

Supporting Information

Catalytic S_NAr reaction of nonactivated fluoroarenes with amines via Ru η^6 -arene complexes

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General

Anhydrous dioxane and tetrahydrofuran (THF) were purchased and dried over activated molecular sieves 4A. All reactions were carried out under an atmosphere of argon in oven-dried glassware with a magnetic stirring bar. Ru(cod)(methylallyl)₂, fluoroarenes, amines, ligands, and trifluoroacetic acid were also commercially available and were used without further purification.

IR spectra were recorded with a JASCO FT210 spectrometer. ¹H and ¹³C NMR spectra were recorded with a JEOL AL-400 spectrometer at 400 MHz and 100 MHz respectively using CDCl₃ as a solvent. ³¹P NMR spectra were recorded with a Lambda-500 (202 MHz) spectrometer using THF-*d*₈ as a solvent. Chemical shift values for protons and carbons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to residual proton and carbon resources of CDCl₃ respectively (δ, 7.26 and 77.0). Chemical shifts for phosphorous are reported in parts per million (ppm, δ scale) referenced to H₃PO₄. ESI-MS spectra were measured with LCQ-DECA. High-resolution mass spectra (HRMS) were measured on a JEOL JMS-GCMateII with EI (Electron Ionization) method.

Experimental Procedure

General Procedure for the Ru-Catalyzed S_NAr reaction of *p*-fluorotoluene with morpholine

(Table 1, entry 9).

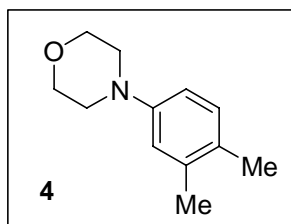
Ru(cod)(2-methylallyl)₂ (6.4 mg, 0.020 mmol), 1,5-bis(diphenylphosphino)pentane (12.3 mg, 0.028 mmol), and TfOH (3.5 μL, 0.040 mmol) were suspended in 0.20 mL of dioxane in a Schlenk tube. To the reaction mixture, *p*-fluorotoluene (2.0 mmol), morpholine (0.40 mmol), triethylamine (0.40 mmol) and triethylsilane (0.40 mmol) were added. The solution was then stirred at reflux for 24 h. After 24 h, the solvent were evaporated. The crude products were purified by thin-layer chromatography (hexane/AcOEt = 10/1) to give analytically pure **1** (72%).

Compound Data of the Products

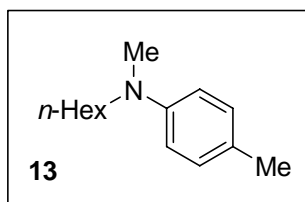
Known compounds:

N-(4-Methylphenyl)morpholine¹ (**1**), *N*-phenylmorpholine¹ (**2**), *N*-(3-methylphenyl)morpholine¹ (**3**),
N-(4-methoxyphenyl)morpholine¹ (**5**), *N*-(3-methoxyphenyl)morpholine¹ (**6**),
N-(2-methoxyphenyl)morpholine² (**7**), *N*-(4-(*N,N*'-dimethylamino)phenyl)morpholine³ (**8**),
N-(4-vinylphenyl)morpholine¹ (**9**), *N*-(4-methylphenyl)piperidine⁴ (**10**),
N-methyl-*N*'-(4-methylphenyl)piperazine⁵ (**11**), *N*-(4-methylphenyl)pyrrolidine⁶ (**12**),
N-benzyl-*N*-methyl-4-methylaniline⁷ (**14**), and *N*-cyclohexyl-4-methylaniline⁸ (**15**)

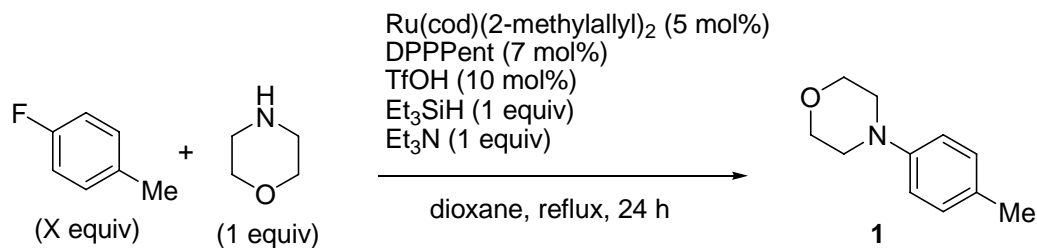
¹H and ¹³C NMR spectra and MS spectra of these compounds were consistent with those in the literatures.

New compounds:*N*-(3,4-Dimethylphenyl)morpholine (**4**)

Colorless oil, $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 2.19 (s, 3H), 2.24 (s, 3H), 3.10 (t, $J = 4.8$ Hz, 4H), 3.85 (t, $J = 4.8$ Hz, 4H), 6.67 (dd, $J = 8.0, 2.0$ Hz, 1H), 6.73 (d, $J = 2.0$ Hz, 1H), 7.03 (d, $J = 8.0$ Hz, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 18.8, 20.2, 50.0, 67.0, 113.4, 117.7, 128.4, 130.2, 137.2, 149.6; IR (neat) 2962, 2854, 2817, 1614, 1506, 1450, 1242, 1122, 804 cm^{-1} ; HRMS (EI^+) Calcd. for: $\text{C}_{12}\text{H}_{17}\text{NO}$ $[\text{M}]^+$ 191.1310. Found: m/z 191.1307.

N-Hexyl-*N*-methyl-4-methylaniline (**13**)

Colorless oil, $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ 0.88 (t, $J = 7.2$ Hz, 3H), 1.28-1.31 (m, 6H), 1.50-1.57 (m, 2H), 2.23 (s, 3H), 2.87 (s, 3H), 3.24 (t, $J = 8.0$ Hz, 2H), 6.62 (d, $J = 8.8$ Hz, 2H), 7.02 (d, $J = 8.8$ Hz, 2H); $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz) δ 14.1, 20.2, 22.7, 26.5, 26.9, 31.8, 38.4, 53.2, 112.6, 125.1, 129.6, 147.5; IR (neat) 2927, 2858, 1620, 1522, 1367, 802 cm^{-1} ; HRMS (EI^+) Calcd. for: $\text{C}_{14}\text{H}_{23}\text{N}$ $[\text{M}]^+$ 205.1830. Found: m/z 205.1818.

Screening of the Amounts of *p*-Fluorotoluene

Entry	X	Yield [%]
1	1	22
2	2	50
3	3	54
4	4	60
5	5	72

ESI-MS and ^{31}P NMR Analyses of the Intermediates

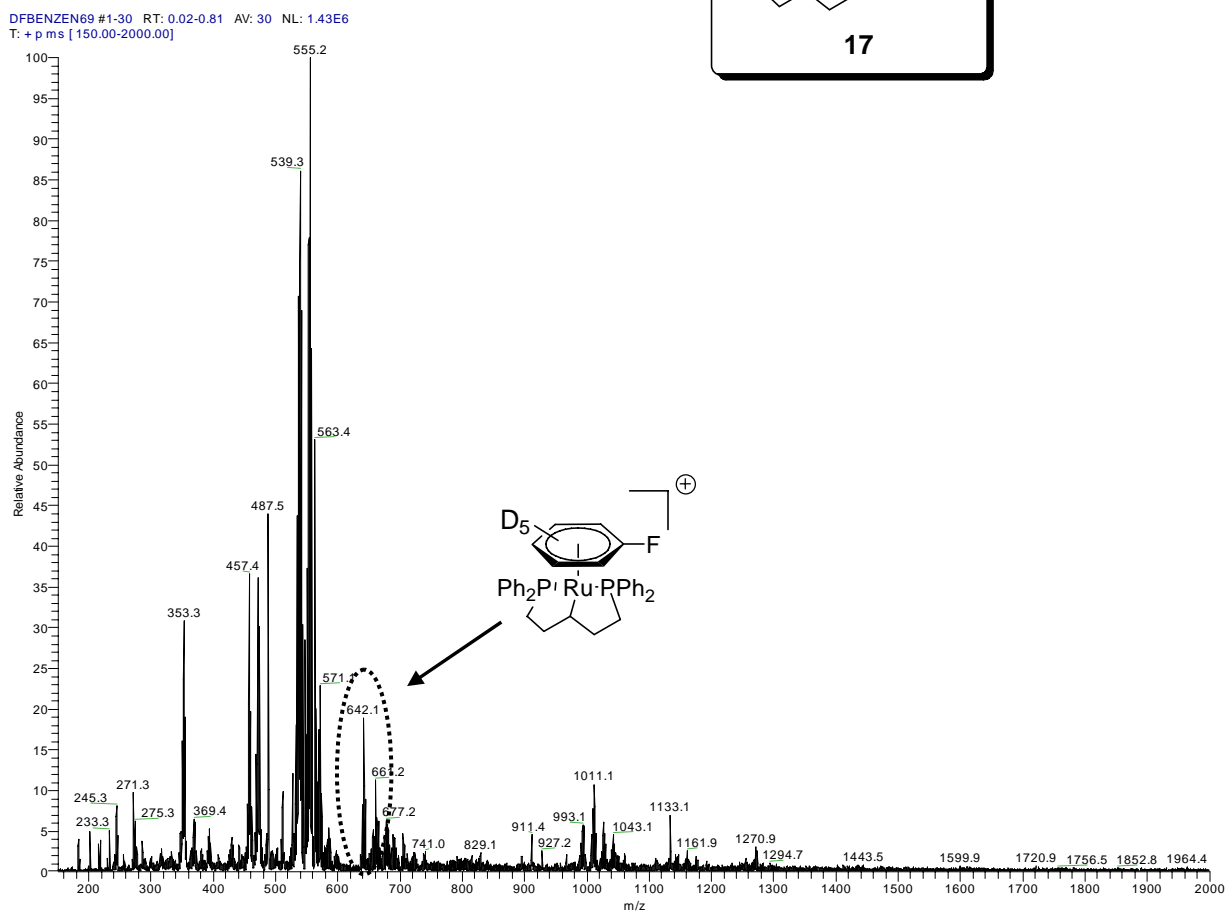
We successfully observed the Ru η^6 -arene complexes **17** and **18** as reaction intermediates by ESI-MS and ^{31}P NMR analyses. As the result of the ESI-MS analyses, the observed isotope patterns of **17** and **18** were consistent with those of the theoretical isotope patterns respectively. Furthermore, both of the ^{31}P NMR spectra of **17** and **18** almost accorded with the spectrum of the pincer-type Ru η^6 -arene complex.⁹ In those NMR analyses, all analytical samples were prepared under argon atmosphere, because these Ru complexes in the samples were air sensitive.

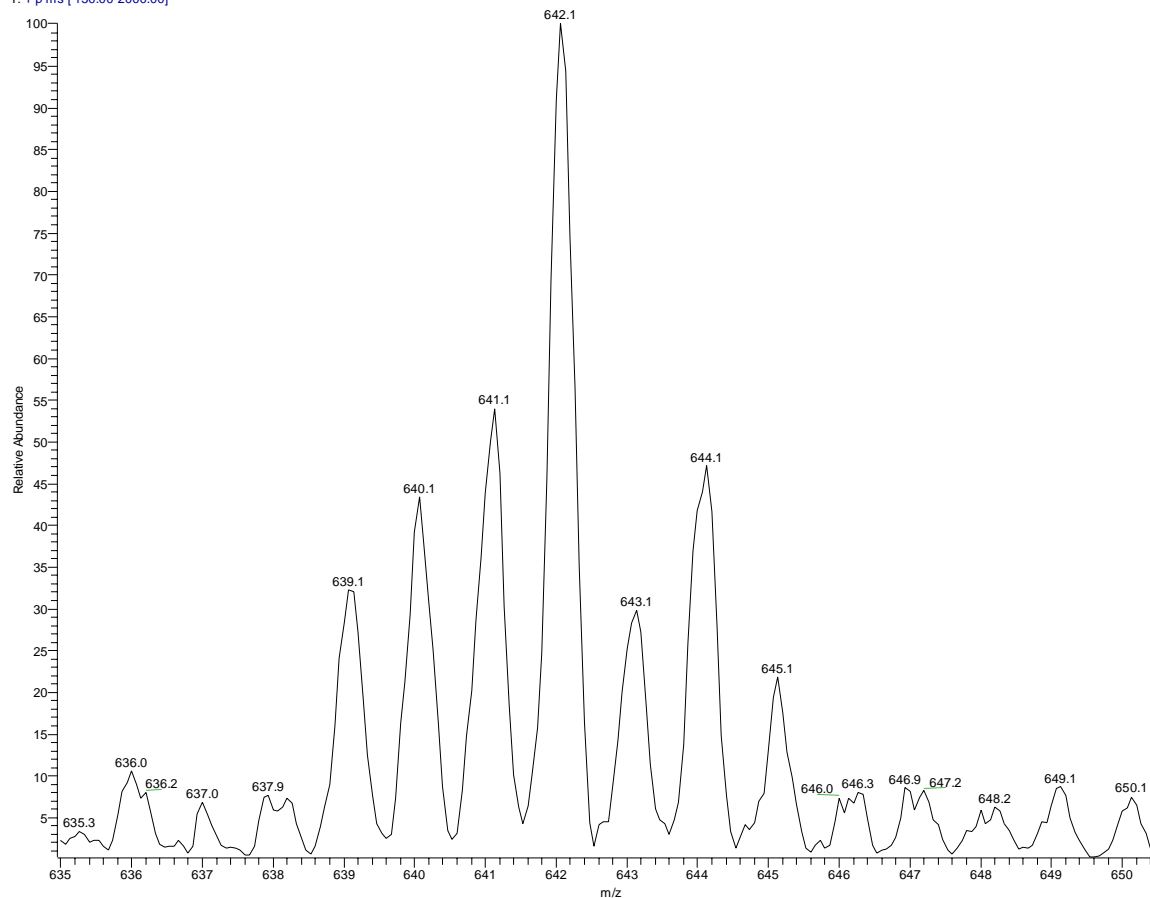
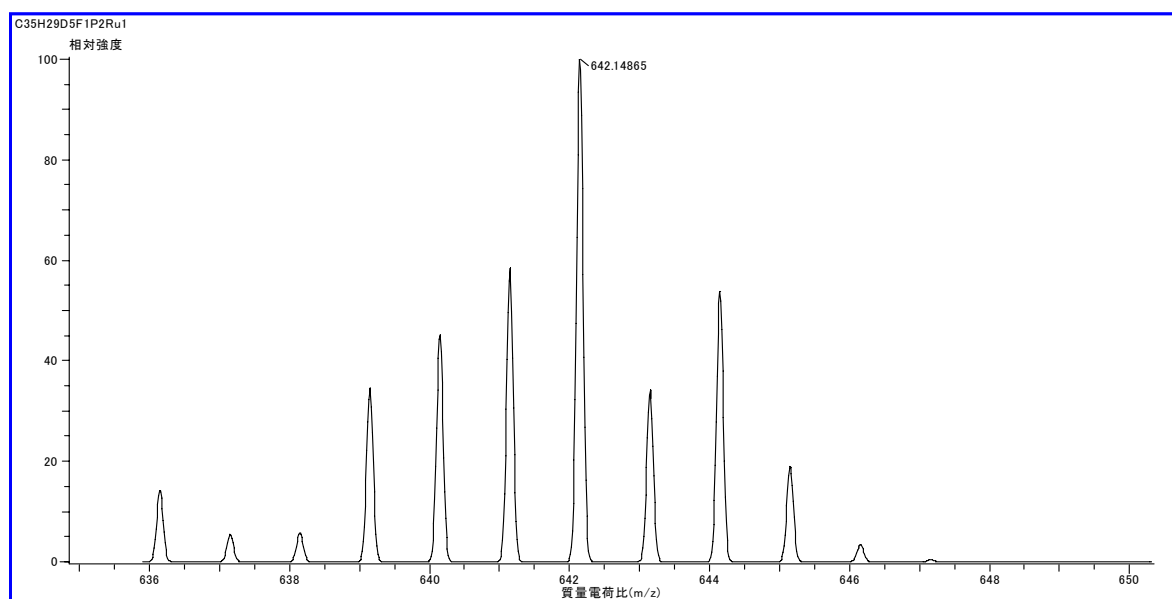
^1H NMR Analyses of the Intermediates **17** and **18**

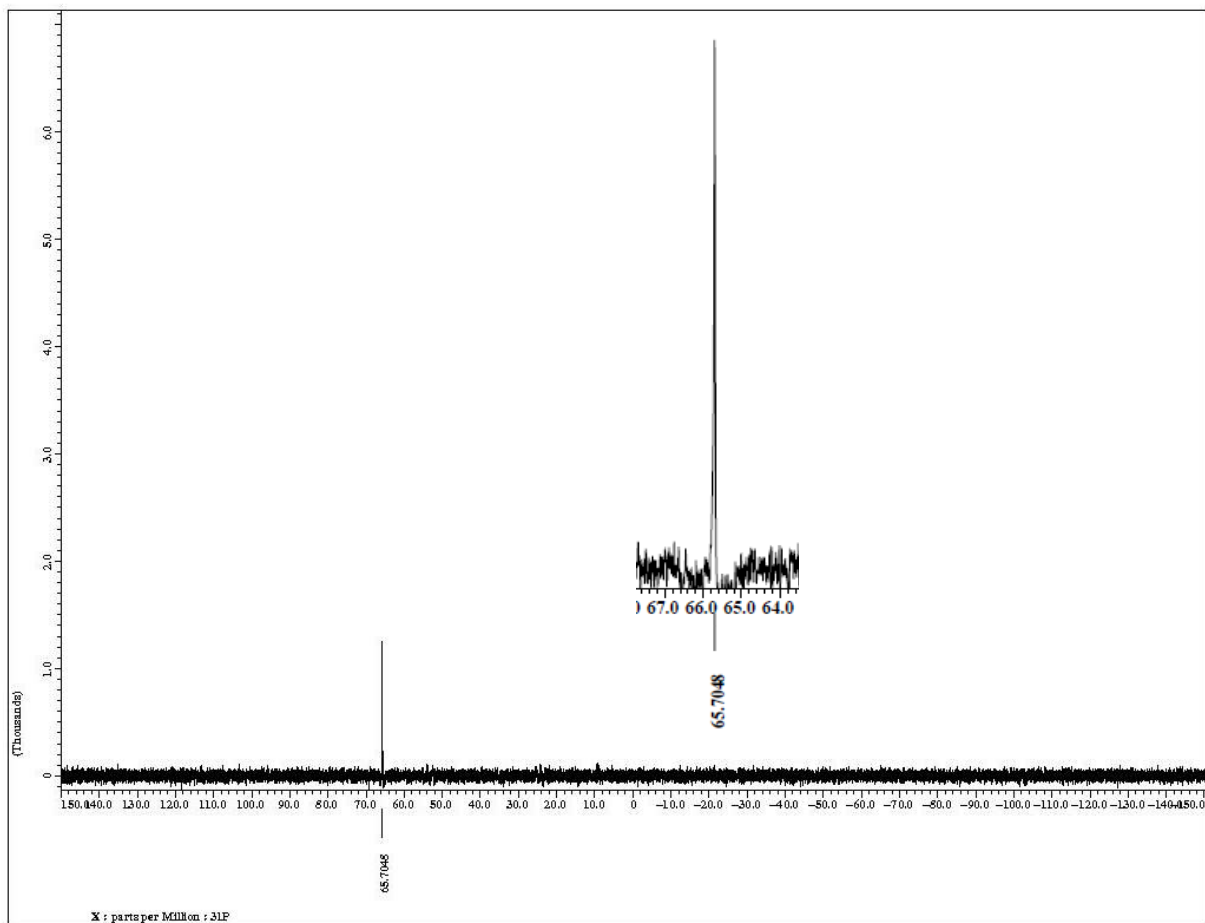
^1H NMR analyses of the Ru η^6 -arene complexes **17** and **18** were also conducted, but we could not assign the ^1H NMR spectra of **17** and **18**, probably because they were not major products in the reaction mixtures. Isolation and full characterization of complexes **17** and **18** could not be achieved yet and they were deferred to a future publication.

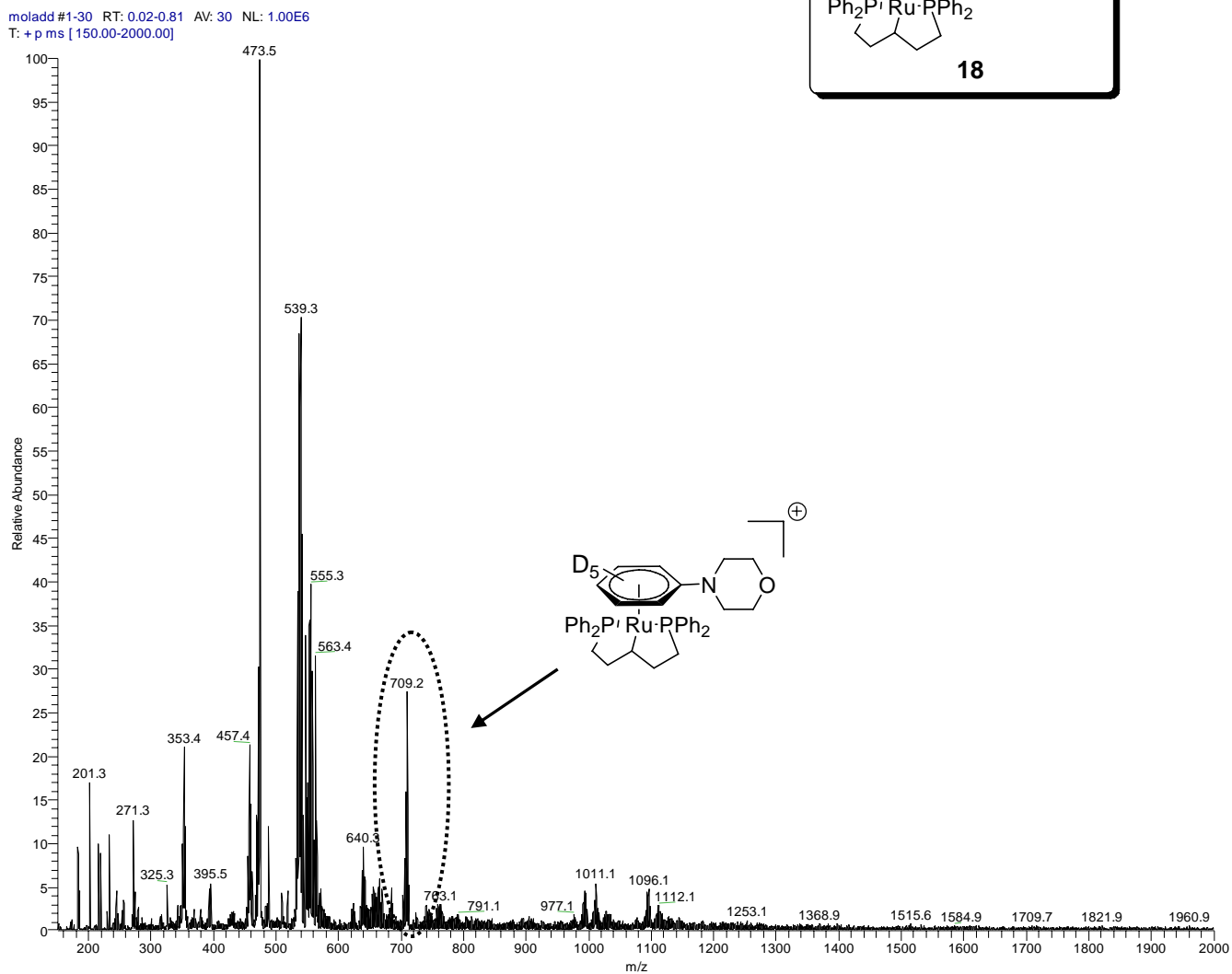
$[\text{Ru}(\text{dpppnt})(\eta^6\text{-fluorobenzene-}d_5)]^+ \text{OTf}^-$ (**17**)

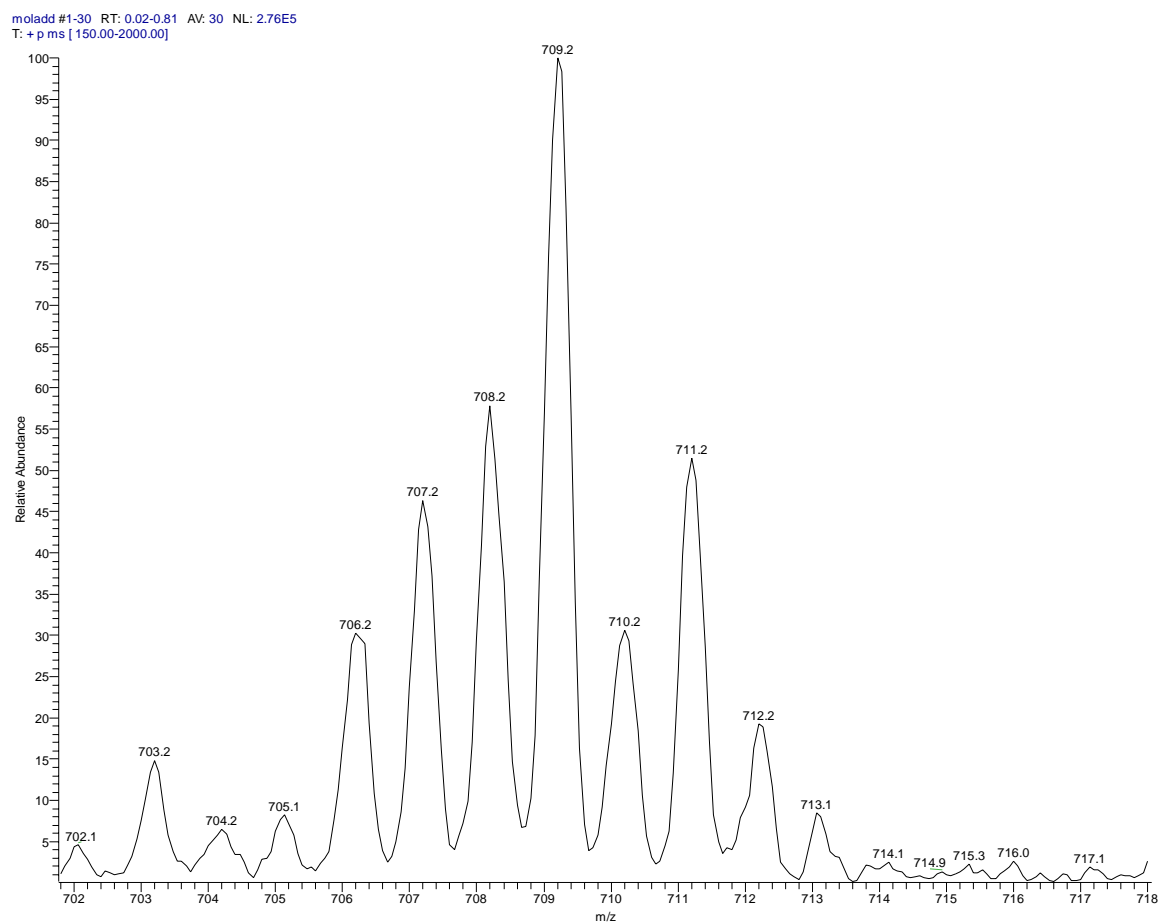
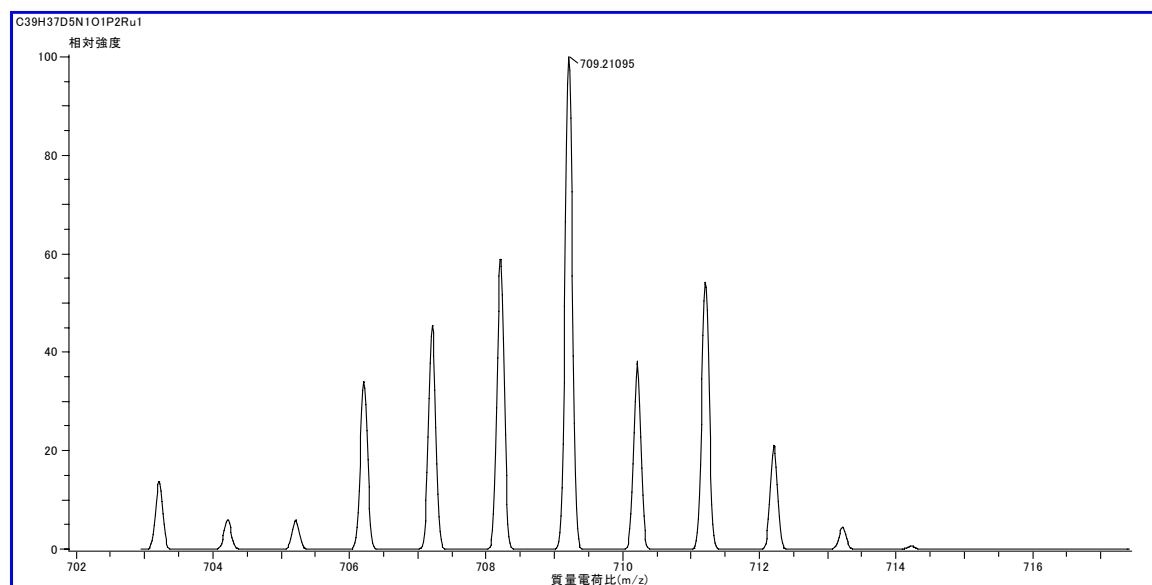
ESI-MS Chart of **17**

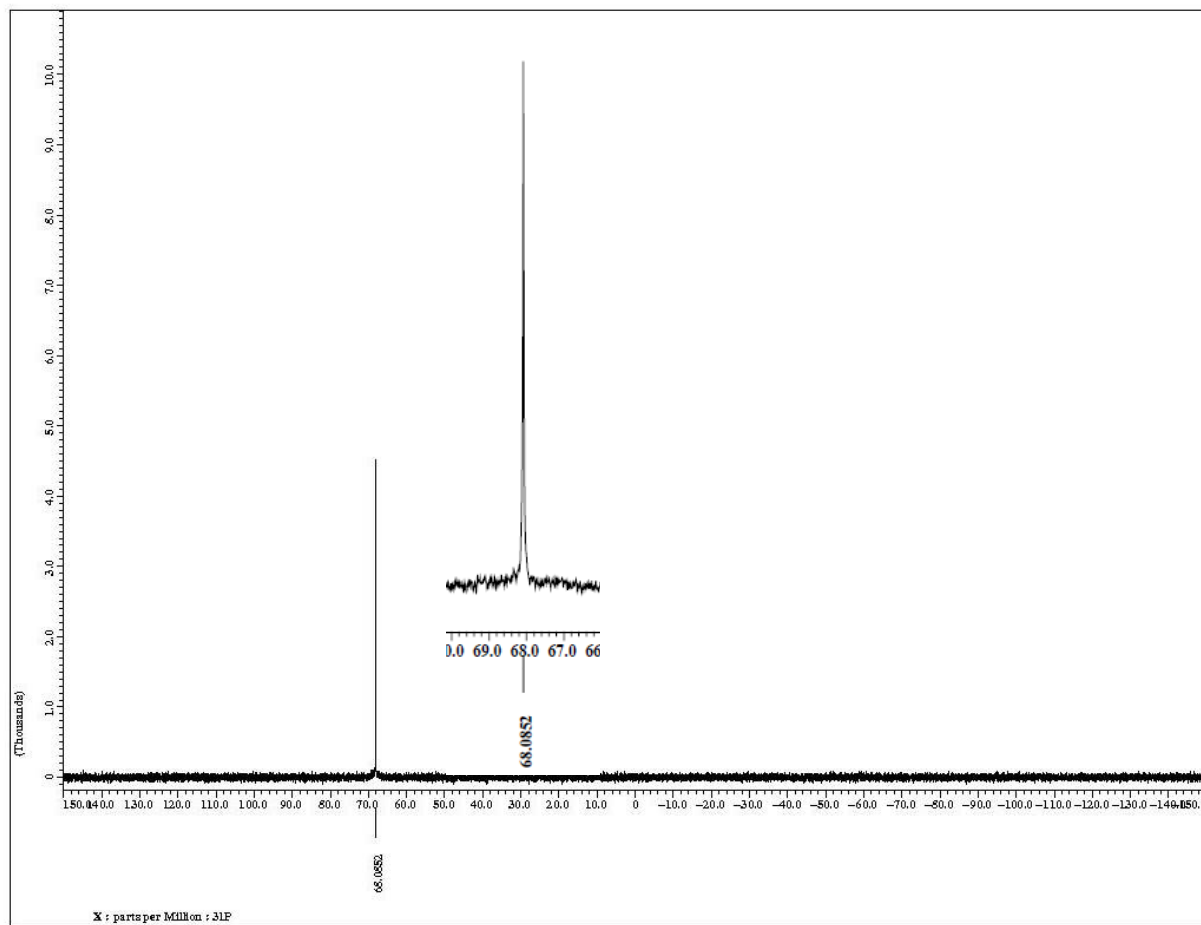


Observed Isotope Pattern of $C_{35}H_{29}D_5FP_2Ru$: $[Ru(dpppent)(\eta^6\text{-fluorobenzene-}d_5)]^+$ DFBENZEN69 #1-30 RT: 0.02-0.81 AV: 30 NL: 2.70E5
T: +p ms [150.00-2000.00]**Theoretical Isotope Pattern of $C_{35}H_{29}D_5FP_2Ru$: $Ru(dpppent)(\eta^6\text{-fluorobenzene-}d_5)]^+$** 

^{31}P NMR Spectrum of 17

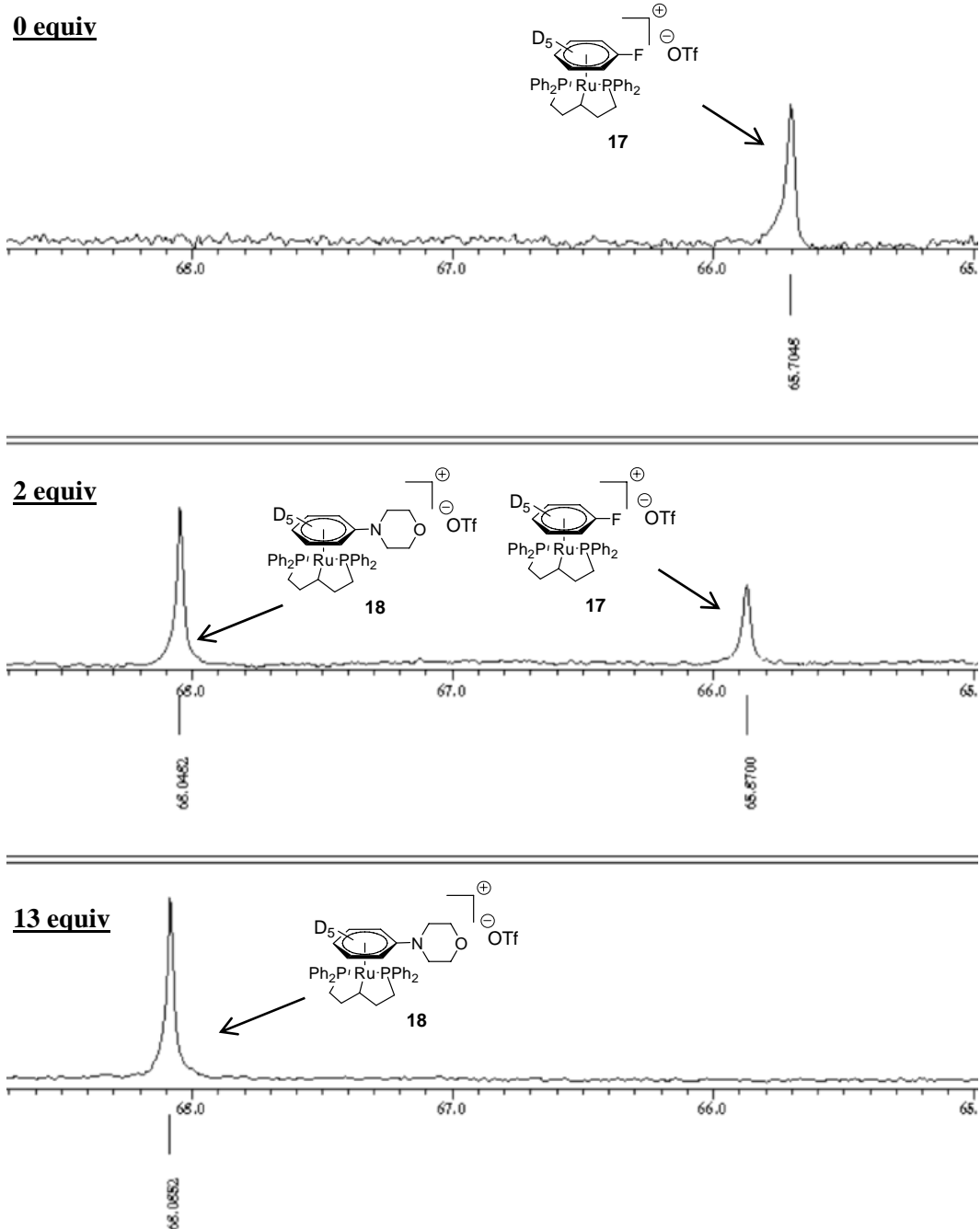
$[\text{Ru}(\text{dpppent})(\eta^6\text{-morpholinobenzene-}d_5)]^+ \text{OTf}^-$ (18)**ESI-MS Chart of 18**

Observed Isotope Pattern of $C_{39}H_{37}D_5NOP_2Ru$: $[Ru(dpppent)(\eta^6\text{-morpholinobenzene-}d_5)]^+$ **Theoretical Isotope Pattern of $C_{39}H_{37}D_5NOP_2Ru$: $Ru(dpppent)(\eta^6\text{-morpholinobenzene-}d_5)]^+$** 

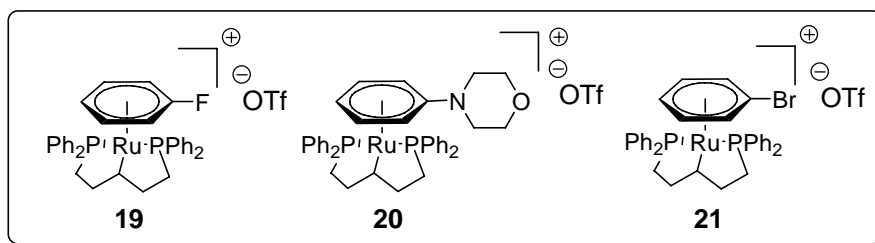
^{31}P NMR Spectrum of 18

The Change of Chemical Shift of ^{31}P NMR; from 17 to 18

We successfully observed that the peak of 17 shifted to the peak of 18 according to the addition of morpholine; monitored by ^{31}P NMR analysis.

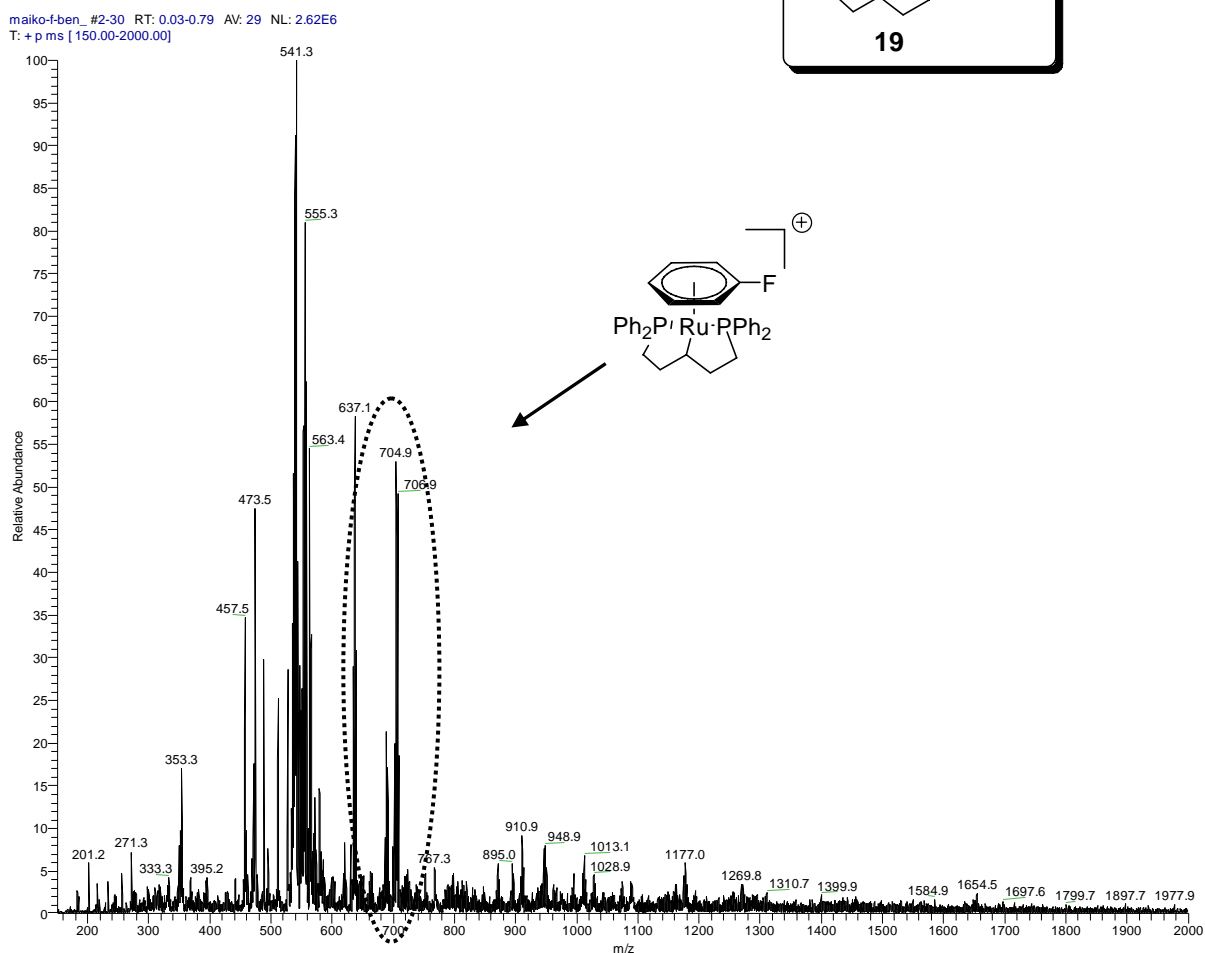


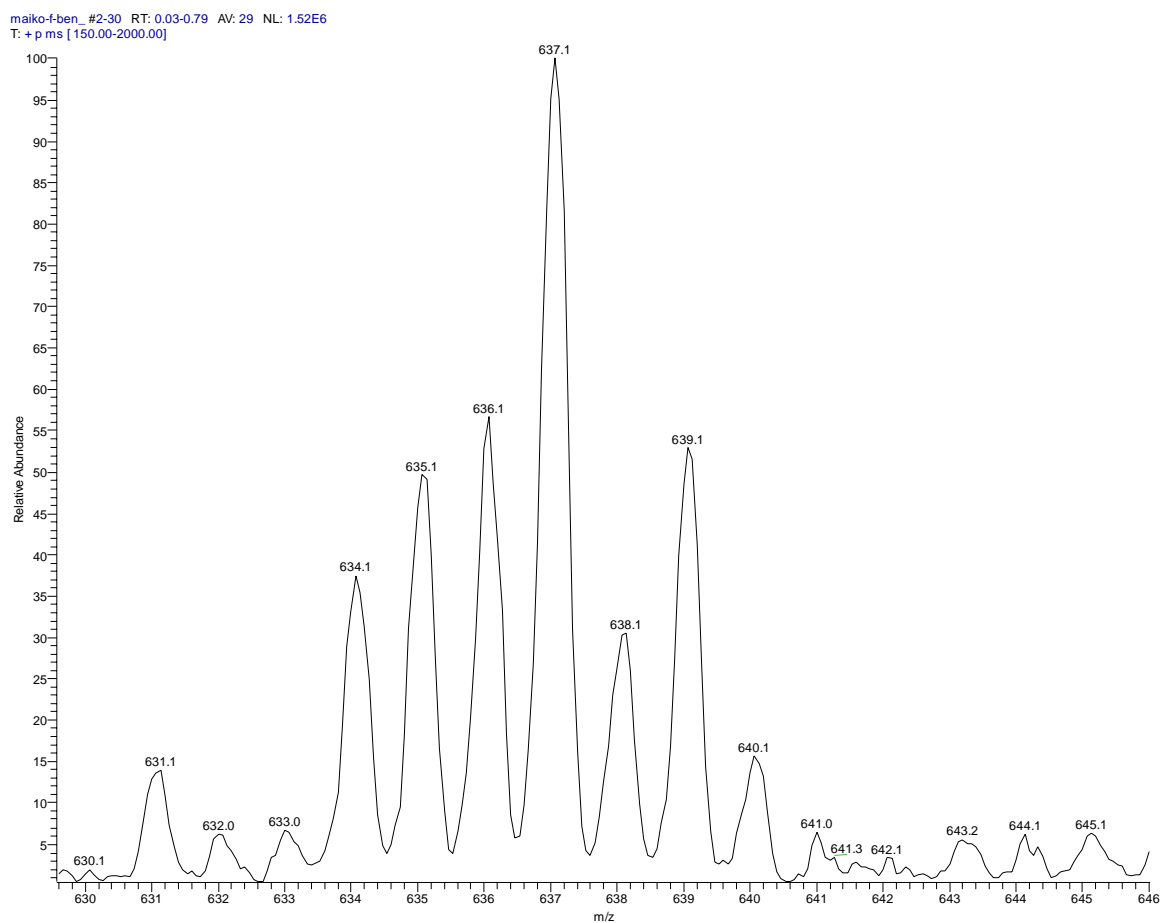
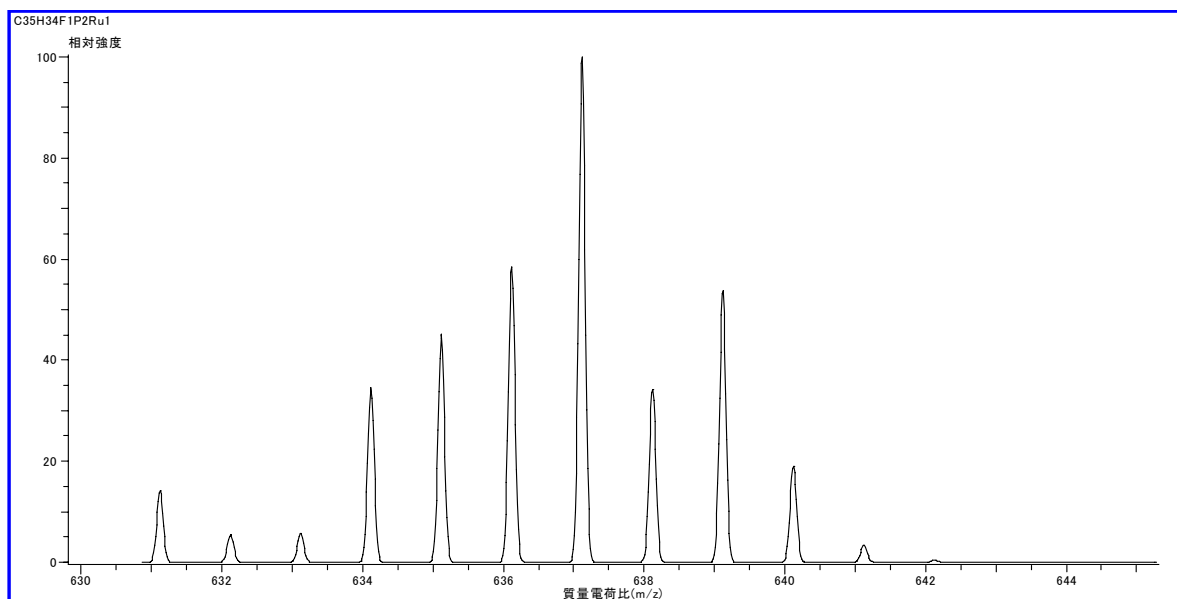
We also achieved the detection of the Ru η^6 -arene complexes **19**, **20**, and **21** by ESI-MS analysis. The observed isotope patterns of **19**, **20**, and **21** were consistent with those of the theoretical isotope patterns respectively. Furthermore, the ^{31}P NMR spectrum of **21** almost accorded with the spectrum of the pincer-type Ru η^6 -arene complex.⁹ In those NMR analysis, the analytical sample was prepared under argon atmosphere, because Ru complexes in the sample were air sensitive.

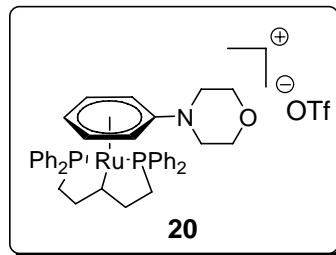
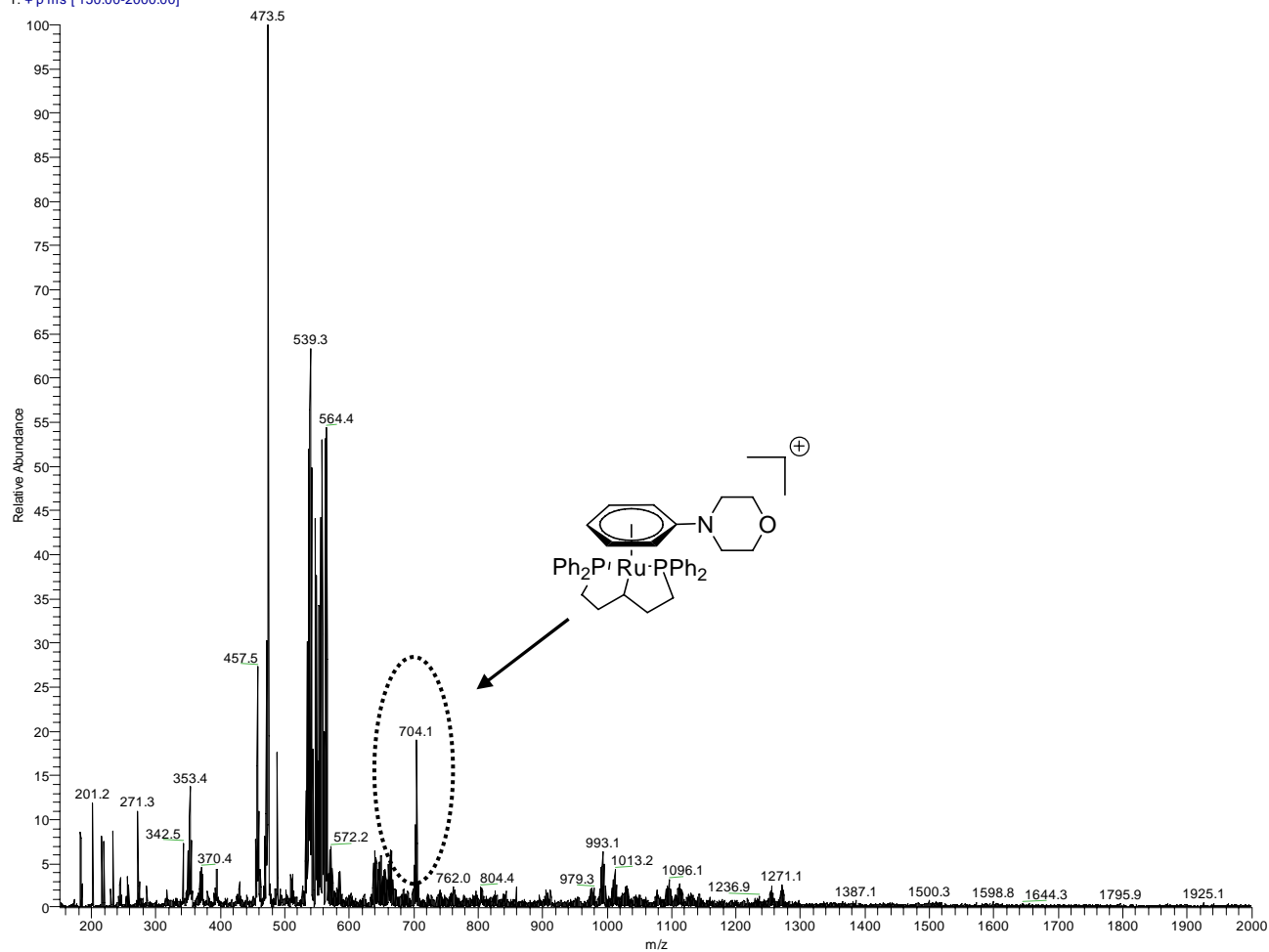


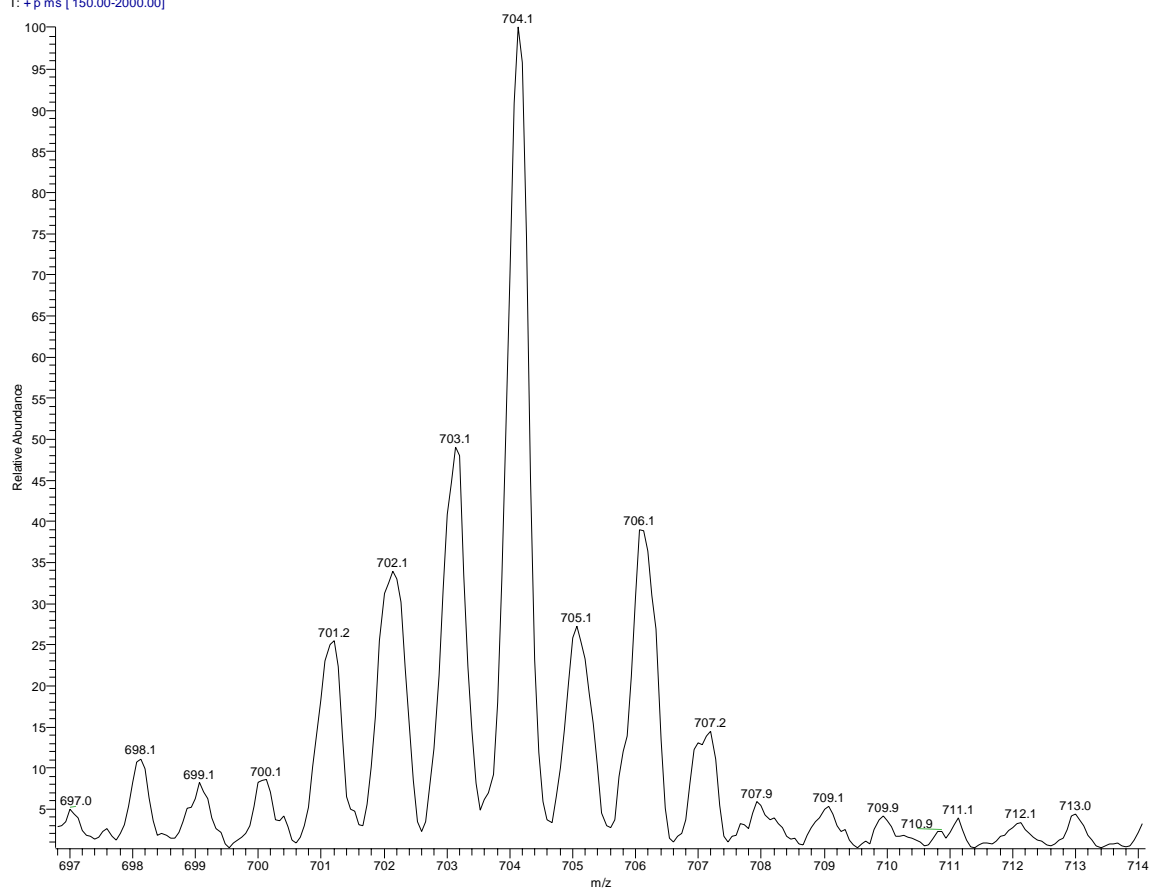
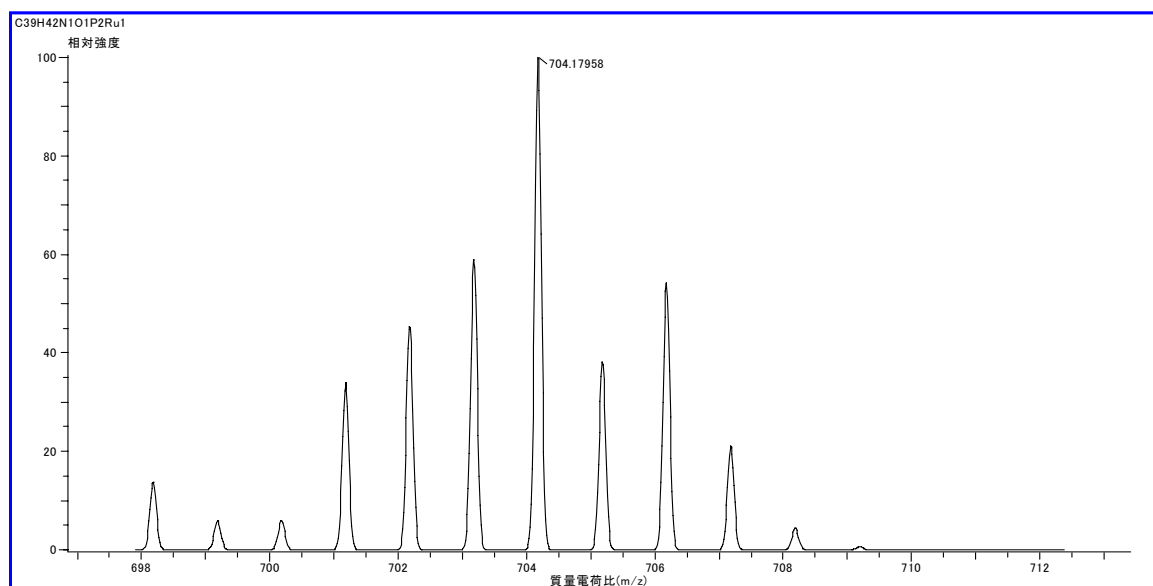
[Ru(dppp)(η^6 -fluorobenzene)]⁺ OTf⁻ (**19**)

ESI-MS Chart of 19



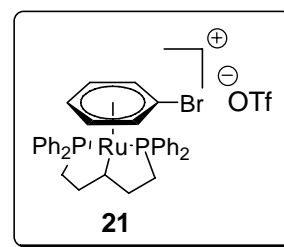
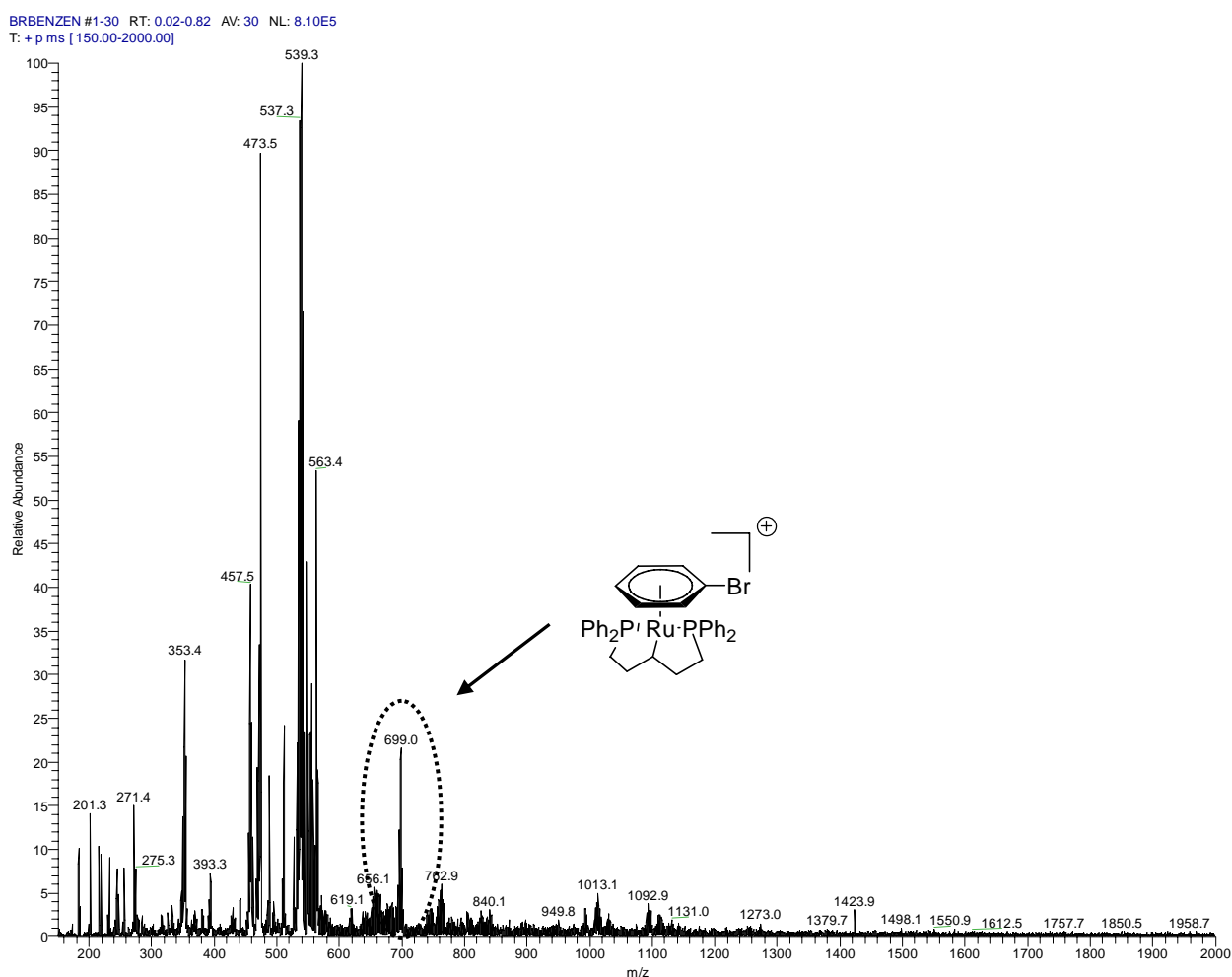
Observed Isotope Pattern of C₃₅H₃₄FP₂Ru: [Ru(dpppnt)(η^6 -fluorobenzene)]⁺**Theoretical Isotope Pattern of C₃₅H₃₄FP₂Ru: [Ru(dpppnt)(η^6 -fluorobenzene)]⁺**

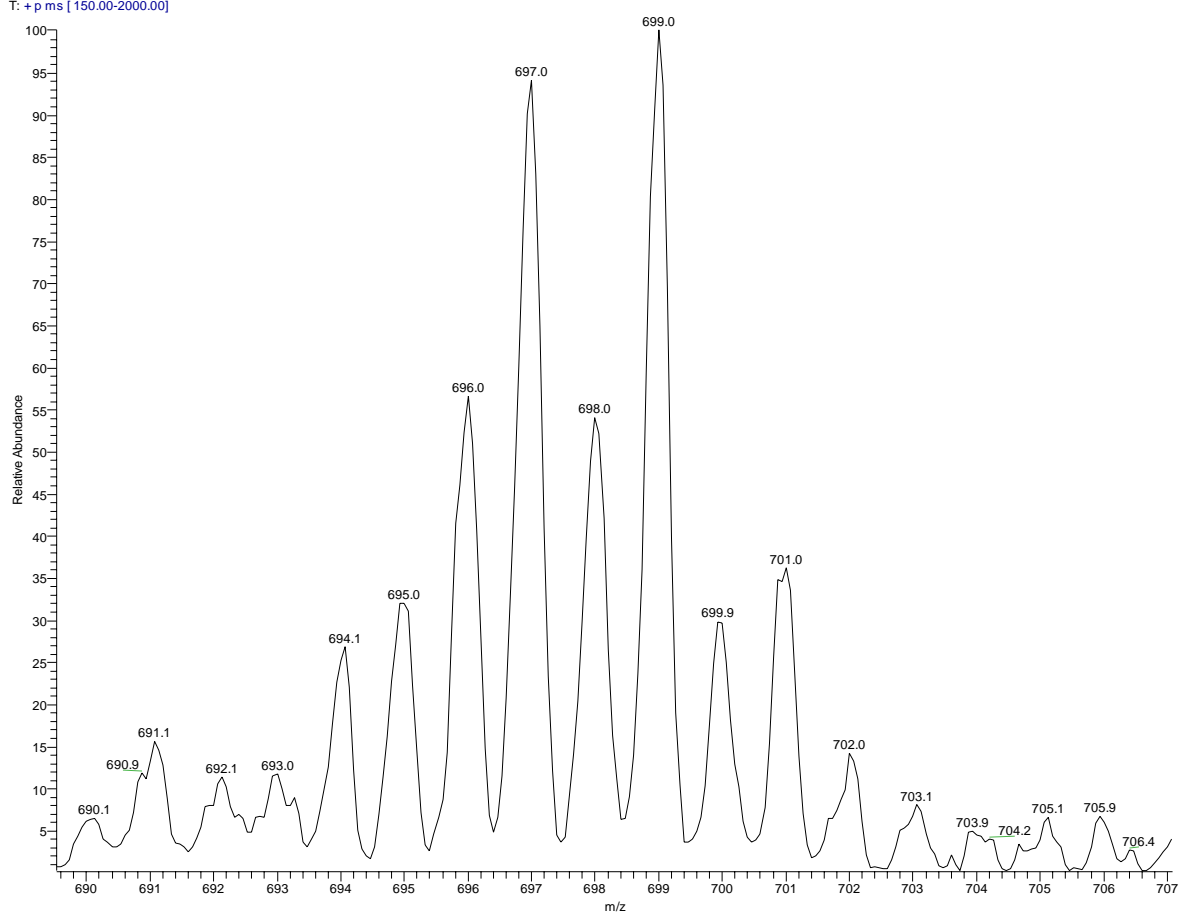
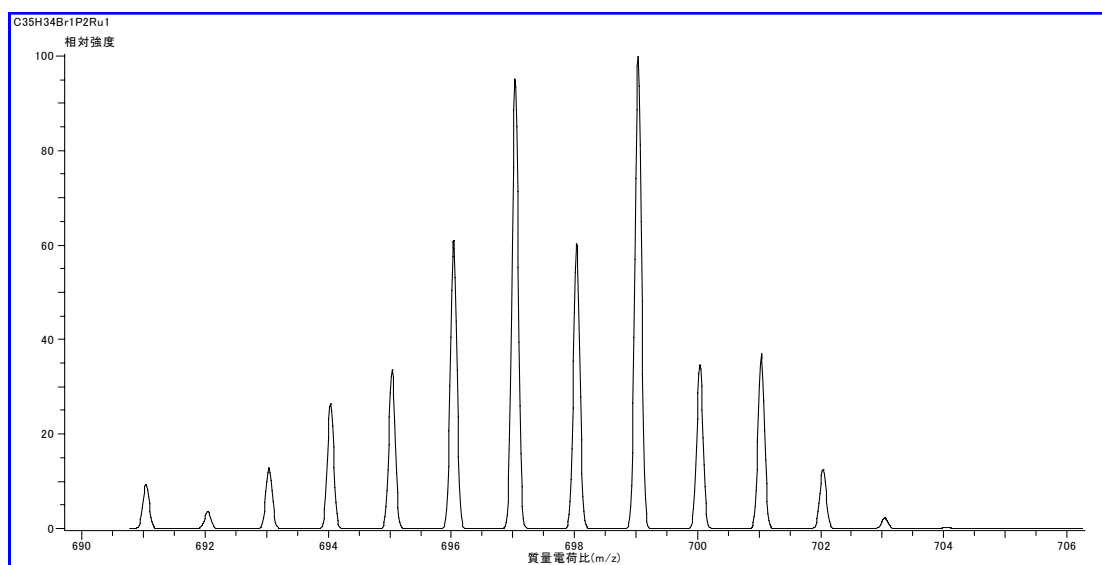
[Ru(dpppent)(η^6 -morpholinobenzene)]⁺ OTf⁻ (20)**ESI-MS Chart of 20**626-mol #1-30 RT: 0.01-0.80 AV: 30 NL: 6.66E6
T: + p ms [150.00-2000.00]

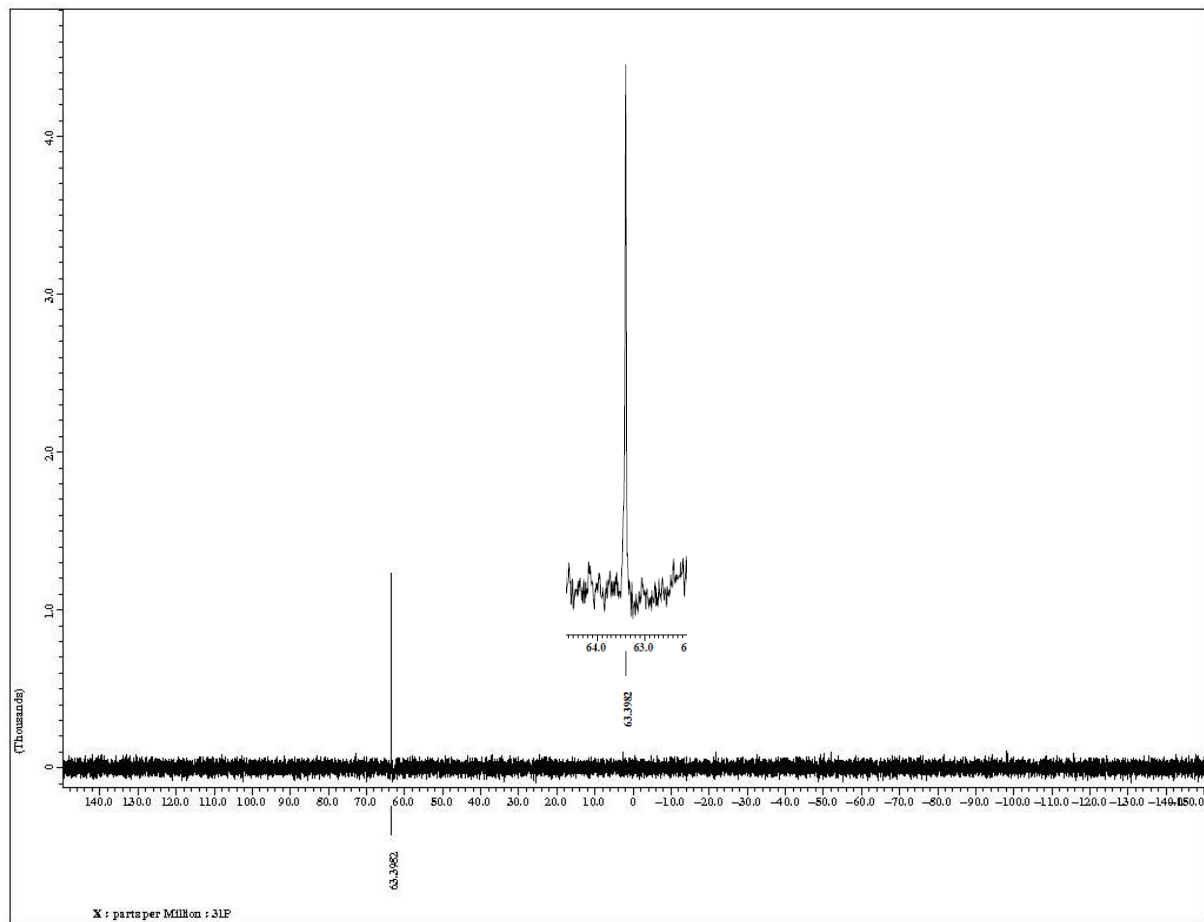
Observed Isotope Pattern of $C_{39}H_{42}NOP_2Ru$: $[Ru(dpppnt)(\eta^6\text{-morpholinobenzene})]^+$ 626-mol#1-30 RT: 0.01-0.80 AV: 30 NL: 1.26E6
T: +p ms [150.00-2000.00]**Theoretical Isotope Pattern of $C_{39}H_{42}NOP_2Ru$: $[Ru(dpppnt)(\eta^6\text{-morpholinobenzene})]^+$** 

[Ru(dpppent)(η^6 -bromobenzene)]⁺ OTf⁻ (21**)**

To the Ru catalyst, an excess amount of bromobenzene was added in THF-*d*₆. [Ru(dpppent)(η^6 -bromobenzene)]⁺ OTf⁻ (**21**) was detected by ³¹P NMR in the reaction solution. Then an excess amount of morpholine was added to the solution and heated to 80 °C for 10 min. As a result, not [Ru(dpppent)(η^6 -morpholinobenzene)]⁺ OTf⁻ (**20**), but (**21**) was detected as a reaction intermediate. (the data of ESI-MS and ³¹P NMR are shown below) This result strongly suggests that the catalytic reaction proceeds by S_NAr reaction.

**ESI-MS Chart of 21**

Observed Isotope Pattern of C₃₅H₃₄BrP₂Ru: [Ru(dpppent)(η^6 -bromobenzene)]⁺BRBENZEN #1-30 RT: 0.02-0.82 AV: 30 NL: 1.75E5
T: + p ms [150.00-2000.00]**Theoretical Isotope Pattern of C₃₅H₃₄BrP₂Ru: [Ru(dpppent)(η^6 -bromobenzene)]⁺**

^{31}P NMR Spectrum of 21

References

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