Diverse Alkanones by Catalytic Carbon Insertion into the Formyl C-H Bond. Concise Access to the Natural Precursor of Achyrofuran.

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SUPPORTING INFORMATION

Background. The experimental procedures reported here for diazoalkane synthesis are based upon reproduction or modification of three modern protocols based on the low-temperature oxidation of hydrazones.[1] One method disclosed by Javed and Brewer involves dehydrogenation with the Swern reagent.[1a] With an optimal solvent and stoichiometry, this method allows pure aryl, diaryl, and aryl-alkyl diazomethanes to be accessed in high yield by simple filtration of triethylammonium chloride away from the reaction mixture. With the exception of the less stable electron-rich diazoindane **14**, all *aryl* diazomethanes used in this study were synthesized according to the Brewer method because of its simplicity and reliance on unprotected hydrazones (details are given below for the preparation of non-commercial aryl hydrazones). Unfortunately, this method is not effective for mono- and dialkyl diazomethanes in general – likely because of their instability in the presence of dimethyl sulfide, a nucleophilic byproduct of the oxidation.[2] Furrow and Myers have described the oxidation of *N-tert*-butyldimethylsilylhydrazones (TSBHs) with (difluoroiodo)benzene as a means to generate diazo compounds *in situ* for acid esterification reactions that are wide in scope.[1b] The temporary use of a bulky *N*-silyl substituent is advantageous, since it prolongs storage of the intermediate hydrazones and shields them against unwanted decomposition to form azines.[3] In addition, Holton and Shechter have reported a $Pb(OAc)_4$–tetramethylguanidine reagent pair for hydrazone oxidation beneficial for yet another reason: the choice of DMF as solvent enables clean and near quantitative extraction of the diazoalkane from the reaction medium upon the addition of cold hexanes or pentane.[1c] Given the fact that attempts to accomplish Sc(III) catalysis of carbon insertion with diazoalkanes generated *in situ*[1b]

(1) (a) Javed, M. I.; Brewer, M. *Org. Lett.* **2007**, *9*, 1789-1792. (b) Furrow, M. E.; Myers, A. G. *J. Am. Chem. Soc.* **2004**, *126*, 12222-12223. (c) Holton, T. L.; Shechter, H. *J. Org. Chem.* **1995**, *60*, 4725-4729. See also: (d) McGuiness, M.; Shechter, H. *Tetrahedron Lett.* **2002**, *43*, 8425-8427.

(2) Catalytic insertion chemistry is inhibited when the nucleophile is grossly impure or generated *in situ* in the presence of other Lewis basic additives or co-products of hydrazone oxidation.

(3) For an informative discussion on this problem, see: Furrow, M. E.; Myers, A. G. *J. Am. Chem. Soc.* **2004**, *126*, 5436-5445.

failed, we have captured the essential features in both the Myers and Shecter methods to form a hybrid protocol for access to the more challenging **14** and aliphatic nucleophiles **16**, **18**, **20**, and **22**. Specifically, a ketone or aldehyde is treated slowly (syringe pump) with triisopropylsilylhydrazine[4] at 0 °C in THF in the presence of powdered 4 Å molecular sieves. The known monosilyl hydrazine reagent was chosen to eliminate the need for Lewis acid catalysis of the condensation and to avoid a high weight trialkylsilanol byproduct.[3] The resulting TIPS hydrazone is, without purification and in the same vessel, subjected to deprotection (TBAF, THF, 0 °C) and oxidation based on the Shechter procedure[1c] designed for free hydrazones (see below for details). The use of $Pb(OAc)_4$ as oxidant and the stoichiometric generation of $Pb(OAc)_2$ as a waste product is certainly a disadvantage associated with the diazoalkane syntheses. In this context, we have recently discovered that $PhI(O_2CCF_3)_2$ can be substituted for $Pb(OAc)_4$ with no impact on the diazoalkane yield, however the hydrocarbon extract does become contaminated with iodobenzene. The experiments reported in this manuscript have not been tested with nucleophiles containing this impurity, but it is possible that there would not be any adverse effect.

Any synthetic chemist who wishes to repeat or adapt experiments reported herein should exercise caution and recognize that all diazoalkanes are likely toxic and shock-sensitive. Diazomethane is a potentially lethal yellow gas at ambient temperature that has been the culprit of several unpredictable and violent explosions. Notwithstanding, a close scrutiny of literature available for its preparation is very informative. One feature that emerges is that published procedures[5] that rely on the use of a volatile organic solvent, including large scale ones such as the Aerojet batch process,[5e,f] have proven safe and robust. Solvents with a high vapor pressure reduce the headspace partial pressure of diazomethane, and this dramatically lowers the explosion hazard. Most recently, a reliable process was developed for the generation of diazomethane at levels of 50-60 metric tons per year in order to feed key intermediates for a new generation of HIV protease inhibitor drugs.[6] As part of this development, careful and controlled detonation studies were carried out. Diazomethane was found to explode when deliberately sparked in the presence of air-free nitrogen. Although the pressures generated were low (<5

(4) Justo de Pomar, J. C.; Soderquist, J. A. *Tetrahedron Lett.* **2000**, *41*, 3285-3289. (b) Thomas W. Lee, Ph.D. Thesis, Harvard University, 2001.

(5) (a) Aldrich Technical Bulletin #AL-180 ("Diazald®, MNNG, and Diazomethane Generators"); this material is freely available under the *Related Information* tab of the Search command at http://www.sigma-aldrich.com. (b) Hudlicky, M. *J. Org. Chem.* **1980**, *45*, 5377-5378. (c) De Boer, T. J.; Backer, H. J. In *Organic Synthesis, Collective Volume IV*; Rabjohn, N., Ed.; John Wiley & Sons: New York, 1963, pp 250-252. (d) Acevedo, O.; Ross, B.; Andrews, R. S.; Springer, R.; Cook, P. D. (Isis Pharmaceuticals) U.S. Patent 549243, 1995. (e) Archibald, T. G.; Huang, D-S.; Pratton, M. H.; Barnard, J. C. (Aerojet General Corporation) U.S. Patent 5817778, 1998. (f) Archibald, T. G.; Barnard, J. C.; Harlan, R. F. (Aerojet General Corporation) U.S. Patent 5854405, 1998.

(6) Proctor, L. D.; Warr, A. J. *Org. Process Res. Dev.* **2002**, *6*, 884-892.

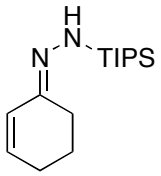
psi), they were of sufficient strength to jar or break the seal of a conventional glass joint.[6] This, in turn, was shown to facilitate the mixing of diazomethane with air, allowing for a more violent diazomethane-oxygen explosion. This finding sheds new light on some older accounts of very startling and unexplainable diazomethane explosions under supposedly inert conditions. In any event, most diazomethane explosions have taken place during its (solvent-free) distillation, and it is important to appreciate that the explosive nature of the reagent is closely a function of its volatility. In this context, it deserves mention that we have safely and without incident applied the two-step procedure given below to a range of higher molecular weight derivatives that exist as solids or viscous oils at or below 23 °C. Although these materials can be assayed in neat form by NMR and IR spectroscopy, our procedures do not require isolation, distillation, or even warming of the potentially unstable diazo compounds. Each of the necessary transfers or manipulations, including reagent storage, can be carried out in solution at low temperature, and the active titer for a given diazo compound is conveniently obtained by acidic quench of a stock solution aliquot with benzoic acid. In the rare case that a volatile diazoalkane (such as 2-diazobutane, **18**) is desired or very large-scale (>1 g) experiments are carried out, adequate precautions should be taken, and the use of safety shields is highly recommended. Gloves must be worn at all times when handling diazoalkane solutions and vessels.

General. Infrared spectra were recorded on a Mettler-Toledo ReactIR iC10 spectrophotometer, ν_{max} in cm^{-1}. Bands are reported as strong (s), medium (m), weak (w), and broad (br). ^{1}H NMR spectra were recorded on a Varian Gemini 2000 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26, $(CH_3)_2SO$: δ 2.50). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR were recorded on a Varian Gemini 2000 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.16, $(CD_3)_2SO$: δ 39.52). High-resolution mass spectra were obtained at the Boston College Mass Spectrometry Facility.

Unless stated otherwise, all reactions were carried out in flame-dried glassware under an atmosphere of nitrogen in dry, degassed solvent with standard Schlenk or vacuum-line techniques. THF, Et_2O, toluene, CH_2Cl_2, DMF, pentane, and hexanes were dispensed from a Glass Contour solvent purification system custom manufactured by SG Waters LLC (Nashua, NH). Triisopropylsilylhydrazine was prepared as previously described.[4] Acetone was dried over calcium sulfate and distilled under

nitrogen. Benzaldehyde (Aldrich), acetophenone (Aldrich), propiophenone (Aldrich), and 1,1,3,3-tetramethylguanidine (Acros) were vacuum distilled over calcium hydride. Dihydrocinnamaldehyde (Aldrich), 2-methoxybenzaldehyde (Aldrich), 4-methoxybenzaldehyde (Aldrich), 2-pyridinecarboxaldehyde (Aldrich), furfural (Aldrich), pivalaldehyde (Aldrich), mesitaldehyde (Aldrich), and 4,5-dimethylthiophene-2-carboxaldehyde (Aldrich) were distilled under vacuum. 4-Trifluoromethylbenzaldehyde (Aldrich), 2-bromobenzaldehyde (Aldrich), 2-chlorobenzaldehyde (Aldrich), 2-butanone (Aldrich), cyclopropyl methyl ketone (Aldrich), and 2-fluorobenzaldehyde (Aldrich) were distilled under nitrogen atmosphere. Geranial was prepared from geraniol by careful oxidation according to a known method.[7] 4-Nitrobenzaldehyde (Aldrich) was recrystallized from water-isopropanol. $Pb(OAc)_4$ (Aldrich), after dissolution in minimal hot glacial acetic acid, deposited as bright white needles upon cooling. The crystals were washed in a fritted Schlenk filter with pentane, dried under vacuum, and then stored in a glovebox at –20 °C. Hydrazine hydrate (Aldrich), TBAF (Acros), 4-dimethylaminobenzaldehyde (Aldrich), 2-methoxy-1-indanone (Aldrich), 2-cyclohexen-1-one (Aldrich), 3-phenyl-2-propynal (Aldrich), powdered 4 Å molecular sieves (Aldrich), and $Sc(OTf)_3$ (Aldrich) were purchased and used as received. Unprotected hydrazones were prepared as described previously.[8] Column chromatography was performed with EMD silica gel 60 (230-400 mesh) and driven with compressed air. Analytical TLC was carried out with EMD silica gel 60 F_{254} precoated plates (250 μm thickness) and a ceric ammonium molybdate or potassium permanganate stain for spot visualization.

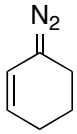
Representative Procedure for Aliphatic Diazoalkane Synthesis and Handling:



2-Cyclohexen-1-one *N*-triisopropylsilylhydrazone. A 50 mL round bottom flask equipped with a Teflon-coated stir bar and a jointed vacuum adapter was charged with powdered 4 Å molecular sieves (4 g) and then flame-dried under vacuum. After backfilling with nitrogen, the vacuum adapter was swapped for a rubber septum, and 2-cyclohexen-1-one (1.06 g, 11.0 mmol, 1.0 equiv) and THF (22 mL) were added successively with stirring. The suspension was then cooled to 0 °C, and triisopropylsilylhydrazine (2.08 g, 11.0 mmol, measured by mass difference into a gas tight syringe) was slowly added dropwise using a syringe pump (2 h). After 30 min of additional stirring, the mixture was filtered through a pad of celite in a sintered glass Schlenk filter into a dry 100 mL round bottom flask cooled to 0 ºC. The original flask, molecular

(7) Piancatelli, G.; Leonelli, F. *Org. Syn.* **2006**, *83*, 18-23.
(8) Pross, A.; Sternhill, S. *Aust. J. Chem.* **1970**, *23*, 989-1003.

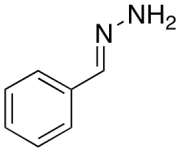
sieves, and celite were washed with two additional 10 mL portions of cold Et_2O. The resulting homogeneous filtrate was concentrated on a rotovap equipped with an oil-free diaphragm pump (3-10 torr) to afford 2.90 g (11.0 mmol, >98%) of product as a colorless oil (~3:2 E:Z mixture, >98% pure by ^{1}H NMR analysis). If not used directly in the subsequent oxidation, this material was stored under nitrogen atmosphere at –20 °C.



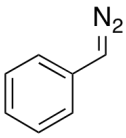
3-Diazocyclohex-1-ene. A flame-dried 50 mL round bottom flask equipped with an oversized Telflon-coated stir bar was charged with 2-cyclohexen-1-one *N*-triisopropylsilylhydrazone (402 mg, 1.51 mmol) and 10 mL of THF. After cooling the colorless solution to 0 ºC, 1.51 mL of TBAF (1.0 M in THF, 1.51 mmol, 1.0 equiv) was added by syringe, at which point a yellow-orange discoloration immediately occurred. The solution was stirred for 10 min and then concentrated under vacuum. Without purification and in the same vessel, the crude hydrazone was freed of residual solvent under vacuum, backfilled with nitrogen, and redissolved in 15 mL of DMF and 4.36 mL 1,1,3,3-tetramethylguanidine (34.7 mmol, 23 equiv). The resulting light pink solution was cooled to –45 °C (dry ice/1:1 ethanol:ethylene glycol) and $Pb(OAc)_4$, finely powdered and weighed into a large vial in a glovebox (736 mg, 1.66 mmol, 1.1 equiv), was added in three portions. After 45 min of stirring at –45 °C, 15 mL of precooled pentane was added and the mixture was stirred vigorously for 1 min. The violet pentane layer was removed with a syringe and transferred to a 100 mL pear-shaped flask cooled to –78 °C. The extraction step was repeated two to three more times (15 mL of pentane) until the extract was no longer colored. The combined pentane layers were washed once with 15 mL of 30% aqueous potassium hydroxide solution and twice with 15 mL portions of saturated aqueous ammonium chloride. In each case, prolonged (>30 sec) vigorous stirring was allowed, the aqueous layer was removed by syringe, and warming above the freezing point (–20 °C) was required for miscibility; these washes serve (respectively) to remove residual DMF and tetramethylguanidine from the organic extract – a prerequisite for efficient catalytic carbon insertion but not esterification. The diazoalkane solution was then transferred with rinsing (freezing the final aqueous wash at –78 °C is most convenient) to a 100 mL round bottom and concentrated under high vacuum at –45 °C to afford 3-diazocyclohex-1-ene as a violet solid. The NMR data that follow represent direct assay of this material without further purification. IR ($PhCH_3$): 2946 (m), 2867 (m), 2038 (s), 1247 (m), 885 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.01 (dt, J = 9.8, 2.0 Hz, 1H), 5.28 (dt, J = 9.8, 4.0 Hz, 1H), 2.61 (t, J = 6.4 Hz, 2H), 2.08 (ddt, J = 6.0, 4.0, 2.0 Hz, 2H), 1.77 (dt, J = 6.4, 6.0, 2H). Typically, the solid is immediately redissolved in toluene and transferred (quantitatively, with rinsing) by cannula to a 1 mL volumetric flask. The active titer is

determined by esterification with benzoic acid. Thus, 100 μL of the stock solution was diluted with 1 mL of THF in a 5 mL round bottom flask, cooled to –45 °C, and treated with benzoic acid dropwise by syringe (166 μL of 1.0 M in THF, 0.166 mmol, 1.1 equiv based on theoretical). Upon slow warming from –45 °C, the reaction mixture became colorless and nitrogen evolution was observed. This mixture was diluted with Et_2O (10 mL) and saturated sodium bicarbonate (10 mL) and transferred to a separatory funnel. After removal of the organic layer, the aqueous layer was washed with two additional 5 mL volumes of Et_2O. The pooled extract was dried over magnesium sulfate and concentrated to a light yellow oil. Purification by silica gel chromatography (TLC R_f = 0.28 in 97:3 hexanes:ethyl acetate) afforded 12.5 mg of the benzoate ester (41% yield, indicative of a 0.62 M stock solution of diazoalkane). Characterization follows for 2-cyclohexene-1-benzoate. IR (thin film): 2937 (w), 2867 (w), 1710 (s), 1451 (w), 1336 (w), 1314 (w), 1266 (s), 1175 (w), 1110 (m), 1069 (w), 1026 (w), 709 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.55 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 2H), 6.01 (ddt, *J* = 10.0, 3.2, 2.0 Hz, 1H), 5.51 (dt, *J* = 5.2, 1.6 Hz, 2H), 2.18-1.95 (m, 3H), 1.92-1.80 (m, 2H), 1.75-1.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 132.9, 132.8, 130.9, 129.7, 128.4, 125.9, 68.8, 28.6, 25.3, 19.2. HRMS (ESI+) Calcd for $C_{13}H_{15}O_2^+$ $[M+H]^+$: 203.1072; Found: 203.1072.

Representative Procedure for Aryl Hydrazone Synthesis:

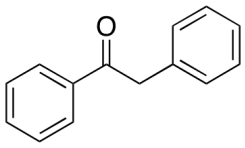


Benzaldehyde hydrazone. In a 2 dram vial equipped with a Teflon-coated stir bar, benzaldehyde (1.00 g, 9.43 mmol) was suspended in 2.0 mL of hydrazine hydrate. After sealing the vial with a Teflon-lined screw cap, the heterogeneous mixture was stirred rapidly with heating at 100 ºC. After 6 h, the mixture was cooled to 23 °C and the product was extracted with three 2 mL portions of CH_2Cl_2. The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 1.10 g (9.16 mmol, 97%) of a colorless oil. This known compound was >98% pure and consisted of a >98:2 *E*:*Z* mixture according to ^{1}H NMR analysis.

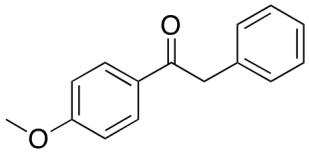


Phenyldiazomethane. Prepared from benzaldehyde hydrazone according to the known procedure.[1a] IR ($PhCH_3$): 2975 (w), 2852 (w), 2062 (s), 1596 (m), 1499 (m), 1381 (m), 1184 (w), 1068 (m), 913 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (t, *J* = 7.6 Hz, 2H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, H), 4.96 (s, 1H).

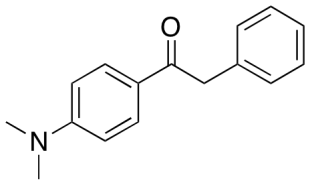
Representative Procedure for Catalytic Homologation:



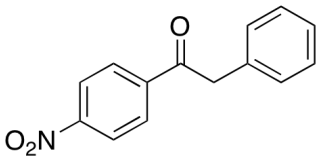
1,2-Diphenylethanone (2a). In a glovebox, a flame-dried 1 dram vial equipped with a Teflon-coated flea stir bar was charged with $Sc(OTf)_3$ (5.0 mg, 0.010 mmol, 0.10 equiv), sealed with a rubber septum, and removed from the glovebox. In a fume hood, toluene (0.50 mL, 0.2 M) was added by syringe, suspending but not dissolving the catalyst. After cooling the mixture to –78 °C, benzaldehyde (10.3 μL, 0.102 mmol, 1.0 equiv) and phenyldiazomethane (1.5 M in toluene, 74.5 μL, 0.112 mmol, 1.1 equiv, solution kept cold at –78 °C) were added in succession to the stirring reaction mixture by syringe. The reaction was stirred for 10 min at –78 °C, at which point the characteristic red color of the nucleophile had dissipated, leaving a turbid light yellow suspension. The reaction mixture was concentrated with a nitrogen purge and purified by flash chromatography (TLC R_f = 0.31 in 9:1 hexanes:ethyl acetate) affording 19.5 mg (0.0996 mmol, 98%) of **2a** as colorless oil. Characterization data for **2a** has been recorded previously.[9]



1-(4-Methoxyphenyl)-2-phenylethanone (2b). Prepared according to the general procedure on a scale of 0.061 mmol of *p*-methoxybenzaldehyde (7.4 μL), 0.067 mmol of phenyldiazomethane (42.4 μL of a 1.68 M solution in toluene, 1.1 equiv), and 0.0060 mmol of $Sc(OTf)_3$ (3.0 mg, 0.10 equiv) in 97% yield (0.0590 mmol, 13.4 mg) after chromatographic purification (TLC R_f = 0.26 in 95:5 hexanes:ethyl acetate. Characterization data for **2b** has been recorded previously.[10]



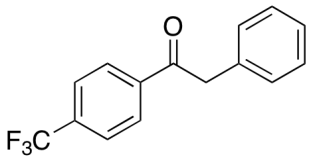
1-(4-Dimethylaminophenyl)-2-phenylethanone (2c). Prepared according to the general procedure on a scale of 0.102 mmol of *p*-(dimethylamino)benzaldehyde (15.2 mg, 1.0 equiv), 0.117 mmol of phenyldiazomethane (76.0 μL of a 1.45 M solution in toluene, 1.1 equiv), and 0.010 mmol of $Sc(OTf)_3$ (4.9 mg, 0.10 equiv) in 98% yield (0.0993 mmol, 23.7 mg) after chromatographic purification (TLC R_f = 0.25 in 90:10 hexanes:ethyl acetate). Characterization data for **2c** has been recorded previously.[11]



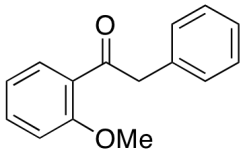
1-(4-Nitrophenyl)-2-phenylethanone (2d). Prepared according to the general procedure on a scale of 0.102 mmol of *p*-nitrobenzaldehyde (15.3 mg), 0.117 mmol of phenyldiazomethane (76.0 μL of a 1.45 M solution in

(9) Li, L.; Cai, P.; Guo, Q.; Xue, S. *J. Org. Chem.* **2008**, *73*, 3516-3522.
(10) Ruan, J.; Saidi, O.; Iggo, J. A.; Xiao, J. *J. Am. Chem. Soc.* **2008**, *130*, 10510-10511.
(11) Dolhem, F.; Barhdadi, R.; Folest, J. C.; Nedelec, J. Y.; Troupel, M. *Tetrahedron* **2001**, *57*, 525-529.

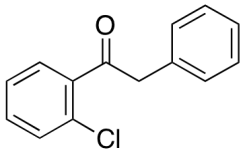
toluene, 1.1 equiv), and 0.010 mmol of $Sc(OTf)_3$ (4.9 mg, 0.10 equiv) in 91% yield (0.0924 mmol, 22.4 mg) after chromatographic purification (TLC R_f = 0.25 in 90:10 hexanes:ethyl acetate). **2d** has been synthesized previously, yet characterization data was not reported.[12] IR (thin film): 1694 (s), 1518 (m), 1351 (m), 746 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.34 (s, 2H), 7.28-7.41 (m, 5H), 8.18 (d, *J* = 8.8 Hz, 2H), 8.34 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.6, 120.1, 123.7, 126.3, 129.1, 129.6, 129.8, 139.1, 152.6, 196.4. HRMS (ESI+) Calcd for $C_{14}H_{12}NO_3^+$ [M+1]$^+$: 242.0772; Found: 242.1100.



1-(4-Trifluoromethylphenyl)-2-phenylethanone (2e). Prepared according to the general procedure on a scale of 0.0830 mmol of *p*-trifluoromethylbenzaldehyde (14.5 mg), 0.091 mmol of phenyldiazomethane (160 μL of a 0.57 M solution in toluene, 1.1 equiv), and 0.0080 mmol of $Sc(OTf)_3$ (4.1 mg, 0.10 equiv) in 97% yield (0.0805 mmol, 21.2 mg) after chromatographic purification (TLC R_f = 0.30 in 90:10 hexanes:ethyl acetate). Characterization data for **2e** has been recorded previously.[13]

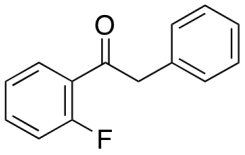


1-(2-Methoxyphenyl)-2-phenylethanone (4a). Prepared according to the general procedure on a scale of 0.104 mmol of *o*-anisaldehyde (15.5 mg), 0.114 mmol of phenyldiazomethane (200 μL of a 0.57 M solution in toluene, 1.1 equiv), and 0.010 mmol of $Sc(OTf)_3$ (4.9 mg, 0.10 equiv) in 96% yield (0.100 mmol, 22.6 mg) after chromatographic purification (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate). Characterization data for **4a** has been recorded previously.[14]

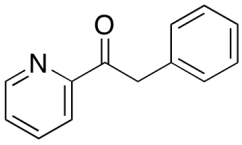


1-(2-Chlorophenyl)-2-phenylethanone (4b). Prepared according to the general procedure on a scale of 0.0830 mmol of *o*-chlorobenzaldehyde (11.7 mg), 0.091 mmol of phenyldiazomethane (55 μL of a 1.66 M solution in toluene, 1.1 equiv), and 0.0080 mmol of $Sc(OTf)_3$ (4.1 mg, 0.10 equiv) in 95% yield (0.078 mmol, 18.2 mg) after chromatographic purification (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate). IR (thin film): 2918 (w), 1699 (s), 1432 (m), 756 (m), 700 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.26 (s, 2H), 7.21-7.44 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.8, 126.7, 127.5, 129.0, 129.2, 129.3, 129.5, 129.7, 131.0, 134.5, 135.6, 201.5. HRMS (ESI+) Calcd for $C_{14}H_{12}ClO^+$ [M+1]$^+$: 231.0532; Found: 231.1096.

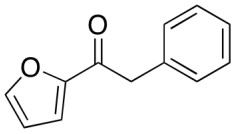
(12) Aggarwal, V. K.; de Vicente, J.; Pelotier, B.; Holmes, I. P.; Bonnert, R. V. *Tetrahedron Lett.* **2000**, *41*, 10327-10331.
(13) Takemiya, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 14800-14801.
(14) Le Bras, G.; Provot, O.; Peyrat, J.; Alami, M.; Brion, J. *Tetrahedron Lett.* **2006**, *47*, 5497-5501.



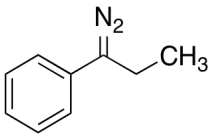
1-(2-Fluorophenyl)-2-phenylethanone (4c). Prepared according to the general procedure on a scale of 0.100 mmol of *o*-fluorobenzaldehyde (10.5 μL), 0.110 mmol of phenyldiazomethane (66.3 μL of a 1.66 M solution in toluene, 1.1 equiv), and 0.010 mmol of $Sc(OTf)_3$ (5.0 mg, 0.10 equiv) in 89% yield (0.0890 mmol, 19.1 mg) after chromatographic purification (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate). **4c** has been synthesized previously.[15] IR (thin film): 3028 (w), 1691 (s), 1109 (m), 907 (m), 732 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.31 (s, 2H), 7.21-7.44 (m, 5H), 7.71 (d, 2H, *J* = 8.6 Hz), 8.10 (d, *J* = 8.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.9, 115.2, 125.3, 127.0, 127.4, 127.5, 129.2, 129.3, 129.6, 134.5, 135.1, 201.4. HRMS (ESI+) Calcd for $C_{14}H_{12}FO^+$ $[M+1]^+$: 215.0827; Found: 215.1098.



2-Phenylacetylpyridine (5). Prepared according to the general procedure on a scale of 0.083 mmol of pyridine-2-carboxaldehyde (8.9 mg), 0.0912 mmol of phenyldiazomethane (61.0 μL of a 1.50 M solution in toluene, 1.1 equiv), and 0.0080 mmol of $Sc(OTf)_3$ (4.1 mg, 0.10 equiv) in 84% yield (0.0698 mmol, 13.8 mg) after chromatographic purification (TLC R_f = 0.30 in 85:15 hexanes:ethyl acetate). Characterization data for **5** has been recorded previously.[16]

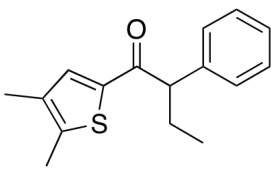


1-(2-Furyl)-2-phenylethanone (6). Prepared according to the general procedure on a scale of 0.10 mmol of furfural (8.3 μL), 0.110 mmol of phenyldiazomethane (66.3 μL of a 1.66 M solution in toluene, 1.1 equiv), and 0.010 mmol of $Sc(OTf)_3$ (4.9 mg, 0.10 equiv) in 90% yield (0.090 mmol, 16.8 mg) after chromatographic purification (TLC R_f = 0.30 in 90:10 hexanes:ethyl acetate). **6** has been synthesized previously, yet characterization data was not reported.[17] IR (thin film): 1669 (s), 1465 (m), 722 (m), 432 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.06 (s, 2H), 6.45 (dd, *J* = 3.5, 1.8 Hz, 1H), 7.10 (dd, *J* = 3.5, 0.7 Hz, 1H), 7.15 (m, 5H), 7.58 (dd, *J* = 1.8, 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.8, 112.6, 118.6, 127.5, 129.2, 129.7, 135.6, 147.1, 152.1, 185.0. HRMS (ESI+) Calcd for $C_{12}H_{11}O_2^+$ $[M+1]^+$: 187.0714; Found: 187.1147.

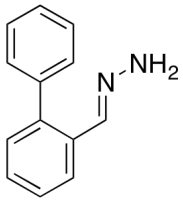


1-Diazo-1-phenylpropane (8). Prepared from propiophenone hydrazone according to the known procedure.[1a] IR ($PhCH_3$): 2044 (s), 1586 (w), 1496 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (t, *J* = 8.5 Hz, 2H), 7.05 (t, *J* = 7.1 Hz, 1H), 6.92 (dd, *J* = 8.8, 1.2 Hz, 2H), 2.21 (q, *J* = 7.9 Hz, 2H), 1.14 (t, *J* = 8.5 Hz, 3H).

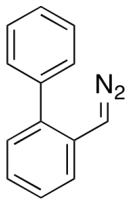
(15) Bak, C.; Praefcke, K. *J. Het. Chem.* **1980**, *17*, 1655-1657.
(16) Easmon, J.; Purstinger, G.; Thies, K.; Heinisch, G.; Hofmann, J. *J. Med. Chem.* **2006**, *49*, 6343-6350.
(17) Firouzabdi, H.; Iranpoor, N.; Nowrouzi, F. *Tetrahedron* **2004**, *60*, 10843-10850.



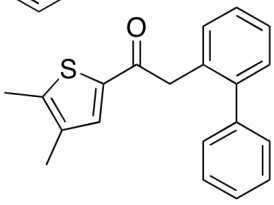
1-(4,5-Dimethylthiophen-2-yl)-2-phenylbutan-1-one (9). Prepared according to the general procedure on a scale of 0.0610 mmol of thiophene carboxaldehyde **7** (7.25 μL, 1.0 equiv), 0.067 mmol of 1-phenyl-1-diazopropane (250 μL of a 0.27 M solution in toluene, 1.1 equiv), and 0.0060 mmol of $Sc(OTf)_3$ (3.0 mg, 0.10 equiv) in 82% yield (0.0503 mmol, 13.1 mg) after chromatographic purification (TLC R_f = 0.30 in 97.5:2.5 hexanes:ethyl acetate). IR (thin film): 2963 (w), 2927 (w), 1640 (s), 1440 (m), 1170 (m) 699 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, *J* = 7.7 Hz, 3H), 2.11 (s, 2H), 2.36 (s, 3H), 4.43 (t, *J* = 7.8 Hz, 1H), 7.18-7.33 (m, 5H), 7.39 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.4, 14.1, 14.3, 27.3, 56.8, 127.0, 127.9, 128.3, 129.0, 129.2, 135.6, 139.5, 140.1, 192.5. HRMS (ESI+) Calcd for $C_{16}H_{19}OS^+$ $[M+1]^+$: 259.1112; Found: 259.1457.



2-Phenylbenzaldehyde hydrazone. In a 2 dram vial equipped with a Teflon-coated stir bar, 2-phenylbenzaldehyde (0.120 g, 0.658 mmol) was dissolved in 0.35 mL (11 equiv) of hydrazine hydrate and 0.66 mL of ethanol. After sealing the vial with a Teflon-lined screw cap, the homogeneous mixture was stirred rapidly with heating at 100 ºC. After 10 h, the mixture was cooled to 23 °C, and the product was extracted with three 4 mL volumes of $CHCl_3$. The combined extracts were concentrated and then dried by azeotropic removal of water with benzene and concentrated under reduced pressure to afford 0.119 g (0.606 mmol, 92%) of a white solid. This material was converted directly to **10** without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.44 (s, 2H), 7.37-7.46 (m, 8H), 7.70 (s, 1H), 7.96 (m, 1H). HRMS (ESI+) Calcd for $C_{13}H_{13}N_2^+$ $[M+1]^+$: 197.1034; Found: 197.1104.

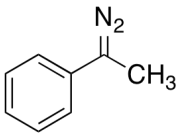


2-(Diazomethyl)biphenyl (10). Prepared from 2-phenylbenzaldehyde hydrazone according to the known procedure.[1a] IR ($PhCH_3$): 2050 (s), 1595 (m), 1381 (w), 1121 (w), 910 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.92 (s, 1H), 7.41-7.51 (m, 8H), 8.35 (m, 1H).

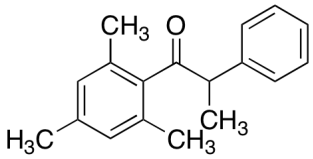


2-(Biphenyl-2-yl)-1-(4,5-dimethylthiophen-2-yl)ethanone (11). Prepared according to the general procedure on a scale of 0.061 mmol of thiophene carboxaldehyde **7** (7.3 μL), 0.0670 mmol of 2-(diazomethyl)biphenyl (213 μL of a 0.314 M solution in toluene, 1.1 equiv), and 0.0060 mmol of $Sc(OTf)_3$ (3.0 mg, 0.10 equiv) in 74% yield (0.0453 mmol, 11.1 mg) after chromatographic purification (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate). IR (thin film): 2922 (w), 1659 (s), 1438 (w), 1187 (m), 719 (w), 704 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.04 (s, 3H), 2.34 (s, 3H), 4.09 (s, 2H), 7.01 (s, 1H), 7.28-7.44 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 14.2, 43.1, 127.0, 127.2, 128.2, 127.7,

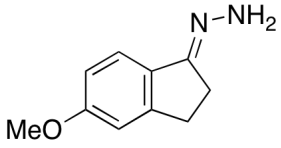
128.3, 129.5, 130.2, 130.6, 134.8, 135.5, 138.7, 141.4, 142.3, 143.9, 190.5. HRMS (ESI+) Calcd for $C_{20}H_{19}OS^+$ [M+1]$^+$: 307.1112; Found: 307.1532.



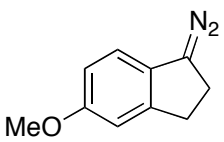
1-Diazo-1-phenylethane (12). Prepared from acetophenone hydrazone according to the known procedure.[1a] IR ($PhCH_3$): 2038 (s), 1596 (w), 1501 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (t, *J* = 8.4 Hz, 2H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.92 (dd, *J* = 8.8, 1.2 Hz, 2H), 2.17 (s, 3H).



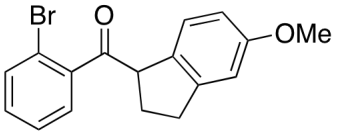
1-Mesityl-2-phenylpropan-1-one (13). Prepared according to the general procedure with adjustment of reaction temperature to –45 °C on a scale of 0.0812 mmol of mesitaldehyde (12.0 μL), 0.162 mmol of 1-diazo-1-phenylethane (144 μL of a 1.13 M solution in toluene, 2.0 equiv), and 0.016 mmol of $Sc(OTf)_3$ (8.0 mg, 0.10 equiv) in 63% yield (0.0512 mmol, 12.9 mg) after chromatographic purification (TLC R_f = 0.30 in 97.5:2.5 hexanes:ethyl acetate). IR (thin film): 2976 (w), 2930 (w), 1697 (s), 1453 (m), 698 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60 (d, *J* = 7.7 Hz, 3H), 1.88 (s, 6H), 2.24 (s, 3H), 4.17 (q, *J* = 7.8 Hz, 1H), 6.78 (s, 2H), 7.18-7.36 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): 16.8, 19.3, 21.2, 54.3, 127.4, 128.5, 128.7, 128.8, 133.5, 138.5, 138.7, 139.2, 209.9. HRMS (ESI+) Calcd for $C_{18}H_{21}O^+$ [M+1]$^+$: 253.1548; Found: 253.1863.



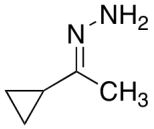
5-Methoxy-indan-1-one hydrazone. In a 2 dram vial equipped with a Teflon-coated stir bar, 2-methoxy-1-indanone (0.20 g, 1.2 mmol) was dissolved in 2.5 mL of ethanol and added to 0.60 mL (10 equiv) of hydrazine hydrate. After sealing the vial with a Teflon-lined screw cap, the homogeneous mixture was stirred rapidly with heating at 100 ºC. After 10 h, the mixture was cooled to 23 °C and the product was extracted with three 8 mL portions of $CHCl_3$. The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 0.193 g (1.10 mmol, 89%) of an ivory solid. This material was taken directly into the oxidation reaction without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.69 (t, *J* = 6.4 Hz, 2H), 3.08 (t, *J* = 6.4 Hz, 2H), 3.81 (s, 3H), 5.03 (br s, 2H), 6.81 (s, 1H), 6.83, (d, *J* = 8.8 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H). HRMS (ESI+) Calcd for $C_{28}H_{31}O_3^+$ [M+1]$^+$: 415.2228; Found: 415.2264.



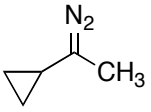
1-Diazo-5-methoxy-indane (14). Prepared from 5-methoxy-indan-1-one hydrazone according to the general procedure for aliphatic diazoalkane synthesis and handling. Used in homologation reactions immediately following the preparation of a concentrated solution in toluene.



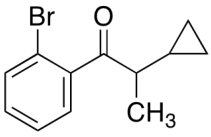
2-Bromophenyl(5-methoxy-indan-1-yl)methanone (15). Prepared according to the general procedure on a scale of 0.122 mmol of 2-bromobenzaldehyde (14.0 μL), 0.134 mmol of 1-diazo-5-methoxy-indane (200 μL of a 0.67 M solution in toluene, 1.1 equiv), and 0.012 mmol of $Sc(OTf)_3$ (6.0 mg, 0.10 equiv) in 62% yield (0.0756 mmol, 25.1 mg) after chromatographic purification (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate). IR (thin film): 2939 (w), 1599 (s), 1489 (m), 1262 (m), 1028 (m), 758 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (t, *J* = 6.8 Hz, 2H), 3.48 (q, *J* = 8.7 Hz, 2H), 3.79 (s, 3H), 3.84 (t, *J* = 6.9 Hz, 1H), 6.65 (d, *J* = 8.8 Hz, 1H), 6.80 (s, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 7.19-7.37 (m, 3H), 7.61 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.2, 32.2, 43.7, 47.0, 55.5, 55.6, 56.4, 71.9, 73.0, 87.3, 110.2, 112.6, 117.1, 119.1, 125.9, 127.4, 128.7, 131.3, 132.5, 133.5, 142.0, 146.5, 159.7, 204.7 HRMS (ESI+) Calcd for $C_{17}H_{16}BrO_2^+$ $[M+1]^+$: 332.0235; Found: 332.0382.



1-Cyclopropylethanone hydrazone. In a 2 dram vial equipped with a Teflon-coated stir bar, cyclopropyl methyl ketone (0.20 mL, 2.1 mmol) was suspended in 1.14 mL (10 equiv) of hydrazine hydrate. After sealing the vial with a Teflon-lined screw cap, the homogeneous mixture was stirred rapidly with heating at 100 ºC. After 10 h, the mixture was cooled to 23 °C and the product was extracted with three 8 mL portions of $CHCl_3$. The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford 0.200 g (2.04 mmol, 95%) of a clear oil. This material was taken directly into the oxidation reaction without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.59-0.71 (m, 2H), 0.77-0.86 (m, 1H), 1.48-1.75 (m, 2H), 1.65 (s, 3H), 4.81 (br s, 2H). HRMS (ESI+) Calcd for $C_5H_{11}N_2^+$ $[M+1]^+$: 99.0878; Found: 99.0736.

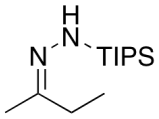


1-Cyclopropyl-1-diazoethane (16). Prepared from 1-cyclopropylethanone hydrazone according to the general procedure for aliphatic diazoalkane synthesis and handling (see compound **18** for isolation procedure). Used in homologation reactions immediately following the preparation of a concentrated solution in toluene.

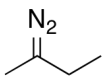


1-(2-Bromophenyl)-2-cyclopropylpropan-1-one (17). Prepared according to the general procedure on a scale of 0.061 mmol of 2-bromobenzaldehyde (8.8 μL,), 0.067 mmol of 1-cyclopropyl-1-diazoethane (60 μL of a 1.10 M solution in toluene, 1.1 equiv), and 0.0060 mmol of $Sc(OTf)_3$ (3.0 mg, 0.10 equiv) in 74% yield (0.0450 mmol, 11.4 mg) after chromatographic purification (TLC R_f = 0.30 in 90:10 hexanes:ethyl acetate). IR (thin film): 2972 (w), 1701 (s), 1429 (m), 1214 (m), 1022 (w), 968 (w), 757 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.10 (m, 2H), 0.48 (m, 2H), 1.30 (d, *J* = 8.6 Hz, 3H), 2.57 (m, 1H), 7.23-7.38 (m, 3H), 7.59 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 3.8, 4.8, 14.7, 15.7, 50.6, 118.6, 127.3, 128.3, 131.0, 133.3, 143.1, 208.1. HRMS (ESI+) Calcd for $C_{12}H_{14}BrO^+$ [M+1]$^+$: 254.0129; Found: 255.0209.

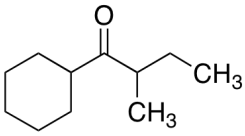


2-Butanone *N*-triisopropylsilylhydrazone. A 10 mL round bottom flask equipped with a Teflon-coated stir bar and a jointed vacuum adapter was charged with powdered 4 Å molecular sieves (4 g) and then flame-dried under vacuum. After backfilling with nitrogen, the vacuum adapter was swapped for a rubber septum and 2-butanone (0.27 mL, 3.0 mmol, 1.0 equiv) and THF (3 mL) were added successively with stirring. After cooling the suspension to 0 °C, triisopropylsilylhydrazine (0.50 g, 3.0 mmol, measured by mass difference into a gas tight syringe) was slowly added dropwise using a syringe pump (2 h). After 30 min of additional stirring, the mixture was filtered through a pad of celite in a sintered glass Schlenk filter into a dry 50 mL round bottom flask cooled to 0 ºC. The original flask, molecular sieves and celite were washed with two additional 5 mL portions of cold Et_2O. The resulting homogeneous filtrate was concentrated on a rotovap equipped with an oil-free diaphragm pump (3-10 torr) with a 0 ºC ice bath, affording 0.70 g (11 mmol, >98%) of product as a colorless oil. If not used directly in the subsequent oxidation, this material was stored under nitrogen at –20 °C.

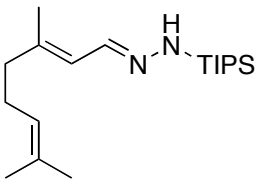


2-Diazobutane (18). A flame-dried 50 mL round bottom flask with an oversized Telflon-coated stir bar was charged with 2-butanone *N*-triisopropylsilylhydrazone (700 mg, 2.95 mmol) and 10 mL of THF. After cooling the colorless solution to 0 ºC, 2.95 mL of TBAF (1.0 M in THF, 2.95 mmol, 1.0 equiv) was added by syringe, at which point a yellow-orange discoloration immediately occurred. The solution was stirred for 10 min and then concentrated with a nitrogen purge. Without purification and in the same vessel, the crude hydrazone was freed of residual solvent under vacuum at –20 ºC, purged with nitrogen, and redissolved in 15 mL of DMF and 5 mL of 1,1,3,3-tetramethylguanidine (59 mmol, 20 equiv). The solution was cooled to –45 °C (dry ice/acetonitrile bath) and $Pb(OAc)_4$, finely powdered and weighed into a large vial in a glovebox (1.40 g, 3.24 mmol, 1.1 equiv) was added in three portions. After 45 min of stirring at –45 °C, distillation glassware was affixed to the reaction flask and the system was placed under static high vacuum for 1.5 h with the reaction flask at 0 °C and a collection flask at –78 °C. Once all coloration had left the reaction flask, the distillation apparatus was swapped for a rubber septum in order to introduce 1 mL of toluene. The concentrated deep orange toluene layer was washed once with 5 mL of precooled 30% aqueous potassium hydroxide solution and twice with 5 mL portions of saturated aqueous ammonium chloride. In each case, prolonged (>30 sec) vigorous stirring was allowed, the aqueous layer was removed by syringe, and

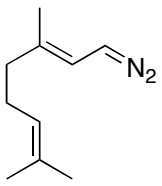
warming above the freezing point (–20 °C) was required for miscibility; these washes serve (respectively) to remove residual DMF and tetramethylguanidine from the distillate. The diazoalkane solution was then transferred quantitatively (freezing the final aqueous wash is most convenient) to a 2 mL volumetric flask for storage and use. The active titer was determined by esterification with benzoic acid. Thus, 100 μL of the stock solution was diluted with 1 mL of THF in a 5 mL round bottom flask, cooled to –45 °C, and treated with benzoic acid dropwise by syringe (295 μL of 1.0 M in THF, 0.295 mmol, 1.0 equiv based on theoretical). Upon slow warming from –45 °C, the reaction mixture became colorless and nitrogen evolution was observed. This mixture was diluted with Et_2O (10 mL) and saturated sodium bicarbonate (10 mL) and transferred to a separatory funnel. After removing the organic layer, the aqueous layer was washed with two additional 5 mL volumes of Et_2O. The pooled extract was dried over magnesium sulfate and concentrated to a light yellow oil. Purification by silica gel chromatography (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate) afforded 13.0 mg of sec-butyl benzoate (25% yield, indicative of a 0.73 M stock solution of diazoalkane **18**).



1-Cyclohexyl-2-methylbutan-1-one (19). Prepared according to the general procedure on a scale of 0.122 mmol of cyclohexane carboxaldehyde (14.7 μL), 0.13 mmol of 2-diazobutane (200 μL of a 0.67 M solution in toluene, 1.1 equiv), and 0.012 mmol of $Sc(OTf)_3$ (6.0 mg, 0.10 equiv) in 78% yield (0.0952 mmol, 16.1 mg) after chromatographic purification (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate). **19** has been synthesized previously, yet characterization data was not reported.[18] IR (thin film): 2928 (w), 2854 (w), 1707 (s), 1450 (m), 1366 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, J = 6.4 Hz, 3H), 1.13 (d, J = 8.5 Hz, 3H), 1.45-1.80 (m, 11H), 2.36 (m, 1H), 2.52 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.1, 15.4, 25.3, 25.4, 25.9, 29.9, 40.5, 47.3, 211.8. HRMS (ESI+) Calcd for $C_{11}H_{21}O^+$ $[M+1]^+$: 169.1548; Found: 169.1573.



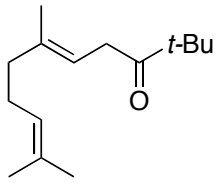
Geranial N-triisopropylhydrazone. Prepared according to the general procedure for diazoalkane synthesis and handling on a scale of 8.15 mmol of geranial (1.24 g), 8.15 mmol of triisopropylsilylhydrazine (1.53 g, 1.0 equiv), and 0.50 g of 4 Å molecular sieves in 10 ml of THF. Isolated a clear oil in 96% yield (2.52 g, 7.82 mmol) that was used directly in the subsequent oxidation without further purification.



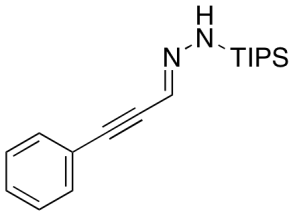
(*E*)-1-Diazo-3,7-dimethylocta-2,6-diene (20). Prepared according to the general procedure for diazoalkane synthesis and handling on a scale of 4.59 mmol geranial N-

(18) Lee, N. R.; Lee, J. I. *Synth. Comm.* **1999**, *29*, 1249-1255.

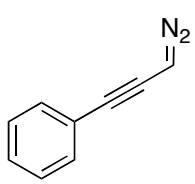
triisopropylhydrazone (1.48 g), 4.59 mmol TBAF (4.59 mL of a 1.0 M solution in THF), and 20 mL of THF. Then 46 mL of DMF, 13.2 mL of 1,1,3,3-tetramethylguanidine (106 mmol, 23.0 equiv), and 5.05 mmol of $Pb(OAc)_4$ (2.24 g, 1.1 equiv) were used in the oxidation. The diazoalkane was processed after extractive workup as a toluene solution for subsequent titration with benzoic acid and usage in homologation reactions.



(E)-2,2,6,10-Tetramethylundeca-5,9-dien-3-one (21). Prepared according to the general procedure with adjustment of the reaction temperature to –20 °C on a scale of 0.100 mmol of pivaldehyde (11.4 μL), 0.110 mmol of (*E*)-1-diazo-3,7-dimethylocta-2,6-diene (133 μL of a 1.19 M solution in toluene, 1.1 equiv), and 0.010 mmol of $Sc(OTf)_3$ (4.9 mg, 0.10 equiv) in 88% yield (0.0881 mmol, 19.6 mg) after chromatographic purification (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate). IR (thin film): 2967 (m), 2870 (m), 1708 (s), 1477 (w), 1450 (w), 1377 (w), 1365 (w), 1309 (w), 1094 (w), 1061 (w), 985 (w), 826 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.15 (s, 3H), 1.59 (s, 3H), 1.61 (d, *J* = 0.8 Hz, 3H), 1.67 (d, *J* = 0.8 Hz, 3H), 2.08-2.03 (m, 4H), 3.22 (dd, *J* = 6.8, 0.8 Hz, 2H), 5.10-5.06 (m, 1H), 5.34-5.30 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.7, 17.9, 25.9, 26.7, 26.8, 36.3, 39.8, 44.4, 116.9, 124.2, 131.6, 138.2, 214.3. HRMS (ESI+) $C_{15}H_{28}O^+$ $[M+1]^+$: Calcd for 223.2062; Found: 223.2054.

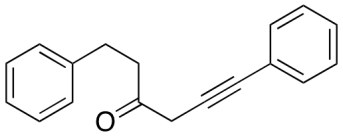


3-Phenylpropiolaldehyde triisopropylsilylhydrazone. A 10 mL round bottom flask equipped with a Teflon-coated stir bar and a jointed vacuum adapter was charged with powdered 4 Å molecular sieves (0.60 g) and then flame-dried under vacuum. After backfilling with nitrogen, the vacuum adapter was swapped for a rubber septum, and 3-phenylpropiolaldehyde (0.122 mL, 1.00 mmol) and THF (2 mL) were added successively with stirring. The suspension was then cooled to 0 °C, and triisopropylsilylhydrazine (188 mg, 1.00 mmol, measured by mass difference into a gas tight syringe) was slowly added dropwise using a syringe pump (2 h). After 30 min of additional stirring, the mixture was filtered through a pad of celite in a sintered glass Schlenk filter into a dry 50 mL round bottom flask cooled to 0 ºC. The original flask, molecular sieves, and celite were washed with two additional 5 mL portions of cold Et_2O. The resulting homogeneous filtrate was concentrated on a rotovap equipped with an oil-free diaphragm pump (3-10 torr), affording 0.29 g (0.97 mmol, 97%) of product as an oil. This material was used directly in the oxidation reaction without purification.

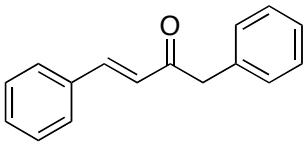


(3-Diazoprop-1-yn-1-yl)benzene (22). Prepared according to the general procedure for diazoalkane synthesis and handling on a scale of 0.890 mmol 3-phenyl-

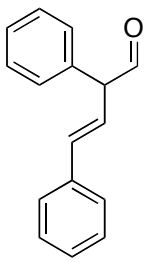
propioaldehyde triisopropylsilylhydrazone (0.267 g), 0.89 mmol of TBAF (0.89 mL of a 1.0 M solution in THF, 1.0 equiv), and 5.0 mL of THF. After concentration of the organic solvent to leave a yellow oil, 9.0 mL of DMF, 2.3 mL of 1,1,3,3-tetramethylguanidine (17.8 mmol, 20 equiv), and 1.8 mmol of $Pb(OAc)_4$ (0.85 g, 2.0 equiv) were added in succession at –45 °C. The diazoalkane was processed after extractive workup as a toluene solution for subsequent titration with benzoic acid and usage in homologation reactions.



1,6-Diphenylhex-5-yn-3-one (23). Prepared according to the general procedure on a scale of 0.15 mmol of dihydrocinnamaldehyde (20 μL), 0.167 mmol of (3-diazoprop-1-ynyl)benzene (100 μL of a 1.56 M solution in toluene, 1.1 equiv), and 0.015 mmol of $Sc(OTf)_3$ (7.5 mg, 0.10 equiv) in 77% yield (0.118 mmol, 29.4 mg) after chromatographic purification (TLC Rf = 0.30 in 95:5 hexanes:ethyl acetate). IR (thin film): 2923 (w), 1684 (s), 1495 (m), 1453 (m), 734 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.98-3.00 (m, 2H), 3.04-3.06 (m, 2H), 3.49 (s, 2H), 7.21-7.24 (m, 3H), 7.29 (s, 1H), 7.31 (s, 1H), 7.32-7.34 (m, 3H), 7.43-7.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.9, 35.2, 43.2, 82.0, 85.0, 123.1, 126.5, 128.52, 128.54, 128.6, 128.8, 128.9, 140.9, 203.9. HRMS (ESI+) Calcd for $C_{18}H_{17}O^+$ $[M+1]^+$: 249.1235; Found: 249.1770.

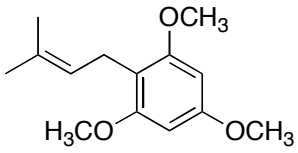


(*E*)-1,4-Diphenylbut-1-en-3-one. Prepared according to the general procedure on a scale of 0.122 mmol of cinnamaldehyde (15.3 μL, 1.0 equiv), 0.134 mmol of phenyldiazomethane (100 μL of a 1.45 M solution in toluene, 1.1 equiv), and 0.012 mmol of $Sc(OTf)_3$ (6.1 mg, 0.10 equiv) in 55% yield (0.067 mmol, 8.9 mg) after chromatographic purification (TLC Rf = 0.30 in 95:5 hexanes:ethyl acetate). IR (thin film): 3027 (w), 1661 (s), 1451 (w), 1172 (w), 980 (w), 734 (m), 688 (m). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.95 (s, 2H), 6.79 (d, *J* = 8.7 Hz, 1H), 7.26-7.31 (m, 5H), 7.32-7.41 (m, 3H), 7.52 (m, 2H), 7.63 (d, *J* = 8.7 Hz, 1H). ^{13}C NMR (125 MHz, CDCl3) δ 197.28, 143.40, 143.39, 134.47, 134.46, 134.41, 134.41, 130.59, 129.52, 129.52, 128.94, 128.94, 128.80, 128.79, 128.40, 128.40, 127.02, 127.02, 125.22, 125.21, 48.39. HRMS (ESI+) Calcd for $C_{16}H_{15}O^+$ $[M+1]^+$: 223.1073; Found: 223.1068.

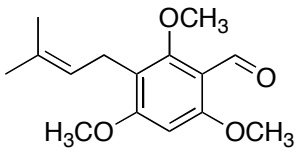


(*E*)-2-Methyl-2,4-diphenylbut-3-enal (24). Prepared according to the general procedure on a scale of 0.122 mmol of cinnamaldehyde (15.3 μL), 0.134 mmol of methyl phenyl diazomethane **12** (400 μL of a 0.32 M solution in toluene, 1.1 equiv), and 0.012 mmol of $Sc(OTf)_3$ (6.1 mg, 0.10 equiv) in 25% yield (0.031 mmol, 6.1 mg) after chromatographic

purification (TLC Rf = 0.35 in 95:5 hexanes:ethyl acetate). Characterization data for **2a** has been recorded previously.[19]



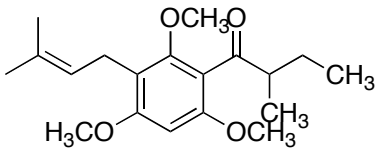
1-Prenyl-2,3,6-trimethoxybenzene. In a 200 mL round bottom flask equipped with a stir bar, 3.89 g (23.1 mmol) of 1,3,5-trimethoxybenzene was dissolved in 46 mL of cyclohexane. The resulting colorless solution was cooled to 0 °C and 20.0 mL of *n*-BuLi (1.62 M in hexanes, 32.4 mmol, 1.4 equiv) was added dropwise, turning the solution pale yellow in color. The reaction mixture was then heated to 65 °C for 30 min, at which point a fine, rust-colored precipitate had formed. After cooling the mixture to 23 °C, 4.0 mL (34.6 mmol, 1.5 equiv) of prenyl bromide was added dropwise from a syringe, and the mixture was again heated near the solvent boiling point for 2 h. Upon cooling to 23 °C, the reaction mixture was yellow in color but remained cloudy. The mixture was diluted with 100 mL of saturated sodium bicarbonate and transferred to a 250 mL separatory funnel with 50 mL of Et_2O. After agitation and removal of the organic layer, the aqueous layer was washed with two additional 50 mL volumes of Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to an orange oil. Due to a minor impurity that co-elutes with the product, purification was best accomplished in two stages by separate chromatographies, first in 1.2:1 CH_2Cl_2:hexanes (TLC R_f = 0.40) and second in 15:1 hexanes:ethyl acetate (TLC R_f = 0.30). Concentration of pure fractions afforded 4.38 g (18.5 mmol, 80%) of a colorless oil that solidified when stored neat at –20 °C. IR (thin film): 2915 (w), 1592 (m), 1453 (m), 1202 (m), 1146 (m), 1114 (s), 809 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.68 (s, 3H), 1.80 (s, 3H), 3.31 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 9H), 5.23 (t, *J* = 6.8 Hz, 1H), 6.18 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.9, 21.8, 25.9, 55.4, 55.9, 90.6, 110.8, 123.8, 130.5, 158.7, 159.4. HRMS (ESI+) Calcd for $C_{27}H_{35}O_4^+$ $[M+1]^+$: 423.2491; Found: 423.2491.



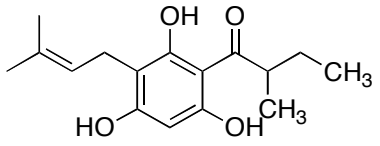
3-Prenyl-2,4,6-trimethoxybenzaldehyde (25). A 50 mL round bottom flask was charged with 322 μL (3.80 mmol, 1.2 equiv) of oxalyl chloride and 15 mL of CH_2Cl_2; the resulting homogeneous solution was cooled to 0 °C. At a rate conducive to the control of gas evolution, 295 μL (3.80 mmol, 1.2 equiv) of dimethylformamide was added by syringe. The reaction mixture was stirred for 30 min and warmed to 23 °C. A solution of 1-prenyl-2,3,6-trimethoxybenzene (750 mg, 3.17 mmol in 6 mL of cyclohexane) was then added through a cannula. The mixture was stirred for 4 h at 23 °C and then diluted with 50 mL of saturated sodium bicarbonate and 50 mL of ethyl acetate. After removal of the organic layer in a separatory funnel, the

(19) Fleming, I.; Rowley, M. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2259.

aqueous layer was washed with two additional 50 mL portions of ethyl acetate. Combined organic layers were dried over magnesium sulfate, filtered, and concentrated to a yellow oil. Purification by silica gel chromatography (TLC R_f = 0.30 in 1:1 hexanes:ethyl acetate) afforded 788 mg (2.98 mmol, 94%) of **25** as a pale yellow oil. IR (thin film): 2932 (w), 1673 (s), 1588 (m), 1224 (m), 1098 (s), 809 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.64 (s, 3H), 1.75 (s, 3H), 3.24 (d, *J* = 8.9 Hz, 2H), 3.79 (s, 3H), 3.88 (s, 6H), 5.11 (t, *J* = 6.8 Hz, 1H), 6.24 (s, 2H), 10.29 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.9, 22.2, 26.0, 55.9, 56.1, 63.2, 91.1, 110.4, 116.6, 123.0, 131.8, 161.9, 162.4, 164.1, 188.1. HRMS (ESI+) Calcd for $C_{28}H_{35}O_5^+$ [M+1]$^+$: 451.2440; Found: 451.2450.

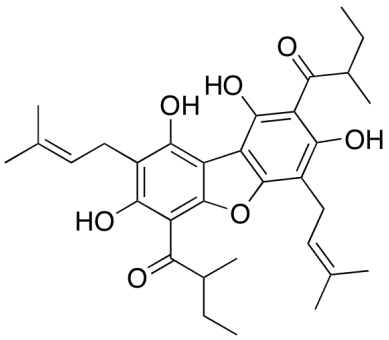


2-Methyl-1-(2,4,6-trimethoxy-3-(3-methylbut-2-enyl)phenyl)butan-1-one (26). Prepared according to the general procedure on a scale of 4.28 mmol of trimethoxybenzaldehyde (1.13 g), 4.7 mmol of 2-diazobutane (7.0 mL of a 0.67 M solution in toluene, 1.1 equiv), and 0.428 mmol of $Sc(OTf)_3$ (211 mg, 0.10 equiv) in 91% yield (3.89 mmol, 1.25 g) after chromatographic purification (TLC R_f = 0.30 in 90:10 hexanes:ethyl acetate). IR (thin film): 2938 (w), 2865 (w), 1694 (s), 1598 (m), 1460 (m), 1106 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, *J* = 7.7 Hz, 3H), 1.11 (d, *J* = 8.8 Hz, 3H), 1.19 (m, 1H), 1.68 (s, 3H), 1.76 (s, 3H), 2.91 (m, 1H), 3.27 (d, *J* = 8.7 Hz, 2H), 3.69 (s, 3H), 3.81 (s, 3H), 3.87 (s, 3H), 5.16 (t, *J* = 6.7 Hz, 1H), 6.26 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.4, 15.2, 22.9, 25.4, 25.9, 49.1, 56.0, 56.1, 63.3, 92.0, 116.2, 123.5, 123.6, 131.7, 155.9, 156.4, 159.9, 208.6. HRMS (ESI+) Calcd for $C_{19}H_{29}O_4^+$ [M+1]$^+$: 321.2066; Found: 321.2075.

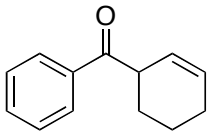


2-Methyl-1-(2,4,6-trihydroxy-3-(3-methylbut-2-enyl)phenyl)butan-1-one (27). To a CH_2Cl_2 solution (0.46 mL) of 0.047 mmol of **26** (15 mg) in a 1 dram vial was added 0.28 mmol of BBr_3 (27 μL, 6.0 equiv) at 23 °C. After sealing the vial with a Teflon-lined screw cap, the solution was heated at 35 °C for 12 h. The reaction mixture was then cooled to 23 °C and washed with an equivalent volume of saturated sodium chloride. The organic layer was dried over magnesium sulfate, filtered, and concentrated. Purification by silica gel chromatography (TLC R_f = 0.30 in 90:10 hexanes:ethyl acetate) delivered a clear oil in 15% yield (0.007 mmol, 2 mg). An alternative and much higher yielding deprotection strategy involves first reduction to the benzylic alcohol, then global demethylation with TMSI, and finally reoxidation with the Dess-Martin periodinane (65% overall, three steps). These details are not disclosed here because we are in the process of rerouting to phloroglucinol as a starting material and incorporating a more readily removable blocking group (benzyl) into the path

of synthesis. IR (thin film): 3422 (br), 2972 (w), 2930 (w), 1626 (s) 1590 (m), 1422 (w), 1229 (m), 1158 (m), 1117 (m), 882 (w), 817 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (t, *J* = 7.7 Hz, 3H), 1.18 (d, *J* = 8.8 Hz, 3H), 1.33 (s, 6H), 1.38 (m, 2H), 1.79 (t, *J* = 6.7 Hz, 1H), 2.59 (t, *J* = 6.7 Hz, 1H), 3.73 (m, 1H), 5.71 (s, 1H), 5.98 (br s, 3H). HRMS (ESI+) Calcd for $C_{16}H_{23}O_4^+$ $[M+1]^+$: 279.1795; Found: 279.1880.



"Pre-achyrofuran" (28). To a slurry of 0.0576 mmol $FeCl_3$ on SiO_2 (0.144 g, 4.0 equiv) in CH_2Cl_2 (0.72 mL, 0.08 M) at 23 °C was added a 0.2 M solution of **27** (4.0 mg, 0.014 mmol) in CH_2Cl_2:CH_3CN (3:1). The faint yellow solution instantly turned dark brown, and after 5 min of rapid stirring the solution was filtered through a celite plug and concentrated to a brown oil. Purification by silica gel chromatography (TLC R_f of **28** = 0.30 in 95:5 hexanes:ethyl acetate) afforded 3.8 mg of the desired product (0.0071 mmol, 51%), 1.6 mg of the uncyclized homodimer (0.0029 mmol, 21%), and 0.9 mg of recovered starting material (0.0031 mmol, 21%). Characterization follows for the desired product dibenzofuran. IR (thin film): 3492 (b), 2927 (w), 1618 (s), 1420 (w), 1230 (w), 1159 (m), 1117 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (t, *J* = 7.5 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.24 (d, *J* = 7.0 Hz, 3H), 1.31 (s, 3H), 1.32 (s, 3H), 1.39 (m, 1H), 1.46 (m, 1H), 1.69 (s, 3H), 1.85 (s, 3H), 1.86-1.92 (m, 2H), 3.47 (m, 1H), 3.73 (m, 1H), 5.69 (br s, 2H), 5.99 (br s, 2H). HRMS (ESI+) Calcd for $C_{32}H_{41}O_7^+$ $[M+1]^+$: 537.1295; Found: 537.1259.

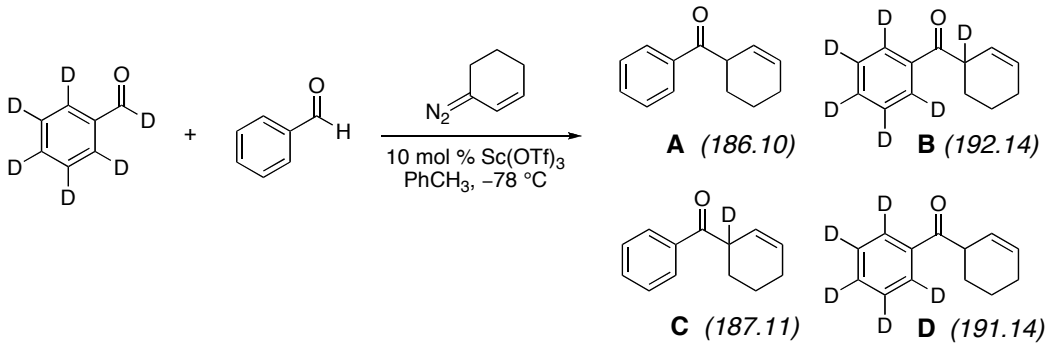


Cyclohex-2-enyl(phenyl)methanone. Prepared according to the general procedure on a scale of 0.162 mmol of benzaldehyde (16.4 μL), 0.179 mmol of 3-diazocyclohex-1-ene (488 μL of a 0.37 M solution in toluene, 1.1 equiv), and 0.016 mmol of $Sc(OTf)_3$ (8.0 mg, 0.10 equiv) in 87% yield (0.141 mmol, 26.4 mg) after chromatographic purification (TLC R_f = 0.30 in 95:5 hexanes:ethyl acetate). IR (thin film): 2935 (w), 1680 (s), 1447 (m), 1209 (m), 960 (m), 695 (w). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.71 (m, 2H), 1.95 (m, 2H), 1.99 (m, 2H), 4.09 (m, 1H), 5.74 (m, 2H), 5.93 (m, 2H), 7.47 (t, *J* = 6.8 Hz, 2H), 7.54 (t, *J* = 6.8 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 25.2, 26.0, 42.0, 125.1, 128.2, 128.3, 130.4, 133.3, 136.4, 202.2. HRMS (ESI+) Calcd for $C_{13}H_{15}O^+$ $[M+1]^+$: 187.1078; Found: 187.1109.

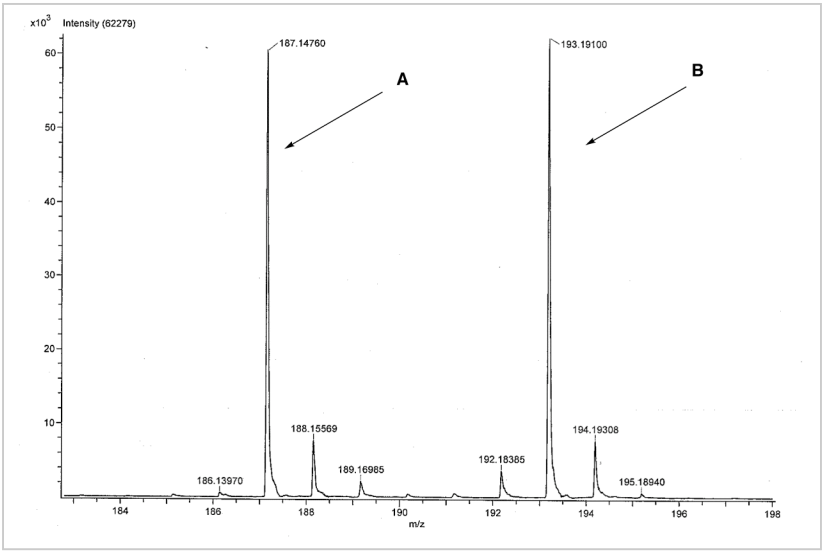
Deuterium Labeling Studies:

In order to distinguish between possible mechanistic pathways (see text of manuscript), the

following experiment was undertaken: In a glovebox, a flame-dried 1 dram vial equipped with a Teflon-coated flea stir bar was charged with $Sc(OTf)_3$ (9.8 mg, 0.020 mmol, 0.10 equiv) and sealed with a rubber septum. In a fume hood, toluene (2.0 mL, 0.1 M) was added by syringe, suspending but not dissolving the catalyst. After cooling the mixture to –78 °C, 10.1 μL benzaldehyde (0.100 mmol, 0.50 equiv), 10.2 μL d_6-benzaldehyde (0.100 mmol, 0.50 equiv), and 470 μL 3-diazocyclohex-1-ene (0.470 M solution in toluene, 0.220 mmol, 1.1 equiv, solution kept cold at –78 °C) were added in succession to the stirring reaction mixture by syringe. The reaction was stirred for 10 min at –78 °C, at which point the characteristic purple color of the nucleophile had dissipated, leaving a turbid light yellow suspension. The reaction mixture was concentrated with a nitrogen purge and purified by flash chromatography (TLC R_f = 0.30 in 19:1 hexanes:ethyl acetate) affording 23.1 mg of a mixture of products **A** and **B**.



The high resolution mass spectrum of the mixture (see Figure) clearly shows a predominance of peaks corresponding to $[M+H]^+$ for structures **A** and **B**. Although the peaks at 188.1557 and 192.1839 could in principle correspond to deuterium crossover structures **C** and **D**, analogous control experiments carried out with just benzaldehyde or d_6-benzaldehyde generate high-resolution mass spectra identical to the individual mass distributions seen in the Figure. The presence of these ions is thus an artifact of the natural abundance of deuterium and the starting level of enrichment in the commercial d_6-benzaldehyde.



STANDARD 1H OBSERVE

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Ambient temperature
GEMINI-400BB "nmr8"

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Pulse 40.4 degrees
Acq. time 3.000 sec
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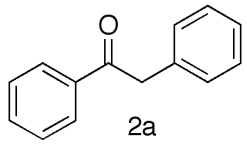
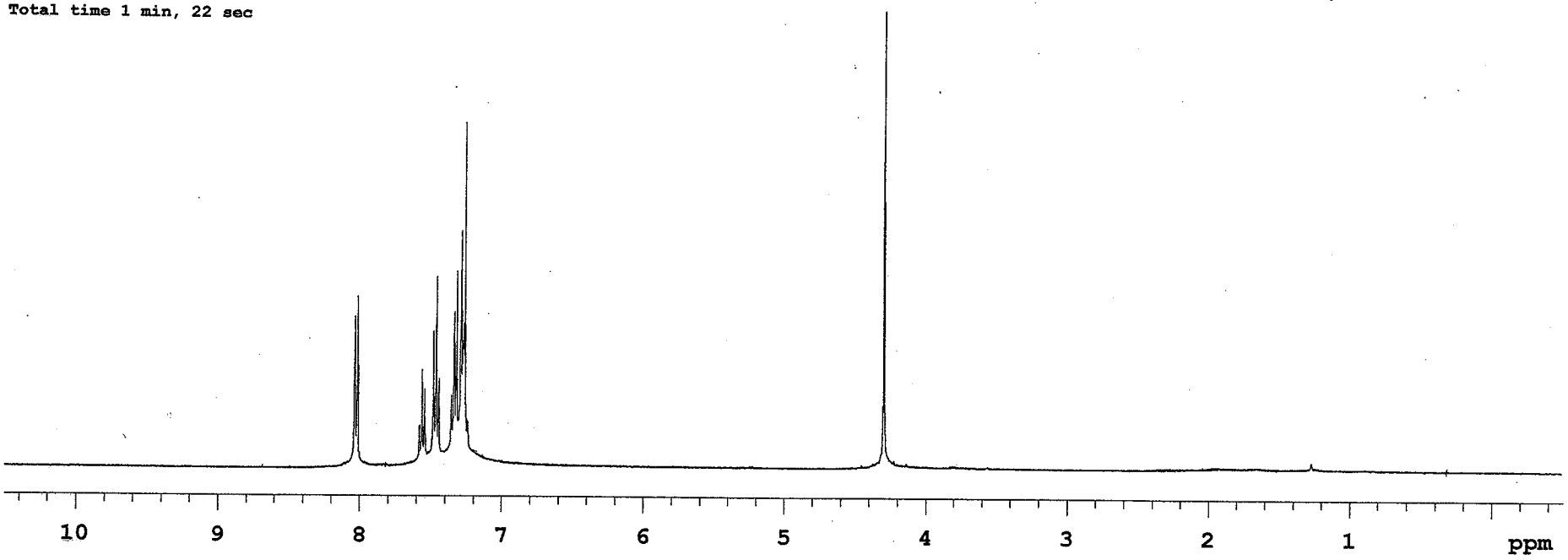
16 repetitions
OBSERVE H1, 400.0268150 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 22 sec



2a



STANDARD 1H OBSERVE

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ACQUISITION		dmm	c
sfrq	400.029	dmf	200
tn	H1	PROCESSING	
at	3.000	wtfile	
np	35992	proc	ft
sw	5998.8	fn	not used
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bs	16	werr	
tpwr	63	wexp	
pw	7.1	wbs	
d1	2.000	wnt	
tof	0		
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ct	16		
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FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
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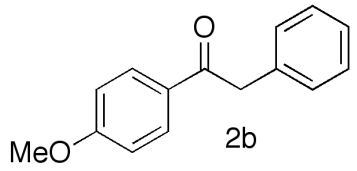
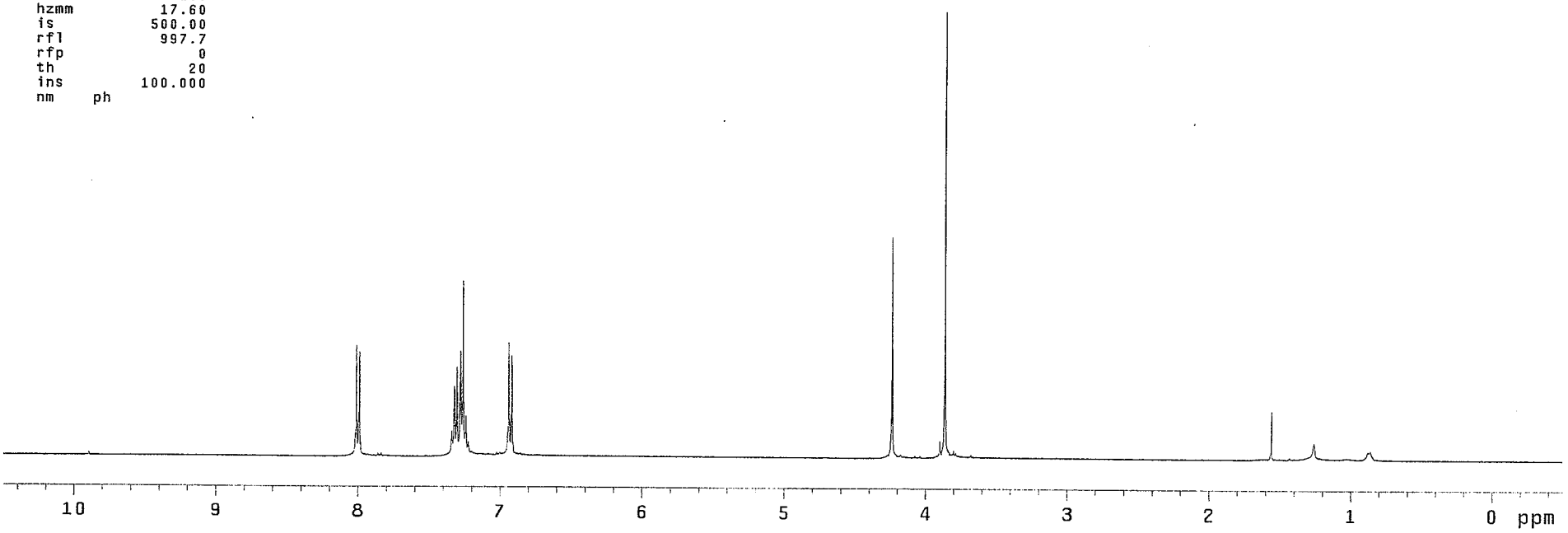
nm	ph		



2b



STANDARD 1H OBSERVE

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ACQUISITION		dmm	c
sfrq	400.029	dmf	200
tn	H1	**PROCESSING**	
at	3.000	wtfile	
np	35992	proc	ft
sw	5998.8	fn	not used
fb	3400		
bs	16	werr	
tpwr	63	wexp	
pw	7.1	wbs	
d1	2.000	wnt	
tof	0		
nt	12		
ct	12		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-200.0		
wp	4400.2		
vs	107		
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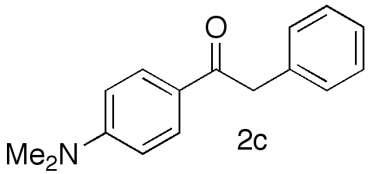
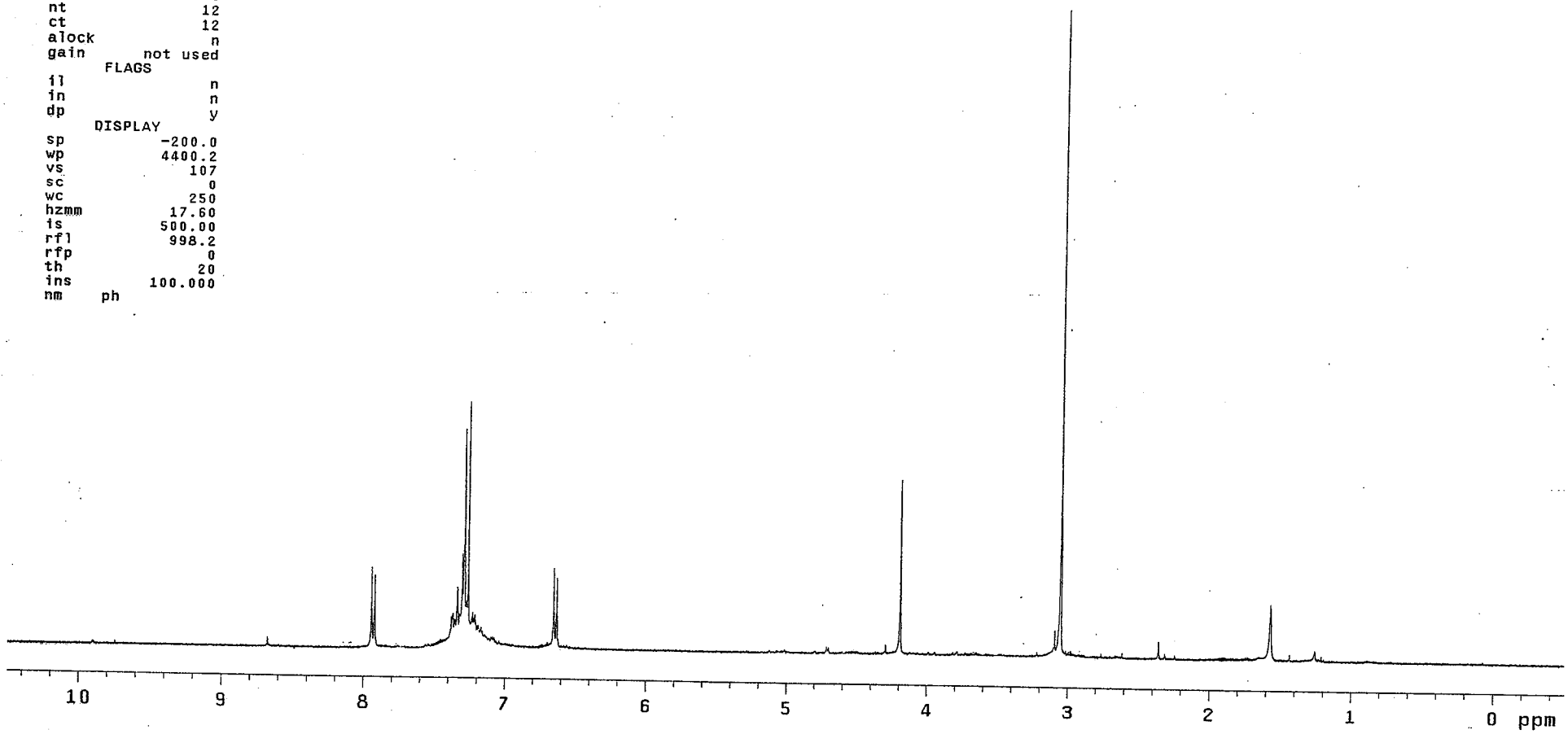
nm	ph		



2c



STANDARD 1H OBSERVE

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ACQUISITION		dmm	c
sfrq	400.029	dmf	200
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sw	5998.8	fn	not used
fb	3400		
bs	16	werr	
tpwr	63	wexp	
pw	7.1	wbs	
d1	2.000	wnt	
tof	0		
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dp	y		
DISPLAY			
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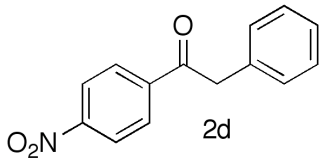
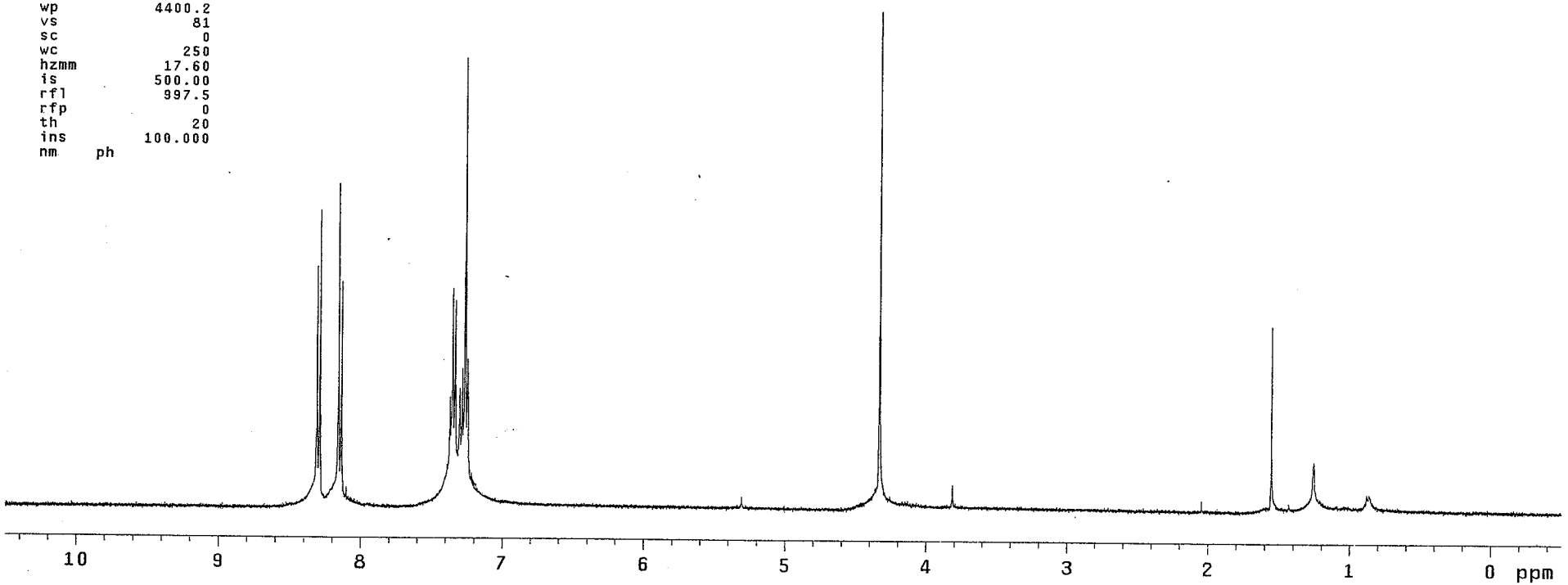
ins	100.000		
nm	ph		





AJW-III-002prod

Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

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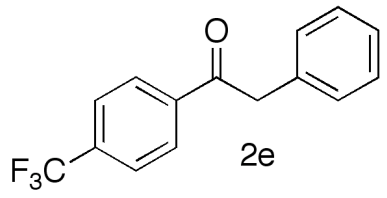
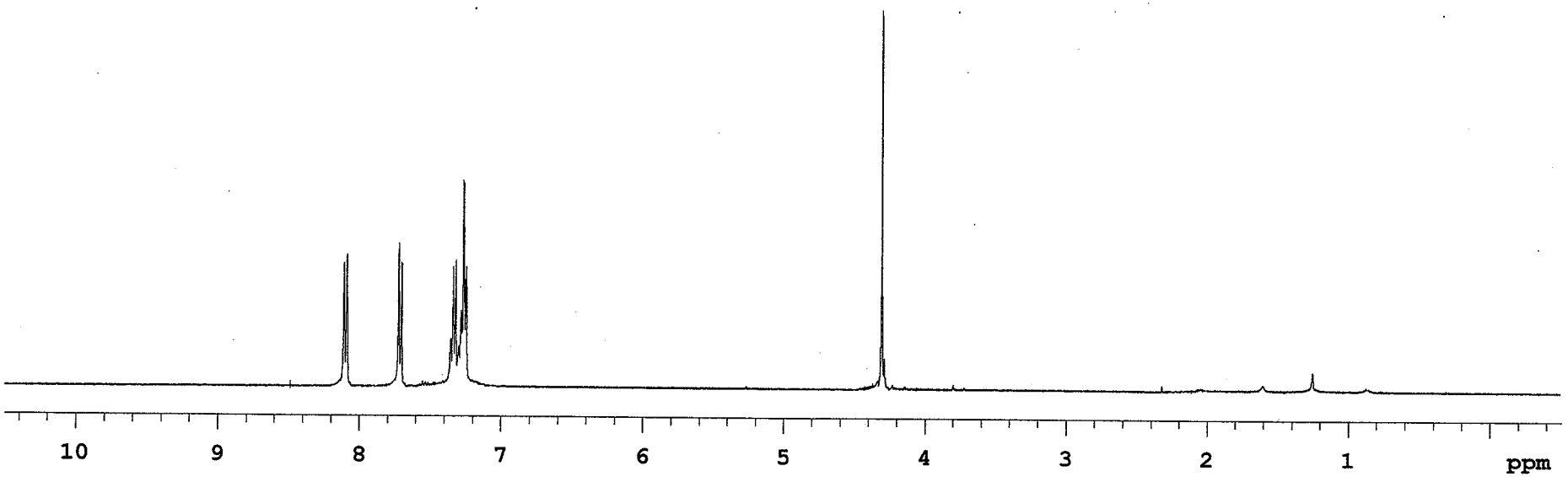
DATA PROCESSING
FT size 65536
Total time 1 min, 2 sec



2e



STANDARD 1H OBSERVE

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bs	16	werr	
tpwr	63	wexp	
pw	7.1	wbs	
d1	2.000	wnt	
tof	0		
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ct	16		
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in	n		
dp	y		
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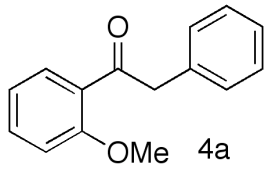
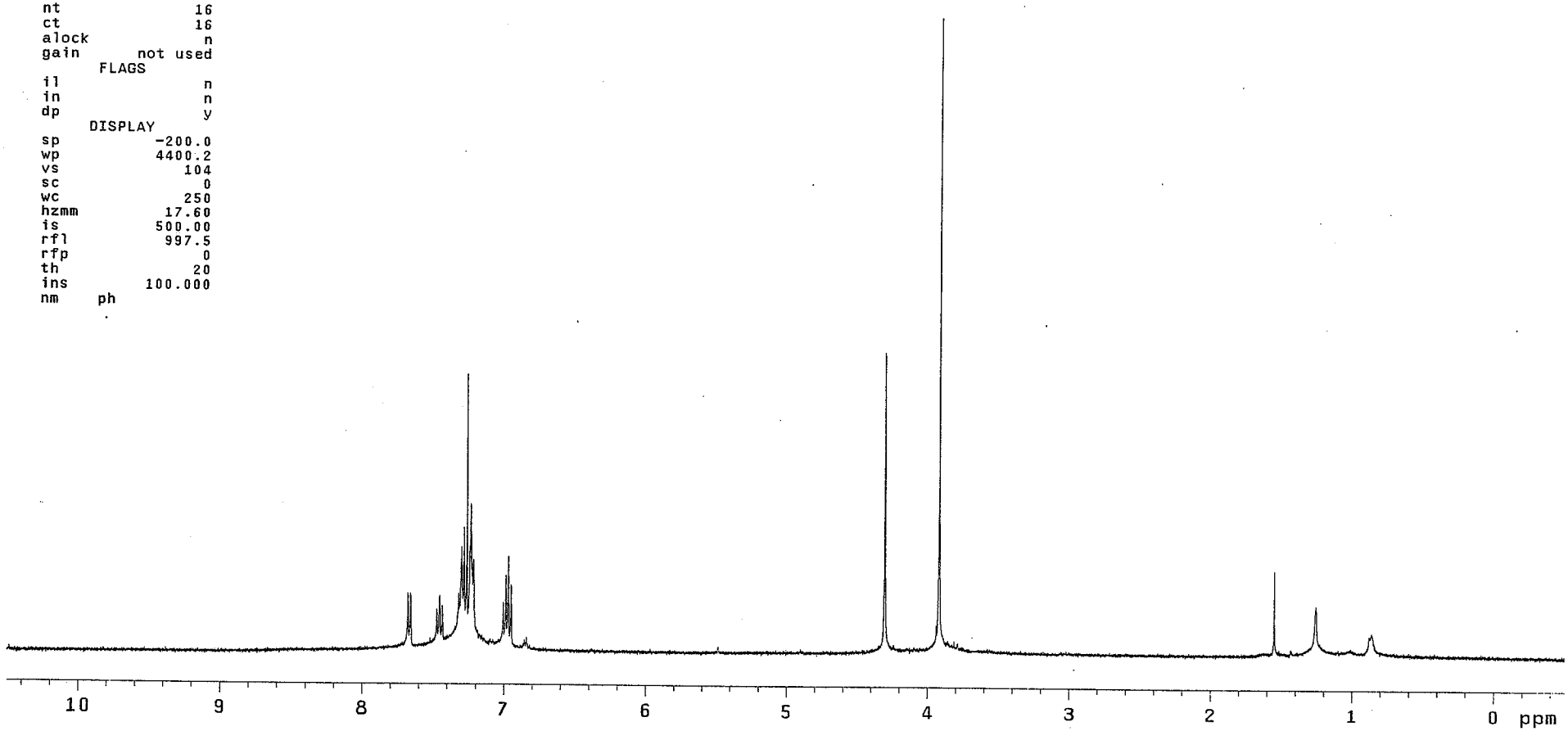
nm	ph		



4a



STANDARD 1H OBSERVE

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np	35992	proc	ft
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tpwr	63	wexp	
pw	7.1	wbs	
d1	2.000	wnt	
tof	0		
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gain	not used		
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in	n		
dp	y		
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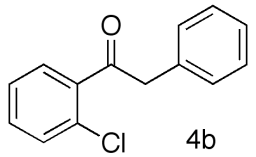
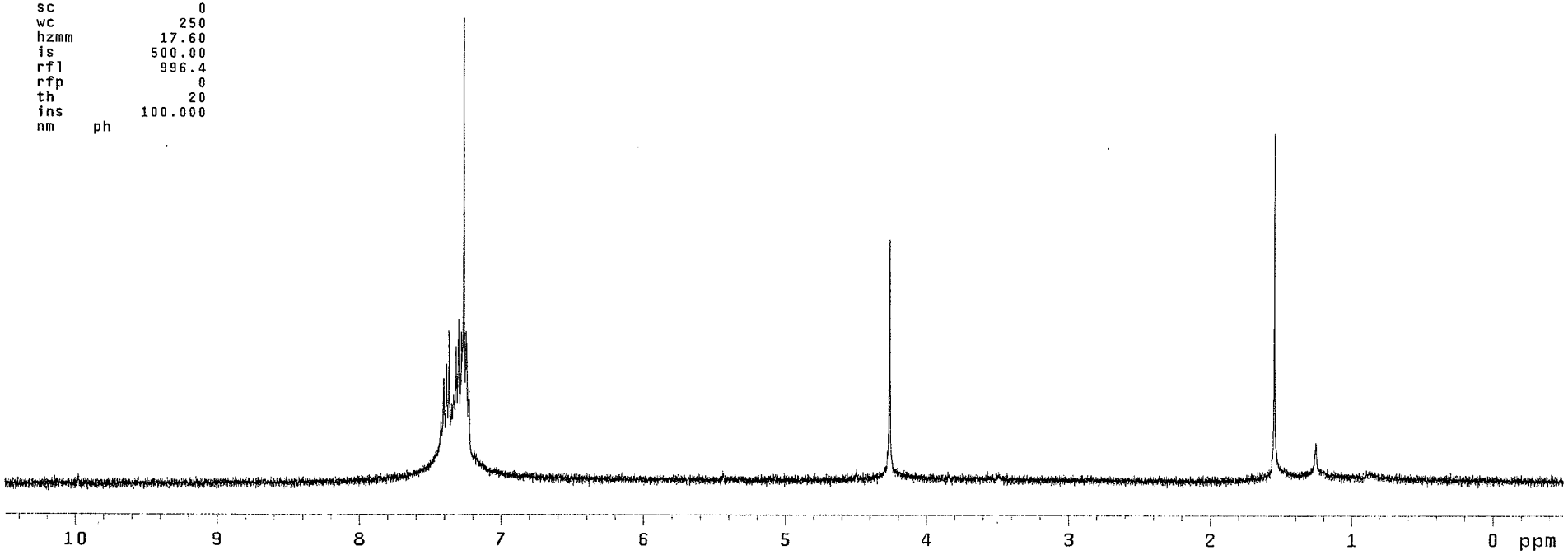
nm	ph		



4b



STANDARD 1H OBSERVE

exp1 std1h

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ACQUISITION		dmm	c
sfrq	400.029	dmf	200
tn	H1	PROCESSING	
at	3.000	wtfile	
np	35992	proc	ft
sw	5998.8	fn	not used
fb	3400		
bs	16	werr	
tpwr	63	wexp	
pw	7.1	wbs	
d1	2.000	wnt	
tof	0		
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ct	16		
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gain	not used		
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in	n		
dp	y		
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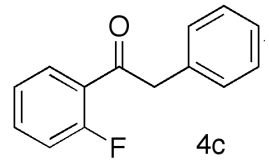
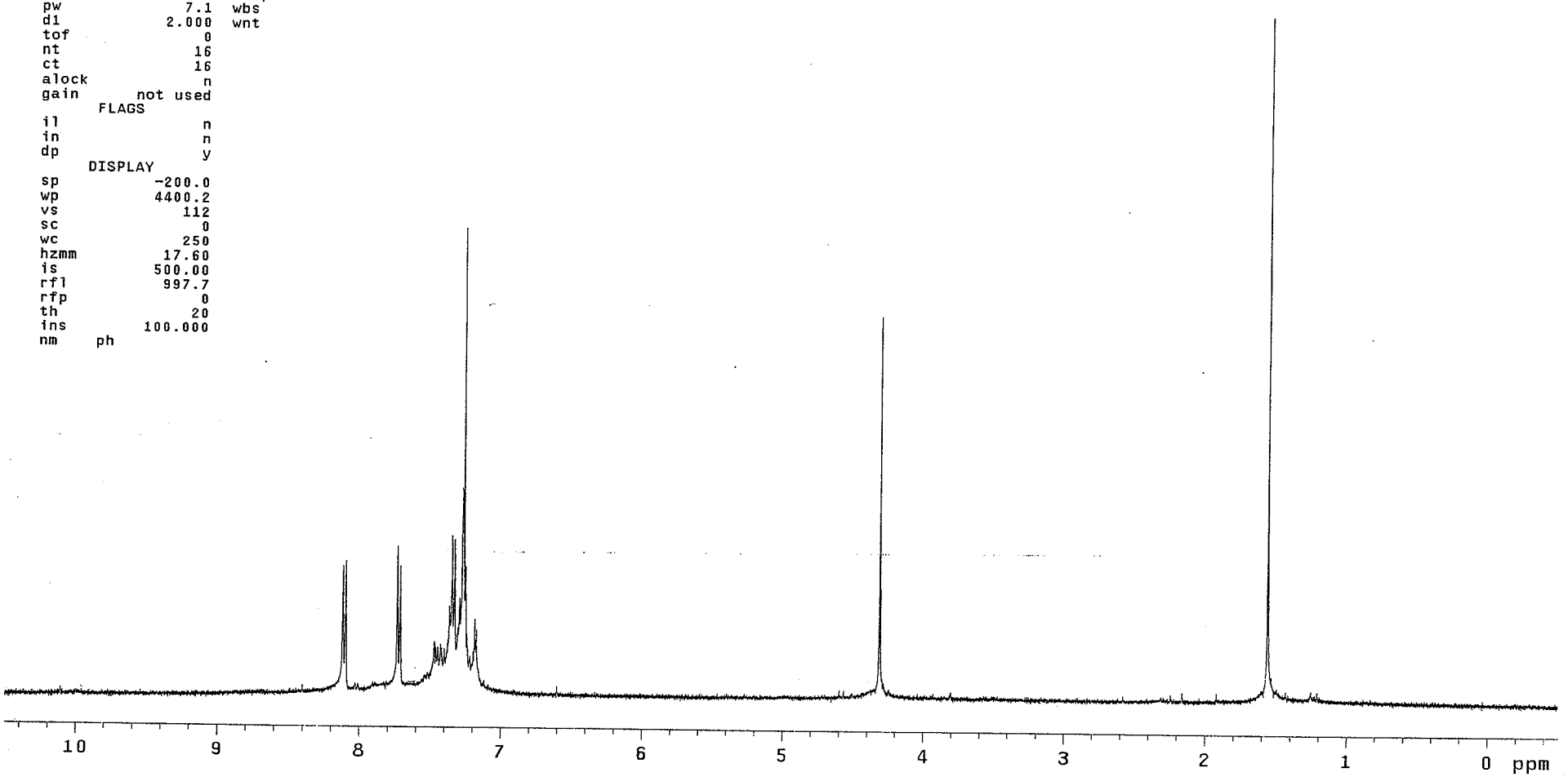
nm	ph		



4c



5

STANDARD 1H OBSERVE

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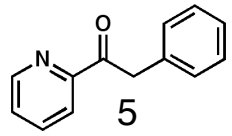
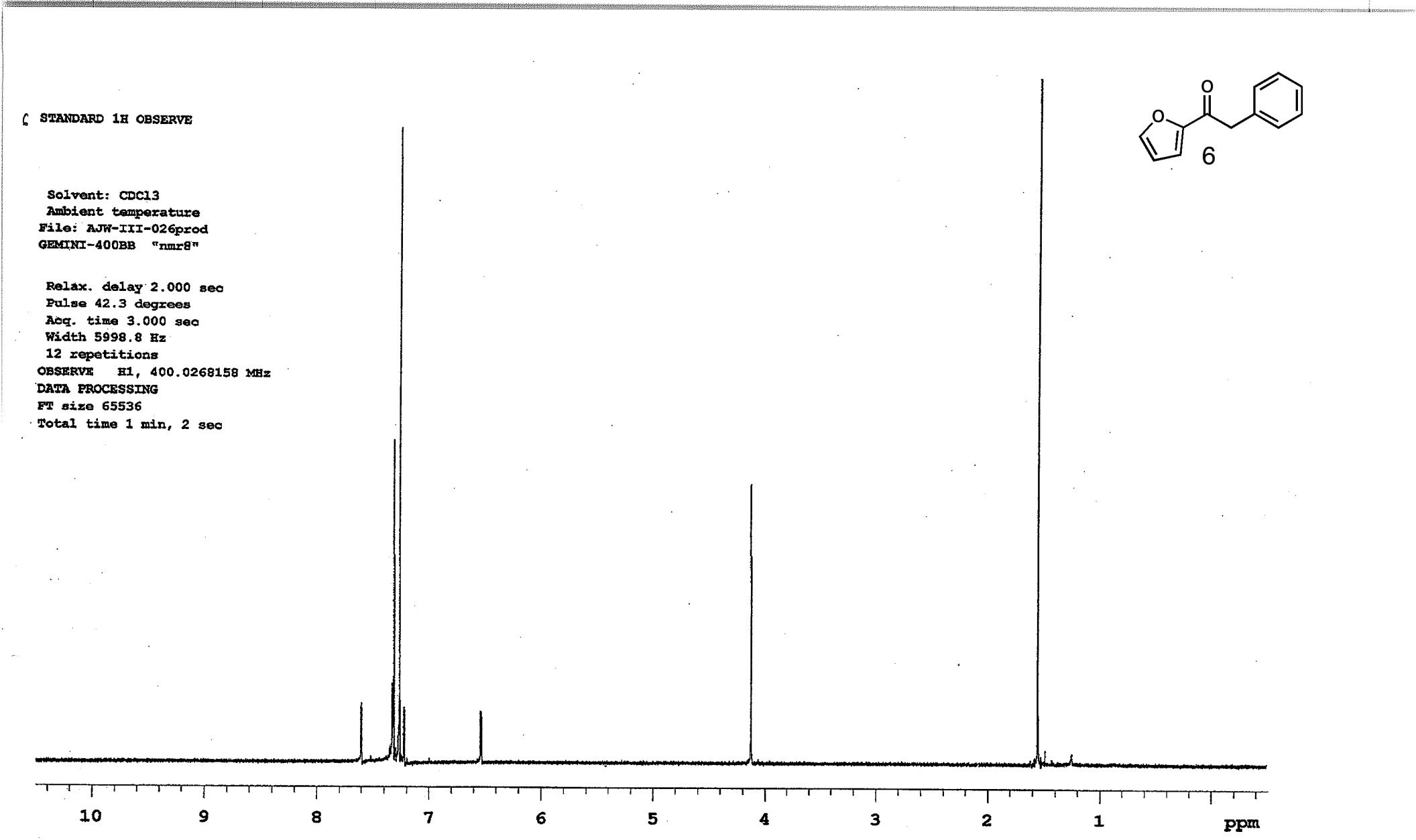
Ambient temperature
File: AJW-III-001spot
GEMINI-400BB "nmr8"

Relax. delay 2.000 sec
Pulse 42.3 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0268150 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 22 sec



5


STANDARD 1H OBSERVE
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Ambient temperature
File: AJW-III-026prod
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 42.3 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
12 repetitions
OBSERVE H1, 400.0268158 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 2 sec
O
O
6
10
9
8
7
6
5
4
3
2
1
ppm

STANDARD 1H OBSERVE

exp1 std1h

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ACQUISITION		dmm	c
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tn	H1	PROCESSING	
at	3.000	wtfile	
np	35992	proc	ft
sw	5998.8	fn	not used
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in	n		
dp	y		
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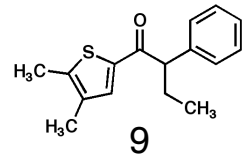
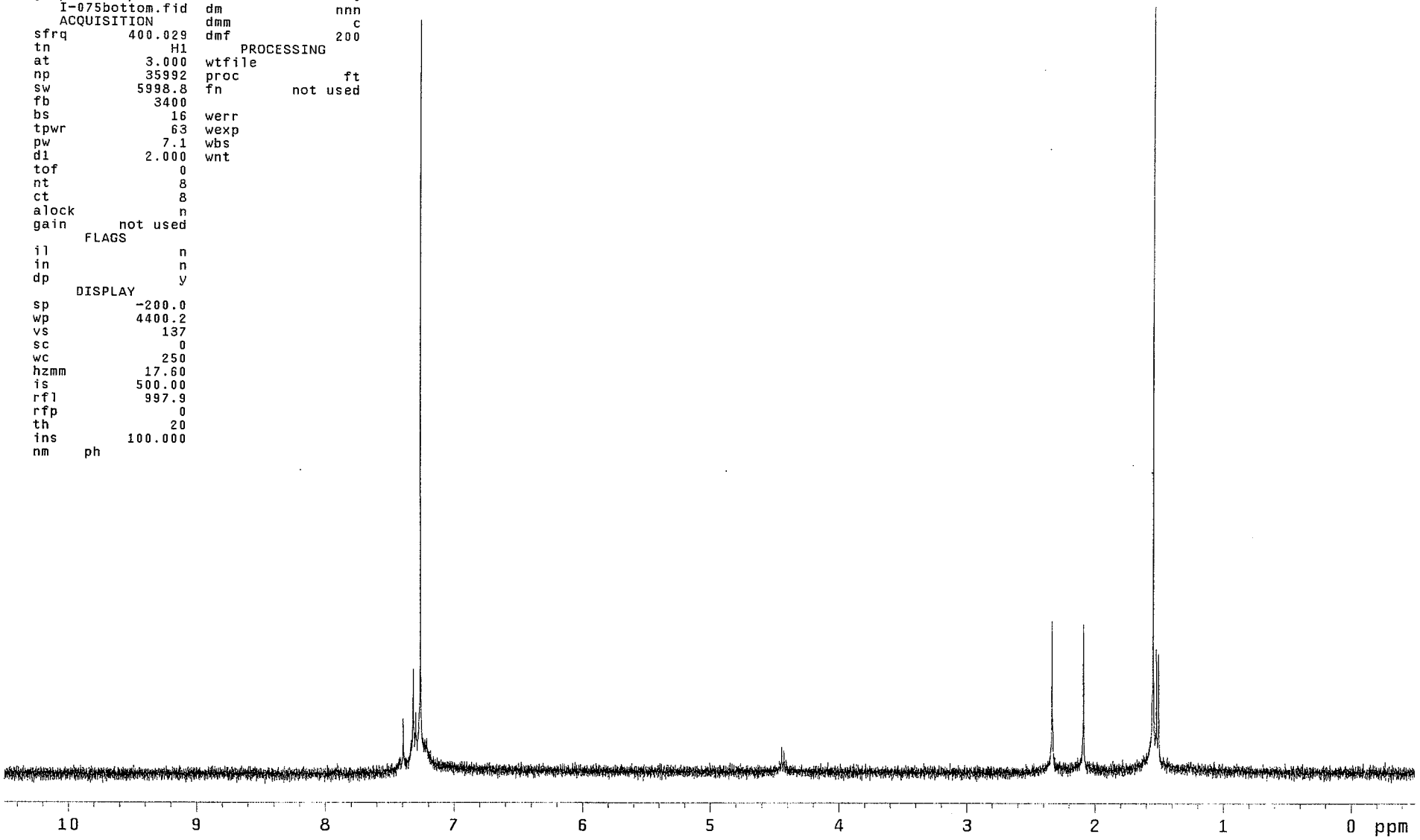
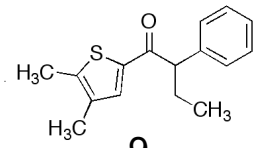
ins	100.000		
nm	ph		



9



13C OBSERVE



9

Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

Relax. delay 4.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
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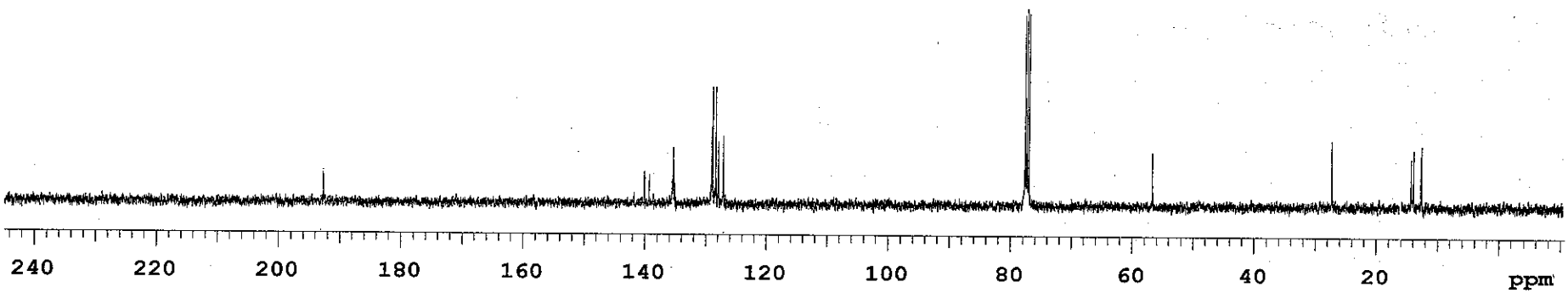
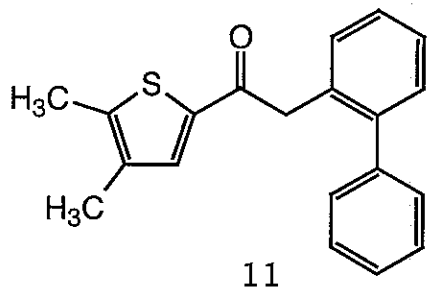
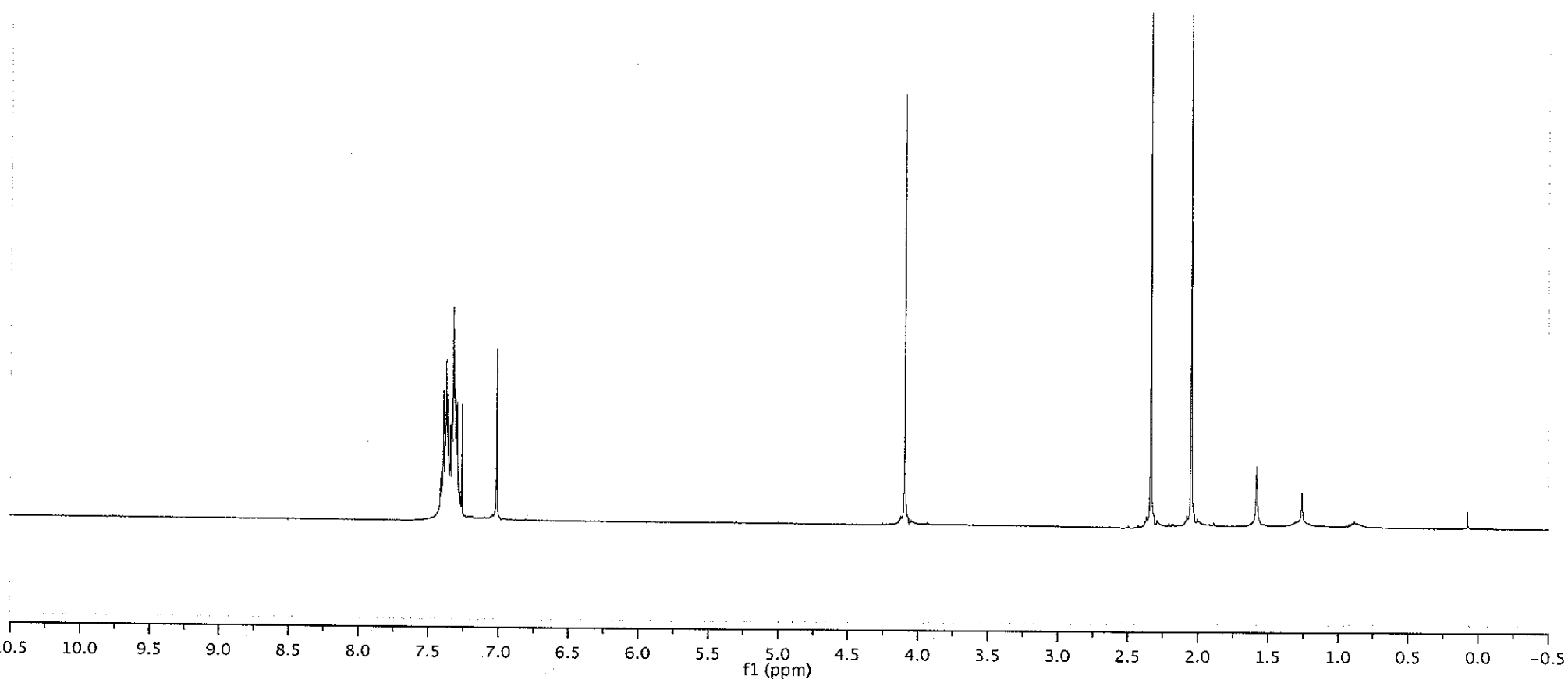
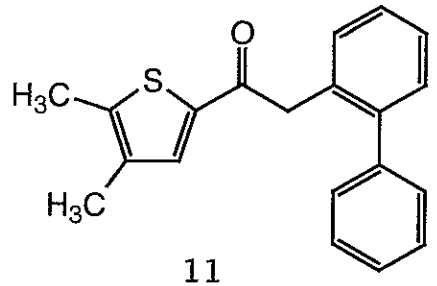
192 repetitions
OBSERVE C13, 100.5868063 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 32 min, 3 sec



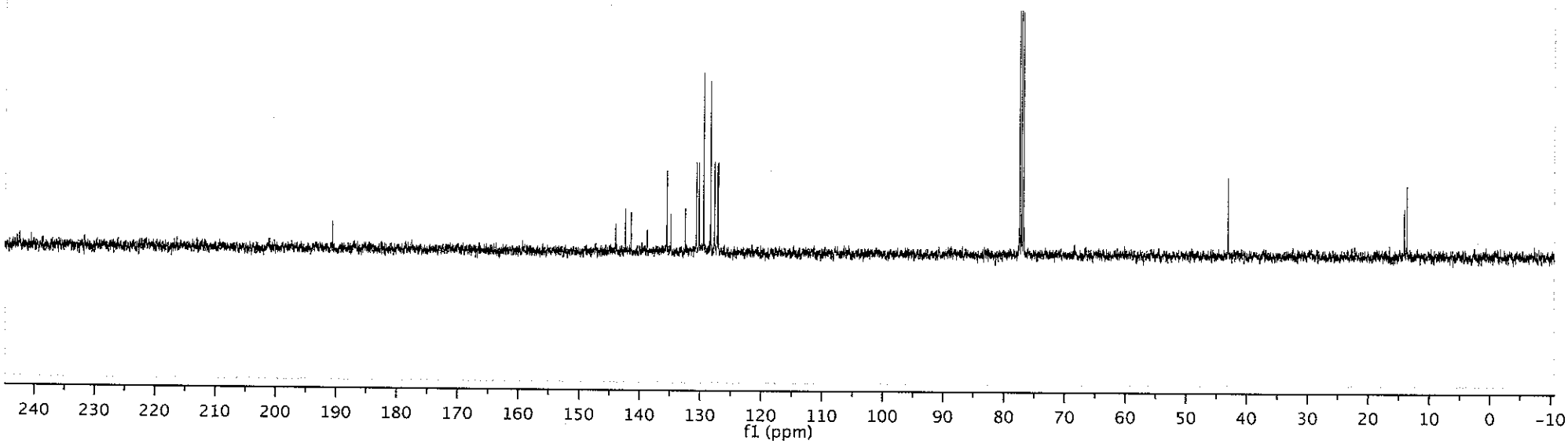

O
S
H3C
H3C

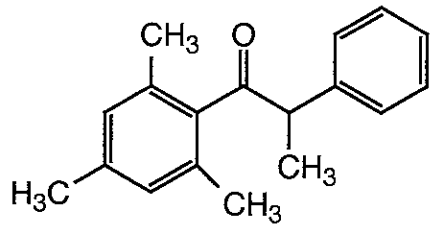
11


10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

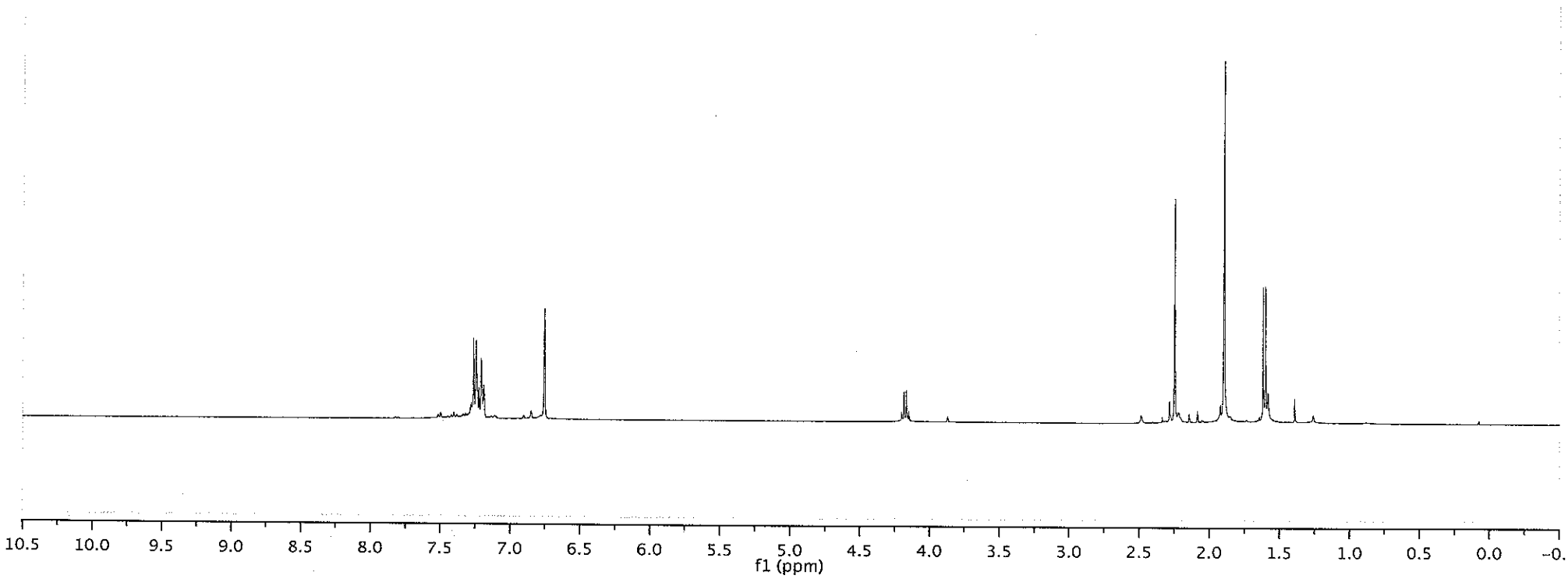

O
S
H3C
H3C

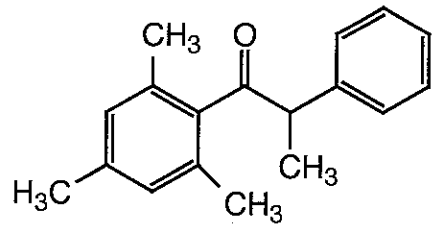
11


240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

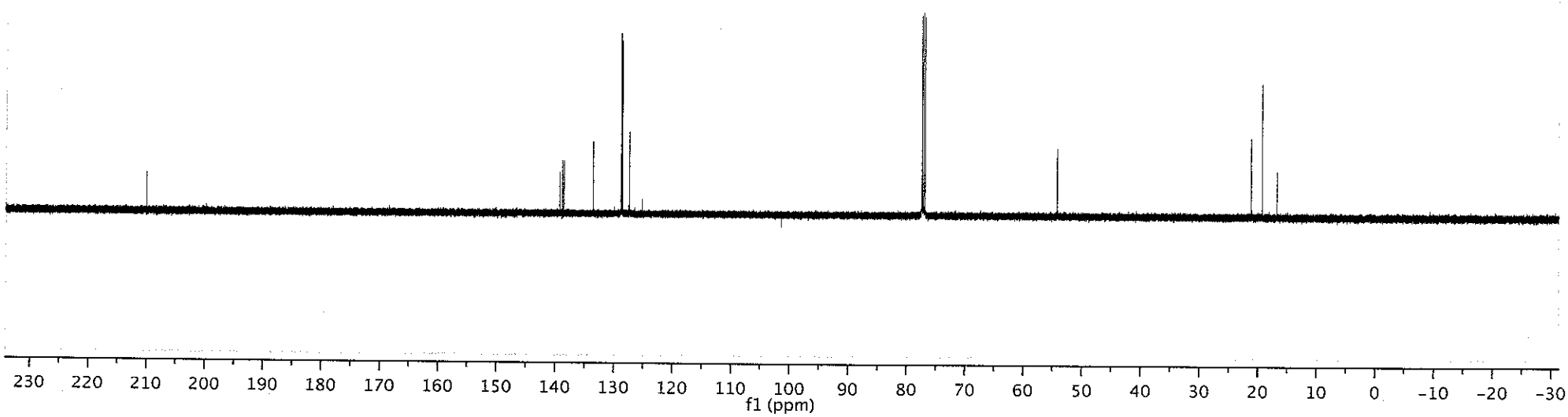

CH3
O
CH3
H3C
CH3

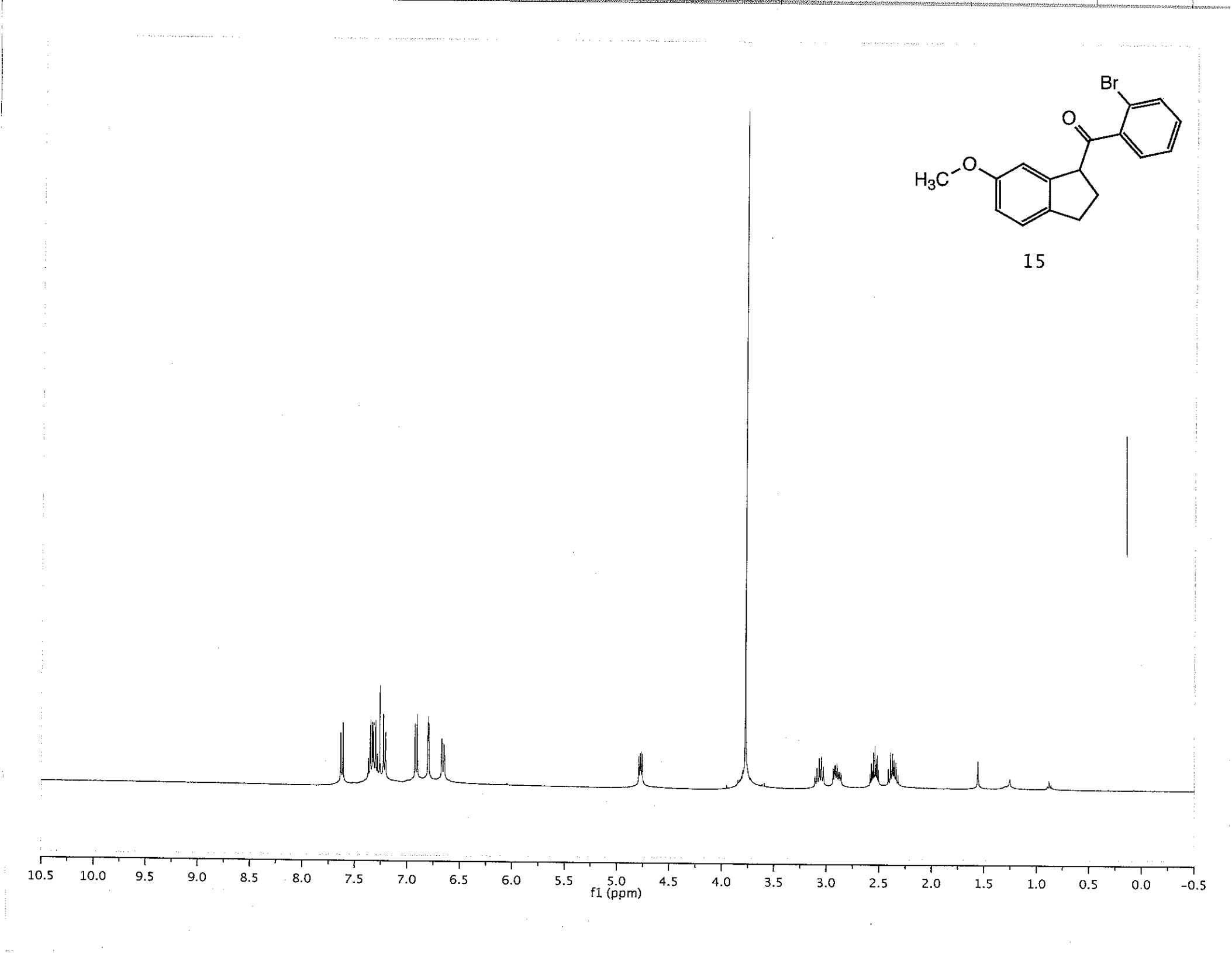
13

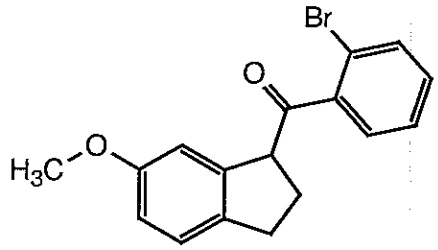

10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


CH3
O
CH3
H3C
CH3

13


230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

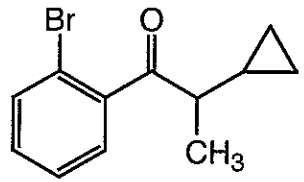

Br
O
H3C
O
15
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



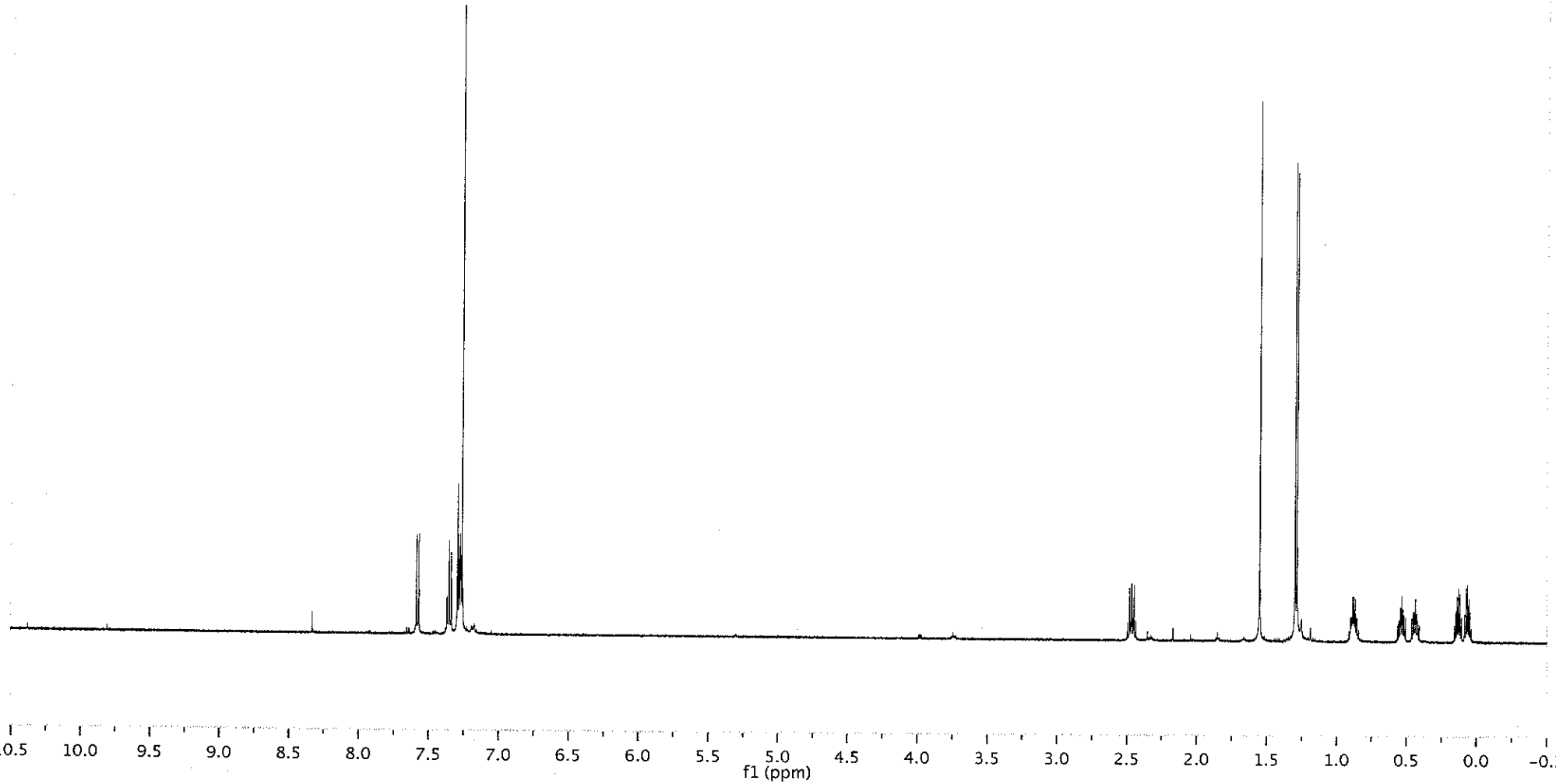
15

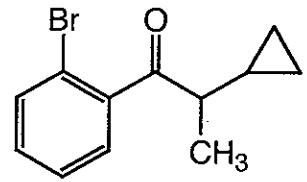
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)


Br
O
CH3

17


10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Br
O
CH3

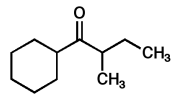
17

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

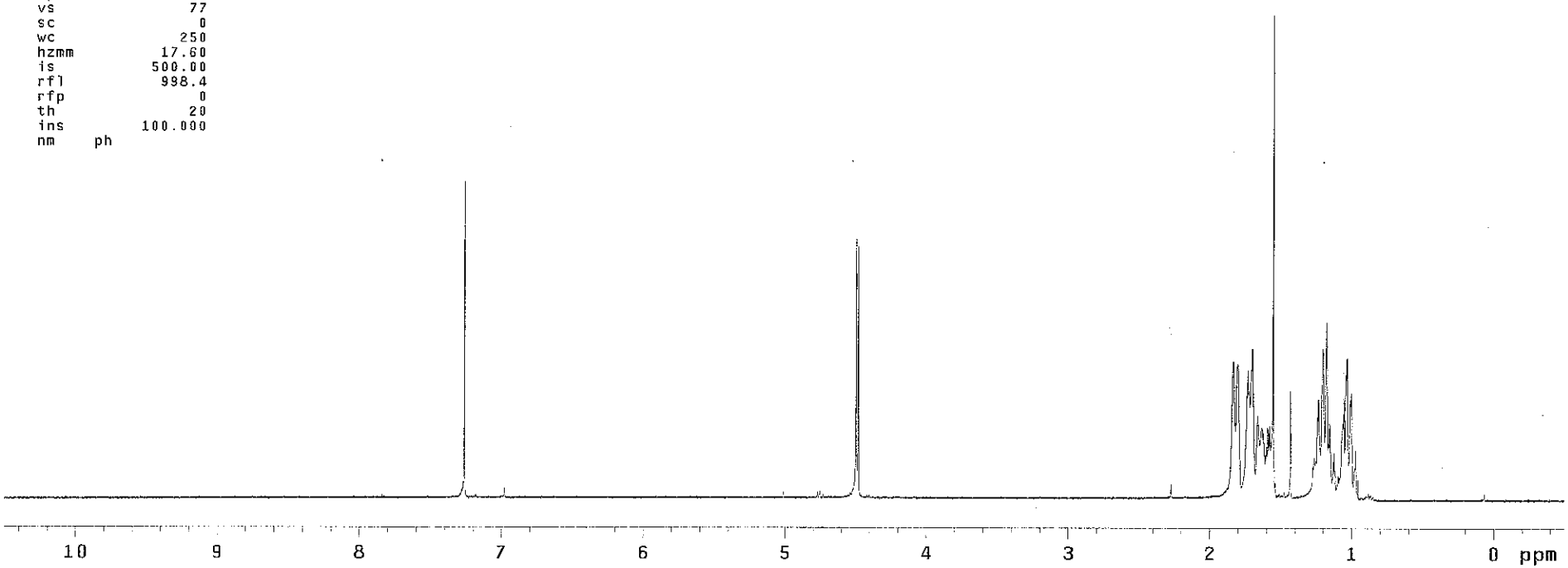
STANDARD 1H OBSERVE

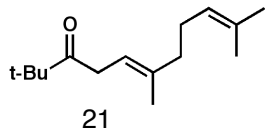
exp1 std1h

SAMPLE		DEC. & VT	
date	Sep 11 2008	dfrq	0
solvent	CDCl3	dn	
file	/export/home/~	dpwr	30
	jsk/wommack/AJW-II~	dof	0
	I-101spot.fid	dm	nnn
ACQUISITION		dmm	c
sfrq	400.029	dmf	200
tn	H1	PROCESSING	
at	3.000	wtfile	
np	35992	proc	ft
sw	5998.8	fn	not used
fb	3400		
bs	16	werr	
tpwr	63	wexp	
pw	7.1	wbs	
d1	2.000	wnt	
tof	0		
nt	16		
ct	16		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-200.0		
wp	4400.2		
vs	77		
sc	0		
wc	250		
hzmm	17.60		
is	500.00		
rfl	998.4		
rfp	0		
th	20		
ins	100.000		
nm	ph		



19



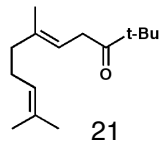


21

STANDARD 1H OBSERVE

Solvent: CDCl3
Ambient temperature
File: DCM-II-268f
GEMINI-400BB "nmr8"

Relax. delay 2.000 sec
Pulse 42.3 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
10 repetitions
OBSERVE H1, 400.0268156 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 39 sec

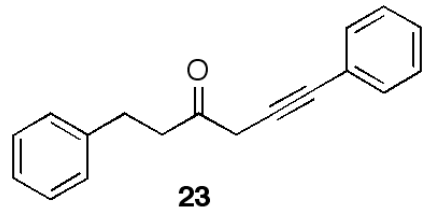


21

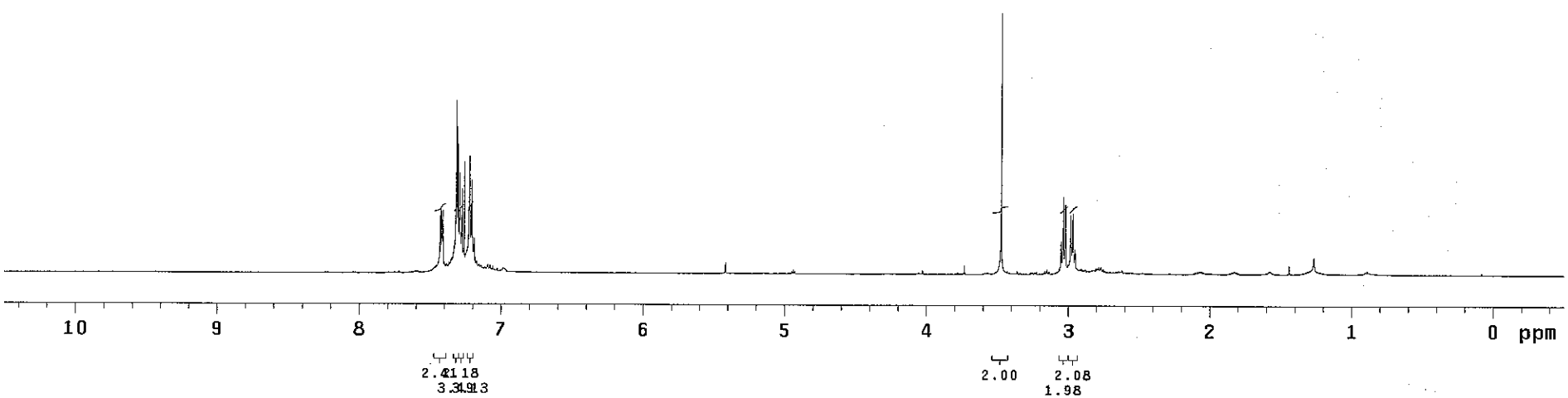
STANDARD PROTON PARAMETERS

exp1 s2pul

SAMPLE		DEC. & VT	
date	Jun 29 2009	dfrq	499.774
solvent	CDCl3	dn	H1
file	/export/home/~	dpwr	30
	jsk/AJW-IV-236prod~	dof	0
	.fid	dm	nnn
ACQUISITION		dmm	c
sfrq	499.774	dmf	200
tn	H1	dseq	
at	5.000	dres	1.0
np	70058	homo	n
sw	7005.9	DEC2	
fb	4000	dfrq2	0
bs	4	dn2	
tpwr	57	dpwr2	1
pw	4.6	dof2	0
d1	0	dm2	n
tof	497.0	dmm2	c
nt	48	dmf2	200
ct	0	dseq2	
alock	n	dres2	1.0
gain	not used	homo2	n
FLAGS		PROCESSING	
il	n	wtfile	
in	n	proc	ft
dp	y	fn	not used
hs	nn	math	f
DISPLAY			
sp	-249.9	werr	
wp	5497.4	wexp	
vs	42	wbs	
sc	0	wnt	wft
wc	250		
hzmm	21.99		
is	33.57		
rfl	4144.3		
rfp	3628.3		
th	7		
ins	2.000		
nm	ph		



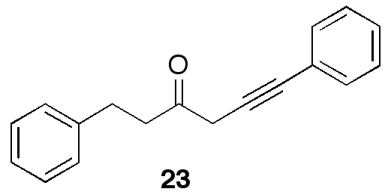
23



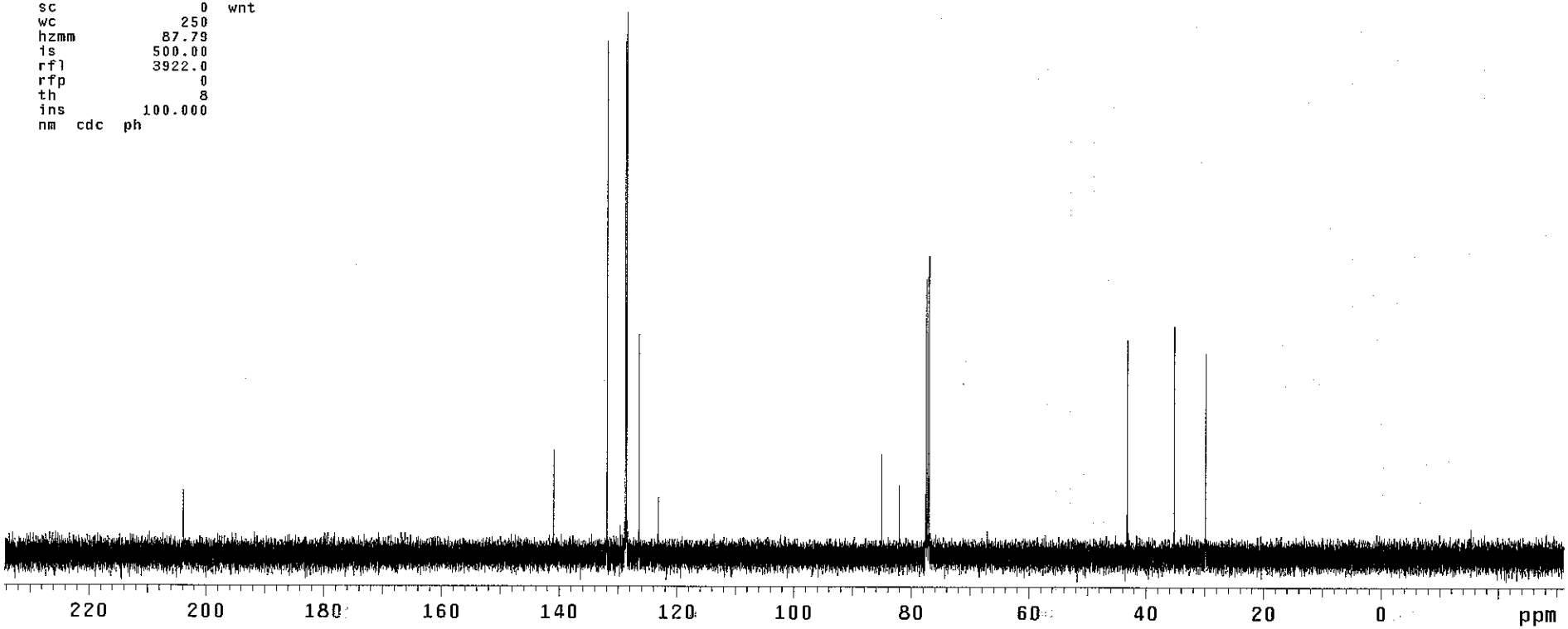
STANDARD CARBON PARAMETERS

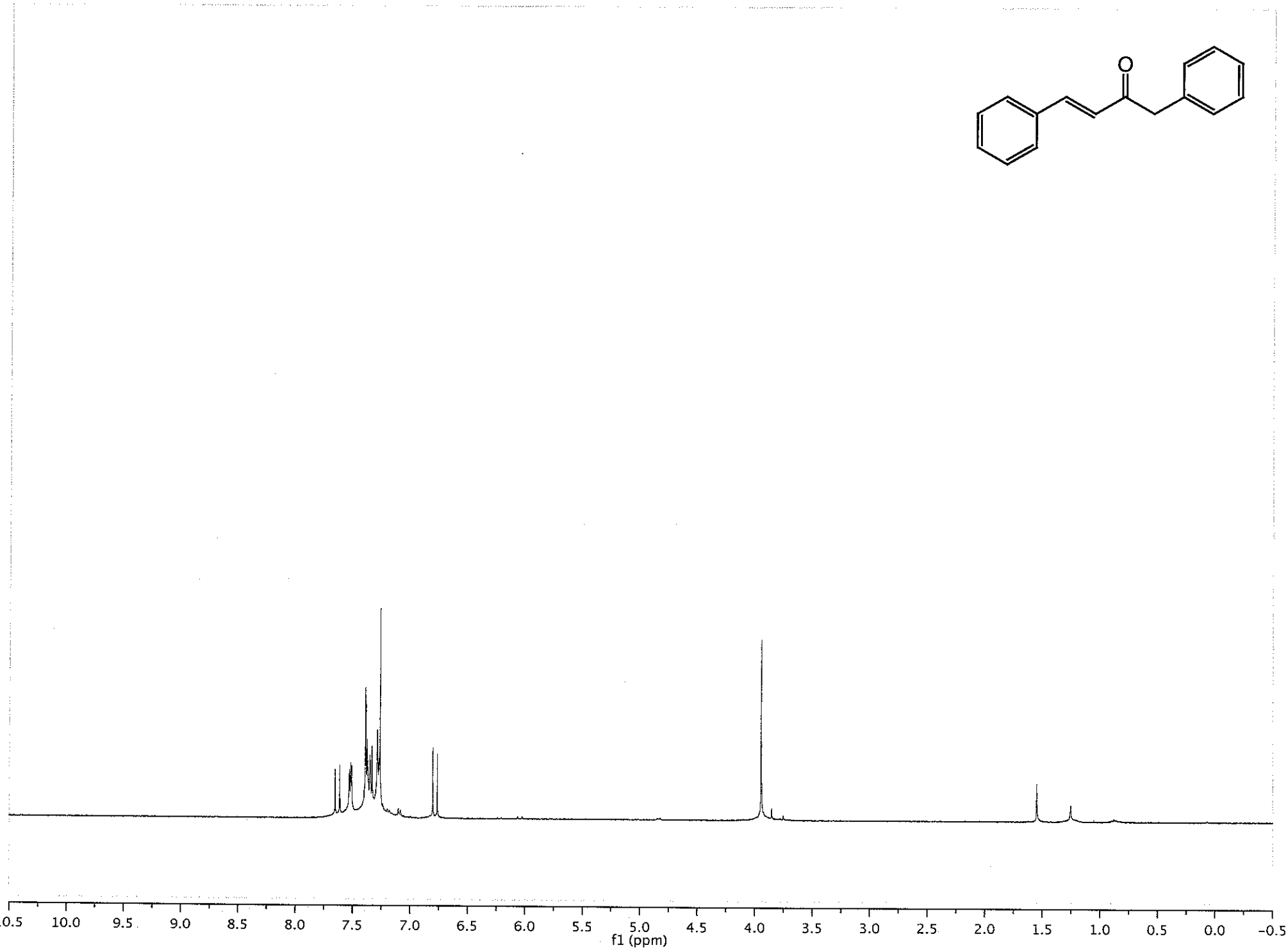
exp1 s2pul

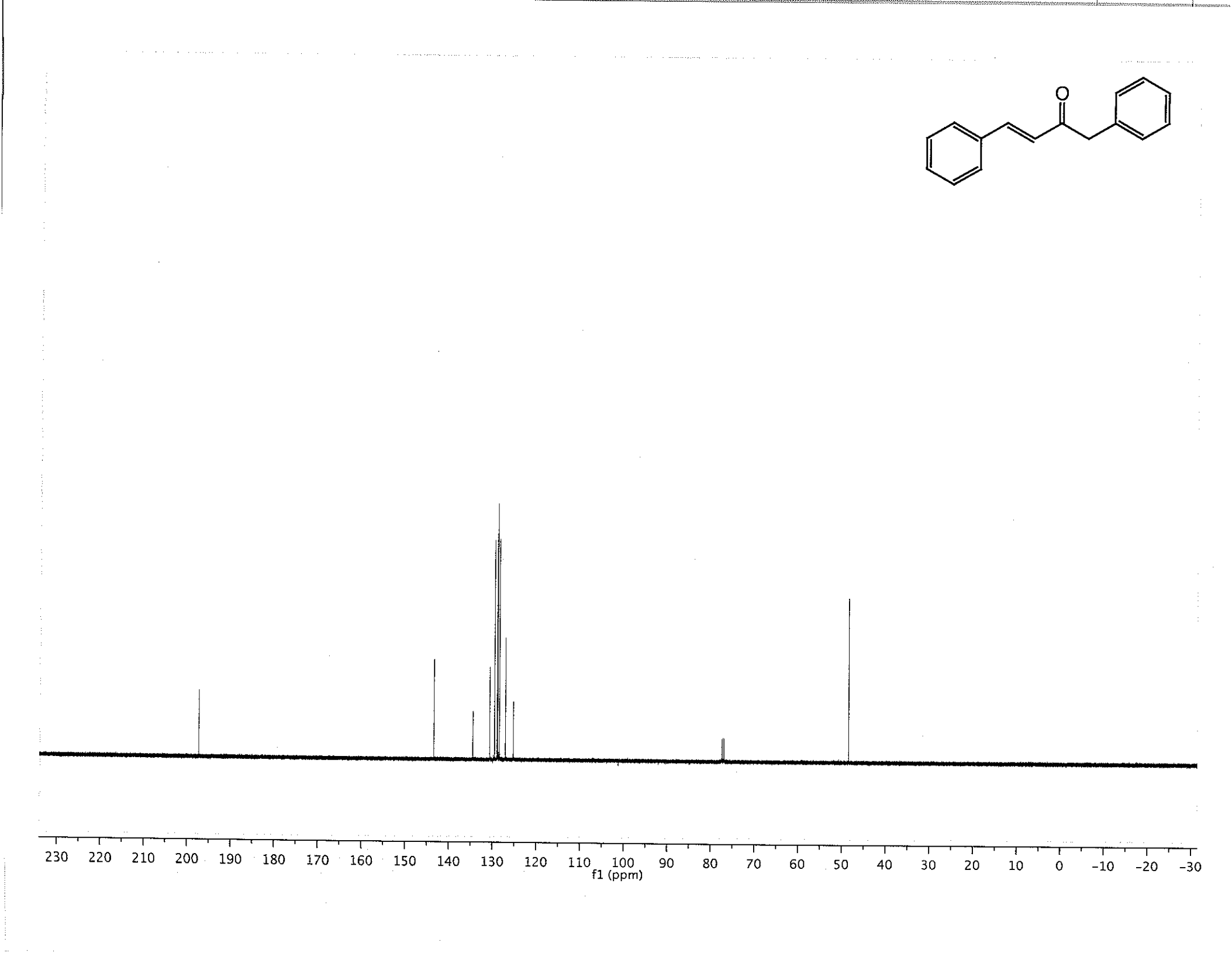
SAMPLE		DEC. & VT	
date	Jun 29 2009	dfrq	499.774
solvent	CDCl3	dn	H1
file	/export/home/~	dpwr	42
	jsk/AJW-IV-236carb~	dof	0
	on1.fid	dm	yyy
ACQUISITION		dmm	w
sfrq	125.680	dmf	7200
tn	C13	dseq	
at	3.000	dres	1.0
np	200168	homo	n
sw	33361.1	DEC2	
fb	18000	dfrq2	0
bs	4	dn2	
tpwr	55	dpwr2	1
pw	7.0	dof2	0
d1	2.000	dm2	n
tof	818.6	dmm2	c
nt	12800	dmf2	10000
ct	0	dseq2	
alock	n	dres2	1.0
gain	not used	homo2	n
FLAGS		PROCESSING	
il	n	wtfile	
in	n	proc	ft
dp	y	fn	not used
hs	nn	math	f
DISPLAY			
sp	-3921.8	werr	
wp	33360.9	wexp	
vs	87	wbs	wft
sc	0	wnt	
wc	250		
hzmm	87.79		
is	500.00		
rfl	3922.0		
rfp	0		
th	8		
ins	100.000		
nm cdc ph			



23



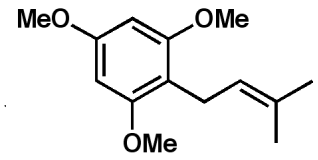

O
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

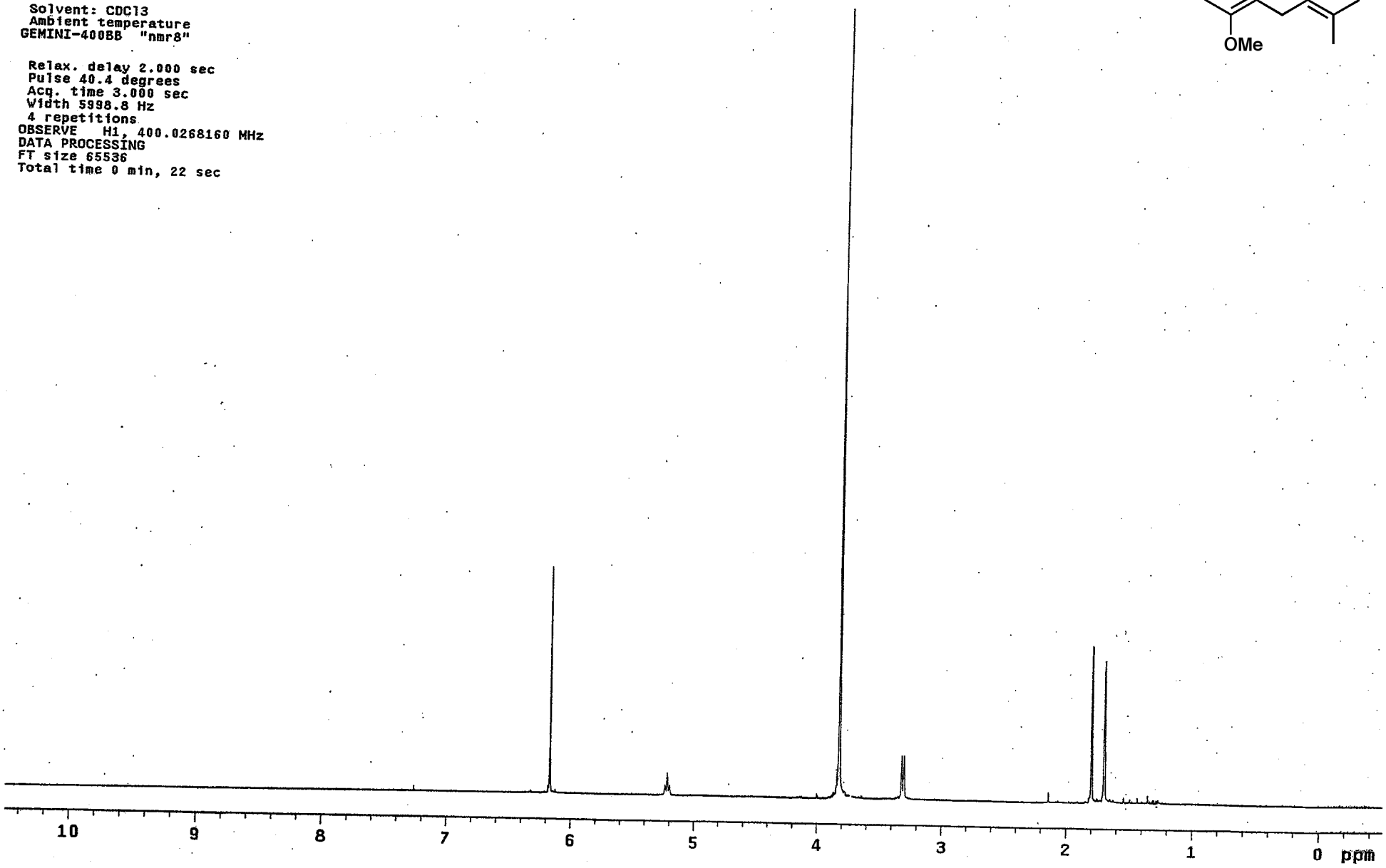

O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
f1 (ppm)

STANDARD 1H OBSERVE

Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

Relax. delay 2.000 sec
Pulse 40.4 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
4 repetitions
OBSERVE H1, 400.0268160 MHz
DATA PROCESSING
FT size 65536
Total time 0 min, 22 sec

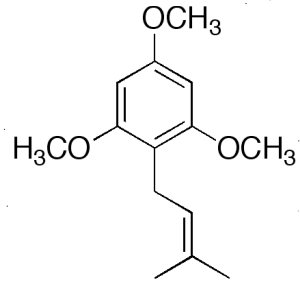


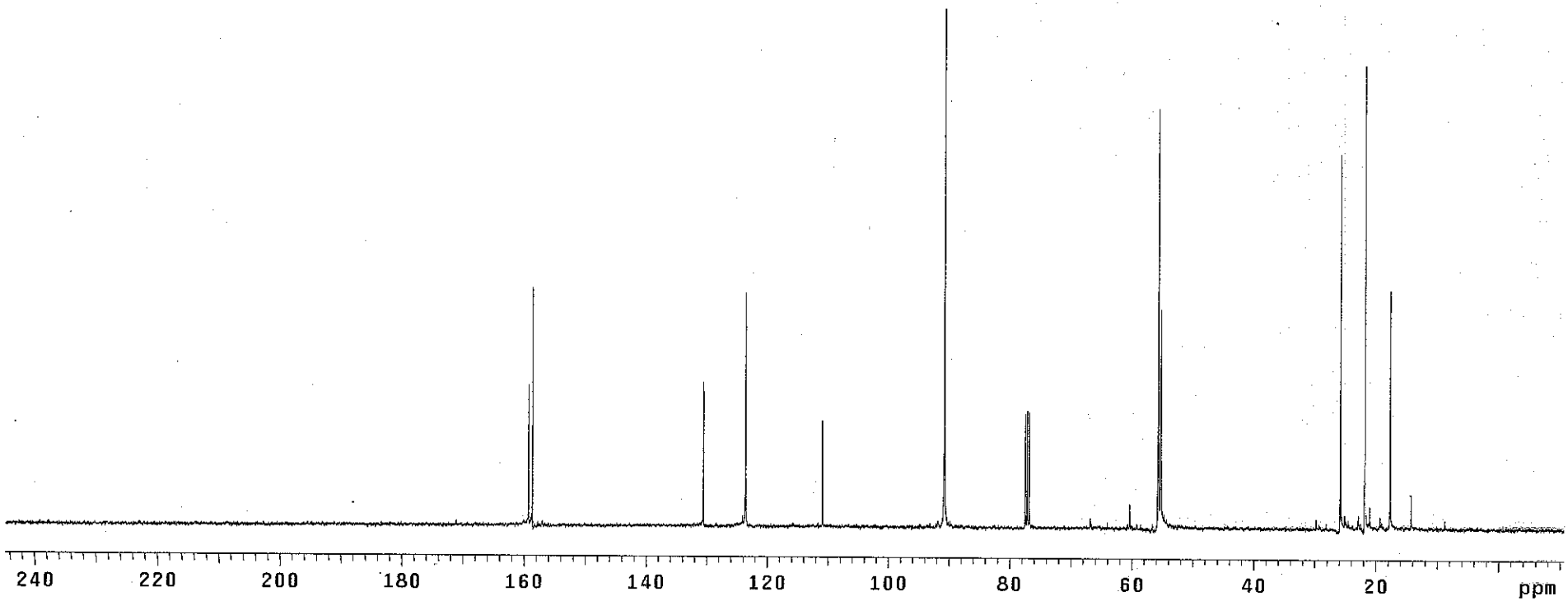


13C OBSERVE

Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

Relax. delay 4.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25683.4 Hz
224 repetitions
OBSERVE C13, 100.5868180 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 17 min, 57 sec



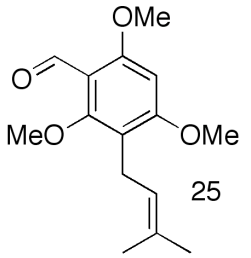


df-iii-114-19

25

Solvent: CDCl3
Ambient temperature
UNITY-300 "nmr2"

Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 5.000 sec
Width 3761.2 Hz
20 repetitions
OBSERVE H1, 299.9403347 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 0 sec

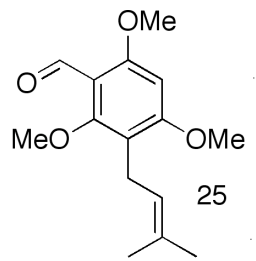


25

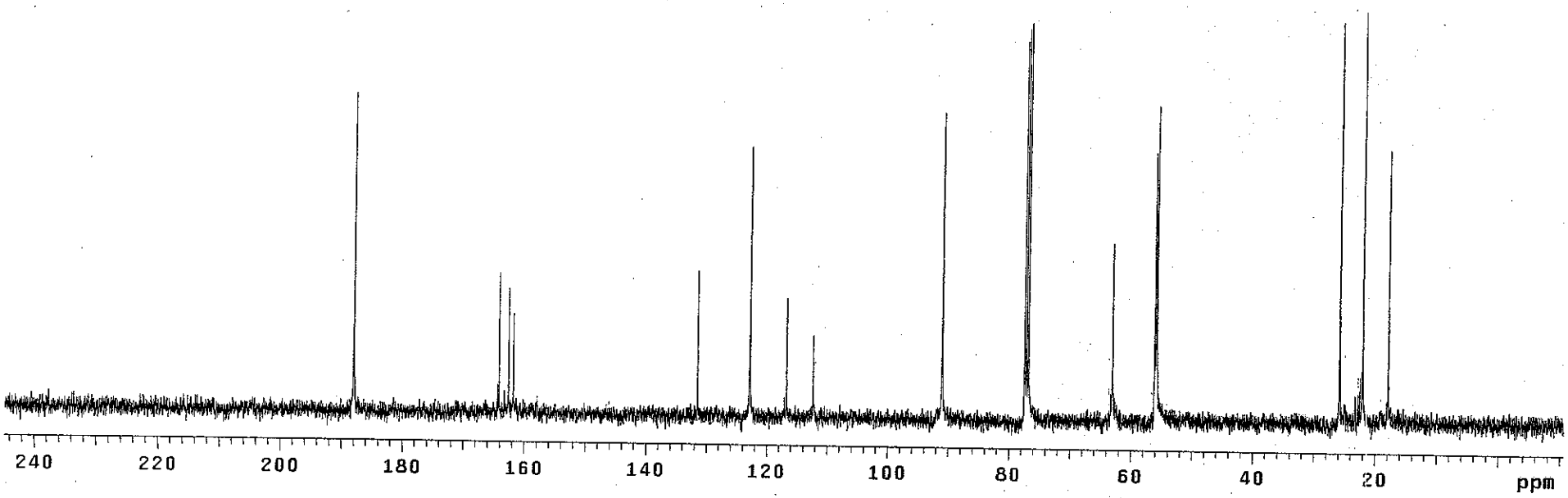
13C OBSERVE

Solvent: CDCl3
Ambient temperature
File: AJW-aldecarbon
GEMINI-400BB "nmr8"

Relax. delay 4.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25683.4 Hz
224 repetitions
OBSERVE C13, 100.5868102 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 19 min, 14 sec



25

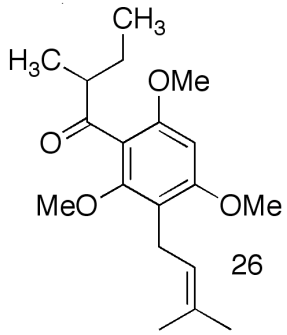


AJW-III-212prod1

26

Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

Relax. delay 2.000 sec
Pulse 42.3 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0268141 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 22 sec

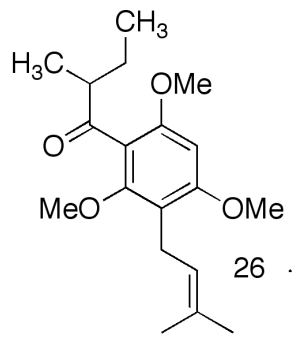


26

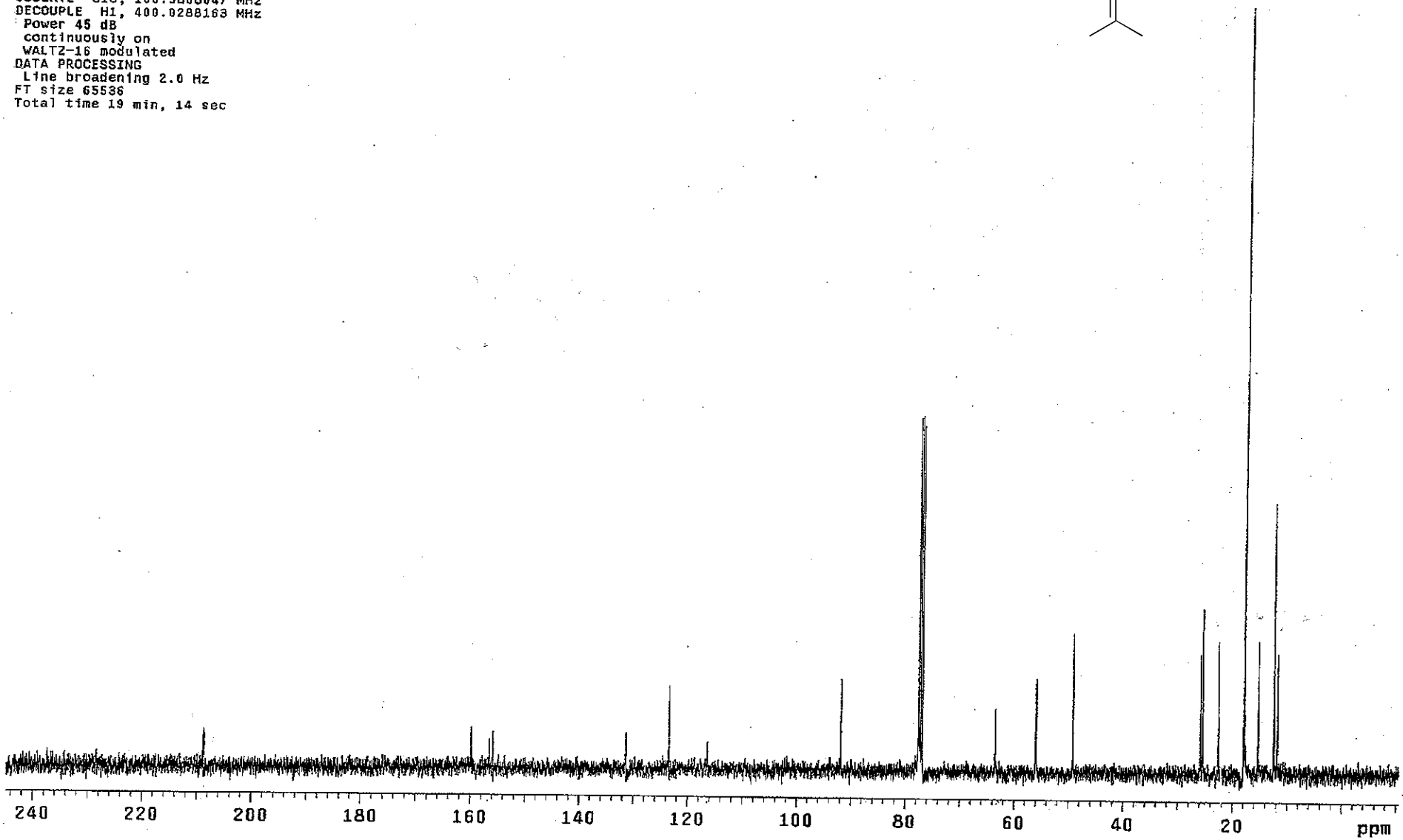
AdW-III-212carbon

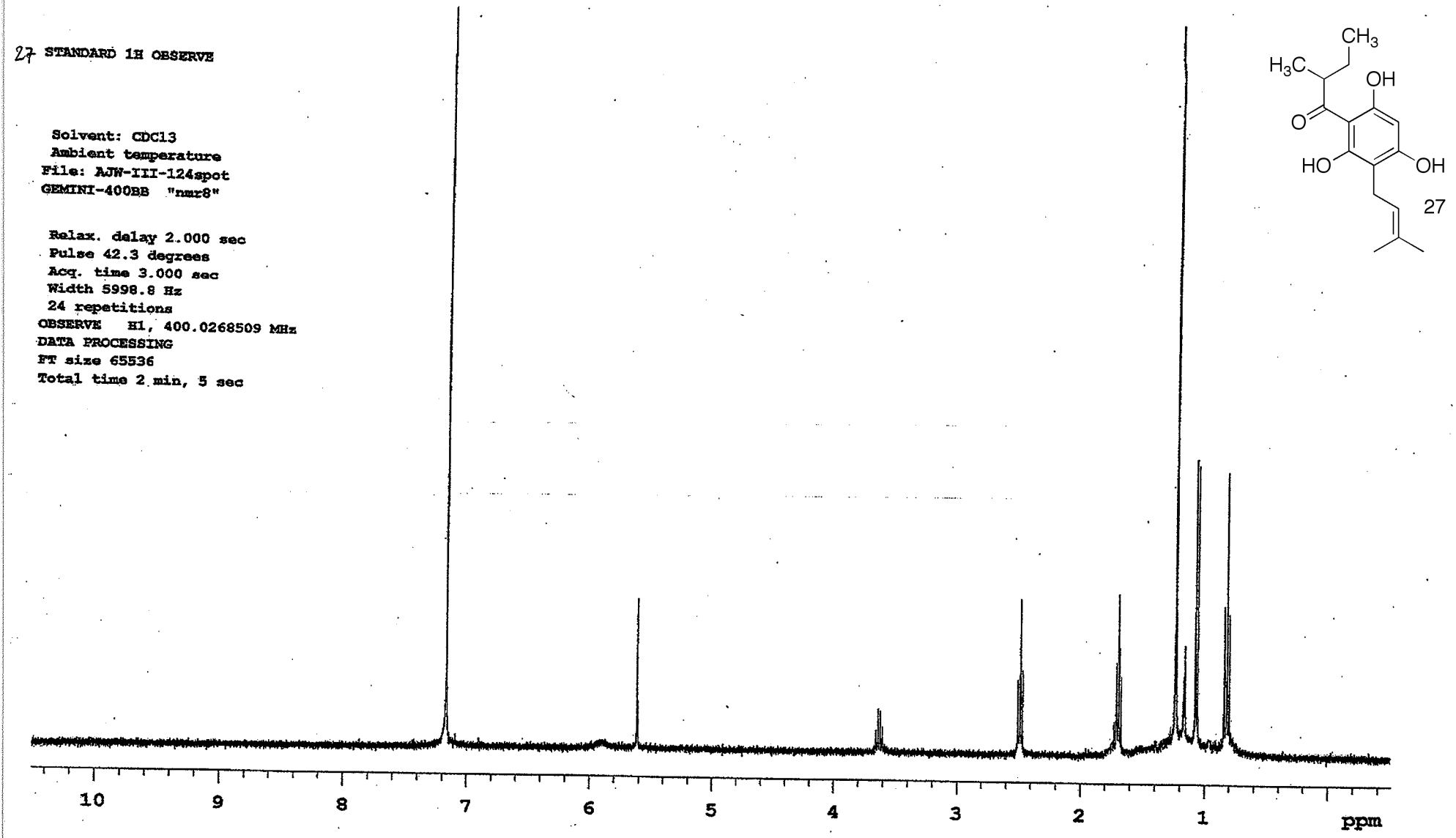
Solvent: CDCl3
Ambient temperature
GEMINI-400BB "nmr8"

Relax. delay 4.000 sec
Pulse 64.8 degrees
Acq. time 0.640 sec
Width 25683.4 Hz
160 repetitions
OBSERVE C13, 100.5868047 MHz
DECOUPLE H1, 400.0288163 MHz
Power 45 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 19 min, 14 sec



26



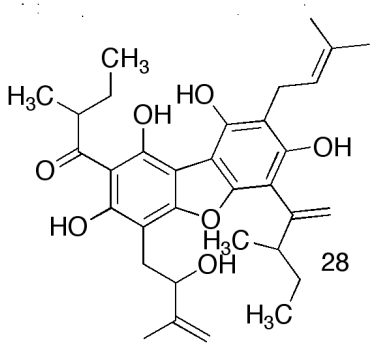

27 STANDARD 1H OBSERVE
Solvent: CDCl3
Ambient temperature
File: AJW-III-124spot
GEMINI-400BB "nmr8"
Relax. delay 2.000 sec
Pulse 42.3 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
24 repetitions
OBSERVE H1, 400.0268509 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 5 sec
CH3
H3C
OH
O
HO
OH
27
10
9
8
7
6
5
4
3
2
1
ppm

28

STANDARD 1H OBSERVE

Solvent: CDCl3
Ambient temperature
File: AJW-III-125prod
GEMINI-400BB "nmr8"

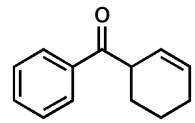
Relax. delay 2.000 sec
Pulse 42.3 degrees
Acq. time 3.000 sec
Width 5998.8 Hz
16 repetitions
OBSERVE H1, 400.0268158 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 22 sec

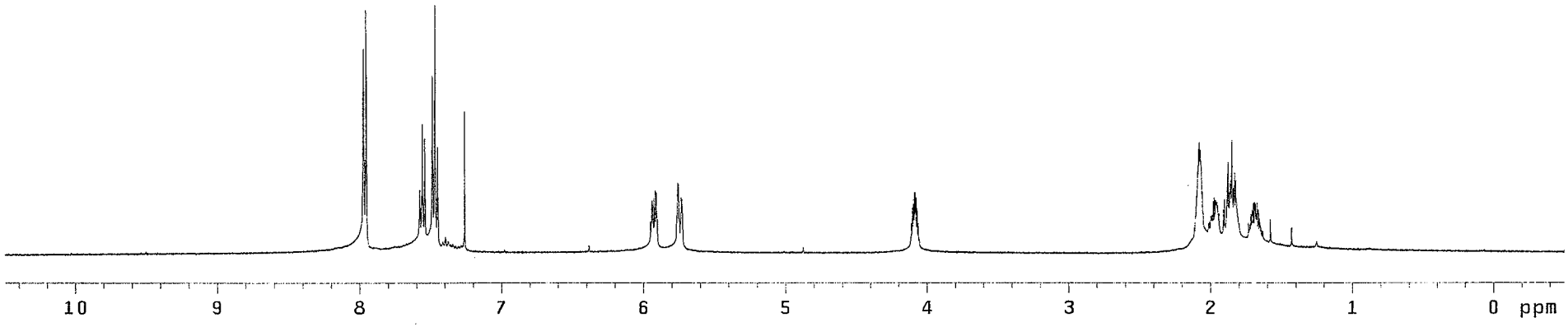


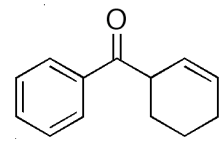
STANDARD 1H OBSERVE

exp1 std1h

SAMPLE		DEC. & VT	
date	Dec 5 2008	dfrq	0
solvent	CDCl3	dn	
file	/export/home/~	dpwr	30
	jsk/wommack/AJW-II~	dof	0
	I-232s2.fid	dm	nnn
ACQUISITION		dmm	c
sfrq	400.029	dmf	200
tn	H1	PROCESSING	
at	3.000	wtfile	
np	35992	proc	ft
sw	5998.8	fn	not used
fb	3400		
bs	16	werr	
tpwr	63	wexp	
pw	7.1	wbs	
d1	2.000	wnt	
tof	0		
nt	16		
ct	16		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-200.0		
wp	4400.2		
vs	39		
sc	0		
wc	250		
hzmm	17.60		
is	500.00		
rfl	998.2		
rfp	0		
th	20		
ins	100.000		
nm	ph		





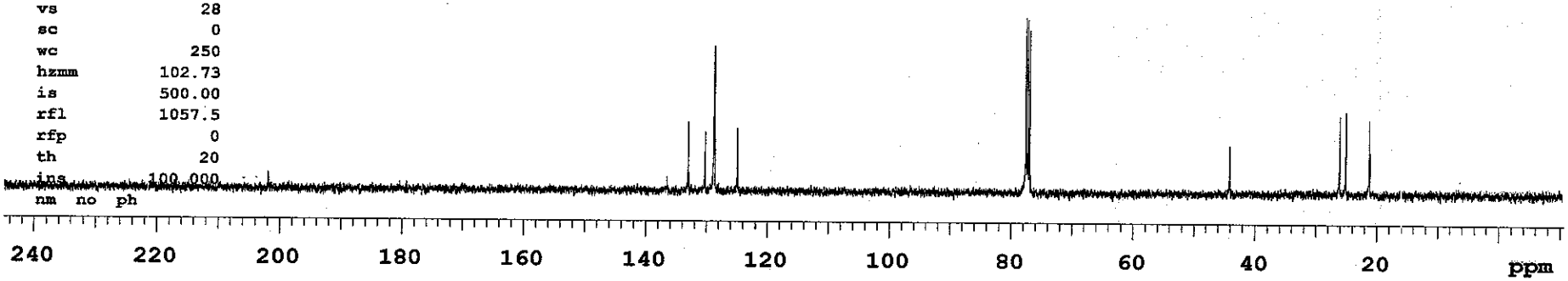


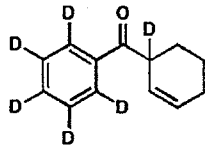
13C OBSERVE

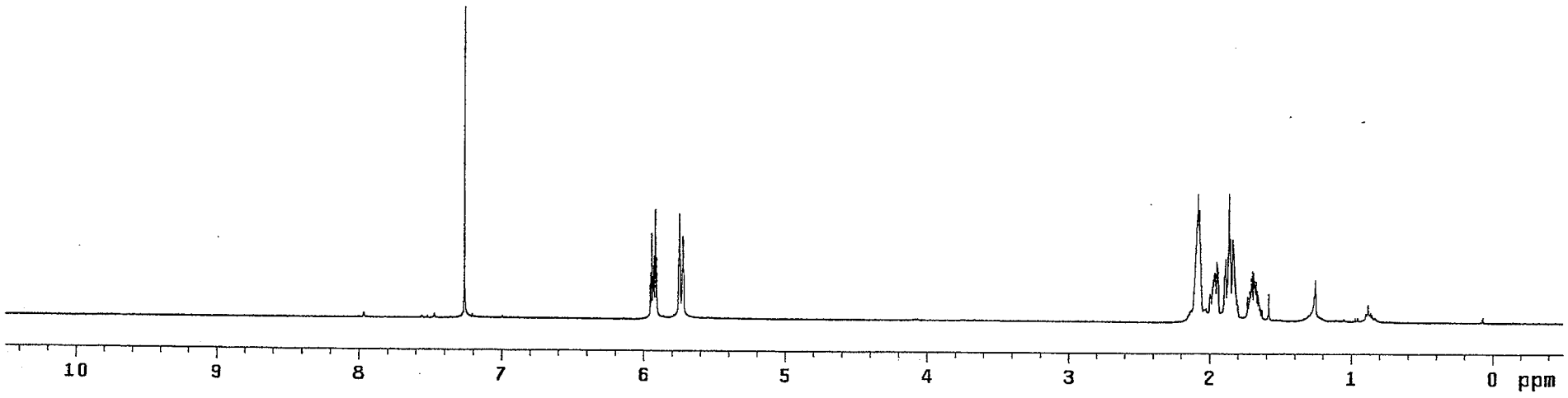
exp1 std13c

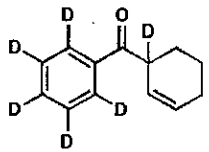
SAMPLE		DEC. & VT	
date	Mar 3 2009	dfrq	400.029
solvent	CDCl3	dn	H1
file	/export/home/~	dpwr	45
	jsk/AJW-III-232car~	dof	0
	bon.fid	dm	yyy
ACQUISITION		dmm	w
sfrq	100.599	dmf	9242
tn	C13	PROCESSING	
at	0.640	lb	2.00
np	32876	wtfile	
sw	25683.4	proc	ft
fb	14200	fn	not used
bs	16		
tpwr	55	werr	
pw	9.0	wexp	
d1	4.000	wbs	
tof	2271.7	wnt	
nt	244		
ct	244		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
DISPLAY			
sp	-1057.5		
wp	25683.4		
vs	28		
sc	0		
wc	250		
hzmm	102.73		
is	500.00		
rfl	1057.5		
rfp	0		
th	20		
ins	100.000		

nm no ph




D
O
D
D
D
D
D


10
9
8
7
6
5
4
3
2
1
0 ppm


D
O
D
D
D
D
D

240
220
200
180
160
140
120
100
80
60
40
20
ppm

Acq. Data Name: DCM-III-086f
Internal Sample Id: moebius*Aldohomo*DCM-III-086f*III-086*Kingsbury
Ionization Mode: ESI+
Acquired m/z Range: 100.00..500.00
Orifice1 Volt Sweep: 20V
Experiment Date/Time: 1/8/2009 2:30:27 PM
Ring Lens Volt: 10[V]