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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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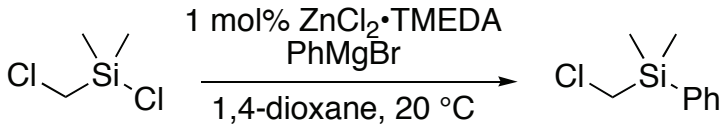
SYNTHESIS OF TETRAORGANOSILANES: (CHLOROMETHYL)DIMETHYLPHENYLSILANE



Submitted by Kei Murakami, Hideki Yorimitsu, and Koichiro Oshima.[1]
Checked by Jane Panteleev and Mark Lautens.

1. Procedure

(Chloromethyl)dimethylphenylsilane. A flame-dried 1-L, three-necked, round-bottomed flask is equipped with a 500-mL pressure equalizing dropping funnel fitted with a septum, a two-way stopcock with an argon inlet, an internal temperature probe, and a 5-cm egg-shaped stirring bar. Dichloro(*N,N,N',N'*-tetramethylethylenediamine)zinc (0.64 g, 2.5 mmol, 1 mol%) (Note 1) is placed in the flask, and the apparatus is purged with argon. 1,4-Dioxane (240 mL) (Note 2) is added to the flask at 23 °C. Chloro(chloromethyl)dimethylsilane (33.8 mL, 250 mmol) (Note 1) is added to the flask through the dropping funnel at 23 °C. The dropping funnel is rinsed with 1,4-dioxane (10 mL). The mixture is cooled in an ice/water bath over 10 min. Phenylmagnesium bromide (Note 3) (1.0 M in THF, 300 mL, 300 mmol, 1.2 equiv) is then transferred to the dropping funnel using a 14 guage metal cannula and is added dropwise to the mixture over 30 min with cooling in an ice/water bath. The addition immediately leads to the formation of white salts. A gentle exothermic reaction takes place. After the completion of the addition, the resulting mixture is allowed to warm to ambient temperature (23 °C) and stirred for an additional 2 h. The reaction mixture is poured over 5 min into a rapidly stirred ice-cold saturated aqueous ammonium chloride solution (150 mL) (Note 2) in a 1-L Erlenmeyer flask equipped with a 5-cm octagonal magnetic stirring bar. The mixture is transferred to a 1-L separatory funnel, and the Erlenmeyer and round-bottomed flasks are rinsed with ethyl acetate (25 mL each) (Note 2). The organic phase is separated, and the aqueous layer is extracted with ethyl acetate (50 mL × 3). The combined organic layers are washed with brine (50 mL), dried once over anhydrous Na_2SO_4 (25 g) (Note 2), filtered through filter paper, and concentrated with a rotary evaporator (35 °C, 34–38

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mmHg). Evaporation is stopped at the time when the volume of the mixture is reduced to approximately 75 mL (Note 4). The mixture is transferred to a 100-mL round-bottomed flask equipped with a magnetic stirring bar. The flask is then equipped with a Vigreux column (20 cm) topped with a distillation head and receiver. Vacuum (23 mmHg) is applied, and remaining 1,4-dioxane is removed until bubbling ceases. The flask is gradually heated in an oil bath to a bath temperature of 155 °C. After the temperature of the fraction reaches 115 °C, a forerun (ca. 1 mL) is collected and discarded. The desired product is then obtained, distilling at 115 °C (23 mmHg). The product weighs 37–38 g (200–203 mmol, 80–81%) and is obtained as a stable, clear, colorless liquid (Notes 5 and 6).

2. Notes

1. Dichloro(*N,N,N',N'*-tetramethylethylenediamine)zinc (98%) and chloro(chloromethyl)dimethylsilane (98%) were purchased from Aldrich Chemical Co., Inc. and used as is.

2. 1,4-Dioxane (99%, anhydrous, water <50ppm), ammonium chloride (99.5%), ethyl acetate (99%), and anhydrous sodium sulfate (99%) were obtained from Wako Pure Chemical Industries Ltd. and were used as received by the submitters. 1,4-Dioxane (99.8%, anhydrous, <0.003% water) and ethyl acetate (>99.5%) were purchased from Aldrich Chemical Co., Inc. and used as received by the checkers. Ammonium chloride (99.5%) and anhydrous sodium sulfate (99%) were purchased from ACP Chemicals Inc., and used as they were by the checkers.

3. Phenylmagnesium bromide solution (1.0M in tetrahydrofuran) was purchased from Aldrich Chemical Co., Inc, and was used as received by the checkers. The submitters synthesized phenylmagnesium bromide (1.0M in tetrahydrofuran).

4. The submitters concentrated the solution using a rotary evaporator (30 °C, 10 mmHg) and noted that the yield of (chloromethyl)-dimethylphenylsilane can be decreased when evaporation is performed under lower pressure or for a prolonged time.

5. The product exhibits the following physicochemical properties: IR (film, NaCl) 3070, 2963, 1427, 1250, 1119, 841, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.42 (s, 6 H), 2.96 (s, 2 H), 7.35–7.44 (m, 3 H), 7.52–7.57 (m, 2 H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ: –4.5, 30.4, 128.0, 129.7, 133.7, 136.1; MS (EI) *m*/*z* (relative intensity): 186 (2), 184 (13), 171 (9), 155

(10), 135 (100); HRMS (EI): *m/z* calcd. for $C_9H_{13}ClSi$ 184.0475; found 184.0473.

6. The purity (99%) was determined by GC using a Phenomenex ZB-5 ms column (30 m × 0.25 mm with 0.25 μm film thickness) (oven temperature: 50 °C for 5 min, ramp 50 °C per min to 300 °C; outlet flow: 1 mL/min; carrier gas: helium; retention time: 6.3 min). The submitters report: Anal. calcd. for $C_9H_{13}ClSi$: C, 58.51; H, 7.09; found: C, 58.45; H, 7.03.

7. The submitters report the reaction proceeded in an 80% yield on a 500-mmol scale.

Waste Disposal Information

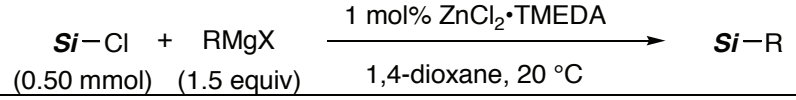
All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

Tetraorganosilanes are quite useful organometallic compounds as reagents and functional materials. The nucleophilic substitution reactions of chlorosilanes with organometallic reagents are commonly used to synthesize tetraorganosilanes. The reactions of chlorosilanes with organolithium reagents generally proceed smoothly, wherein functional group compatibility is not sufficiently wide due to the high reactivity of organolithium reagents.[2] On the other hand, the substitution reactions with the less reactive organomagnesium reagents often require prolonged reaction times and high temperatures to go to completion. Toxic cyanide or thiocyanate salts are known to catalyze the substitution reactions of chlorosilanes with organomagnesium reagents.[3] Very recently, silver nitrate proved to facilitate the substitution reaction.[4] However, the scope of the Grignard reagents in the silver-catalyzed reaction is not satisfactorily wide, i.e., limited to arylmagnesium reagents. Finally, zinc chloride, a very cheap inorganic salt, is found to catalyze the substitution reactions with a much wider variety of organomagnesium reagents (Table 1).[5] The zinc-catalyzed reaction seems to be the best method at present, comprehensively taking the efficiency, scope, operability, scalability, cost, and toxicity into account. The product, (chloromethyl)dimethylphenylsilane, is the precursor of useful

dimethylphenylsilylmethylmagnesium chloride[6] and serves also as an important building block in organic synthesis.[7]

Table 1. Zinc-Catalyzed Substitution Reactions of Chlorosilanes with Grignard Reagents



Entry	***Si***	RMgX	Time [h]	Yield [%]
1	$PhMe_2Si$	2-MeC_6H_4MgBr	5	92
2	$PhMe_2Si$	4-$MeOC_6H_4MgBr$	1	87
3	$PhMe_2Si$	3-$CF_3C_6H_4MgBr$	3	99
4	Ph_2MeSi	4-MeC_6H_4MgBr	15	89
5[a]	$PhMe_2Si$	CH_2=$CMeMgBr$	3	84
6[a]	Ph_2MeSi	CH_2=$CHMgBr$	2	71
7[a]	*i*-Pr_3Si	CH_2=$CHCH_2MgCl$	12	91
8[a]	*t*-$BuMe_2Si$	$PhCH_2MgCl$	7	70
9[a,b]	*t*-$BuMe_2Si$	CH_2=$CHCH_2MgCl$	8	71
10	(4-NCC_6H_4)Me_2Si	4-MeC_6H_4MgBr	1	75

[a] THF was used as a solvent. [b] Performed on a 50-mmol scale.

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Appendix
Chemical Abstract Nomenclature; (Registry Number)

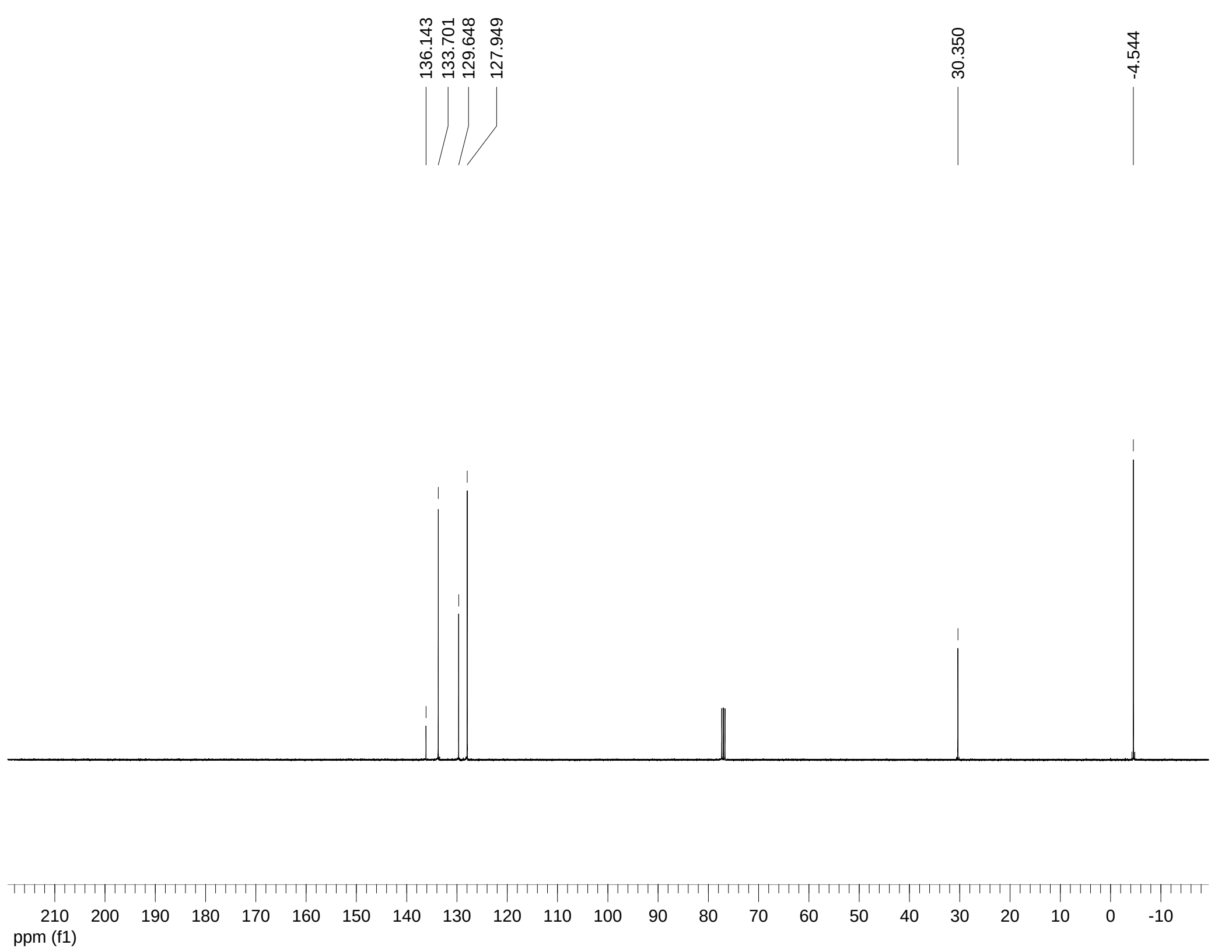
Bromobenzene; (108-86-1)
Magnesium; (7439-95-4)
Dichloro(*N,N,N',N'*-tetramethylethylenediamine)zinc; (28308-00-1)
Chloro(chloromethyl)dimethylsilane; (1719-57-9)
(Chloromethyl)dimethylphenylsilane; (1833-51-8)

Koichiro Oshima was born in Hyogo, Japan, in 1947. He obtained his B.S. in 1970 and Ph.D. in 1975 from Kyoto University under the guidance of Professor Hitosi Nozaki. He then worked as a postdoctoral fellow with Professor Barry Sharpless at MIT and became an Assistant Professor at Kyoto University in 1977. He was promoted to Lecturer in 1984, Associate Professor in 1986, and Professor in 1993. His research interests include the development of new reactions utilizing radical intermediates and organometallic reagents. He received the Award for Young Chemists of the Society of Synthetic Organic Chemistry, Japan in 1983, the Japan Synthetic Organic Chemistry Award in 2004, and the Chemical Society of Japan Award for 2006.

Kei Murakami was born in Osaka, Japan, in 1985. He completed his undergraduate education at Kyoto University in 2007 and is currently pursuing his Ph.D. studies under the tutelage of Professor Koichiro Oshima. He has been a JSPS research fellow since 2009, developing new metal-catalyzed reactions for carbon–carbon and carbon–silicon bond formation.

Hideki Yorimitsu was born in Kochi, Japan, in 1975. He obtained his B.S. in 1997 and Ph.D. in 2002 from Kyoto University under the supervision of Professor Koichiro Oshima. He then served as a JSPS postdoctoral fellow, working with Professor Eiichi Nakamura at the University of Tokyo. He became an Assistant Professor at Kyoto University in 2003 and has been an Associate Professor since 2008. His research program focuses on the development of new organic reactions useful for synthesizing biologically interesting compounds, novel coordinating structures, and organometallic compounds. He received the Chemical Society of Japan Award For Young Chemists for 2008.

Jane Panteleev received her Bachelor of Science degree in Biochemistry at Queen's University, Ontario, in 2007. During that time she had the opportunity to work in the research lab of Prof. Victor Snieckus. She is currently pursuing her Ph.D. degree under the supervision of Prof. Mark Lautens at the University of Toronto. Her current research is in the area of asymmetric transition metal catalysis.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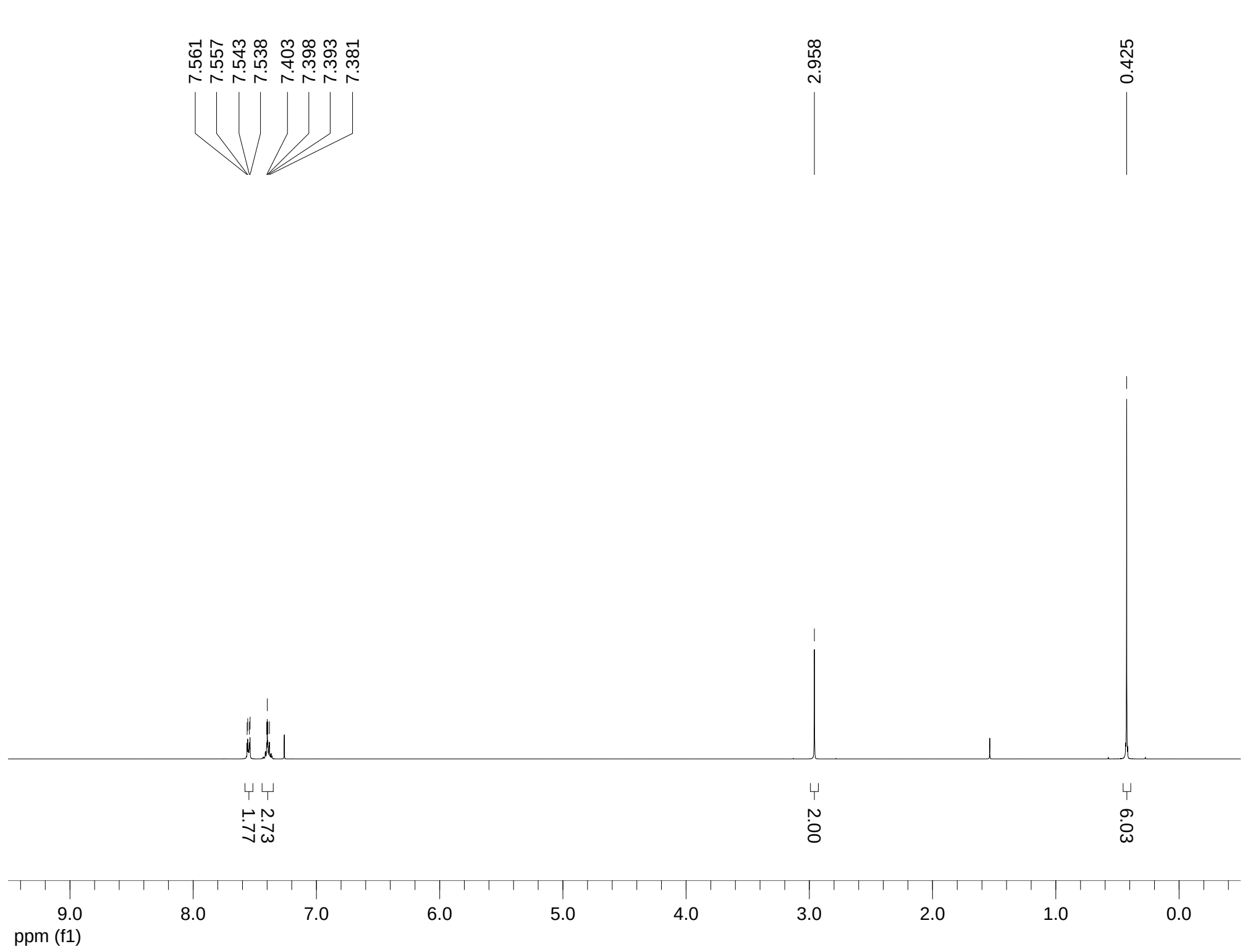
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