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Experimental Procedures

2-(*o*-Nitrobenzenesulfonyl)-2-azabicyclo[2.2.1]hept-5-en-3-one (3a)

To a solution of 2-azabicyclo[2.2.1]hept-5-en-3-one (**2**) (1.09 g, 10 mmol) in THF (31 ml) at -78 °C was added BuLi-n-hexane solution (1.56 M) (6.41 ml, 10 mmol of BuLi) under Ar atmosphere with stirring. The mixture was stirred for 30 min at the same temperature. To the resulting solution was added a solution of *o*-nitrobenzenesulfonyl chloride (2.44 g, 11 mmol) in THF (4 ml) during the period of 1 h at -75— -70°C with stirring. After being stirred for 2 h at -75°C, the reaction mixture was neutralized with AcOH (0.12 g, 2 mmol). The mixture was diluted with toluene (50 ml), washed with 10% brine (50 ml), and dried over $MgSO_4$. The solvent was removed *in vacuo* to give 2.44 g (83%) of **3a**, mp 94°C (from AcOEt—hexane); exact mass (EI) calcd for $(C_{12}H_{10}N_2O_5S+H)^+$ 295.0389, found 295.0353.

2-(Diphenylphosphoryl)-2-azabicyclo[2.2.1]hept-5-en-3-one (3b)

To a solution of **2** (1.05 g, 9.6 mmol) in THF (20 ml) was added BuLi-n-hexane solution (1.56 M) (6.73 ml, 10.5 mmol of BuLi) at -78°C with stirring. The mixture was stirred for 30 min at the same temperature. The resulting solution was added to a solution of diphenyl chlorophosphate (2.17 ml, 10.5 mmol) in THF (10 ml) with stirring under ice-cooling. The mixture was stirred under ice-cooling for 5 min. To the resulting reaction mixture was added saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc, and the organic layer was dried over $MgSO_4$. After evaporation of the solvent *in vacuo* , the residue was submitted to silica gel column chromatography. Elution with hexane-EtOAc (3:1) afforded a crystalline substance, which was purified by recrystallization from hexane-EtOAc to give 2.12 g (88%) of **3b**, mp 51°C, exact mass (EI) calcd for $(C_{18}H_{16}NO_4P)^+$ 341.0817, found 341.0825.

6-Chloro-9-[*c*-4-(N-*o*-nitrobenzenesulfonyl)carbamoyl-cyclopent-2-en-*r*-1-yl]-9*H*-purine (6)

To a solution of $Pd[P(O^iPr)_3]_4$ (0.1 mmol) prepared from $Pd(OAc)_2$ (22.4 mg, 0.1 mmol) and $P(O^iPr)_3$ (0.148 ml, 0.6 mmol) in THF (5 ml) was added a solution of 6-chloropurine tetrabutylammonium salt (395 mg, 1 mmol) in THF (5 ml) and a solution of **3a** (294 mg, 1 mmol) in THF (5 ml) with stirring at room temperature. The mixture was stirred for 2.5 h at room

temperature. After removal of the solvent *in vacuo*, the residue was submitted to silica gel column chromatography. Elution with $CHCl_3$-*iso*-PrOH-AcOH (10:1:0.1) gave 267 mg (60%) of **6**, mp 212°C (from $CHCl_3$-MeOH), exact mass (EI) calcd for $(C_{17}H_{13}ClN_6O_5S)^+$ 448.0356, found 448.0360.

6-Chloro-9-[*c*-4-(N-diphenylphosphoryl)carbamoyl-cyclopent-2-en-*r*-1-yl]-9*H*-purine (7)

To a suspension of NaH (60% oil dispersion) (22 mg, 0.55 mmol) in N-methylpyrrolidone (NMP) (1 ml) was added a solution of 6-chloropurine (85 mg, 0.55 mmol) in NMP (1 ml) at 0°C with stirring. After being stirred for 1 h at 60°C, to the solution were added a solution of $Pd(OAc)_2$ (11 mg, 0.05 mmol) in THF (0.5 ml), $P(O^iPr)_3$ (0.074 ml, 0.3 mmol), and a solution of **3b** (63 mg, 0.5 mmol) in NMP (1 ml) with stirring under ice-cooling, successively. After being stirred at room temperature for 1 h, the resulting mixture was neutralized with AcOH. After evaporation of the solvent *in vacuo*, the residue was submitted to silica gel column chromatography. Elution with hexane-EtOAc (1:5) afforded 137 mg (55%) of **7**. mp 187°C (from EtOAc); exact mass (EI) calcd for $(C_{23}H_{19}ClN_5O_4P)^+$ 495.0863, found 495.0870.

6-Chloro-2-formylamino-6-Chloro-9-[*c*-4-(N-*o*-nitrobenzenesulfonyl)carbamoylcyclopent-2-en-*r*-1-yl]-9*H*-purine (8)

To a solution of 2-formylamino-6-chloropurine tetrabutylammonium salt (2.63 g, 6.0 mmol) in THF (20 ml) was added $Pd(OAc)_2$ (56.0 mg, 0.25 mmol), and $P(O^iPr)_3$ (360 mg, 1.73 mmol), successively. After being stirred at 50°C for 30 min, to the mixture was added a solution of **3a** (1.47 g, 5.0 mmol) in THF (5 ml) during the period of 2 h at room temperature. After being stirred for 1 h at room temperature, the mixture was neutralized with AcOH, and concentrated *in vacuo* to give a residue, which was submitted to silica gel column chromatography. Elution with $CHCl_3$-MeOH (15:1) afforded 1.36 g (55%) of **8**. mp 218-220°C (dec.) (from $CHCl_3$-MeOH); exact mass (EI) calcd for $(C_{18}H_{14}ClN_7O_6S)^+$ 491.0415, found 491.0420.

6-Chloro-9-[*c*-4-(N-methyl-N-*o*-nitrobenzene-sulfonyl)carbamoylcyclopent-2-en-*r*-1-yl]-9*H*-purine (10)

To a solution of **6** (30 mg, 0.067 mmol) in THF-CH_2Cl_2 (1:1) (2 ml) was added MeOH (8.0 μl, 0.20 mmol), PPh_3(53 mg, 0.20 mmol), and diethyl azodicarboxylate (90%, 0.036 ml, 0.21 mmol) under Ar atmosphere with stirring at room temperature. After being stirred

for 30 min, the solvent was evaporated *in vacuo* to give a crystalline residue, which was submitted to silica gel column chromatography. Elution with hexane-EtOAc (1:2) gave 30 mg (97%) of **10**. mp 215-217°C (from hexane-AcOEt-$CHCl_3$): ^{1}HNMR ($CDCl_3$, 300 MH_Z) δ 2.30 (dt, J=3.71, 14.56 Hz, 1H), 2.99 (dt, J=9.07, 14.56 Hz, 1H), 4.20-4.27 (m, 1H), 5.85-5.93 (m, 1H), 6.08 (dt, J=2.20, 5.77 Hz, 1H), 6.30 (dt, J=2.20, 5.22 Hz, 1H), 7.74-7.88 (m, 3H), 8.09 (s, 1H), 8.34-8.41 (m, 1H), 8.73 (s, 1H); exact mass (EI) calcd for $(C_{18}H_{15}ClN_6O_5S)^+$ 462.0513, found 462.0532.

6-Chloro-9-(*c*-4-hydroxymethylcyclopent-2-en-*r*-1-yl)-9*H*-purine (11)

To a solution of **10** (30 mg, 0.065 mmol) in MeOH (2 ml) was added $NaBH_4$ (25 mg, 0.66 mmol) under ice-cooling with stirring. The mixture was stirred at room temperature for 5 min, and neutralized with AcOH. After evaporation of the solvent, the residue was submitted to silica gel column chromatography. Elution with AcOEt gave 15 mg (92%) of **11** and 13 mg (93%) of **12**. **11**: ^{1}HNMR ($CDCl_3$, 300 MH_Z) δ 1.96 (dt, J=5.22, 14.29 Hz, 1H), 2.91 (dt, J=9.20, 14.29 Hz, 1H), 3.10-3.20 (m, 1H), 3.74 (dd, J=4.26, 10.58 Hz, 1H), 3.89 (dd, J=4.26, 10.58 Hz, 1H), 5.77-5.86 (m, 1H), 5.92 (dt, J=2.27, 5.77 Hz, 1H), 6.25 (dt, J=2.06, 5.77 Hz, 1H), 8.34 (s, 1H), 8.75 (s, 1H). **12**: ^{1}HNMR ($CDCl_3$, 300 MH_Z) δ 2.80 (d, J=5.22 Hz, 1H), 5.19-5.29 (m, 1H), 7.72-7.81 (m, 2H), 7.84-7.93 (m, 1H), 8.11-8.19 (m, 1H).

2-Amino-6-chloro-9-(*c*-4-hydroxymethylcyclopent-2-en-*r*-1-yl)-9*H*-purine (15)

To a suspension of NaH (60% oil dispersion)(0.44 g, 11 mmol) in THF (50 ml) was added **8** (2.46 g, 5.0 mmol) portionwise under ice-cooling with stirring. After being stirred with ice-cooling for 1 h, to the mixture was added di-*tert*-butyl dicarbonate (2.18 g, 10.0 mmol). The resulting mixture was stirred for 2 h at room temperature, and then stirred for 3 h at 50°C. After cooling, methyl iodide (7.1 g, 50 mmol) was added to the mixture. The reaction mixture was stirred overnight at room temperature, and poured into water. The resulting mixture was extracted with AcOEt. The organic layer was washed with saturated brine, dried over anhydrous $MgSO_4$, and condensed *in vacuo* to give 2.90 g of **13**. Without further purification, the crude **13** was used for the next reaction. To a solution of crude **13** in MeOH (100 ml) was added $NaBH_4$ (0.19 g, 5.0 mmol) portionwise with stirring at -20°C. During this period, the internal temperature was kept below 0°C. The mixture was then stirred at room temperature for 8 h. After the reaction mixture was neutralized with 5% H_2SO_4, the solvent was evaporated off *in vacuo*. To the residue was added

water. The mixture was extracted with AcOEt. The extract was dried over $MgSO_4$, and condensed *in vacuo* to give 2.8 g of **14.** Without further purification, the crude **14** was used for the next reaction. The crude **14** was dissolved in 90% aqueous AcOH (10 ml). The solution was heated at 50°C for 8 h. After removal of the solvent, the residue was submitted to silica gel column chromatography. Elution with $CHCl_3$-MeOH (40:1) afforded 0.96 g (72% from **8**) of **15**. mp 160-162°C (lit.[2a] mp 145-147°C for $C_{11}H_{12}ClN_5O \cdot 3/4\ H_2O$); ^{1}HNMR (DMSO-$d_6$, 300 MHz) δ 1.88 (dt, J=13.7, 5.5 Hz, 1H), 2.62 (dt, J=13.7, 8.8 Hz, 1H), 2.87 (m, 1H), 3.44 (m, 2H), 4.78 (t, J=5.2Hz, 1H), 5.44 (m, 1H), 5.89 (m, 1H), 6.13 (m, 1H), 6.86 (brs, 2H), 7.38 (d, J=8.0 Hz, 2H), 7.78 (d, J=8.0 Hz, 2H), 8.02 (s, 1H); ^{13}CNMR (DMSO-d_6, 75 MHz) δ 160.0, 154.0, 149.7, 141.6, 139.2, 129.6, 123.9, 64.1, 59.5, 48.1, 34.3.

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chiku NBS-ABH

exp1 stdih

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tof	600.0	wbs	
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in	n		
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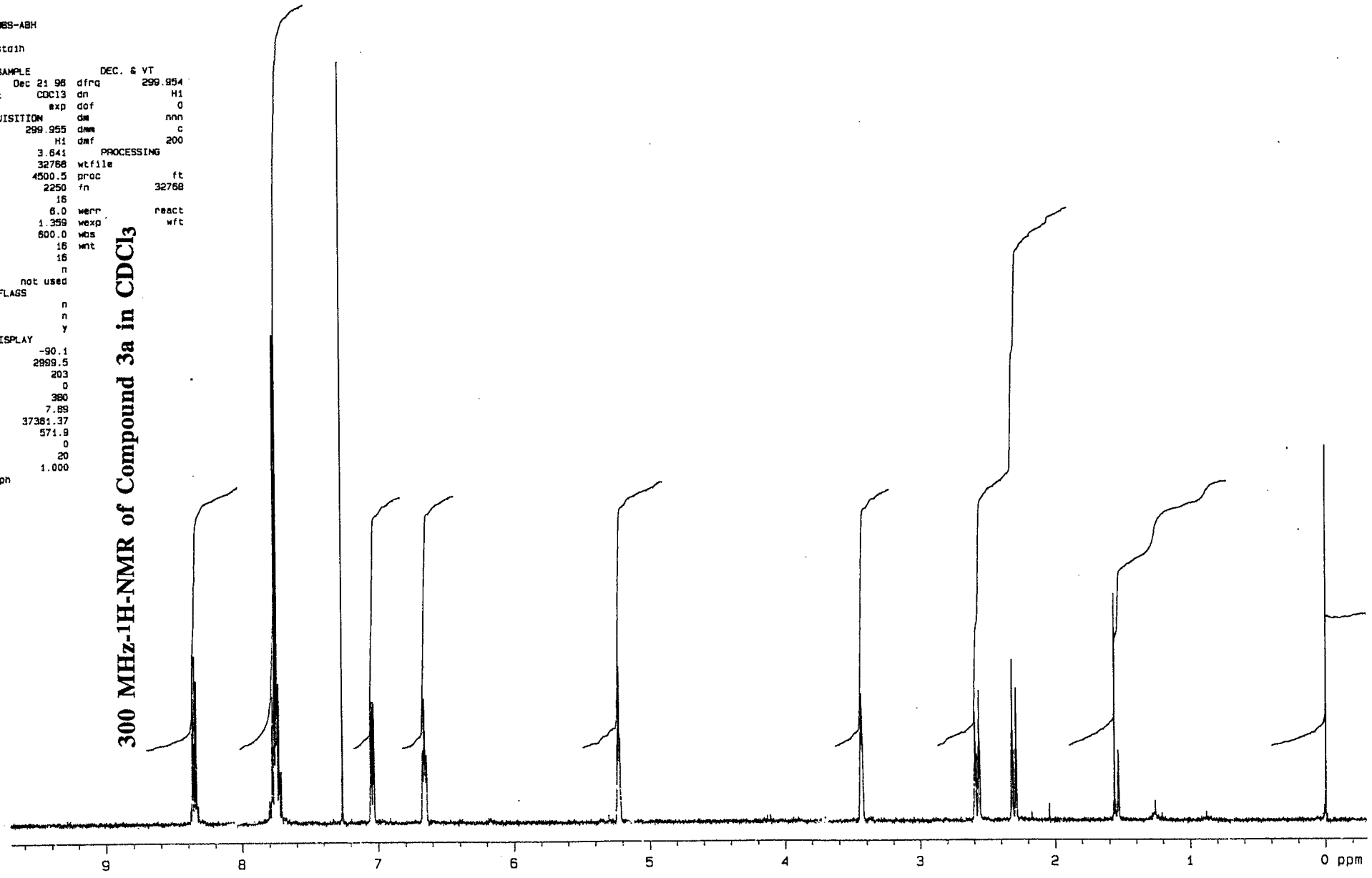
300 MHz-^{1}H-NMR of Compound 3a in $CDCl_3$



N-diphenylphosphino ABH

expl stdin

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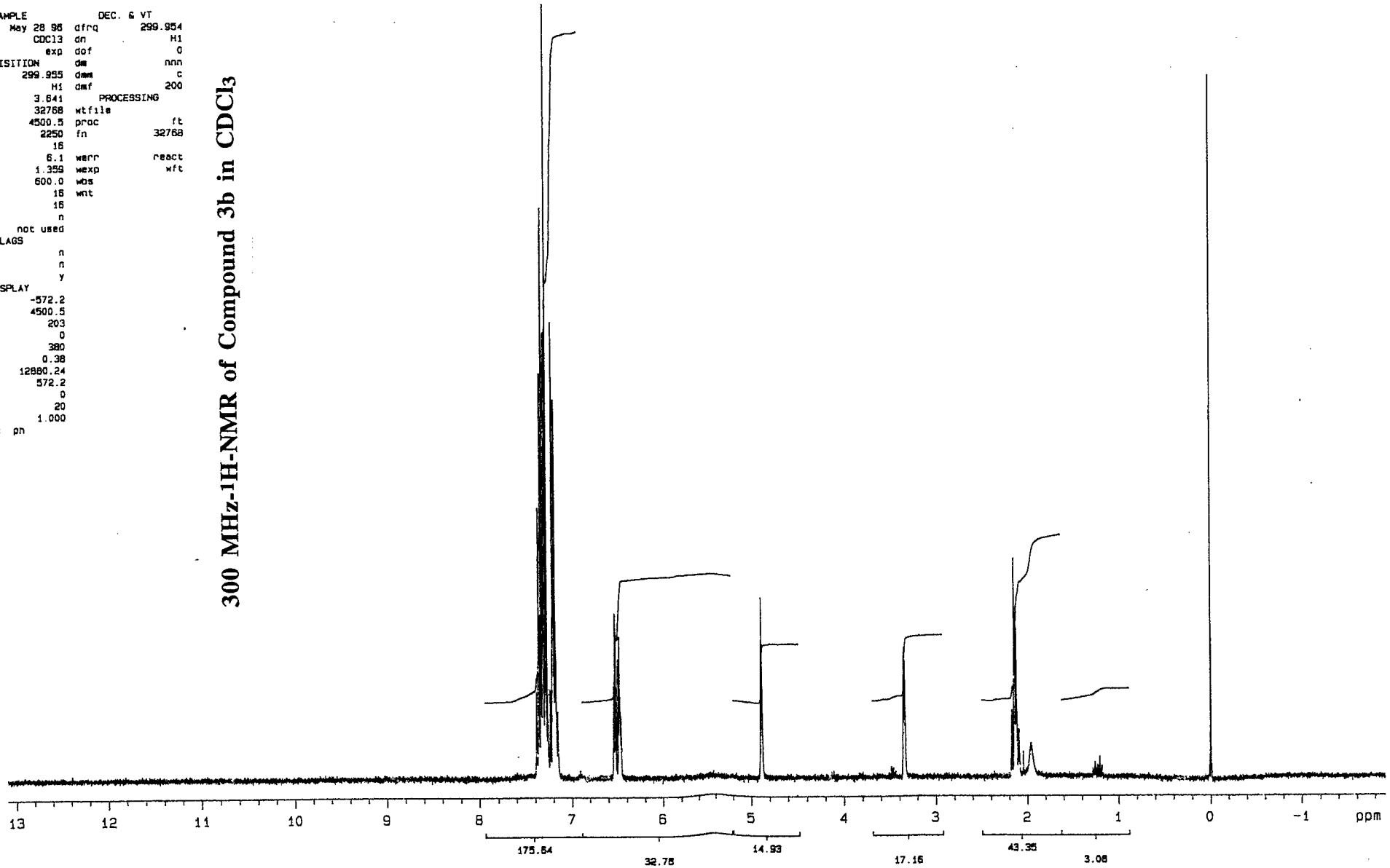
nm cdc pn			

300 MHz-^{1}H-NMR of Compound 3b in $CDCl_3$



STANDARD 1H OBSERVE

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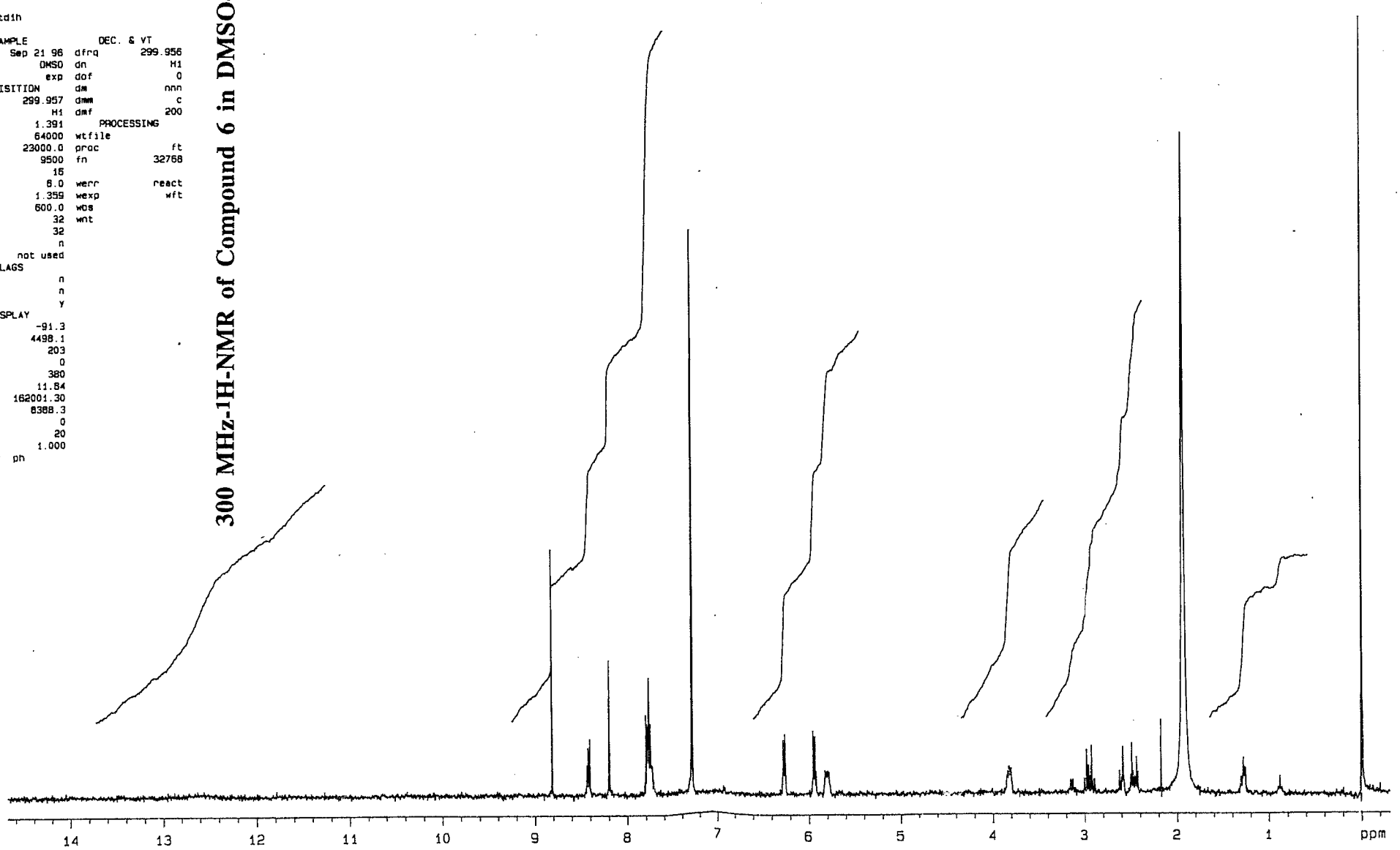
nm cdc ph

300 MHz-^{1}H-NMR of Compound 6 in DMSO-d$_6$



chiku phosphine-4

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nm cdc ph			

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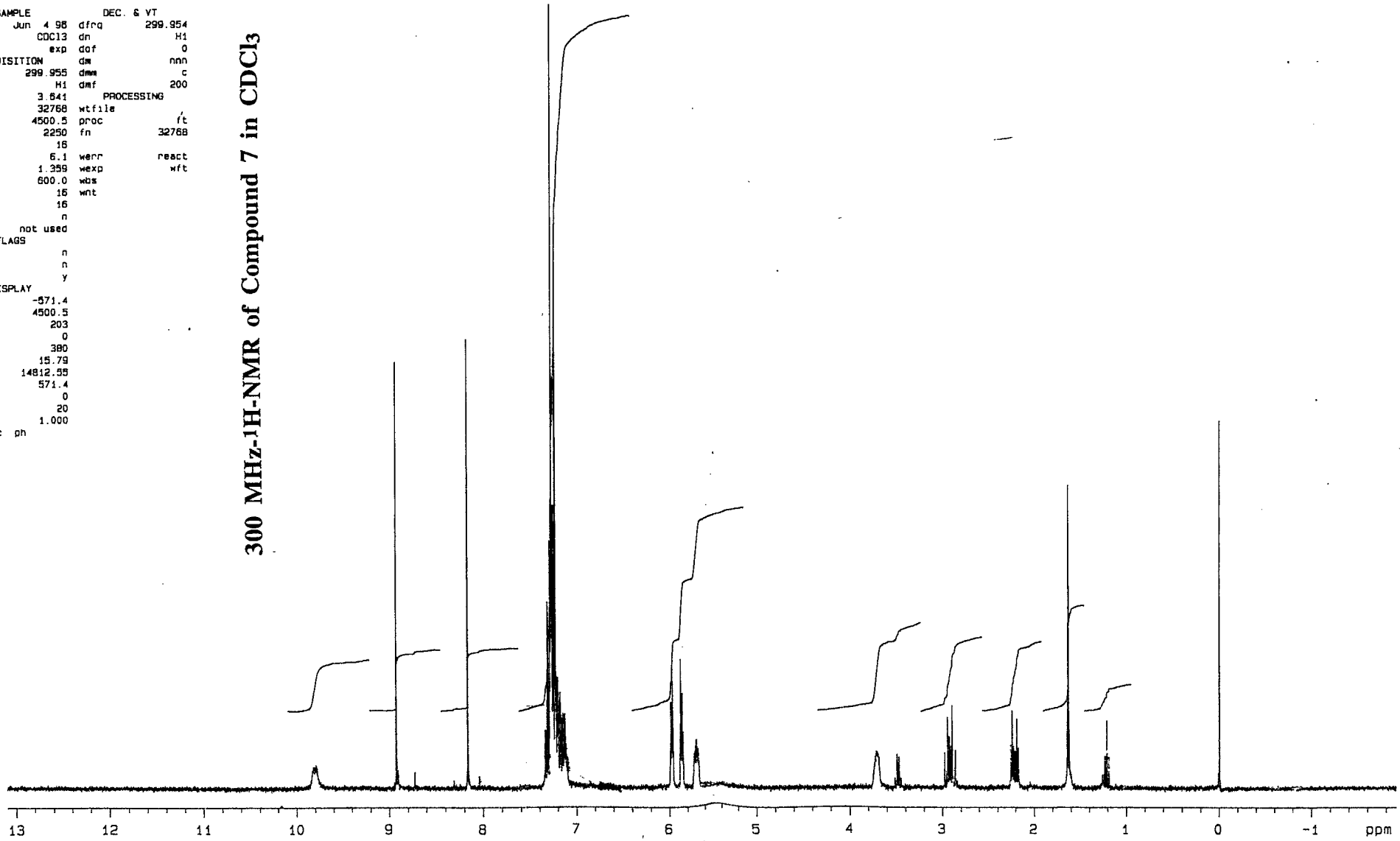
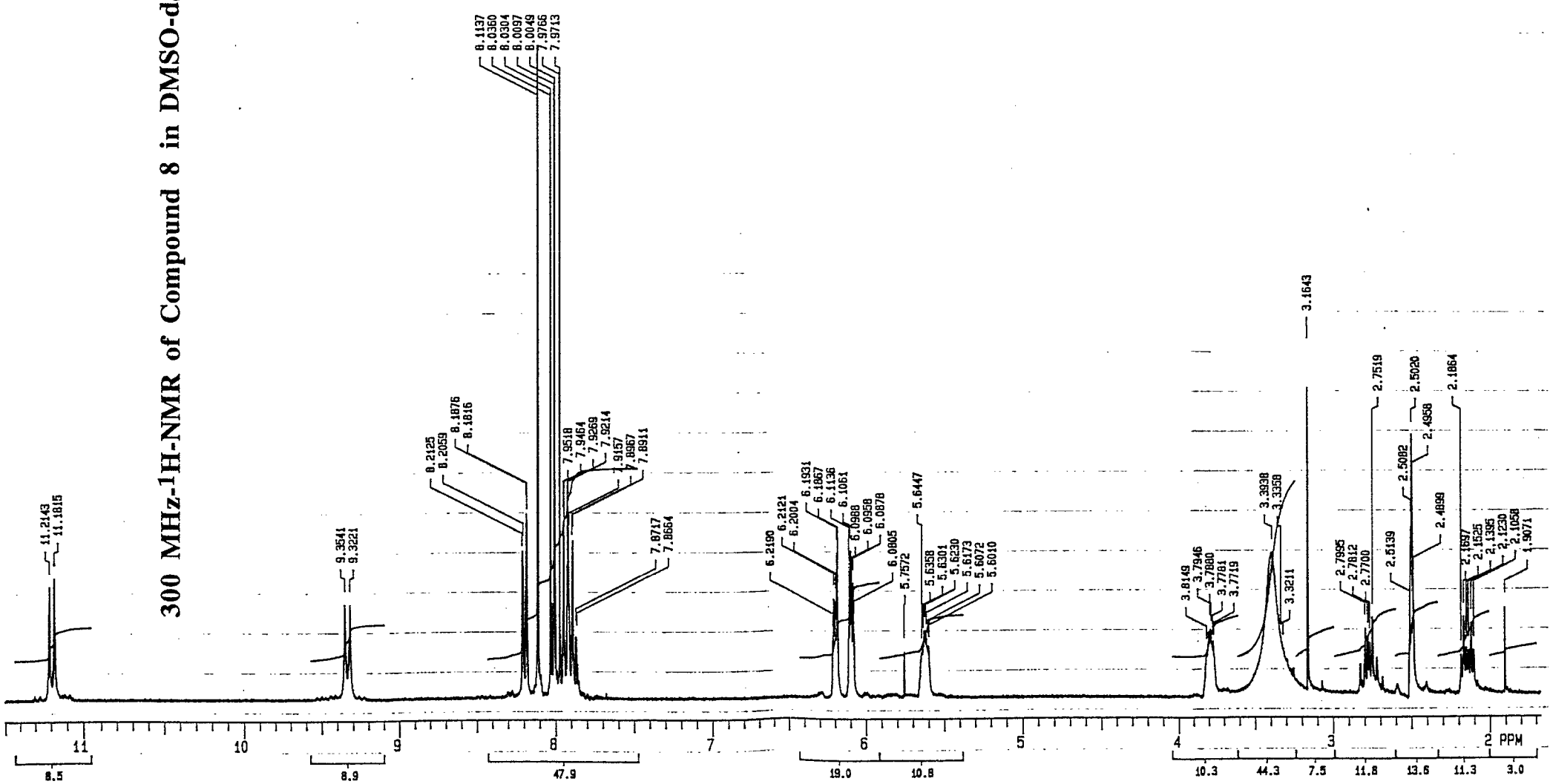


9

300 MHz-^{1}H-NMR of Compound 8 in DMSO-d_6



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Acq. Time	2.993 sec	Delay	0.222 sec	Modulation Mode	C	Freq.	200 Hz	Width	2948.9 Hz/ppm	Start	502.2 Hz/ppm			Temp.	°C
Pulse Width	9.6 μsec	Transients	16	Pulse Width	μsec	Power Mode	1.0	Reference						Solvent	DMSO

SAMPLE

EQ97241
FACP - ABH-NBS
MAIN PRODUCT

Number
File H
Date 01-31-95
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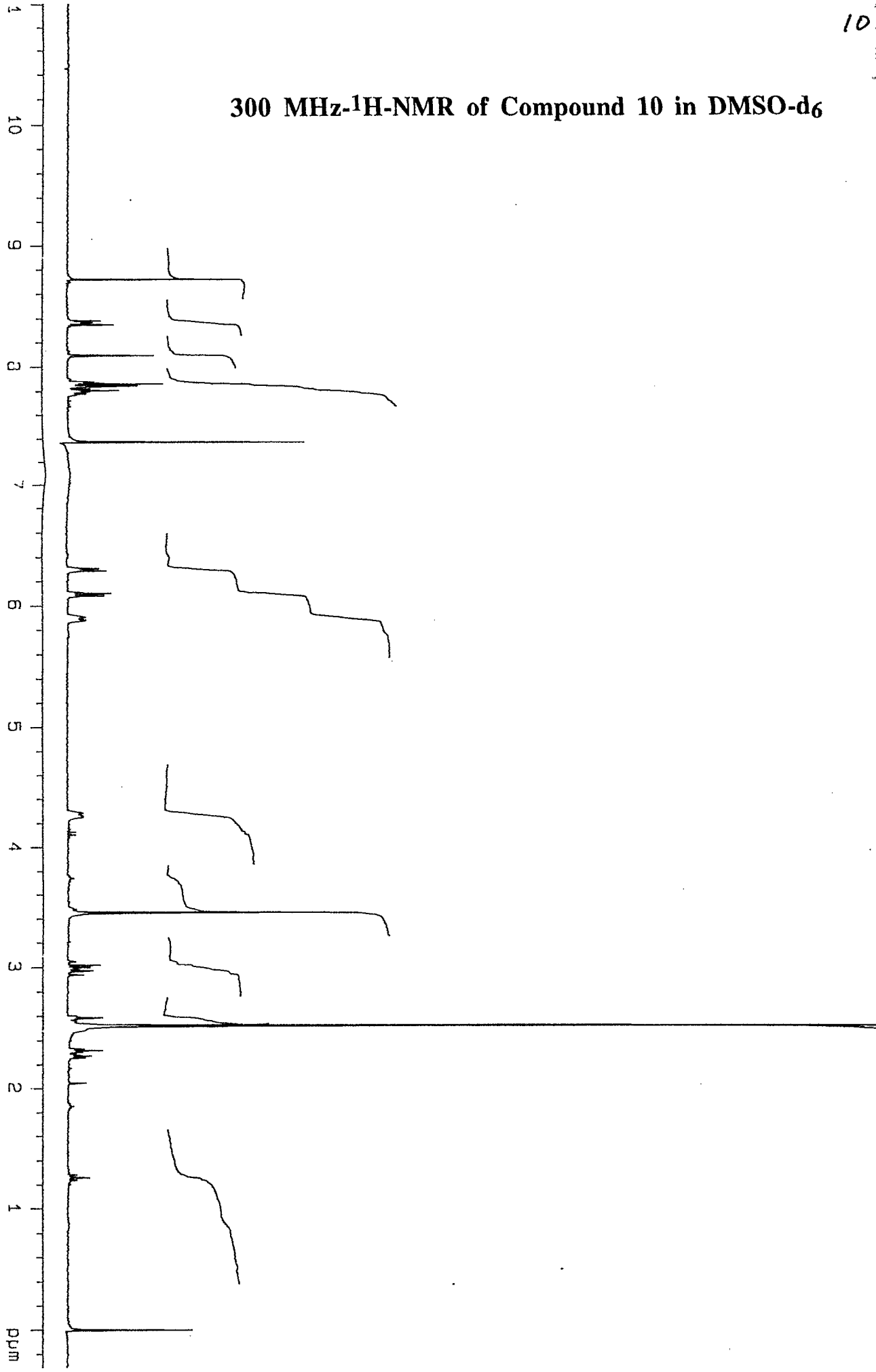
xL-BCH 300

KURARAY Co., LTD

300 MHz-^{1}H-NMR of Compound 10 in DMSO-d_6



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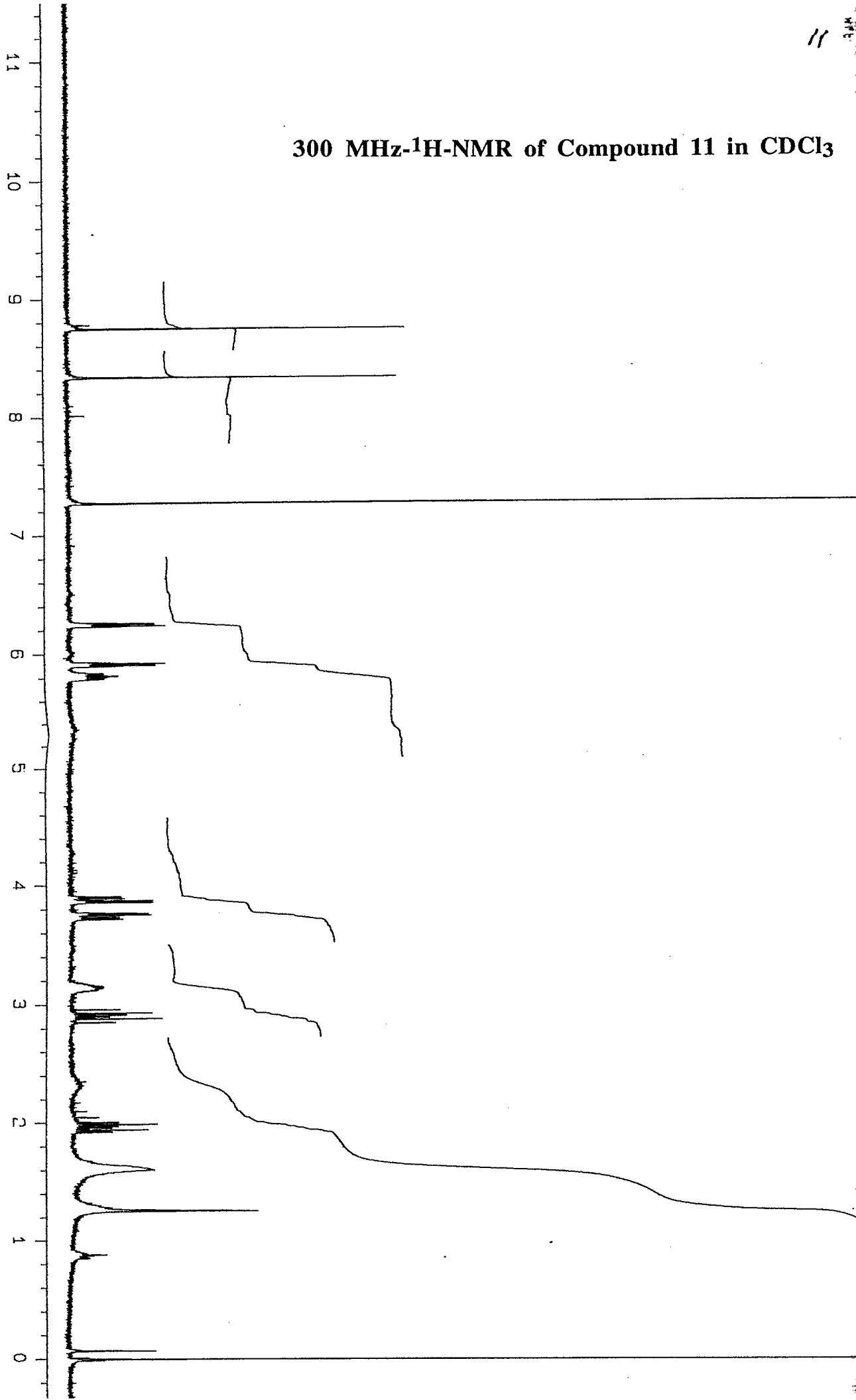
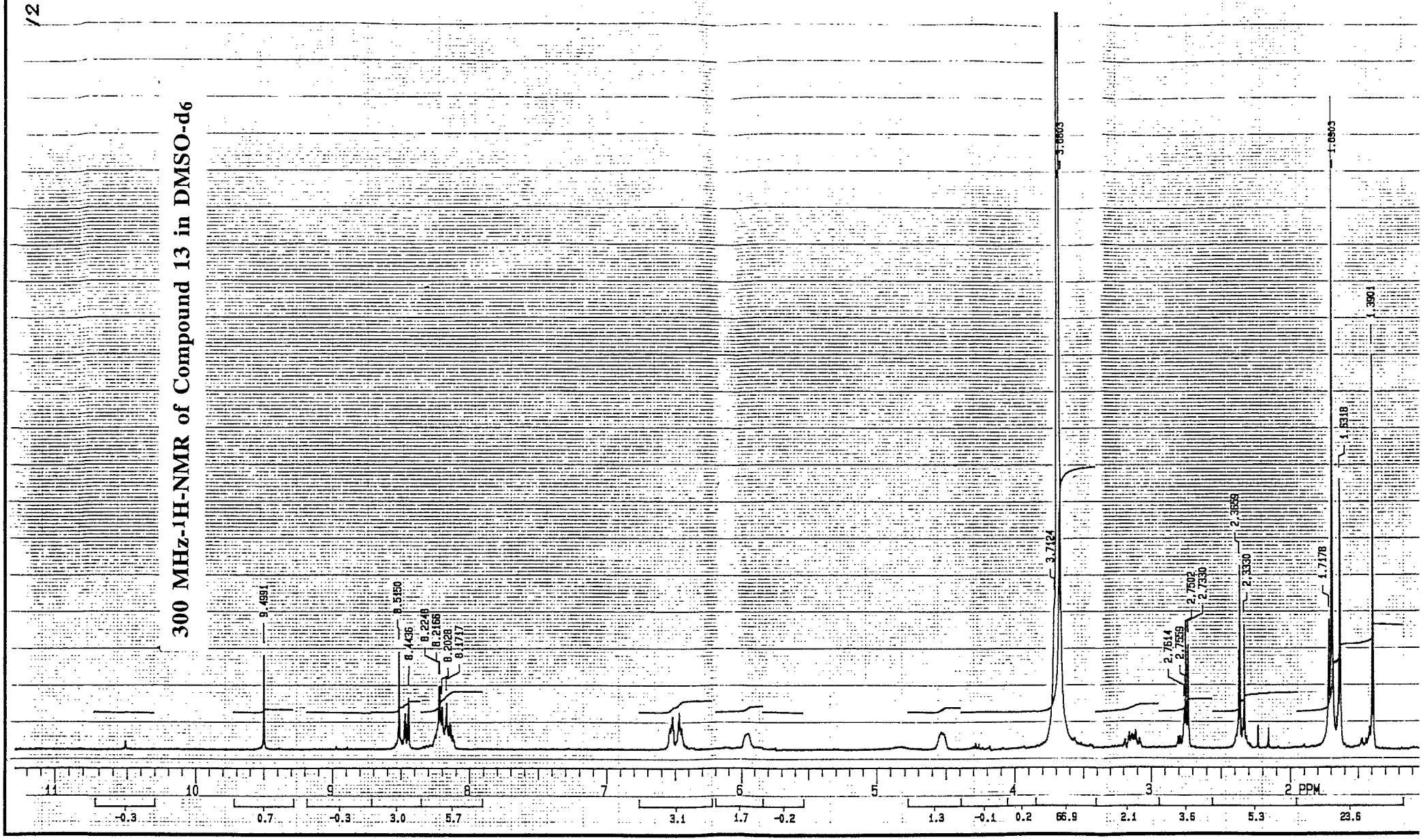


/2

300 MHz-^{1}H-NMR of Compound 13 in DMSO-d_6



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PLOT/PROCESSING: FN 32 K | RE sec | CD sec | LB Hz | AF sec | CCD | Width 3086.8 Hz/ppm | Start 300.2 Hz/ppm | Reference

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SAMPLE: EXP7540 N-BOC-N-ME

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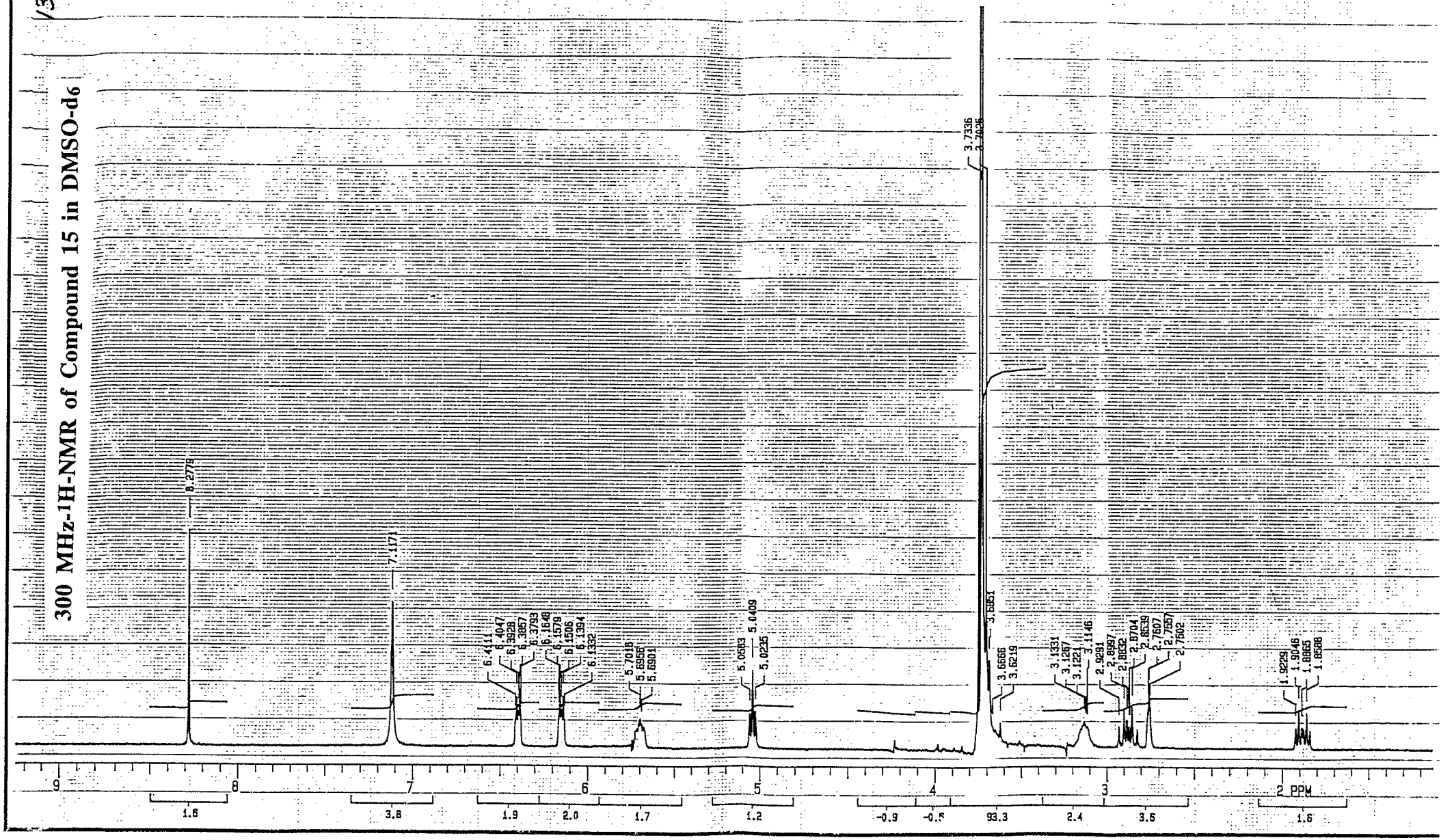
KURARAY Co., LT

13

300 MHz-^{1}H-NMR of Compound 15 in DMSO-d_6



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PLOT/PROCESSING: FN 32 K RE sec CD sec | LB Hz AF sec CCD | Width 2436.5 Hz/ppm Start 339.8 Hz/ppm | Reference

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KURARAY Co., LTD