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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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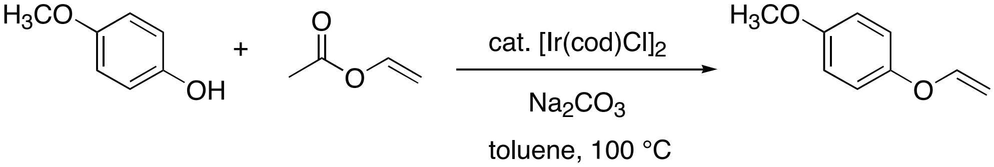
# IRIDIUM-CATALYZED SYNTHESIS OF VINYL ETHERS FROM ALCOHOLS AND VINYL ACETATE

## (1-Methoxy-4-vinyloxybenzene)



Submitted by Tomotaka Hirabayashi, Satoshi Sakaguchi and Yasutaka Ishii.[1,2]
Checked by Paul W. Davies and Alois Fürstner.
Discussion Addendum *Org. Synth.* **2012**, *89*, 307

## 1. Procedure

A 100-mL, two-necked round-bottomed flask is fitted with a magnetic stirbar, a reflux condenser connected to an argon/vacuum line, and a rubber septum. The equipment is flame dried under vacuum and then flushed with argon. Di-μ-chloro-bis(1,5-cyclooctadiene)diiridium(I), $[Ir(cod)Cl]_2$, (0.34 g, 0.01 eq., 0.5 mmol) (Note 1) and sodium carbonate (3.18 g, 30 mmol, 0.6 eq.) (Note 2) are rapidly weighed in air and added to the flask which is resealed, evacuated and backfilled with argon. Toluene (50 mL) (Note 3), *p*-methoxyphenol (6.21 g, 50 mmol) (Note 4) and vinyl acetate (8.61 g, 100 mmol) (Note 5) are successively introduced and the flask is placed into a preheated oil-bath at 100 °C with magnetic stirring. The reaction mixture changes from a yellow color after the addition of the vinyl acetate to a wine red color within 30 minutes of heating (Note 6) and continues to darken over the course of the reaction. After heating for 2 h, the reaction mixture is allowed to cool to ambient temperature before being transferred to a separatory funnel. Portions of EtOAc used to rinse the flask (3 × 50 mL) are added to the separatory funnel. The combined organic fractions are washed with water (3 × 100 mL) and brine (50 mL) before being dried over $MgSO_4$. The solution is filtered, the cake is washed with EtOAc (2 × 20 mL), and the combined filtrates are evaporated (Note 7). The resulting crude product is applied to a pre-packed silica gel column (50 × 3.5 cm) (Note 8) and eluted with hexanes/EtOAc (4:1) giving 1-methoxy-4-vinyloxybenzene as a pale yellow liquid after evaporation of the solvent (6.85 g, 91%) (Notes 7, 9, 10)

## 2. Notes

1. $[Ir(cod)Cl]_2$ can be prepared according to the literature method.[3] This complex is commercially available from Aldrich Chemical Company, Inc. The checkers used $[Ir(cod)Cl]_2$ purchased from Strem without further purification.

2. $Na_2CO_3$ purchased from Wako Pure Chemical Industries Ltd. was used as received. The checkers, however, found that the use of moist $Na_2CO_3$ led to lower yields of the desired product and increased amounts of the acetate side-product. Well reproducible results were obtained by using $Na_2CO_3$ dried under high vacuum ($10^{-4}$ Torr) at 80 °C overnight before use.

3. Toluene was dried by distillation over Na under Ar atmosphere.

4. *p*-Methoxyphenol was purchased from Wako Pure Chemical Industried Ltd. or Acros and used as received.

5. Vinyl acetate purchased from commercial suppliers (Wako Pure Chemical Industries Ltd., or Acros) was dried over MS 4Å and distilled at normal pressure (bp 72 °C) under Ar.

6. This characteristic color change is much slower if insufficiently dried $Na_2CO_3$ is used, thus leading to longer overall reaction times.

7. To avoid any loss of product during the evaporation of the solvent, the vacuum was set to $\geq$ 20 mbar and the temperature of the water bath should not exceed 40 °C.

8. Silica gel (230-400 mesh) from Kanto Kagaku Reagent Division was used. The checkers used Merck silica gel (230-400 mesh).

9. A small amount (< 3%) of 1-acetoxy-4-methoxybenzene was observed as a side product. The checkers obtained somewhat larger amounts of this compound (0.52 g, 6%).

10. Analytical data: $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.97-6.84 (m, 4H), 6.59 (dd, $J$ = 6.2, 13.8 Hz, 1H), 4.64 (dd, $J$ = 1.7, 13.8 Hz, 1H), 4.34 (dd, $J$ = 1.7, 6.2 Hz, 1H), 3.79 (s, 3H); $^{13}C$ NMR (101 MHz, $CDCl_3$) δ 155.8, 150.7, 149.6, 118.8, 114.8, 93.7, 55.8; IR (film) 2953, 2835, 1639, 1500, 1209, 1147, 1034, 954, 830 $cm^{-1}$. Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H 6.71; Found: C, 71.85; H, 6.67.

## Safety and 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

Vinyl ethers are conventionally prepared by mercury-catalyzed transfer vinylation,[4] base- or transition metal-catalyzed isomerization of allyl ethers,[5]

**Table 1.** Iridium-Catalyzed Synthesis of Various Vinyl Ethers

| Entry | Alcohol | Product | Time | GLC Yield | Isolated Yield |
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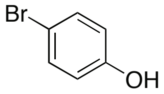
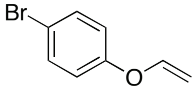
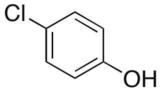
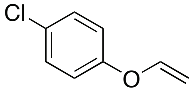
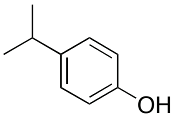
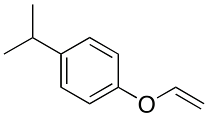
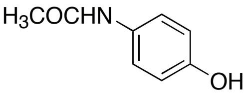
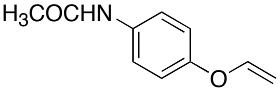
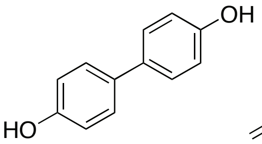
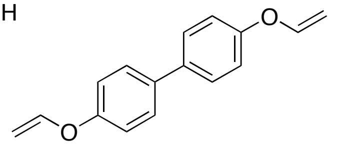
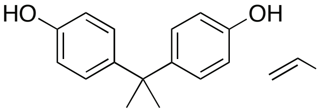
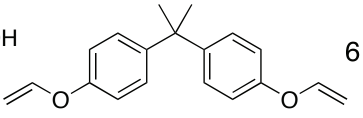
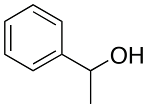
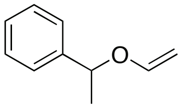
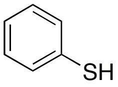
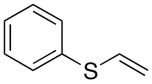
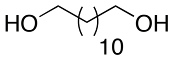
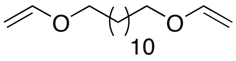
| 1 |  |  | 3 h | 91% | 88% |
| 2 |  |  | 3 h | 92% | 49% |
| 3 |  |  | 3 h | 98% | 92% |
| 4 |  |  | 15 h | 84% | 79% |
| 5[a] |  |  | 6 h | 88% | 80% |
| 6[a] |  |  | 6 h | 90% | 86% |
| 7 |  |  | 2 h | 95% | - |
| 8[b] |  |  | 24 h | 92% | - |
| 9[a] |  |  | 6 h | 95% | 83% |

[a] 4 eq. of vinyl acetate and 2 eq. of $Na_2CO_3$ were used. [b] See text.

or elimination reactions.[6] Quite recently, the synthesis of allyl and alkyl vinyl ethers by the transfer vinylation of alcohols with butyl vinyl ether in the presence of a palladium catalyst has been reported.[7]

The present method uses commercially available $[Ir(cod)Cl]_2$ as the precatalyst for the synthesis of vinyl ethers which are very difficult to prepare otherwise.[2] The reaction is thought to proceed through an addition-elimination sequence of alcohol and acetic acid in the presence of the iridium complex as a catalyst and $Na_2CO_3$ as the base. Representative examples are compiled in the Table. The method can also be applied to the synthesis of vinyl ethers derived from secondary alcohols (entry 7) and holds promise for the preparation of alkyl vinyl ethers (entry 9). Although sulfur compounds frequently inhibit transition metal-catalyzed reactions, thiophenol reacts with vinyl acetate to form phenylvinyl thioether in excellent yield (entry 8); this compound, however, is unstable in air and is therefore difficult to isolate in analytically pure form (~15 %).

**1**. Department of Applied Chemistry, Faculty of Engineering, Kansai University, Suita, Osaka 564-8680, Japan.

**2**. Okimoto, Y.; Sakaguchi, S.; Ishii, Y. *J. Am. Chem. Soc.* **2002**, *124*, 1590.

**3**. Herde, J. L.; Lambert, J. C.; Senoff, C. V. *Inorg. Synth.* **1974**, *15*, 18.

**4**. Watanabe, W. H.; Conlon, L. E. *J. Am. Chem. Soc.* **1956**, *79*, 2828.

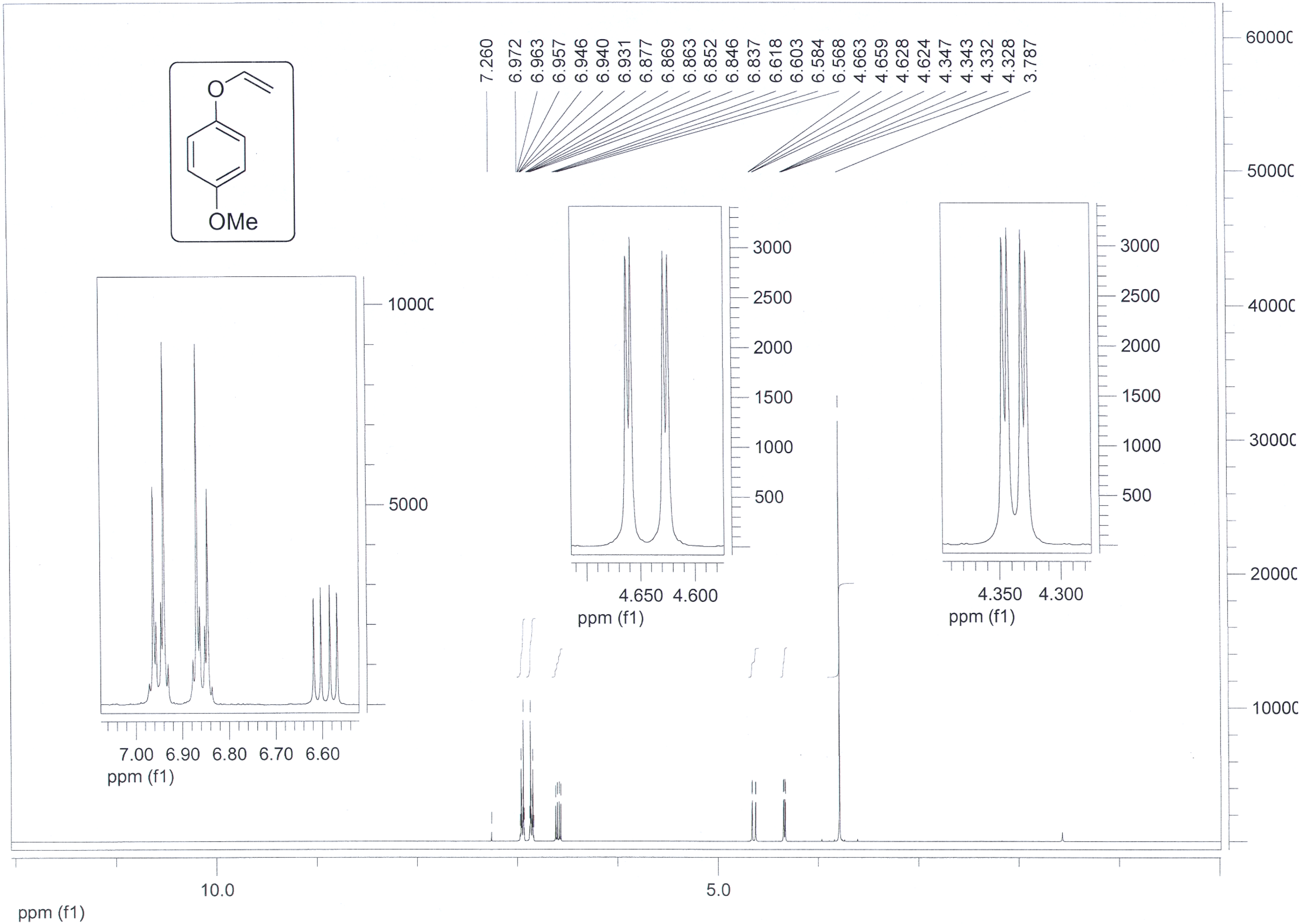
**5**. Larock, R. C. *Comprehensive Organic Transformations,* 2nd ed.; Wiley-VCH: New York, **1999**, pp. 222 and 225-226.

**6**. Nerdel, F.; Buddrus, J.; Brodowski, W.; Hentschel, P.; Klamann, D.; Weyerstahl, P. *Justus Liebigs Ann. Chem.* **1967**, *710*, 36.

**7**. Bosch, M.; Schlaf, M. *J. Org. Chem.* **2003**, *68*, 5225.

## Appendix
## Chemical Abstracts Nomenclature; (Registry Number)

Di-μ-chloro-bis(1,5-cyclooctadiene)diiridium(I): Iridium,
di-μ-chlorobis[(1,2,5,6-η)-1,5-cyclooctadiene]di-; (12112-67-3)
Sodium carbonate: Carbonic acid disodium salt; (497-19-8)
Toluene: Benzene, methyl-; (108-88-3)
*p*-Methoxyphenol: Phenol, 4-methoxy-; (150-76-5)
Vinyl acetate: Acetic acid ethenyl ester; (108-05-4)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ppm (f1)
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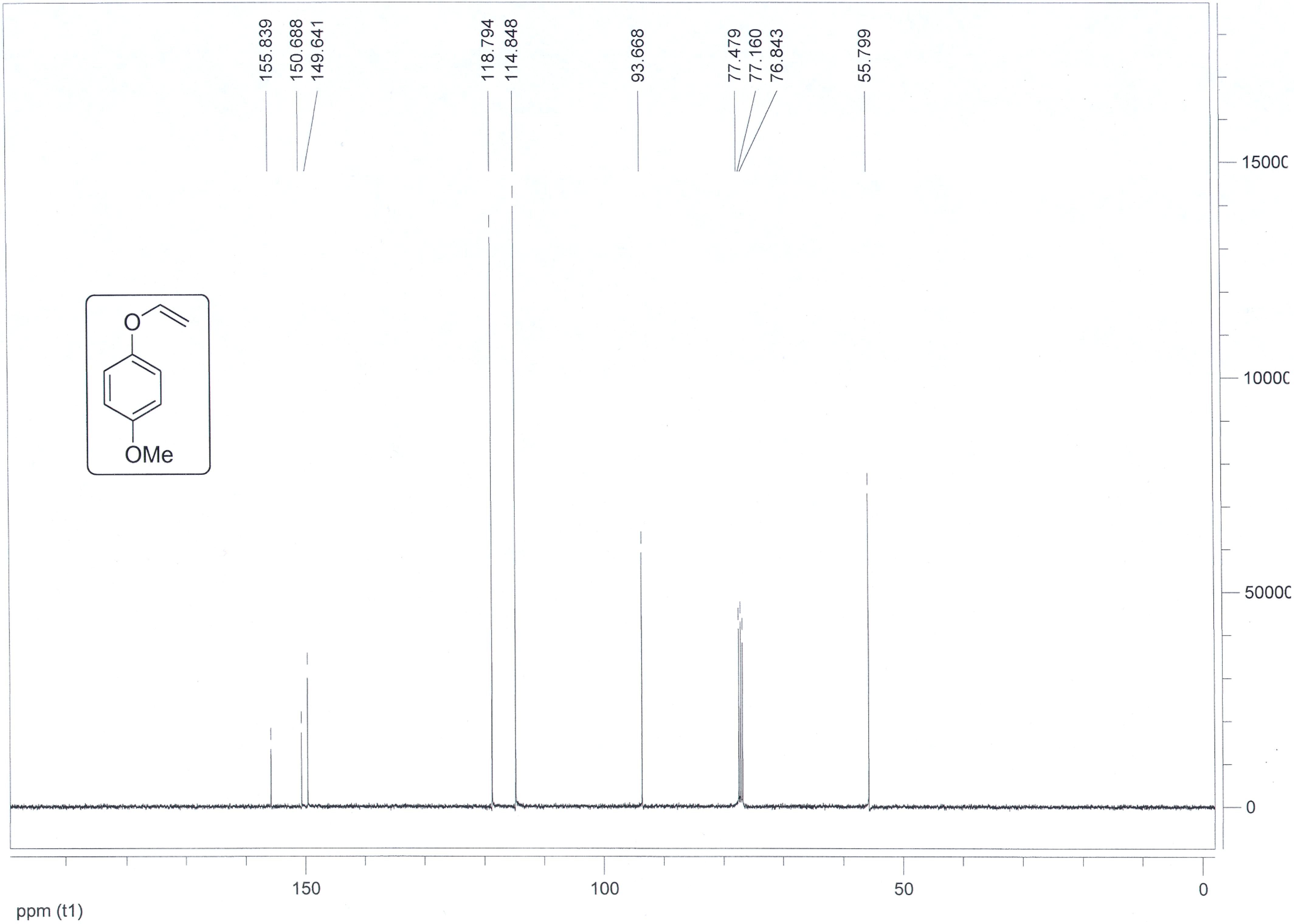
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