Formation of Enamides via Palladium(II)-Catalyzed Vinyl Transfer from Vinyl Ethers to Nitrogen Nucleophiles

Jodie L. Brice, James E. Meerdink, and Shannon S. Stahl*

University of Wisconsin – Madison
1101 University Ave.
Madison, WI 53706

Email: stahl@chem.wisc.edu

Supporting Information

General Considerations.

All commercially available compounds were used as received, and all were purchased from Aldrich except DIPHOS and $Pd(OCOCF_3)_2$ (Strem), $Pd(OAc)_2$ and $PdCl_2$ (DuPont), $HgSO_4$ (Mallinckrodt Chemical Works), and $HgCl_2$ (Allied Chemical).

^1H, ^{13}C, and ^{19}F NMR spectra were recorded on Bruker AC-300 MHz spectrometers, and $CDCl_3$ was purchased from Cambridge Isotope Laboratories, Inc. The chemical shifts (δ) are given in parts per million relative to internal TMS (0 ppm for ^1H), $CDCl_3$ (77.2 ppm for ^{13}C), and internal (capillary) CF_3CO_2H (-76.5 ppm for ^{19}F).

Flash chromatography was performed on silica gel 60 (particle size 0.040-0.063mm, 230-400 mesh ASTM, purchased from EMD) with hexanes/diethyl ether or methylene chloride.

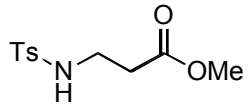
(DPP)$Pd(OCOCF_3)_2$ was prepared by a literature procedure,[1] and (DPP)$Pd(OAc)_2$, (Phen)$Pd(OCOCF_3)_2$, (TMEDA)$Pd(OCOCF_3)_2$, $(PPh_3)_2Pd(OCOCF_3)_2$, and (DIPHOS)$Pd(OCOCF_3)_2$ were prepared analogously. (DPP)$PdCl_2$ was prepared by a known method.[2]

General procedure for catalyst screening.

To a disposable culture tube were added 2-oxazolidinone (0.19 mmol, 16.8 mg), catalyst (9.5 μmol), and 1,3,5-tri-*tert*-butylbenzene (0.063 mmol, 15.8 mg) internal standard. The reaction was started by adding butyl vinyl ether (BVE) (1.93 mmol, 250 μL) and immediately heating to 75 °C. The culture tube was left open to air, and the contents were vortexed for 3 minutes. The reactions were halted by removing BVE under vacuum and cooling to –78 °C within 45 seconds. Product yield was evaluated by ^{1}H NMR spectroscopy relative to internal standard.

Synthesis of N-tosyl-N-vinyl-β-alanine methyl ester.

The amine functionality of β-alanine was tosylated with TsCl according to literature procedure, 48%.[3] Subsequent methylation[4] to the ester by TMS-CHN_2 furnished quantitative yield of this substrate for transfer vinylation. Characterization data agrees with literature.[5]

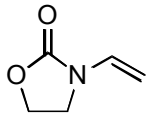


Representative procedure for transfer vinylation.

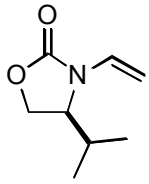
2-Oxazolidinone (5.7 mmol, 500 mg), BVE (57.4 mmol, 7.43 mL), and (DPP)Pd($OCOCF_3$)$_2$ (0.28 mmol, 189 mg) were combined in a round bottom flask equipped with a magnetic stir bar. The flask was capped by a rubber septum with an 18 gauge needle punctured through it. The reaction was stirred at 75 °C in an oil bath and monitored for completion by ^{1}H NMR aliquots. Upon completion, the reaction mixture was allowed to cool and loaded directly onto a chromatography column packed with silica (elution solvent = hexanes/ether 1:9).

Product Characterization Data.

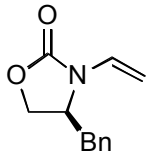
3-vinyl-2-oxazolidinone. 91%, light yellow oil. Characterization data matches literature report.[6]



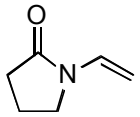
(S)-4-isopropyl-3-vinyl-2-oxazolidinone. Column chromatography (hexanes/ether 25:75) yielded a off-white solid, 95%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78 (dd, J = 16.2, 9.3 Hz, 1H), δ 4.49-4.08 (m, 4H), δ 4.05 (dt, J = 4.8, 3.6 Hz, 1H), δ 2.45 (septet d, J = 6.9, 3.3 Hz, 1H), δ 0.94 (d, J = 6.9 Hz, 3H), δ 0.85 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.8, 129.0, 94.2, 63.1, 58.1, 26.0, 18.0, 14.0. HRMS: m/z (EI) calculated $[M]^{\bullet+}$ = 155.0946, measured 155.0942. $[\alpha]_D^{25}$ = +51.5 (c = 1.1, CH_2Cl_2) .



(S)-4-benzyl-3-vinyl-2-oxazolidinone. Column chromatography (hexanes/ether 25:75) yielded a light yellow oil, 92%. Characterization data matches literature report.[7]



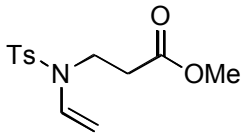
1-Vinyl-2-pyrrolidinone. Column chromatography (hexanes/ether 1:9) yielded a pale yellow oil, 89%. ^{1}H NMR spectra matches known reports for commercially available compound.[8]



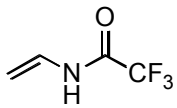
N-methyl-N-vinyl-p-toluenesulfonamide.[9] Column chromatography (CH_2Cl_2) yielded a white crystalline solid, 64%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 6.75 Hz, 2H), δ 7.31 (d, J = 6.25 Hz, 2H), δ 7.00 (dd, J = 15.8, 9.0 Hz, 1H), δ 4.33 (d, J = 9.0 Hz, 1H), δ 4.18 (d, J = 15.5 Hx, 1H), δ 2.86 (s, 3H), δ 2.43 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$)

δ 143.6, 134.6, 129.6, 126.8, 92.9, 31.1, 21.3. HRMS: m/z (ESI) calculated $[M+Na+MeOH]^+$ = 266.0827, measured = 266.0835.

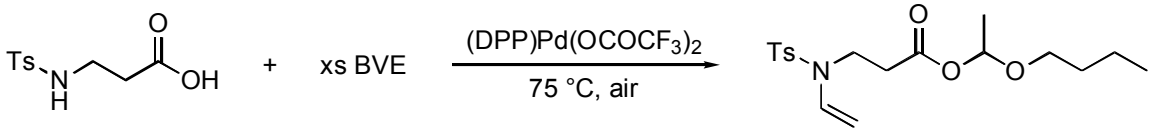
N-tosyl-N-vinyl-β-alanine methyl ester. Column chromatography (CH_2Cl_2) yielded a pale yellow viscous oil, 87%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 6.6 Hz, 2H), δ 7.31 (d, J = 8.7 Hz, 2H), δ 6.88 (dd, J = 15.9, 9.3 Hz, 1H), δ 4.36 (d, J = 9.6 Hz, 1H), δ 4.28 (d, J = 15.9 Hz, 1H), δ 3.69 (s, 3H), δ 3.64 (m, 2H), δ 2.65 (m, 2H), δ 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 171.6, 144.2, 136.0, 131.8, 130.0, 127.0, 92.9, 52.0, 40.4, 32.0, 21.7. HRMS: m/z (ESI) calculated $[MNa]^+$ = 306.0776, measured = 306.0763.



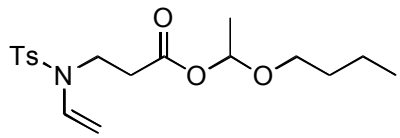
N-vinyl-2,2,2,-trifluoroacetamide.[10] Due to difficulties encountered during purification of N-vinyl trifluoroacetamide, ethyl vinyl ether was used in place of butyl vinyl ether and the reaction was run at room temperature. Column chromatography (CH_2Cl_2) yielded a white solid, 76%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (br., 1H), δ 6.89 (ddd, J = 18.9, 15.6, 9.0 Hz, 1H), δ 5.01 (d, J = 9.0 Hz, 1H), δ 4.79 (d, J = 9.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 155.0 (q, J = 38.2 Hz), δ 126.4 (s), δ 115.8 (q, J = 287 Hz), δ 102.0 (s). ^{19}F NMR (282 MHz, $CDCl_3$) δ 74.7. HRMS: m/z (EI) calculated $[M]^{\bullet+}$ = 139.0245, measured = 139.0247.



Incompatibility of the described transfer vinylation conditions with the carboxylic acid functionality.



Column chromatography (CH_2Cl_2) yielded a pale yellow oil, 12%. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 6.9 Hz, 2H), δ 7.31 (d, J = 7.8 Hz, 2H), δ 6.88 (dd, J = 16.2, 9.3 Hz, 1H), δ 5.91 (q, J = 5.4 Hz, 1H), δ 4.37 (d, J = 9.0 Hz, 1H), δ 4.28 (d, J = 15.6 Hz, 1H), δ 3.66-3.45 (m, 4H), δ 2.66 (t, J = 6.6 Hz, 2H), δ 2.43 (s, 3H), δ 1.55 (m, 2H), δ 1.39 (d, J = 5.1 Hz, 3H), δ 1.36 (m, 2H), δ 0.92 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 170.5, 143.8, 135.6, 131.4, 129.7, 126.7, 96.8, 92.6, 68.9, 39.9, 31.9, 31.3, 21.3, 20.5, 18.9, 13.6. HRMS: m/z (ESI) calculated $[MNa]^+$ = 392.1508, measured = 392.1522.



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(S)-4-isopropyl-3-vinyl-2-oxazolidinone
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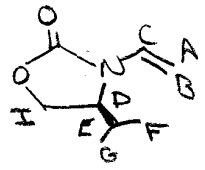

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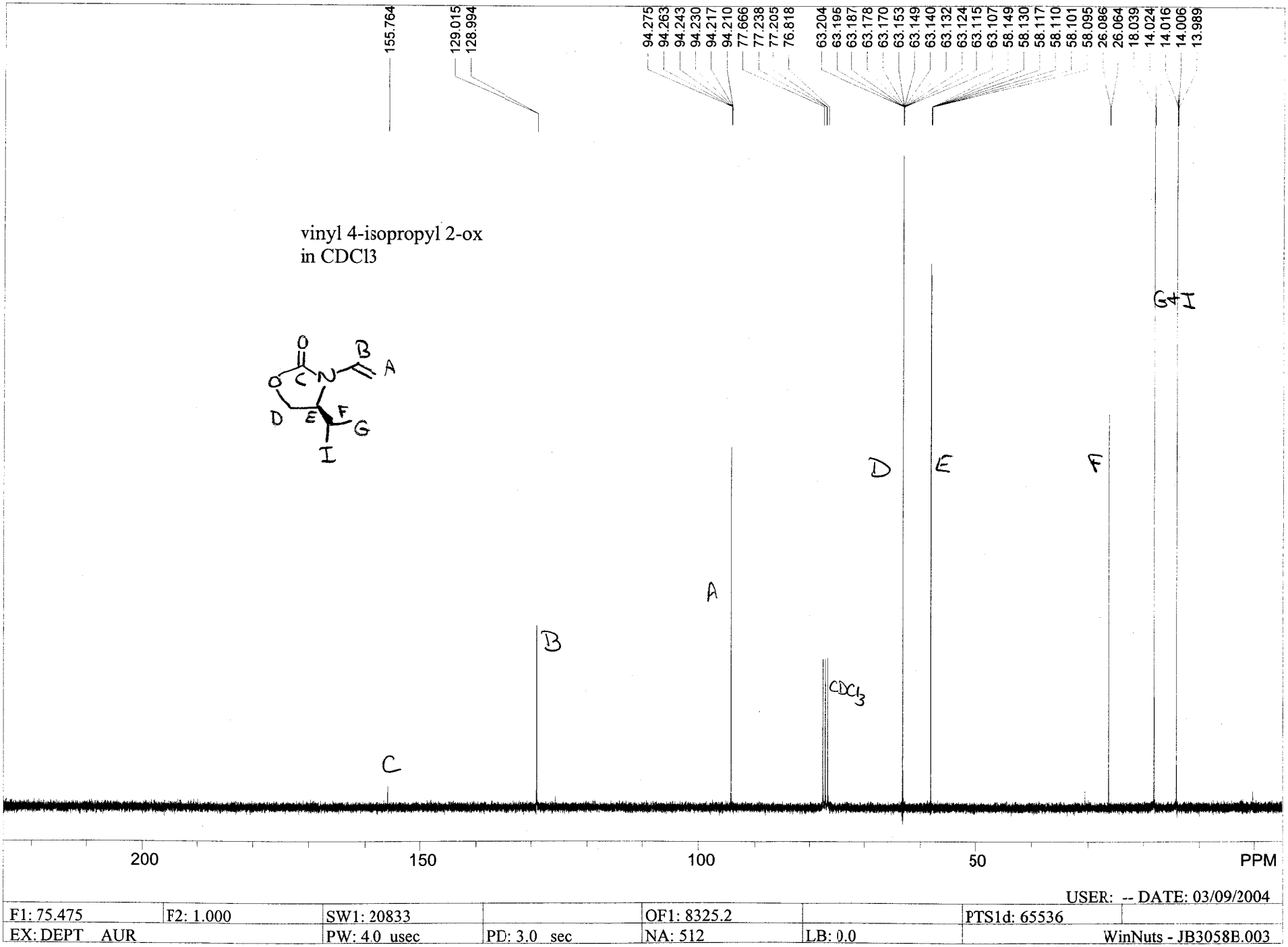

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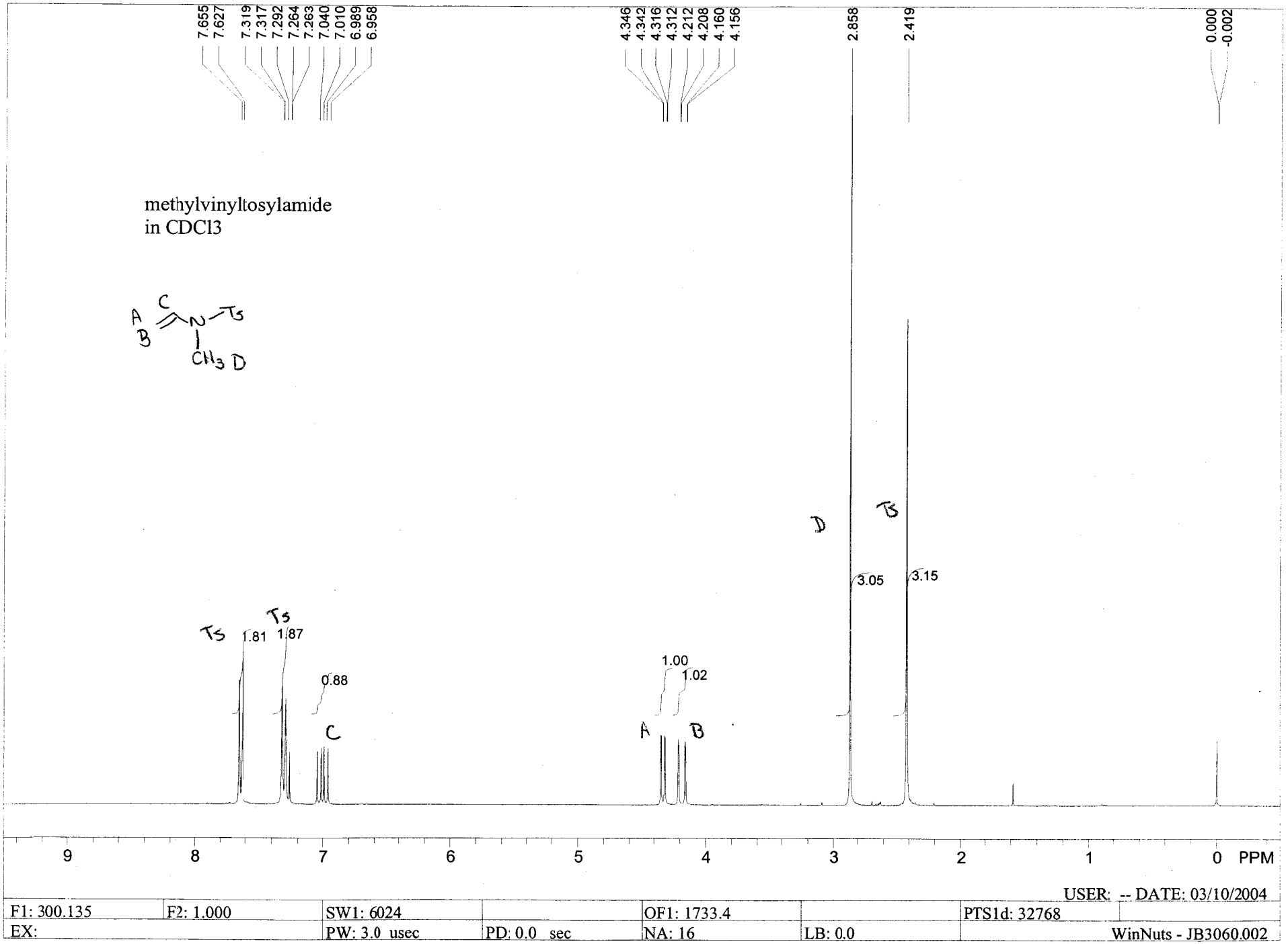

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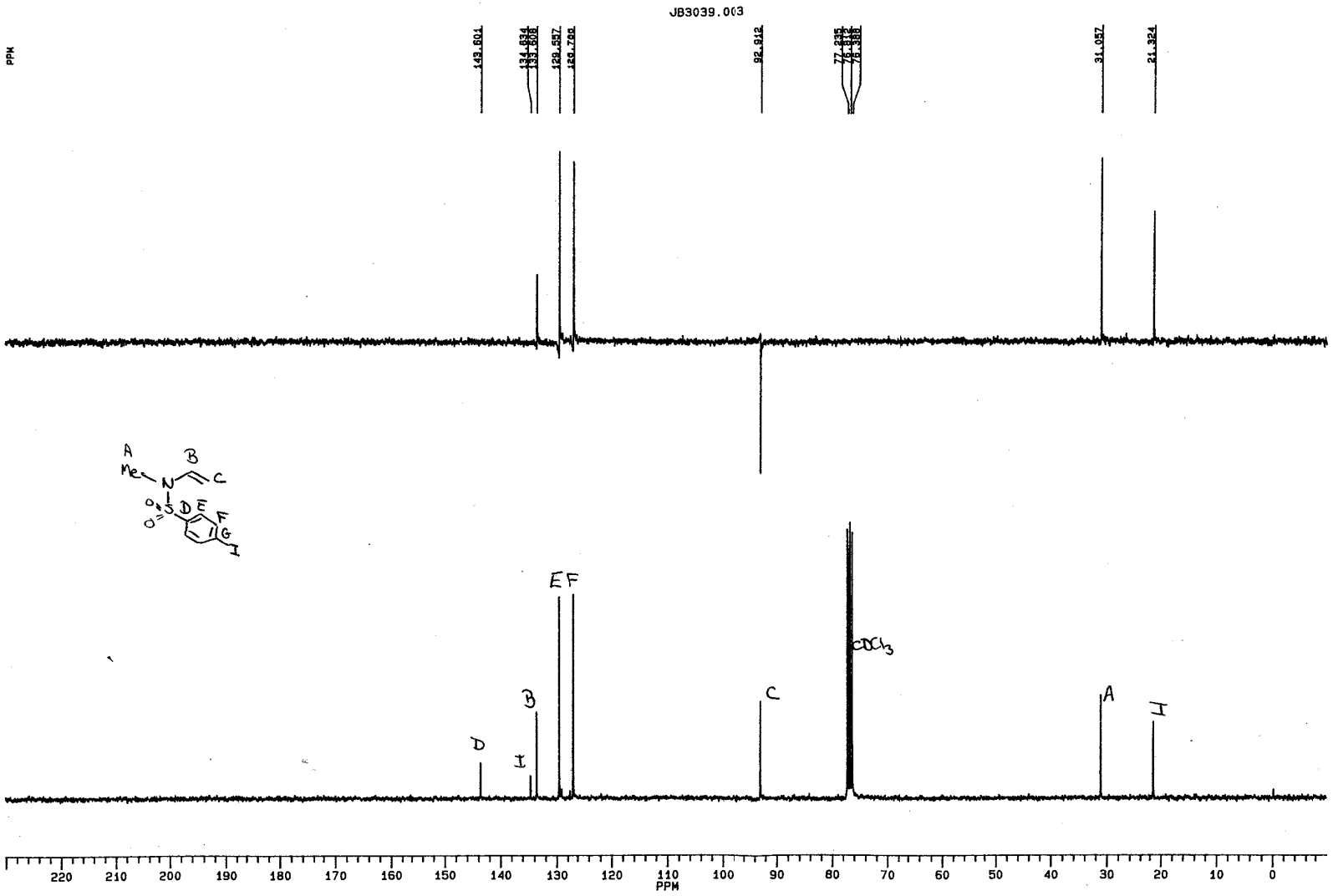

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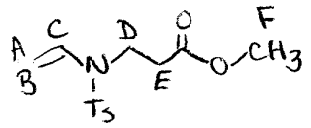
in CDCl3



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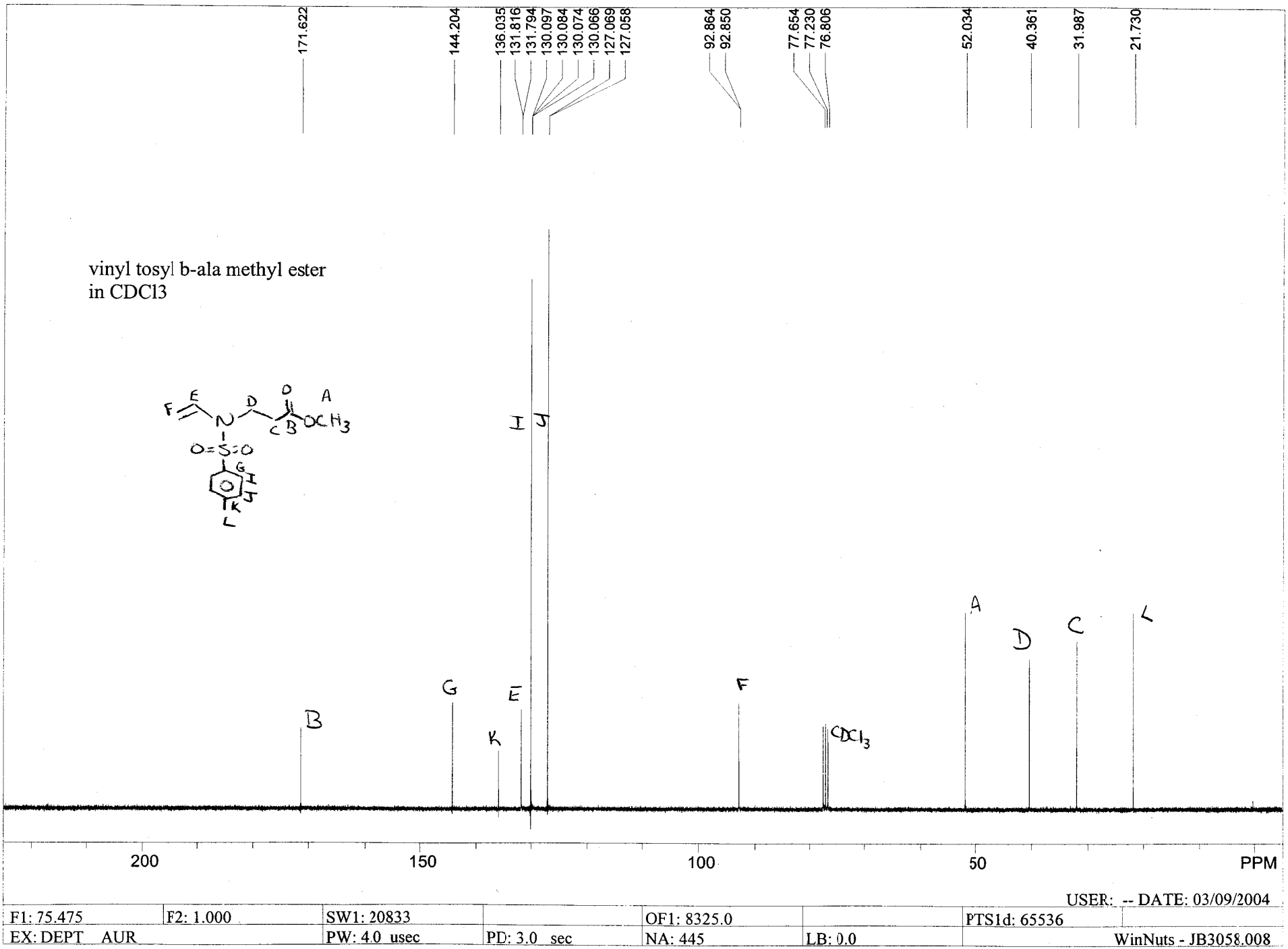

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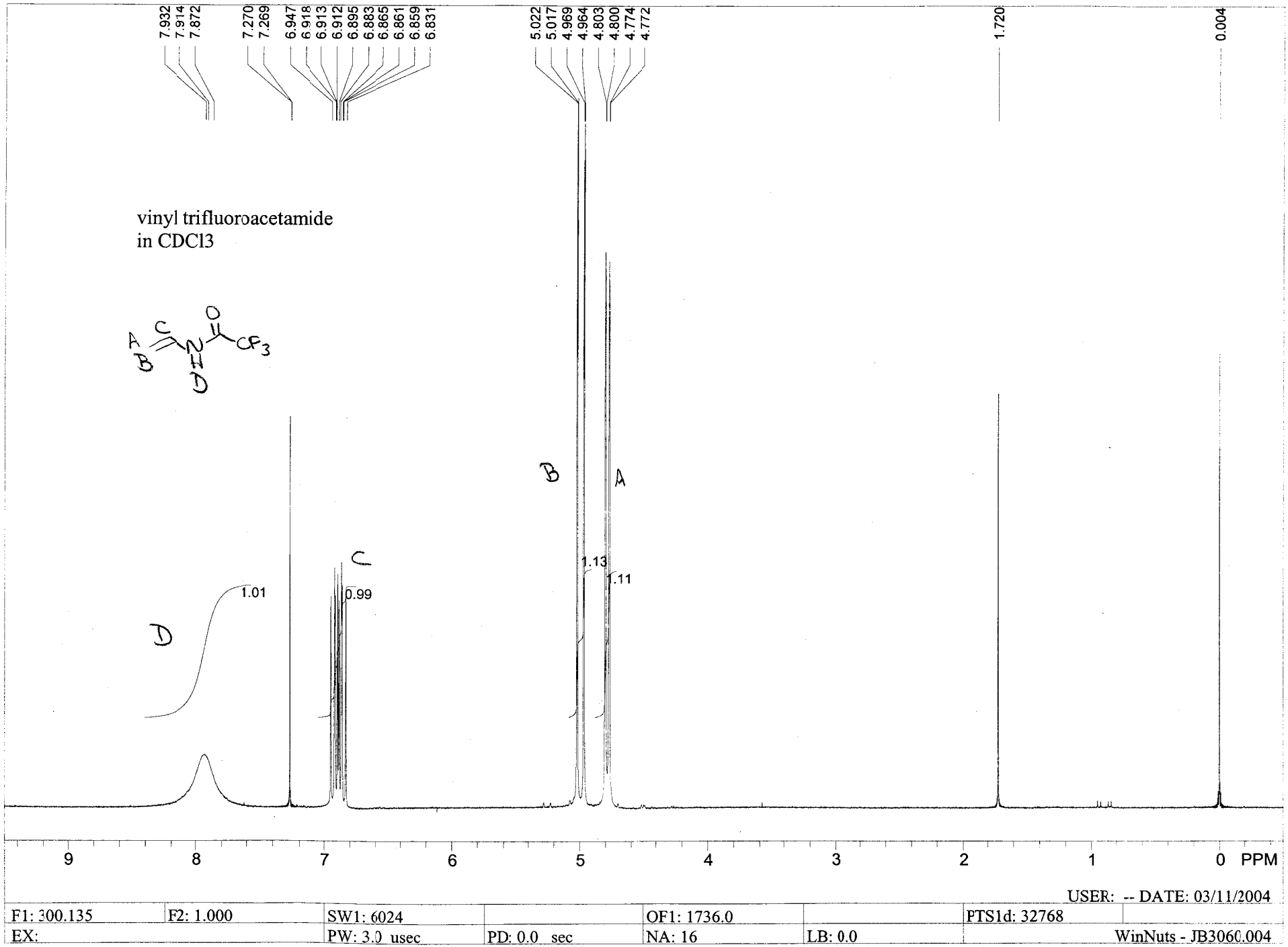

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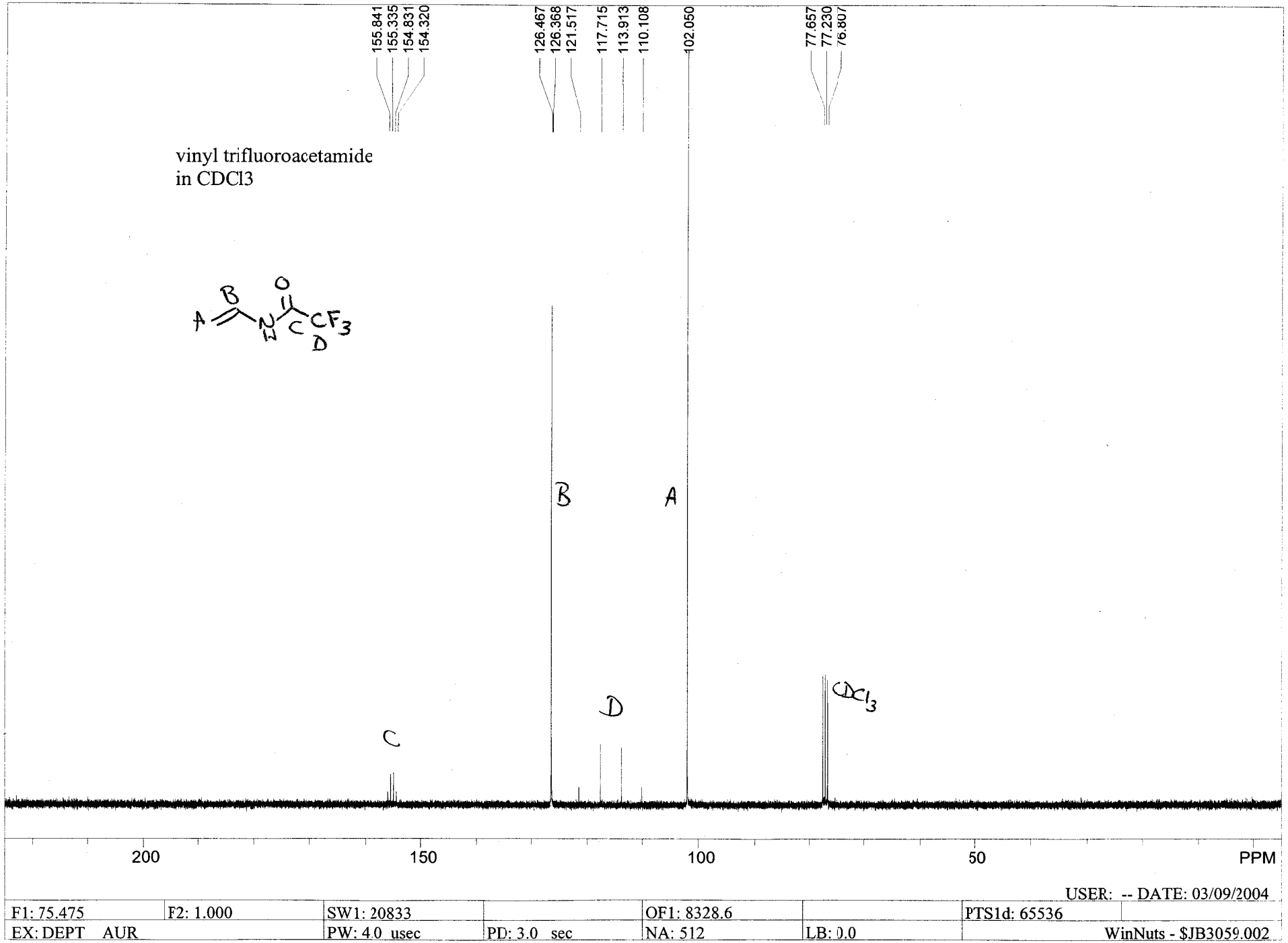

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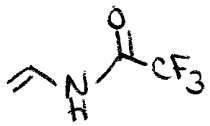
vinyl trifluoroacetamide
TFA std.
in CDCl3



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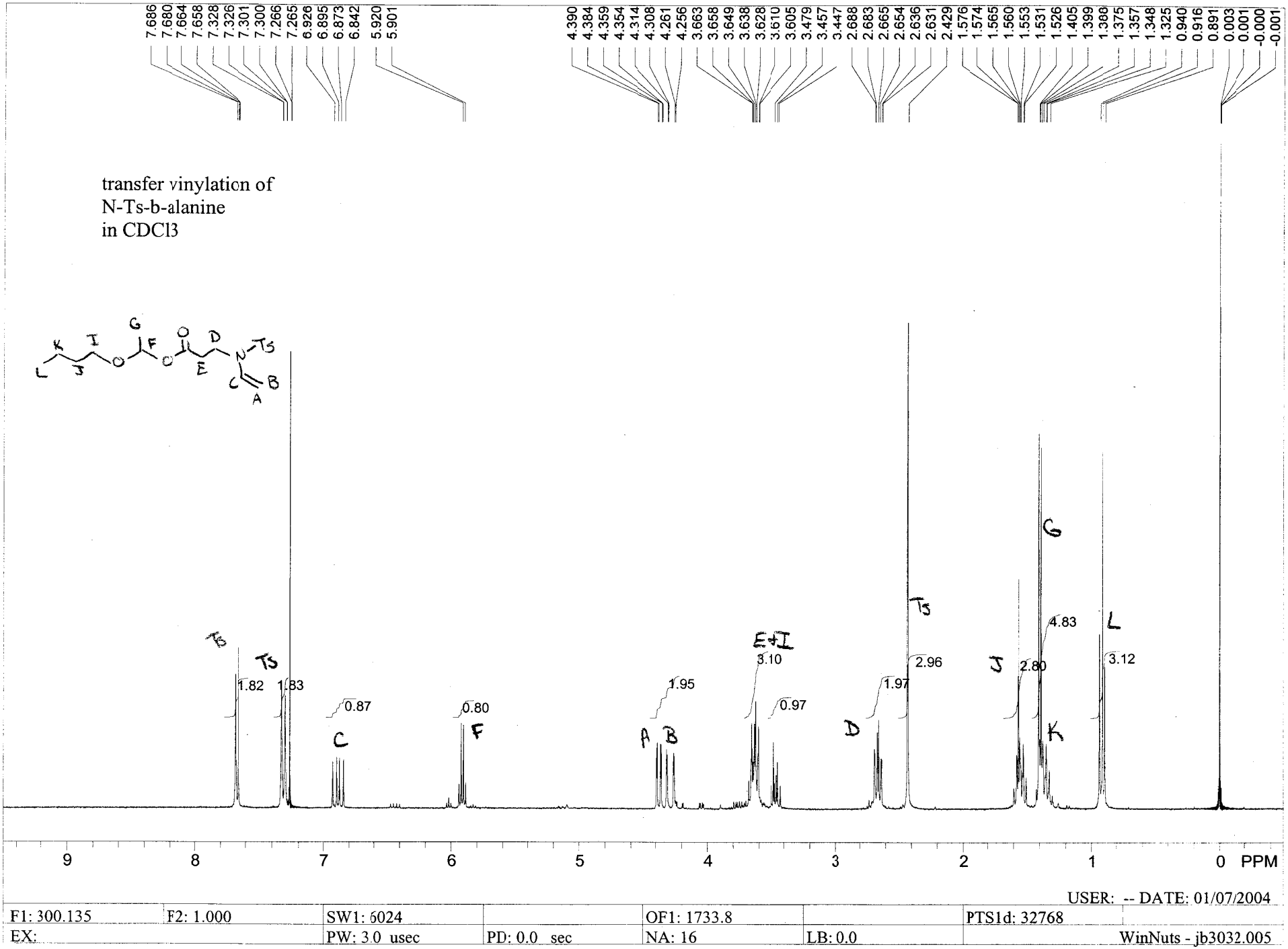

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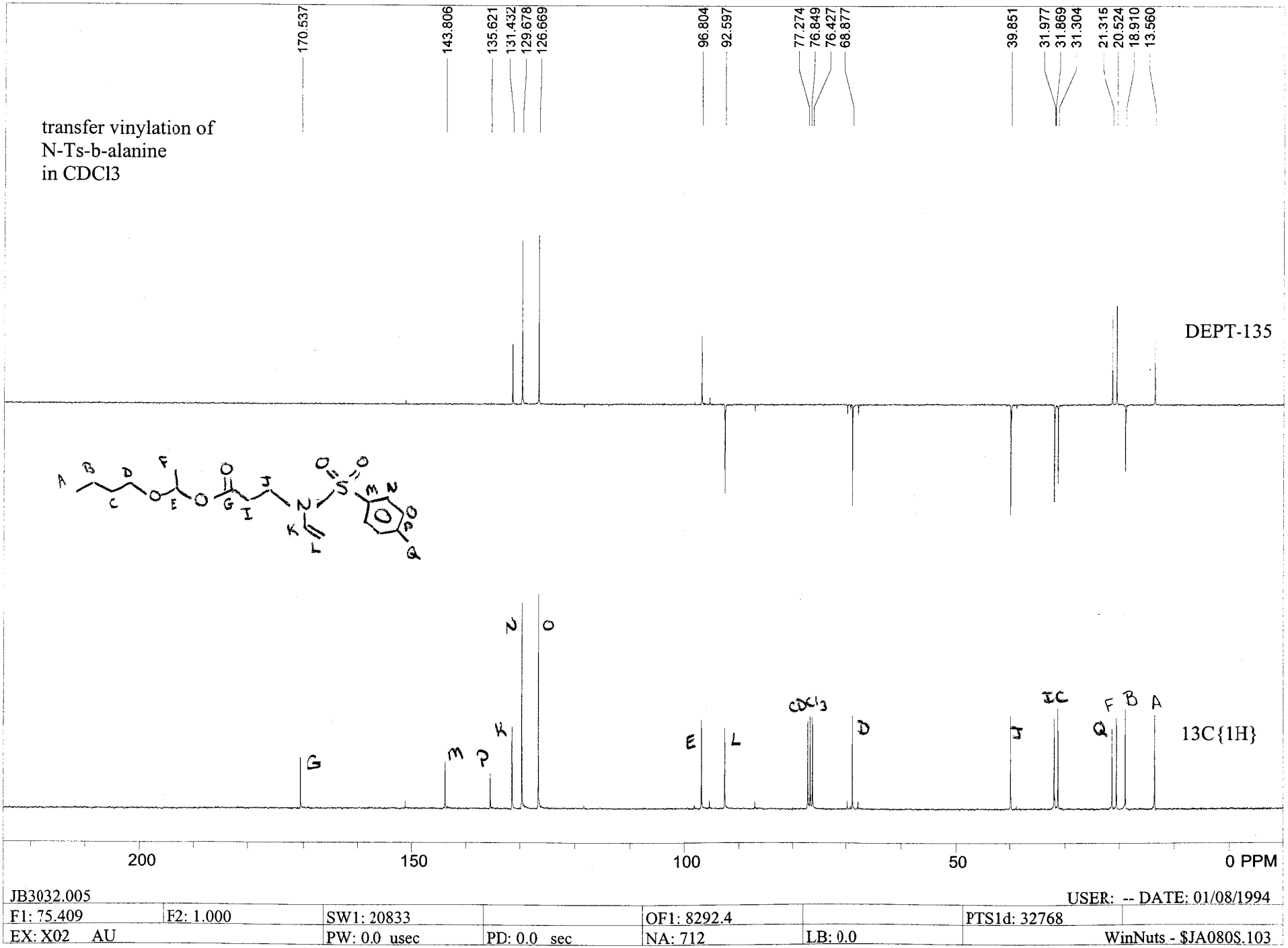

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