09; IR (neat) cm^{-1}: 1694, 1266.

1-Phenyl-2-trifluoromethyl-1-pentanone (7c)

Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2c** (320 mg, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7c** (160 mg, 35%). **7c**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 0.91 (t, 3H, *J* = 7.3 Hz), 1.33 (m, 2H), 1.86 (m, 1H), 2.09 (m, 1H) , 4.21 (m, 1H), 7.52 (m, 2H), 7.64 (m, 1H), 7.97 (m, 2H); ^{13}C NMR ($CDCl_3$) δ: 13.9, 20.3, 29.0 (q, *J* = 2.1 Hz), 49.1 (q, *J* = 25.1 Hz), 124.9 (q, *J* = 280.2 Hz), 128.4, 128.8, 133.8, 136.8, 194.5 (q, *J* = 1.4 Hz); ^{19}F NMR ($CDCl_3$) δ: -3.48 (d, 3F, *J* = 8.3 Hz); MS *m*/*z*: 230 (M^+); HRMS Calc. $C_{12}H_{13}OF_3$: 230.09 (M^+), Found: 230.09; IR (neat) cm^{-1}: 1696, 1240.

3-Trifluoromethyl-2-nonanone (7e)

Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2e** (0.33 mL, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7e** (280 mg, 67%). **7e**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 0.88 (t, 3H, *J* = 7.1 Hz), 1.29 (m, 8H), 1.75 (m, 1H), 1.86 (m, 1H), 2.28 (s, 3H), 3.17 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: 14.0, 22.5, 25.7 (q, *J* = 2.5 Hz), 26.8, 28.9, 30.0 (q, *J* = 2.2 Hz), 31.4, 56.5 (q, *J* = 25.4 Hz), 124.9 (q, *J* = 279.6 Hz), 202.0 (q, *J* = 1.2 Hz); ^{19}F NMR ($CDCl_3$) δ: -4.14 (d, 3F, *J* = 8.9 Hz); MS *m*/*z*: 210 (M^+); HRMS Calc. $C_{10}H_{17}OF_3$: 210.12 (M^+), Found: 210.12; IR (neat) cm^{-1}: 2964, 2936, 1734, 1262, 1166, 1130, 1108.

2-Methyl-1,1,1-trifluoro-3-octanone (7f)

Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2f** (0.29 mL, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted

with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7f** (233 mg, 59%). **7f**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 0.90 (t, 3H, *J* = 7.2 Hz), 1.24-1.35 (m, 4H), 1.32 (d, 3H, *J* = 7.6 Hz), 1.60 (q, 2H, *J* = 7.4 Hz), 2.52 (dt, 1H, *J* = 17.9, 7.2 Hz), 2.60 (dt, 1H, *J* = 17.9, 7.5 Hz), 3.27 (qq, 1H, *J* = 9.0, 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ: 10.5 (q, *J* = 3.1 Hz), 13.9, 22.4, 22.9, 31.1, 42.3 (q, *J* = 1.8 Hz), 49.9 (q, *J* = 26.6 Hz), 125.1 (q, *J* = 279.4 Hz), 204.2 (q, *J* = 1.7 Hz); ^{19}F NMR ($CDCl_3$) δ: -5.72 (d, 3F, *J* = 9.0 Hz); MS *m*/*z*: 196 (M^+); HRMS Calc. $C_9H_{15}OF_3$: 196.11 (M^+), Found: 196.11; IR (neat) cm^{-1}: 2964, 2880, 1732, 1262, 1176, 1110.

Methyl 4-(3-oxo-2-trifluoromethyl-butyl)benzoate (7g)

Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2g** (408 mg, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7g** (357 mg, 65%). **7g**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.11 (s, 3H), 3.09 (dd, 1H, *J* = 13.6, 4.0 Hz), 3.26 (dd, 1H, *J* = 13.6, 10.7 Hz), 3.59 (m, 1H), 3.91 (s, 3H), 7.25 (m, 2H), 7.98 (m, 2H); ^{13}C NMR ($CDCl_3$) δ: 31.6 (q, *J* = 2.4 Hz), 31.8 (q, *J* = 1.4 Hz), 52.1, 57.2 (q, *J* = 25.0 Hz), 124.2 (q, *J* = 281.1 Hz), 128.8, 129.1, 130.1, 141.8, 166.6, 200.7; ^{19}F NMR ($CDCl_3$) δ: -4.24 (d, 3F, *J* = 7.6 Hz); MS *m*/*z*: 274 (M^+); HRMS Calc. $C_{13}H_{13}O_3F_3$: 274.08 (M^+), Found: 274.08; IR (neat) cm^{-1}: 1728, 1286, 1184, 1160, 1112.

4,4,4-Trifluoro-3-(4-methoxybenzyl)-2-butanone (7h)

Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2h** (352 mg, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7h** (322 mg, 65%). **7h**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.07 (s, 3H), 3.01 (dd, 1H, *J* = 13.8, 4.0 Hz), 3.12 (dd, 1H, *J* = 13.8, 10.7 Hz), 3.52 (m, 1H), 3.78 (s, 3H), 6.83 (m, 2H), 7.08 (m, 2H); ^{13}C NMR ($CDCl_3$) δ: 31.1 (q, *J* = 2.6 Hz), 31.9 (m), 55.2, 57.8 (q, *J* = 24.6 Hz), 114.2, 124.4 (q, *J* = 280.3 Hz), 128.3, 129.8, 158.6, 201.6; ^{19}F NMR ($CDCl_3$) δ: -4.42 (d, 3F, *J* = 7.6 Hz); MS *m*/*z*: 246 (M^+); HRMS Calc. $C_{12}H_{13}O_2F_3$: 246.09 (M^+), Found: 246.09; IR (neat) cm^{-1}: 1732, 1252, 1036.

2-Trifluoromethylcyclohexanone (7i)

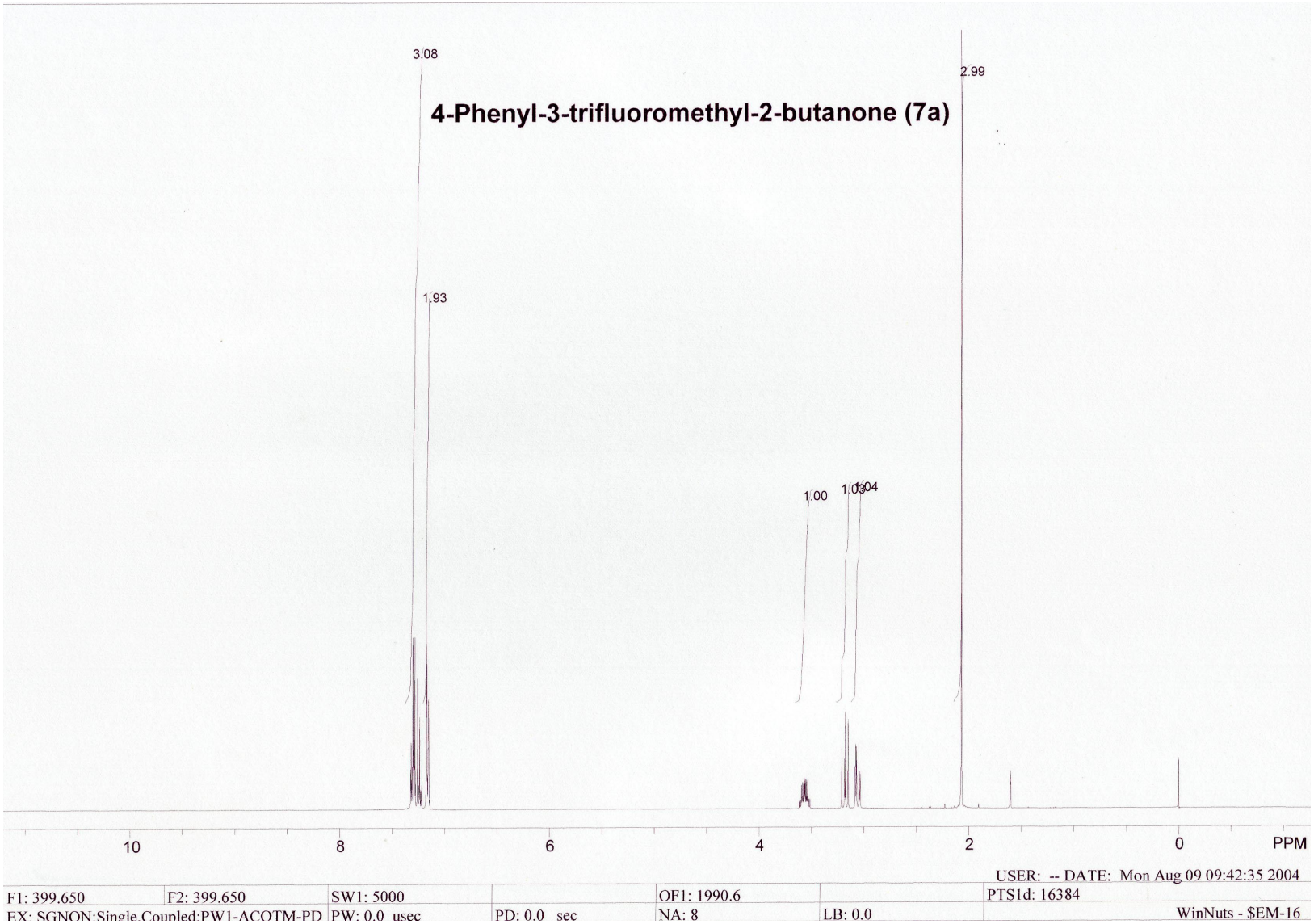
Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2i** (0.20 mL, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7i** (182 mg, 55%). **7i**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 1.67-1.88 (m, 3H), 1.99-2.03 (m, 1H), 2.07-2.15 (m, 1H), 2.31-2.39 (m, 2H), 2.48-2.53 (m, 1H), 3.08 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: 23.8, 27.1, 27.6 (q, J = 2.5 Hz), 42.2 (q, J = 1.6 Hz), 53.7 (q, J = 25.5 Hz), 124.6 (q, J = 278.6 Hz), 202.9; ^{19}F NMR ($CDCl_3$) δ: -6.02 (d, 3F, J = 8.3 Hz); MS *m*/*z*: 166 (M^+); HRMS Calc. $C_7H_9OF_3$: 166.06 (M^+), Found: 166.06; IR (neat) cm^{-1}: 2956, 2880, 1730, 1394, 1274.

4,4-Dimethyl-2-trifluoromethylcyclohexanone (7j)

Under an atmosphere of Ar, a solution of **1** (ca 1 mL) in THF (2 mL) was added to a mixture of **2j** (0.26 mL, 2 mmol) and $RhCl(PPh_3)_3$ (37 mg, 2 mol%) in THF (6 mL) at -30 °C. 1.0 M Et_2Zn in hexane (3 mL, 3 mmol) was gradually added to the solution at 0 °C, and then the solution was stirred at RT for 0.5 h. The solution was quenched with 10% HCl, and extracted with Et_2O. The Et_2O layer was washed with sat. NaCl and dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by column chromatography (AcOEt : Hexane = 1 : 9) to give **7j** (204 mg, 53%). **7j**: colorless oil; ^{1}H NMR ($CDCl_3$) δ: 1.09 (s, 3H), 1.24 (s, 3H), 1.67-1.81 (m, 3H), 1.99 (m, 1H), 2.35 (m, 1H), 2.49 (m, 1H), 3.19 (m, 1H); ^{13}C NMR ($CDCl_3$) δ: 24.0, 30.2, 31.1, 38.4 (q, J = 1.7 Hz), 39.3, 39.6 (q, J = 2.5 Hz), 49.9 (q, J = 24.9 Hz), 124.7 (q, J = 280.0 Hz), 203.1; ^{19}F NMR ($CDCl_3$) δ: -6.19 (d, 3F, J = 7.6 Hz); MS *m*/*z*: 194 (M^+); HRMS Calc. $C_9H_{13}OF_3$: 194.09 (M^+), Found: 194.09; IR (neat) cm^{-1}: 2968, 2880, 1734, 1388, 1310, 1286, 1264, 1174, 1146, 1082.

References

1. Ohno, H.; Okumura, M.; Maeda, S.; Iwasaki, H.; Wakayama, R.; Tanaka, T. *J. Org. Chem.* **2003**, *68*, 7722-7732.
2. Frattini, S.; Quai, M.; Cereda, E. *Tetrahedron Lett.* **2001**, *42*, 6827-6829.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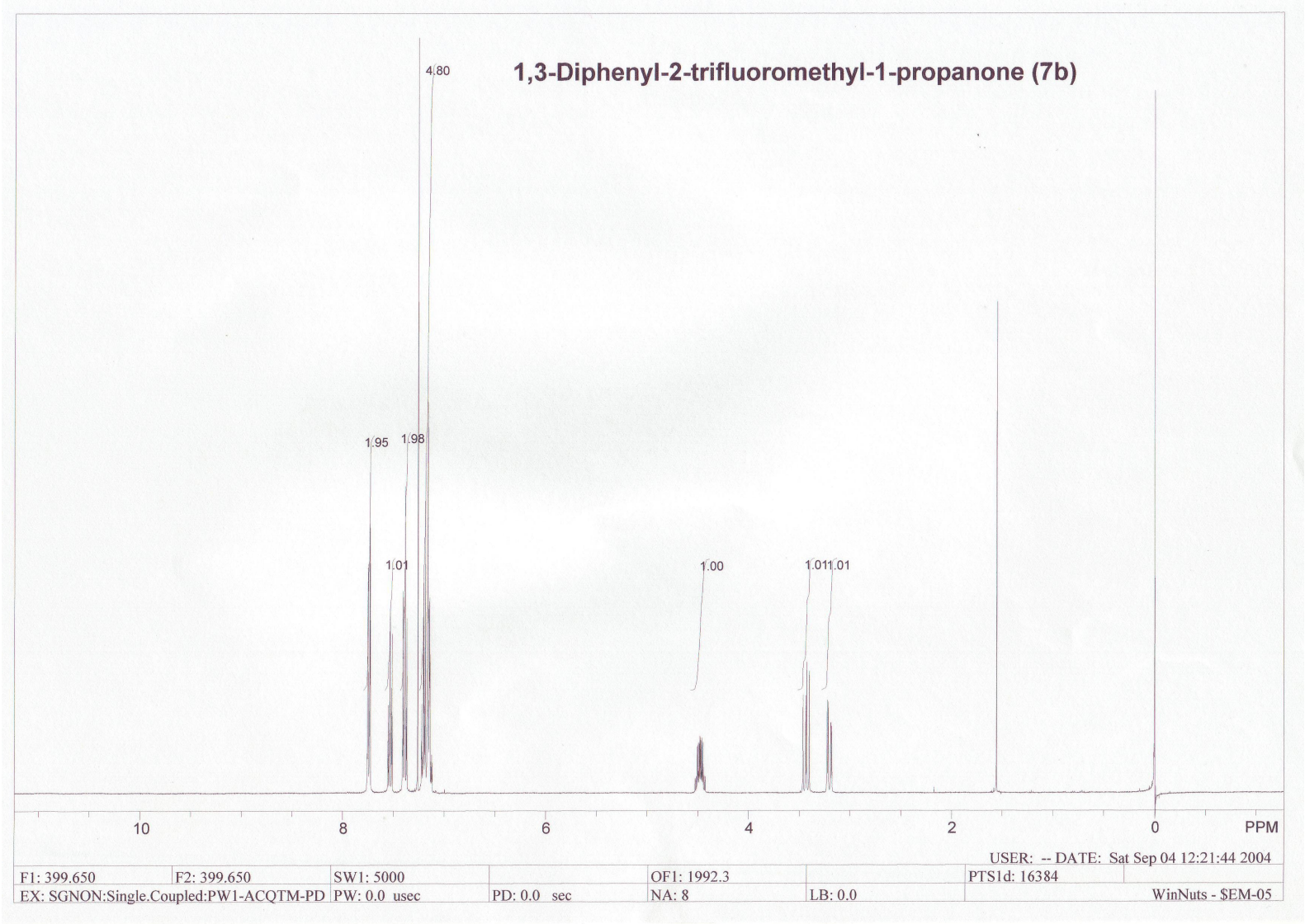
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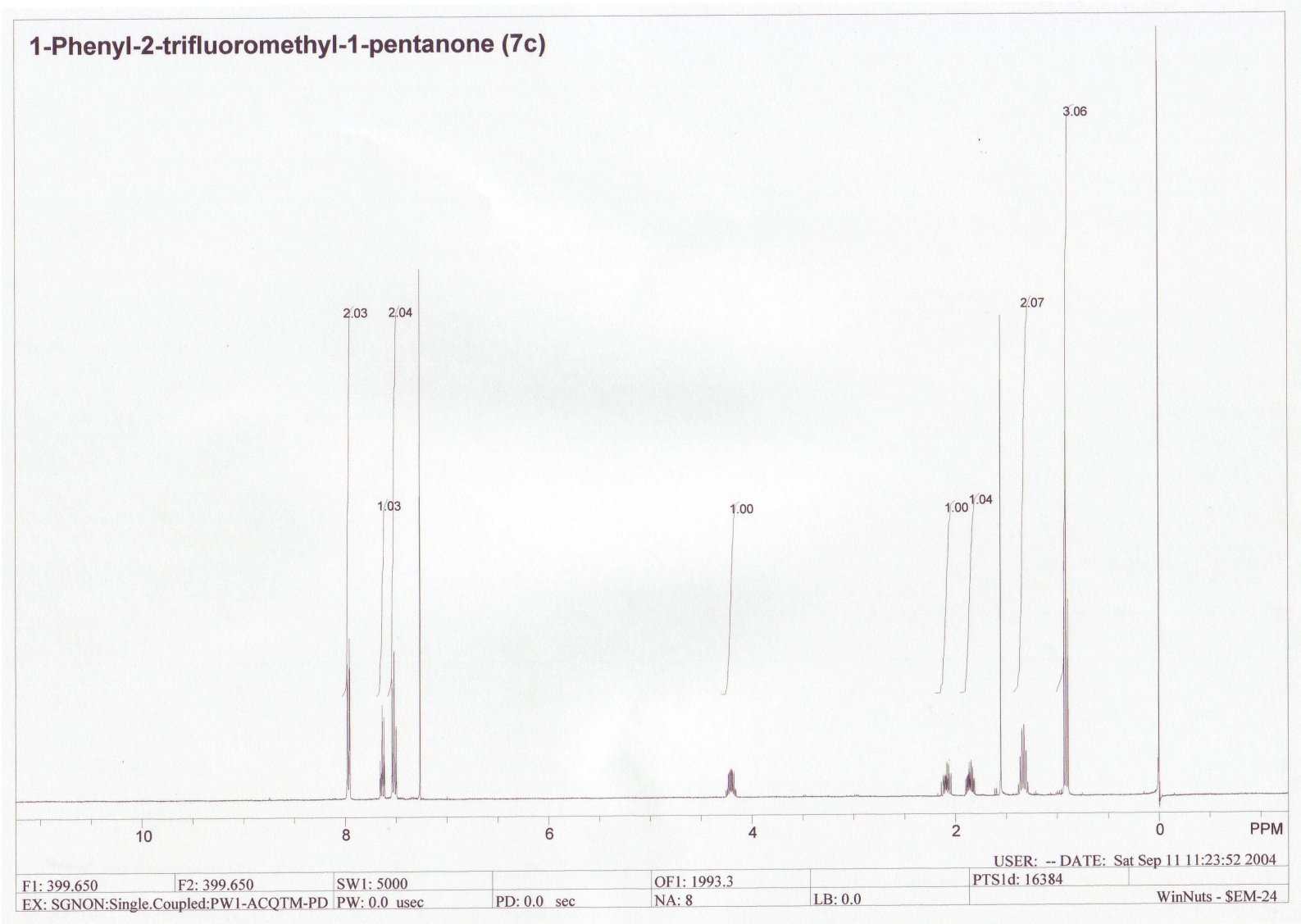
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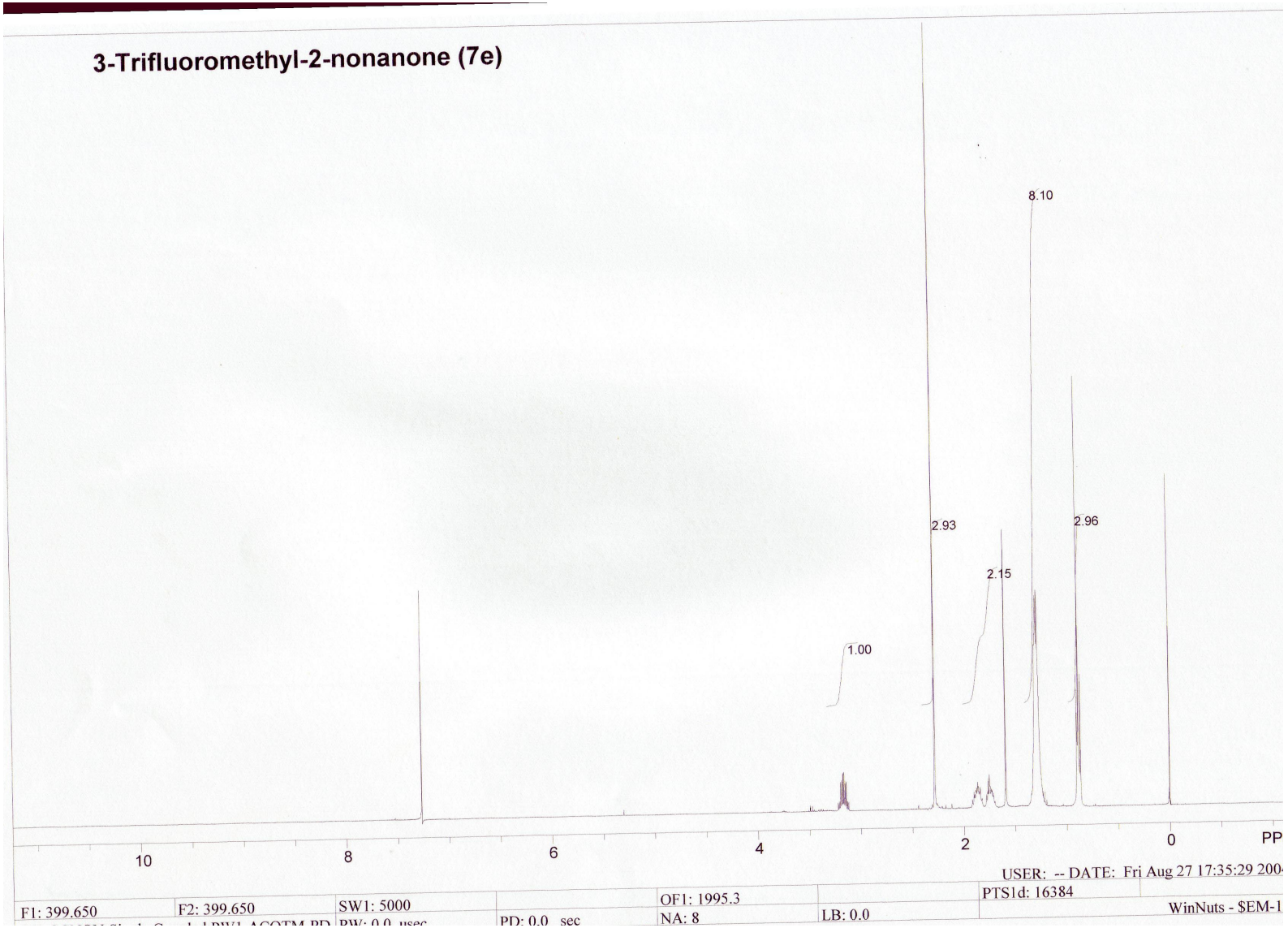
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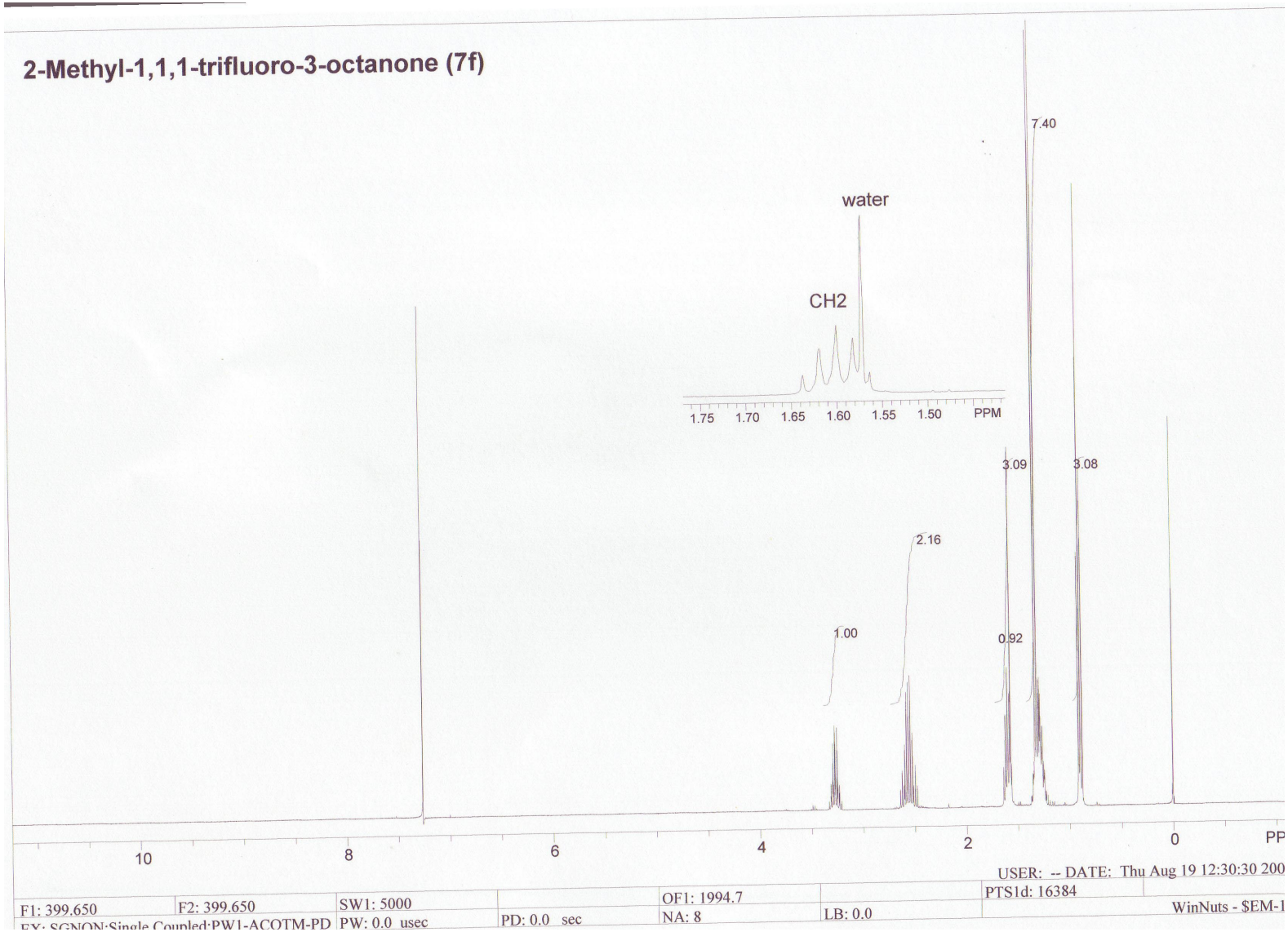
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1.00
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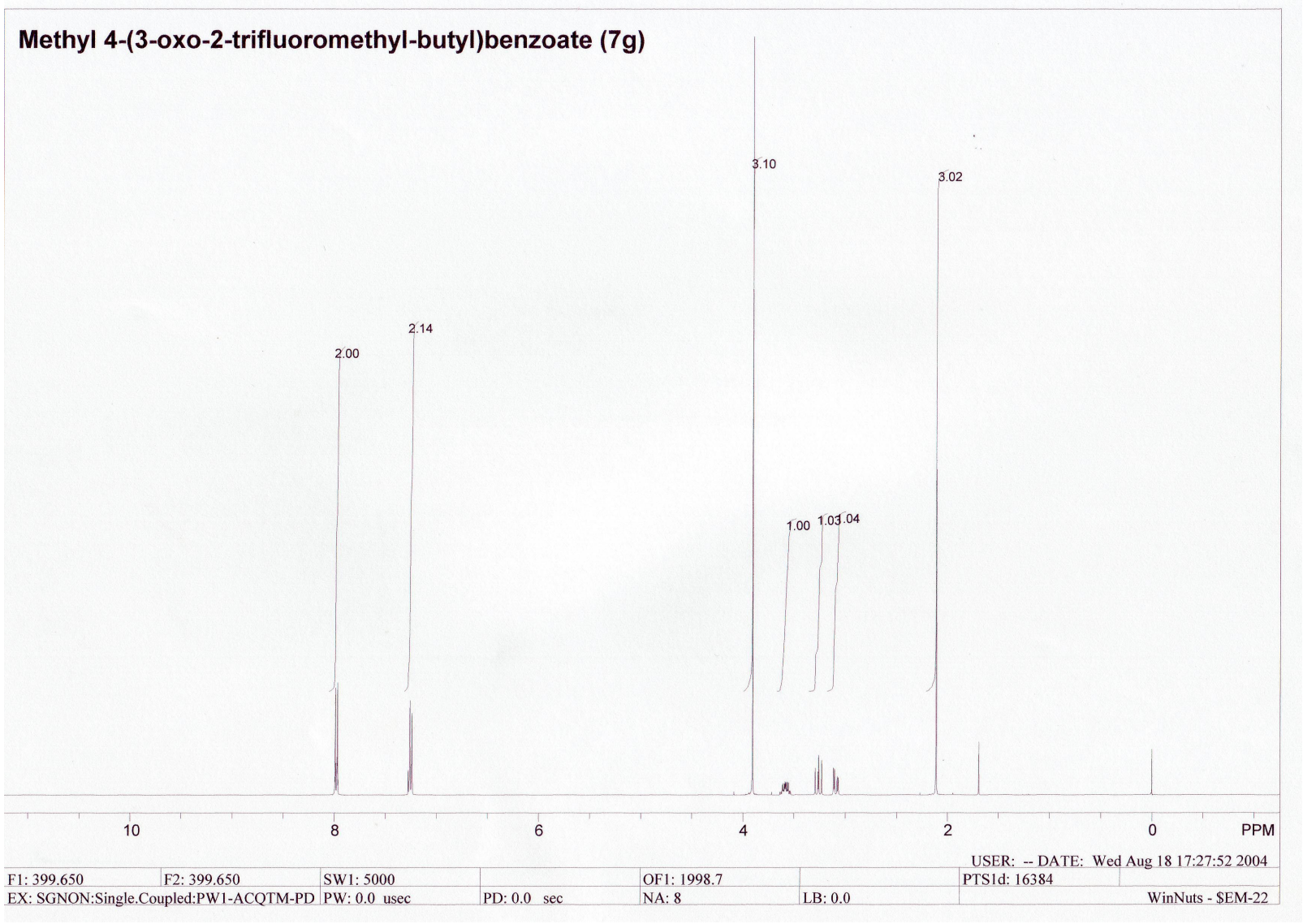
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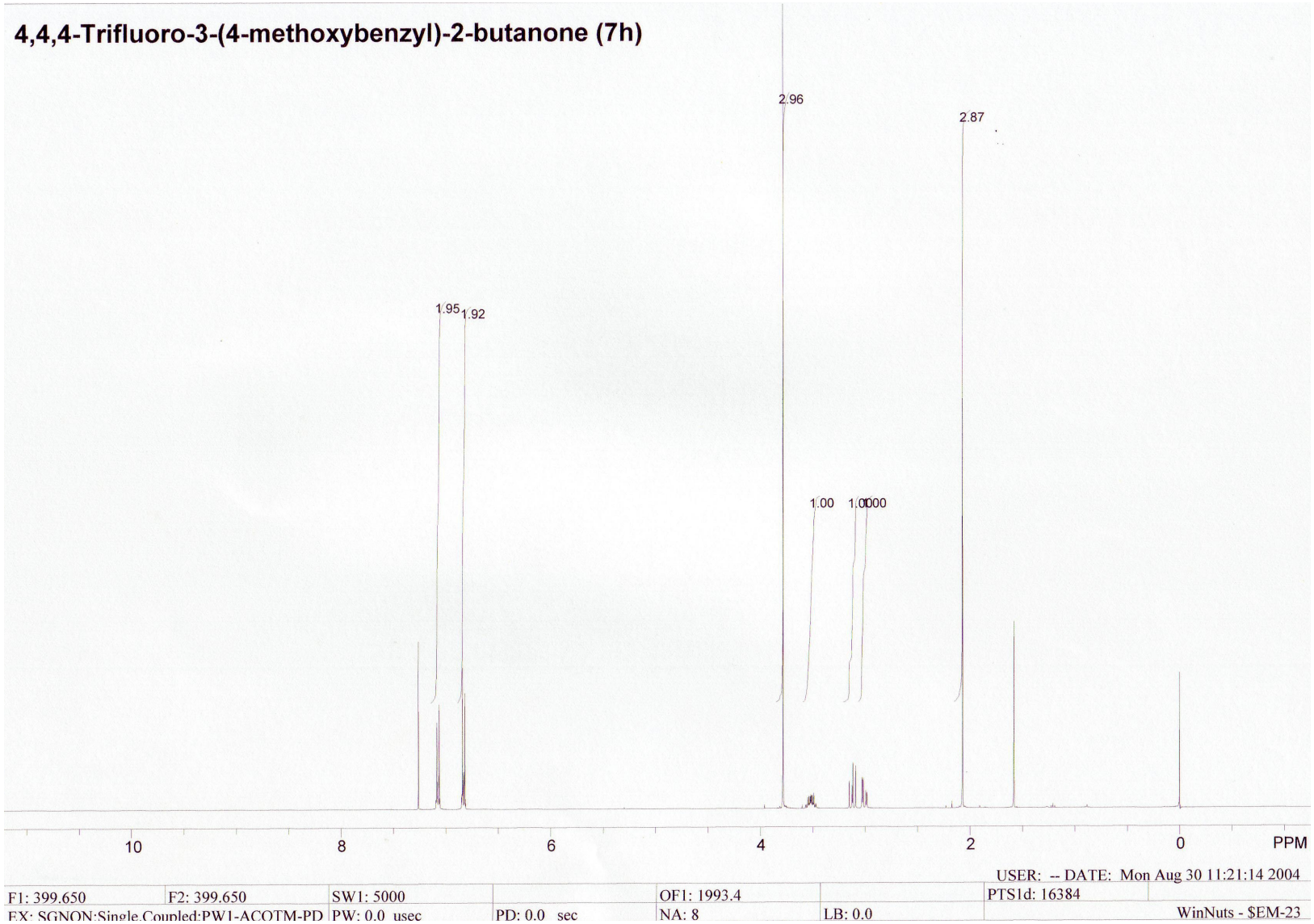
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2
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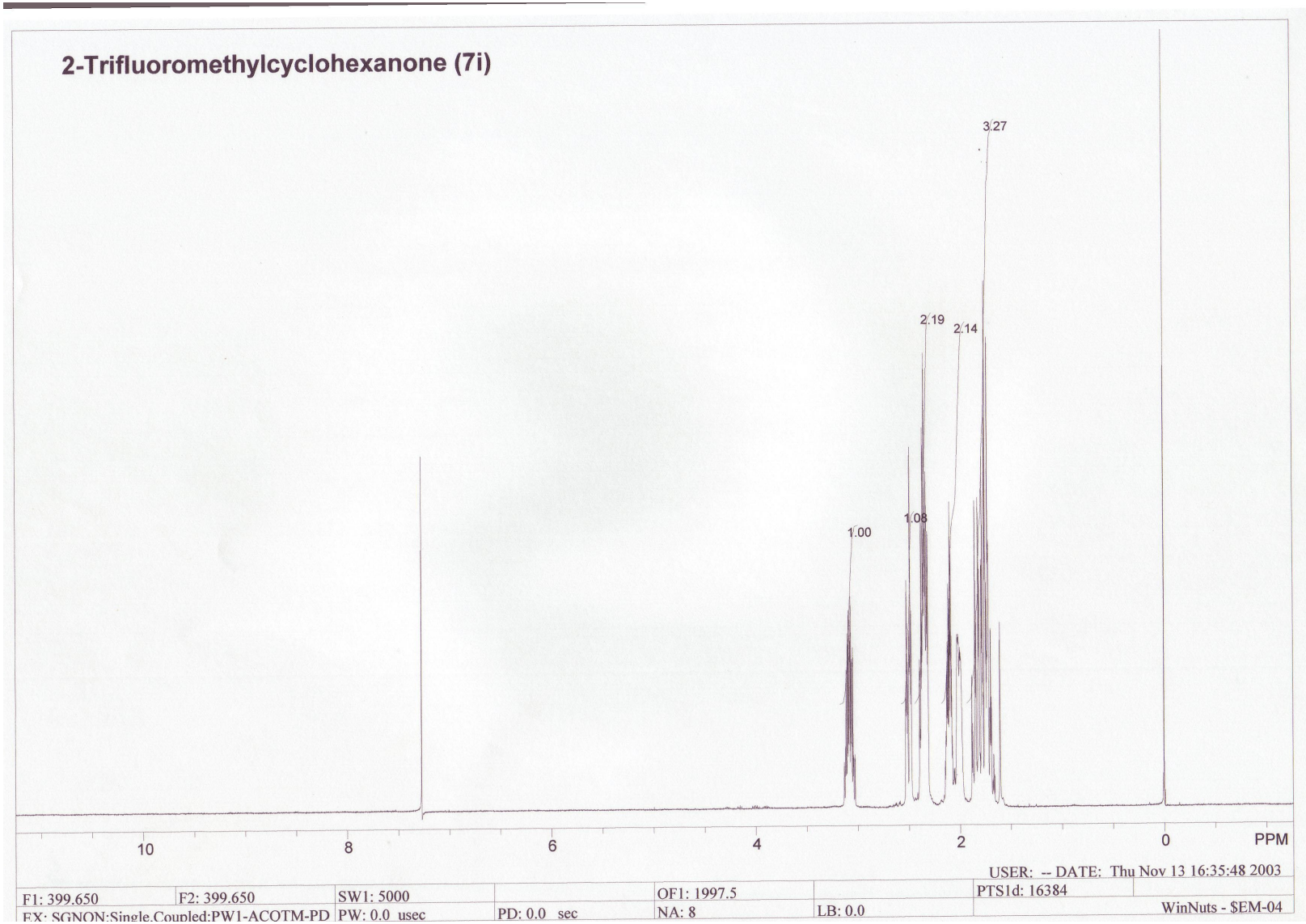
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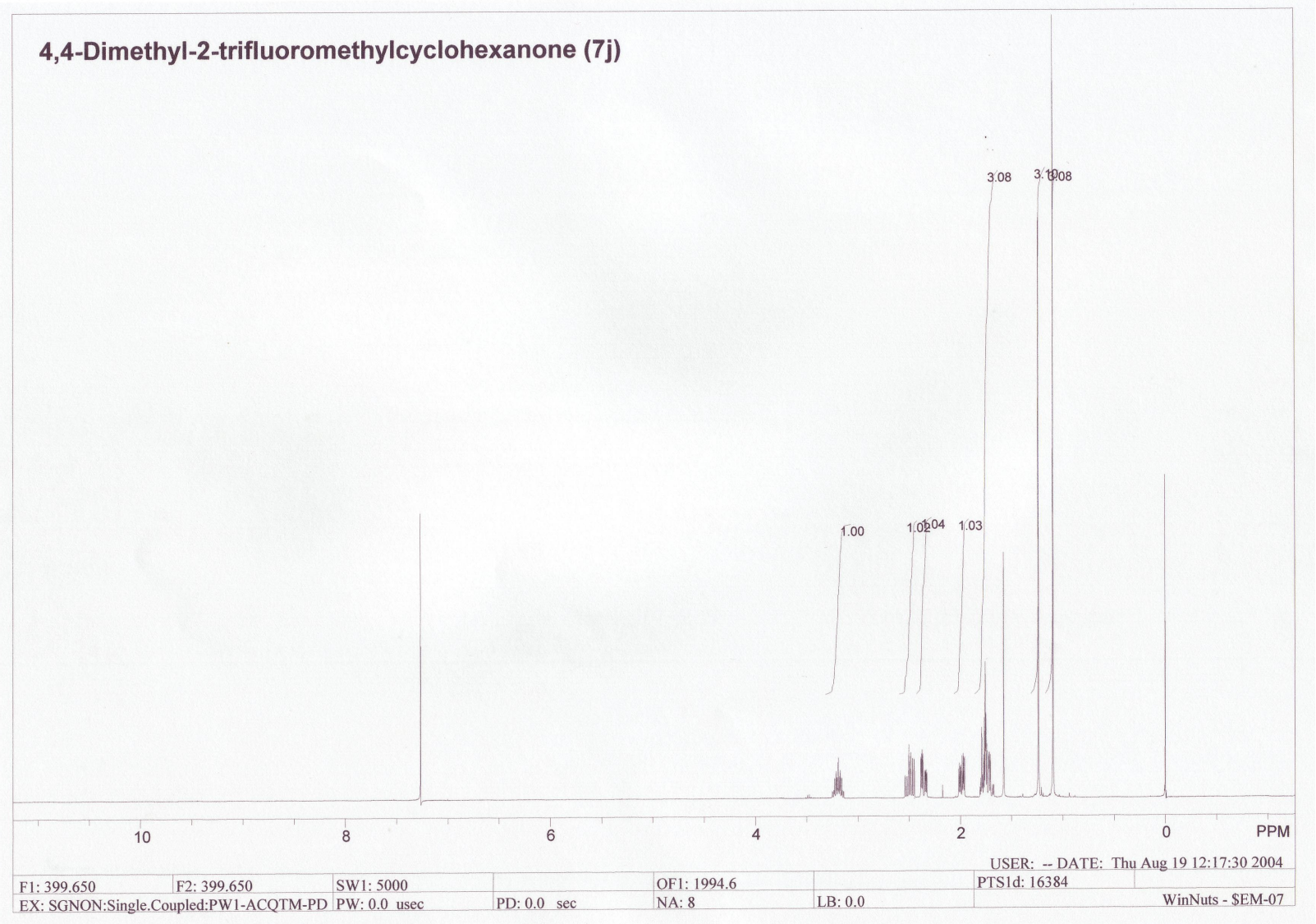
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1.04
1.03
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6
4
2
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