Ru/PNNP-Catalyzed Asymmetric Imine Aziridination by Diazoester Activation

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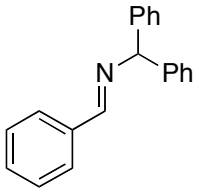
Supporting Information

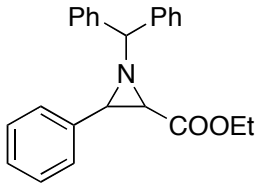
General. Reactions with air- or moisture-sensitive materials were carried out under an argon atmosphere using Schlenk techniques or in a glove box under purified nitrogen. CH_2Cl_2 and CD_2Cl_2 were distilled from CaH and degassed (3 × freeze/pump/thaw) under argon prior to use. ^{1}H, ^{13}C, ^{15}N, and ^{31}P NMR spectroscopic experiments were run on Bruker AVANCE DPX 250, 300 and 500 spectrometers. ^{1}H and ^{13}C positive chemical shifts in ppm are downfield from tetramethylsilane. ^{15}N NMR spectra are referenced to external CH_3NO_2 (neat). ^{31}P NMR spectra are referenced to external 85% H_3PO_4. Optical rotations were measured using a Perkin Elmer 341 polarimeter with a 1 dm cell. 2-^{13}C-glycine (98% ^{13}C) and $Na^{15}NO_2$ (98% ^{15}N) were purchased from Cambridge Isotope Labs.

Synthesis of *N*-benzylidene-1,1-diphenylmethanamine (5)



A mixture of benzaldehyde (8.4 g, 72 mmol), diphenylmethaneamine (14.8 g, 72 mmol), and $ZnCl_2$ (125 mg, 0.92 mmol) in toluene (500 mL) was refluxed overnight with a Dean-Stark apparatus. $ZnCl_2$ was filtered off, the solvent evaporated under reduced pressure, and the crude product was recrystallized several times from hot ethanol to give white crystals. Yield: 19.2 g, 88 %. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (*s*, 1H, C*H*=N), 7.88 (*m*, 2H, arom.), 7.45 – 7.23 (*m*, 13H, arom.), 5.63 (*s*, 1H, C*H*Ph_2).

Catalytic procedures for the synthesis of enantiomerically enriched *cis*-ethyl 1-benzhydryl-3-phenylaziridine-2-carboxylate (6)



Method 1: [RuCl(PNNP)]PF_6 (2) as catalyst (Table 1, run 1). [$RuCl_2$(PNNP)] (19.9 mg, 0.024 mmol) and $TlPF_6$ (8.4 mg, 0.024 mmol) were dissolved in CH_2Cl_2 (1 mL) and stirred at room temperature overnight. Then, the precipitate was filtered off with a glass fiber filter, and imine **5** (130 mg, 0.48 mmol) was added to the mother liquor. The mixture was stirred at room temperature for 10 minutes, and EDA (55 mg, 0.48 mmol) in CH_2Cl_2 (3 mL) was added over 8 hours by syringe pump. The mixture was stirred room temperature for 24 hours, the solvent removed under reduced pressure, and the crude product purified by column chromatography (hexane/ethylacetate 95:5) to obtain a white solid. Yield: 28%. ee: 25% (2*S*,3*S*).

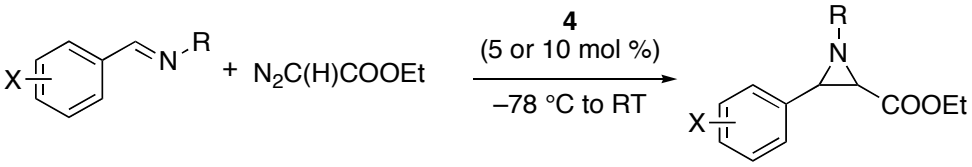
Method 2: [RuCl(H_2O)(PNNP)]PF_6 (3) as catalyst (Table 1, runs 3,4). [$RuCl_2$(PNNP)] (20.7 mg, 0.025 mmol) and $TlPF_6$ (8.7 mg, 0.025 mmol) were stirred in CH_2Cl_2 (2 mL) at room temperature overnight. The precipitate was filtered off with a glass fiber filter, and H_2O (2.1 μL, 0.114 mmol) and imine **5** (135 mg, 0.50 mmol) were added to the solution.[1] The solution was stirred at room temperature for 10 min, and EDA (57 mg, 0.50

mmol) was added thereto. After stirring at room temperature for 24 h, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (hexane/ethylacetate 95:5) to obtain a white solid. Yield: 18%. ee: 61% (2*R*,3*R*).

Method 3: [RuCl(Et$_2$O)(PNNP)]PF$_6$ (4) as catalyst. [RuCl$_2$(PNNP)] (40 mg, 0.048 mmol) and (Et$_3$O)PF$_6$ (12.0 mg, 0.048 mmol) were dissolved in CH_2Cl_2 (3 mL), and the solution was stirred at room temperature overnight. Imine **5** (135 mg, 0.49 mmol) was added to the mixture, which was then cooled at –78 °C in a 2-propanol/dry ice bath. EDA (56 mg, 0.49 mmol) was added, the mixture was stirred for 5 min and then warmed up to room temperature with a 2-propanol bath. The course of the reaction was monitored by TLC until complete EDA consumption (usually after 4 h). Then, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (hexane/ethylacetate 95:5) to give a white solid. Yield: 26%. ee: 84%. In another experiment, the yield was determined by ^{1}H NMR spectroscopy by adding a known amount of 1,3,5-trimethoxybenzene as internal standard to the crude mixture at the end of the reaction. Yield (**6**): 27%. Yield (**7**): 27%. ^{1}H NMR (300 MHz, $CDCl_3$): δ7.65 – 7.18 (*m*, 15H, arom.), 3.98 (*s*, 1H, C*H*Ph$_2$), 3.97 (*q*, 2H, $^2J_{H,H'}$ = 7.1 Hz, COOC*H*$_2$), 3.25 (*d*, 1H, $^3J_{H,H'}$ = 6.9 Hz, NC*H*COOEt), 2.71 (*d*, 1H, $^3J_{H,H'}$ = 6.9 Hz, NC*H*Ph), 1.01 (*t*, 1H, $^2J_{H,H'}$ = 7.1 Hz, C*H*$_3$). $[a]_D^{20}$ = +32.3° ± 0.1 @ 84% ee (c = 2.0, CH_2Cl_2) (2*R*,3*R*).[2]

Method 3, which gave the best results for substrate **5**, was used to screen imines with different substituents and nitrogen-protecting groups (see Table S1 below).

Table S1. Substrate screening.[a]



R	X	**4** (mol %)	yield (%)	ee (%)
$CHPh_2$	4-F	5	10	84
$CHPh_2$	4-F	10	10	87
$CHPh_2$	4-F_3C	5	11	30
$CHPh_2$	4-MeO	5	3	nd
$CHPh_2$	2-MeO	5	2	nd
$CHPh_2$	4-Me_2N	5	0	–
$CHPh_2$	4-Me	10	5	nd
CPh_3	H	5	0	–
CH_2Ph	H	10	0	–

[a] Reactions performed according to **Method 3** (see above). Yields were determined by ^{1}H NMR spectroscopy by adding a known amount of 1,3,5-trimethoxybenzene as internal standard to the crude mixture at the end of the reaction.

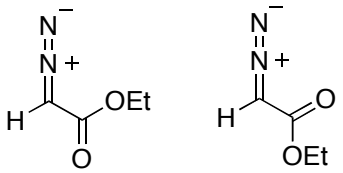
Synthesis of ^{13}C- and ^{15}N-Labeled EDA

Ethyl 2-^{13}C-glycine hydrochloride.[3] 2-^{13}C-glycine (98% 2-^{13}C, 0.50 g, 4.85 mmol) was suspended in ethanol, and the mixture cooled down to –20 °C (ice-salt bath). $SOCl_2$ (0.58 mL, 8.00 mmol) was added, the temperature raised to room temperature, and another equivalent of solid 2-^{13}C-glycine (0.50 g, 4.85 mmol) was slowly added. The mixture was refluxed for 2 h. After cooling the colorless solution to room temperature, the solvent was evaporated under reduced pressure. The resulting white solid was dried in high vacuum for 2 h and recrystallized from ethanol. Yield: 1.10 g, 95 %. m.p. = 145–147 °C.

Ethyl 2-^{13}C-diazoacetate (^{13}C-EDA).[4] Ethyl 2-^{13}C-glycine hydrochloride (1.00 g, 7.1 mmol) was mixed with H_2O (2 mL) and CH_2Cl_2 (4 mL) in a two-necked flask equipped with

septum, argon inlet, and internal thermometer. The colorless mixture was cooled down to –5 °C, and an ice-cold solution of $NaNO_3$ (0.59 g, 8.5 mmol) in H_2O (2 mL) was added. The resulting mixture was cooled to –9 °C, and a 5% (w/w) H_2SO_4 solution (0.679 g) was slowly added. As higher temperature might decrease the yield, the temperature was never let to above +1 °C during the addition. Thereafter, the mixture was stirred for 20 min between –9 °C and +1 °C, and then poured into an ice-cold separating funnel. The yellow organic layer was recovered, and the water phase was extracted with CH_2Cl_2 (2 × 3 mL). The combined organic phase was washed with a 5% ice-cold $NaHCO_3$ solution (6 mL), the organic phase was separated, and the water phase was extracted with CH_2Cl_2 (2 × 3 mL). The combined organic phase was dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The resulting yellow oil was dried in vacuum for 15 min, and the product distilled with cold distillation under high vacuum. Yield: g (0.74 g, 81%). ^{1}H NMR (500 MHz, CD_2Cl_2, 298 K): δ 4.80 (*d*, 1H, $^1J_{C,H}$ = 205 Hz, $N_2{}^{13}CH$), 4.23 (*q*, $^2J_{H,H'}$ = 7.1, 2H, OCH_2CH_3), 1.30 (*t*, $^2J_{H,H'}$ = 7.1, 3H, OCH_2CH_3). ^{13}C NMR (126 MHz, CD_2Cl_2, 298 K): δ 46.3 (*s*, N_2CH).

In the low-temperature ^{1}H and ^{13}C NMR spectra of EDA, We observed signal broadening and decoalescence to resolved signals in a 5:4 ratio. We attribute this dynamic phenomenon to the interconversion between the *s-cis* and *s-trans* isomers, which are in fast equilibrium on the NMR time-scale at room temperature. The ^{1}H and ^{13}C NMR spectroscopic data at –80 °C are given below.



s-trans *s-cis*

Low-temperature data: ^{1}H NMR (500 MHz, CD_2Cl_2, 195 K): δ 5.01 (*d*, 1H, $^1J_{C,H}$ = 205 Hz, $N_2{}^{13}CH$), 4.72 (*d*, 1H, $^1J_{C,H}$ = 205 Hz, $N_2{}^{13}CH$), 4.20 (*q*, $^2J_{H,H'}$ = 7.1, 2H, OCH_2CH_3),

4.17 (*q*, $^{2}J_{H,H'}$ = 7.1, 2H, OCH_2CH$_3$), 1.29 (*t*, $^{2}J_{H,H'}$ = 7.1, 3H, OCH$_2$CH_3), 1.25 (*t*, $^{2}J_{H,H'}$ = 7.1, 3H, OCH$_2$CH_3). ^{13}C NMR (126 MHz, CD_2Cl_2, 195 K): δ 47.5 (*s*, N_2*C*H), 46.5 (*s*, N_2*C*H).

Synthesis of ethyl ^{15}N-diazoacetate. (^{15}N-EDA).[4] ^{15}N-EDA was prepared analogously to ^{13}C-EDA from ethyl glycine hydrochloride (1.00 g, 7.1 mmol) and Na$^{15}NO_2$ (98% ^{15}N, 0.60 g, 8.5 mmol). ^{1}H NMR (500 MHz, CD_2Cl_2, 298 K): δ 4.80 (*br s*, 1H, N_2C*H*), 4.23 (*q*, $^{2}J_{H,H'}$ = 7.1, 2H, OCH_2CH$_3$), 1.30 (*t*, $^{2}J_{H,H'}$ = 7.1, 3H, OCH$_2$CH_3). ^{15}N NMR (50.7 MHz, CD_2Cl_2, 298 K): δ 4.05 (*br s*, 1N, ^{15}*N*NC). Low-temperature data: ^{1}H NMR (500 MHz, CD_2Cl_2, 195 K): δ 5.04 (*s*, 1H, N_2C*H*), 4.74 (*s*, 1H, N_2C*H*), 4.20 (*q*, $^{2}J_{H,H'}$ = 7.1, 2H, OCH_2CH$_3$), 4.17 (*q*, $^{2}J_{H,H'}$ = 7.1, 2H, OCH_2CH$_3$), 1.29 (*t*, $^{2}J_{H,H'}$ = 7.1, 3H, OCH$_2$CH_3), 1.25 (*t*, $^{2}J_{H,H'}$ = 7.1, 3H, OCH$_2$CH_3). ^{15}N NMR (50.7 MHz, CD_2Cl_2, 195 K): δ 7.6 (*s*, 1N, ^{15}*N*NC), –1.29 (*s*, 1N, ^{15}*N*NC).

NMR Spectroscopic Studies: General. The reactions described below were run under argon in NMR tubes fitted with serum septa and were monitored by NMR spectroscopy as detailed below. Additions of reagents were performed by microsyringe. A 2-PrOH bath at the appropriate temperature was used to keep the sample temperature at the values indicated below during all manipulations and transfers from and to the spectrometer.

Experiment 1. The goal of the experiment was to establish whether the carbene complex *trans*-[RuCl(C(H)COOEt)(PNNP)]$^+$ (**8**) reacts with imine **5**. Thus, labeled **8** was prepared by adding ^{13}C-EDA (1 equiv) to a CD_2Cl_2 solution of [RuCl(OEt$_2$)(PNNP)]$^+$ (**4**) and imine **5** (**4**:**5**:EDA = 1:1:1).

Preparation of **4**: [$RuCl_2$(PNNP)] (30.0 mg, 0.036 mmol) and (Et_3O)PF_6 (9.0 mg, 0.036 mmol) were dissolved in CD_2Cl_2 (0.5 mL) and stirred overnight at room temperature. The ^{31}P and ^{1}H NMR spectra at 195 K (Figure S1) are consistent with the formulation of the complex as *cis*-β-[RuCl(OEt$_2$)(PNNP)]$^+$.[5]

Then, imine **5** (9.8 mg, 0.036 mmol) was added to the mixture at room temperature, and the ^{31}P and ^{1}H NMR spectra were recorded at 298 K and at 195 K. Along with unreacted **4**, the signals of an unknown product (**C**, AX system, 13%, δ 42.3 (*d*, $^{2}J_{P,P'}$ = 24.8 Hz), 36.3

(*d*, $^{2}J_{P,P'}$ = 24.8 Hz)) were observed (Figure S2). This species is not the imine complex [RuCl(**5**)(PNNP)]$^{+}$, as confirmed by (^{1}H,^{1}H)-NOESY analysis and by the observation that it is formed in small amounts in the reaction of **4** with EDA.

After extracting the sample from the NMR spectrometer, EDA (9.0 μL, 0.036 mmol) was added by microsyringe to the solution at 195 K. The sample was transferred immediately to the precooled NMR spectrometer (195 K) and the ^{31}P and ^{1}H NMR spectra were recorded (Figure S3). The ^{31}P NMR spectrum of the reaction solution shows that **4** is quantitatively converted to *trans*-[RuCl(C(H)COOEt)(PNNP)]$^{+}$ (**8**) (74%, δ 42.3 (*d*, $^{2}J_{P,P'}$ = 24.8 Hz), 36.3 (*d*, $^{2}J_{P,P'}$ = 24.8 Hz)[3], and an apparently C_2-symmetric dinitrogen complex (**10**, see below) featuring singlet **D** (15%, δ 42.3) in the ^{31}P NMR spectrum. Upon warming to room temperature in 20 K steps, the composition of the solution did not change, and no aziridine was formed, as indicated by (^{13}C,^{1}H)-HMQC experiments. The signals of impurity **C** (11%) remained unchanged up to room temperature and disappeared within 4 h time. After 4 h at room temperature, all the species had converted to dinitrogen complex **10** (signal **D**, 60%) and to [RuCl(CH_2COOEt)(PNNP)] (**E**, 40%, δ 47.8, AB system) (see below) (Figure S4).

The ^{31}P NMR signal **E** is a tight AB pattern δ 47.9 (*d*, $^{2}J_{P,P'}$ = 28.2 Hz), 47.8 (*d*, $^{2}J_{P,P'}$ = 28.2 Hz) (202 MHz, CD_2Cl_2, 298 K) and is assigned to the new complex *trans*-[RuCl(CH_2COOEt)(PNNP)] on the basis of the ^{1}H NMR signals of the RuCH_2COOEt moiety, which were identified by means of (^{31}P,^{1}H)-HMQC and (^{13}C,^{1}H)-HMQC experiments: ^{1}H NMR (500 MHz, CD_2Cl_2, 298 K): δ 3.79 (*d*, 1H, $^{2}J_{H,H'}$ = 11.2 Hz, RuC*H*H'COOEt), 3.36 (*d*, 1H, $^{2}J_{H,H'}$ = 11.2 Hz, RuCH*H'*COOEt).

Figure S1. ^{1}H (500 MHz) and ^{31}P (202 MHz) NMR spectra of **4** at 195 K in CD_2Cl_2.

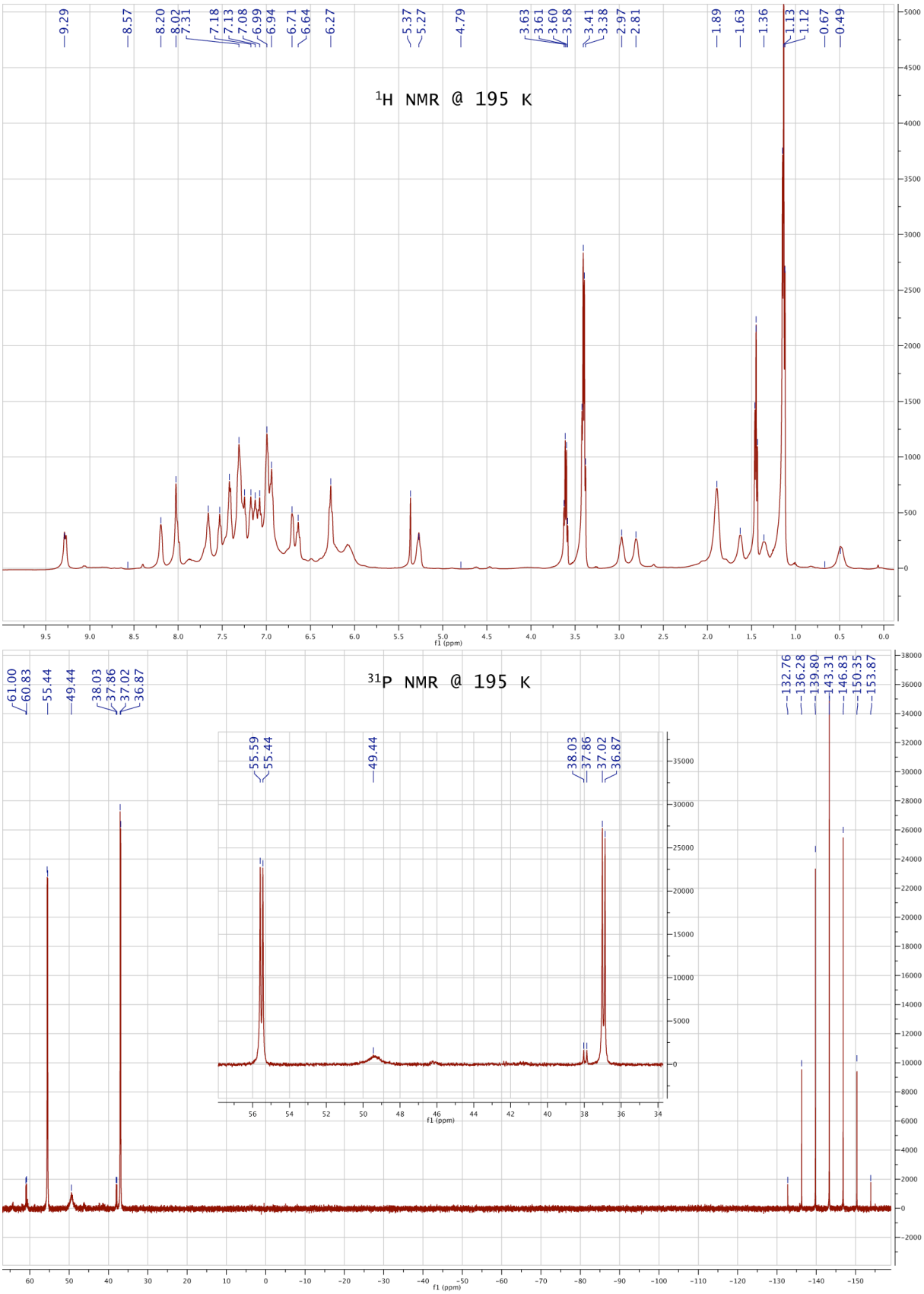
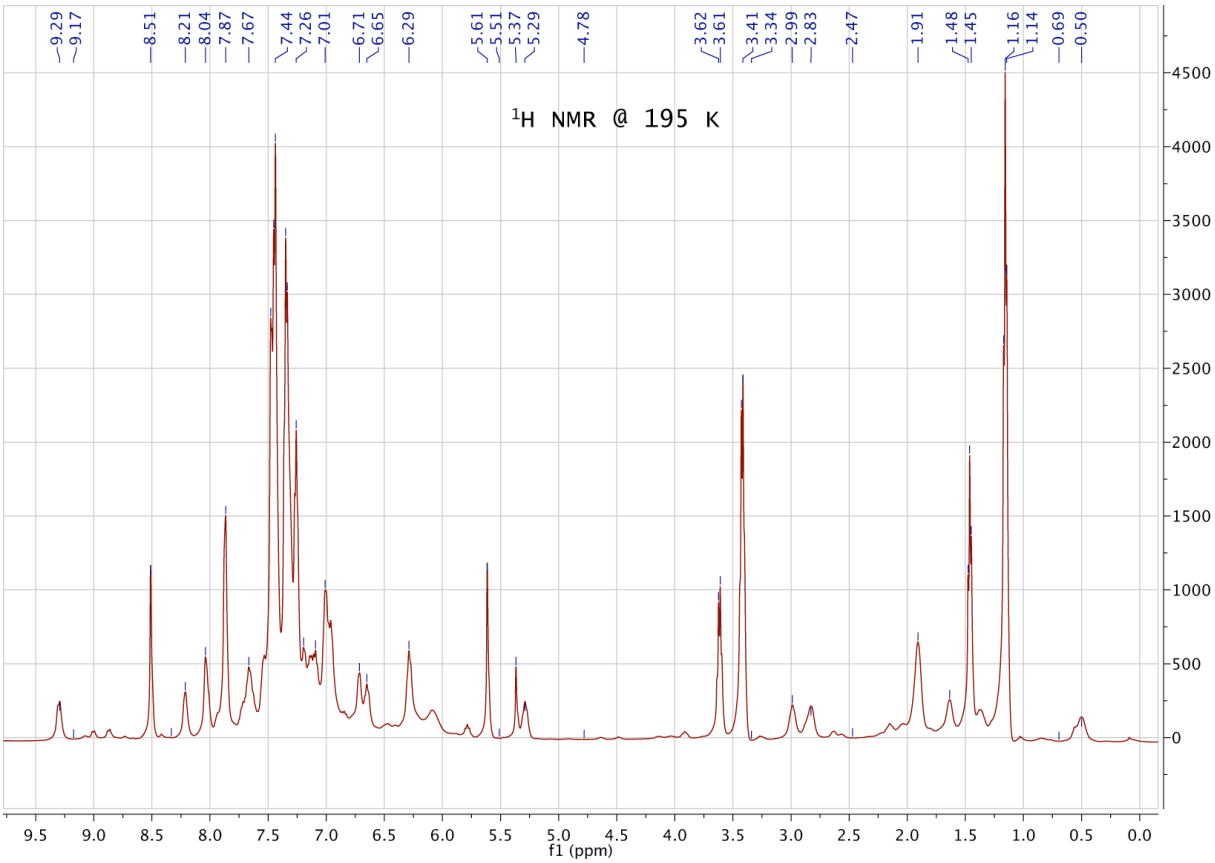


Figure S2. ^{1}H (500 MHz) and ^{31}P (202 MHz) NMR spectra after imine addition at 195 K in CD_2Cl_2.



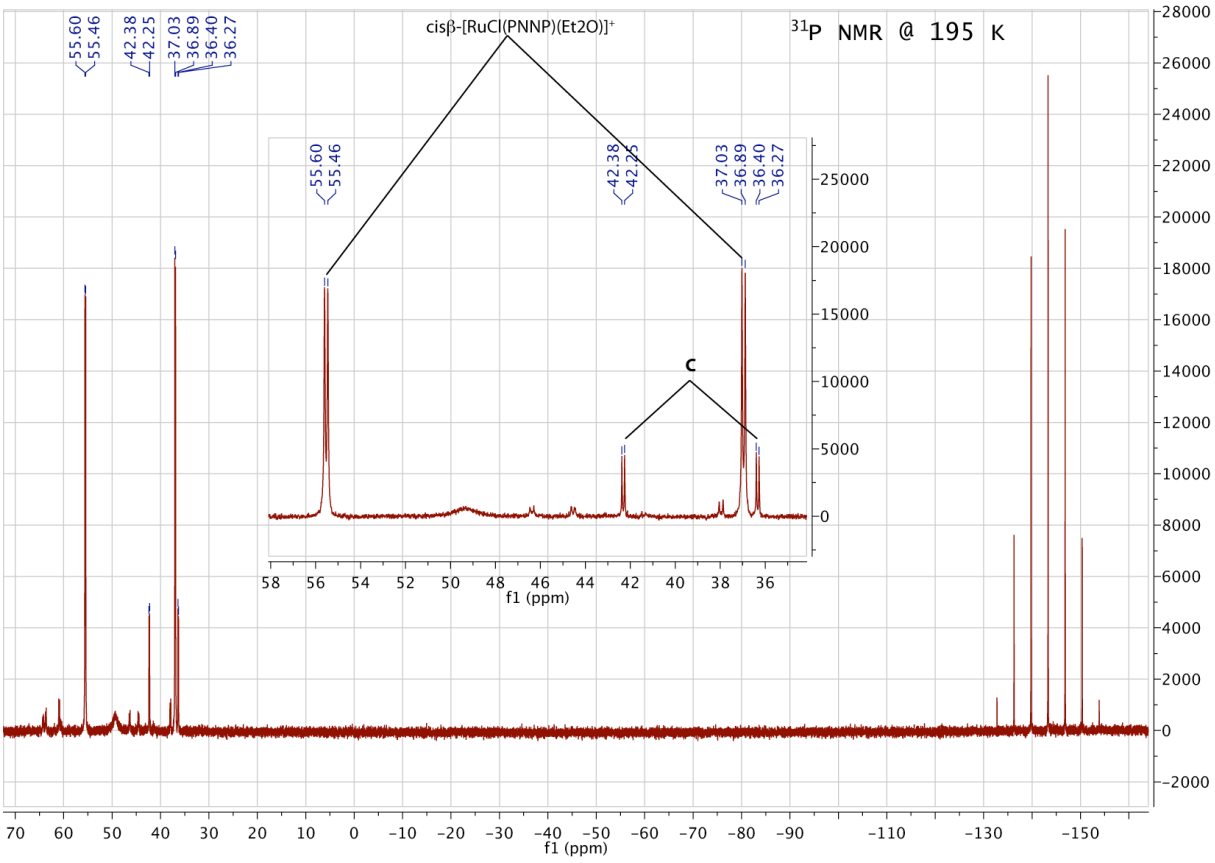
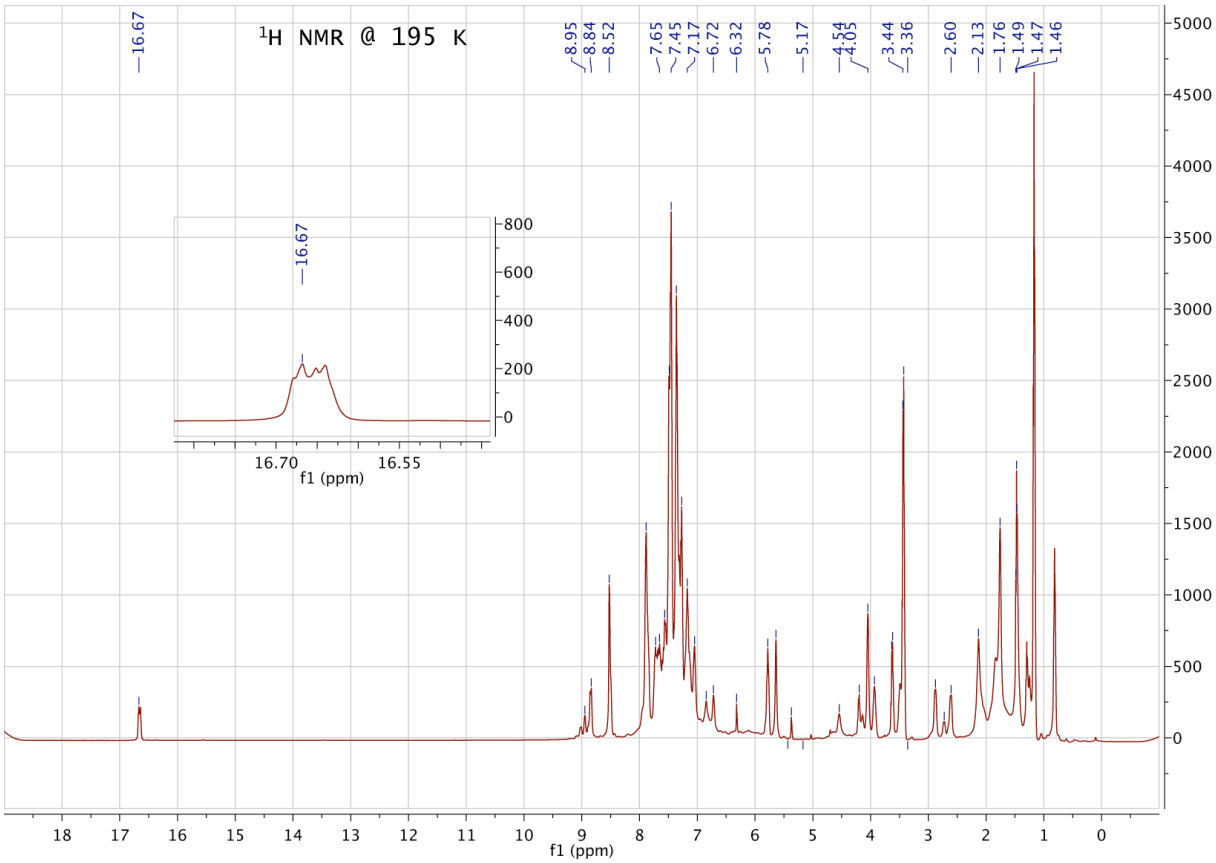


Figure S3. ^{1}H (500 MHz) and ^{31}P (202 MHz) NMR spectra after ^{13}C-EDA addition at 195 K in CD_2Cl_2.



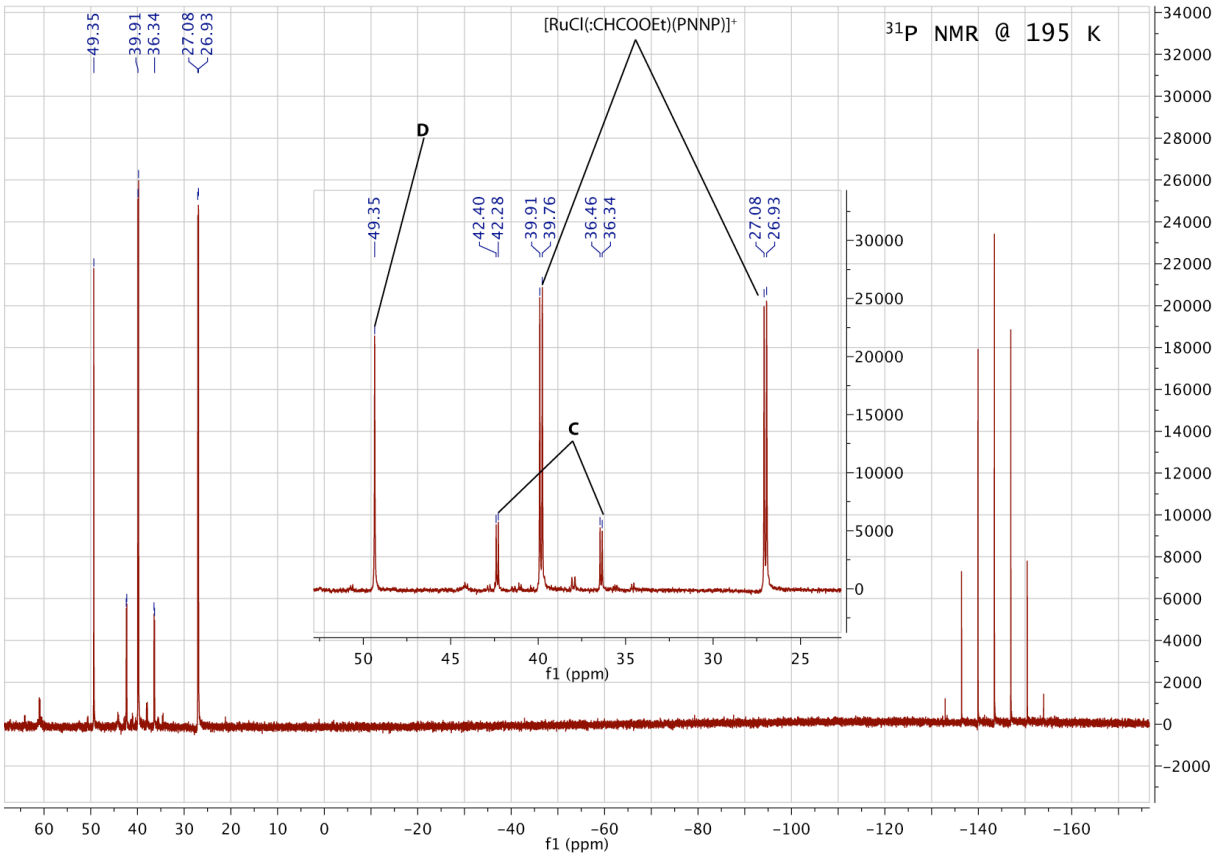
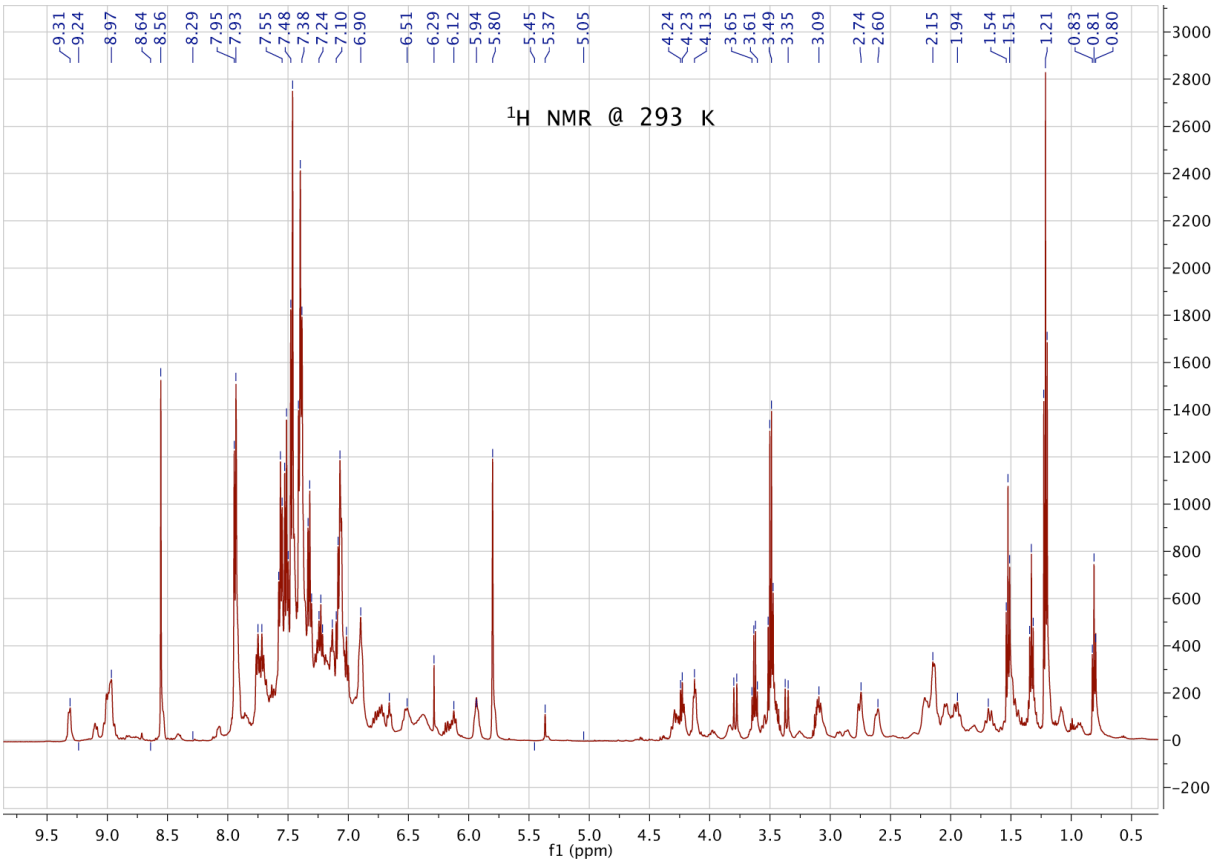
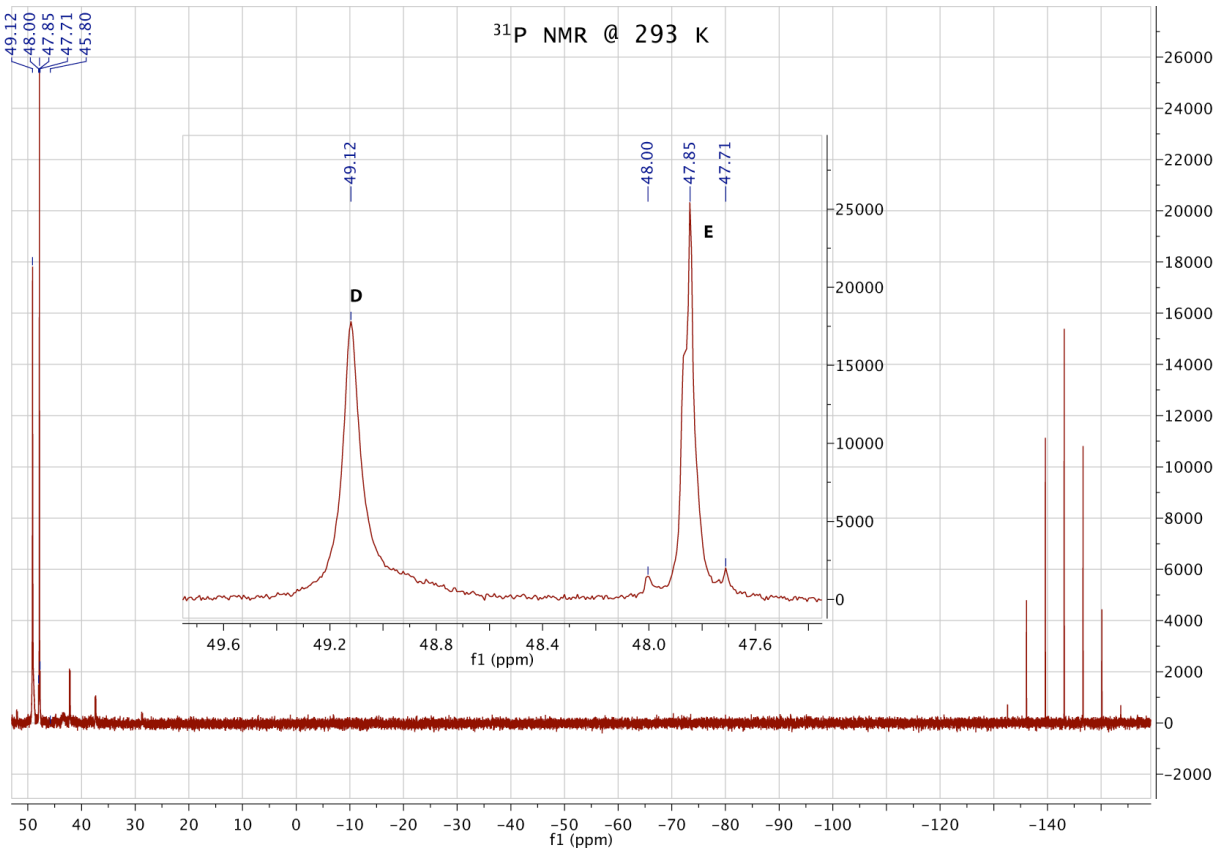


Figure S4. ^{1}H (500 MHz) and ^{31}P (202 MHz) NMR spectra after 4 h at 293 K in CD_2Cl_2.





Experiment 2. An excess of ^{13}C-EDA (10 equiv) was added to a CD_2Cl_2 solution of complex $[RuCl(OEt_2)(PNNP)]^+$ (**4**) and imine **5** (**4**:**5**:EDA = 1:1:10) as described below.

Complex **4** was prepared by treating $[RuCl_2(PNNP)]$ (24.3 mg, 0.029 mmol) with $(Et_3O)PF_6$ (7.3 mg, 0.029 mmol) in CD_2Cl_2 (0.5 mL). After stirring the solution at room temperature overnight, the formation of **4** was confirmed by the ^{31}P and ^{1}H NMR spectra at 298 K and 195 K. Then, imine **5** (7.9 mg, 0.029 mmol) was added to the solution, which was cooled again. EDA (32.2 μL, 0.293 mmol) was added at 195 K, and the ^{13}C, ^{1}H, and ^{31}P NMR spectra were run at the same temperature, as well as a (^{13}C,^{1}H)-HMQC experiment. The (^{13}C,^{1}H)-HMQC correlation showed the signals of unreacted ^{13}C-EDA as major product, along with those of *trans*-[RuCl(PNNP)(^{13}C(H)COOEt)]$^+$ (traces), ^{13}C-maleate (traces) (Figure S5). The signal (**F**) of an additional ^{13}C-containing species with a $J_{C,H}$ comparable to that of ^{13}C-EDA is present, but disappears after heating to –20 °C. As this signal has never been observed at temperatures higher than –20 °C, we deem it immaterial for the further discussion. The ^{31}P NMR spectrum showed the quantitative conversion of **4** to several unknown species.

As no aziridine **6** was observed at 193 K, the sample was carefully warmed up to 253 K. At this temperature, (^{13}C,^{1}H)-HMQC correlation experiment indicated that a small amount of ^{13}C-aziridine had formed. To slow down the reaction, the sample was cooled to 213 K, at which temperature a (^{13}C,^{1}H)-HMQC experiment revealed new signals that we assign to the coordinated ^{13}C-EDA of the new complex *trans*-[RuCl($N_2{}^{13}$C(H)COOEt)(PNNP)]$^+$ (**9**) (Figure S6). At the same temperature, the ^{31}P NMR spectrum shows the signals of dinitrogen complex **10** (signal **D**, 31 %) and the same AB system observed in **Experiment 1** upon addition of imine to **4** (**C**, δ 42.3 (*d*, $^2J_{P,P'}$ = 24.2 Hz), 36.2 (*d*, $^2J_{P,P'}$ = 24.2 Hz)) (9 %) (Figure S7). The main feature of the spectrum consists of two AB patterns in equal ratio, **A** (31%) and **B** (31%) (δ(**A**) 42.4 (*d*, $^2J_{P,P'}$ = 25.3 Hz) and 35.8 (*d*, $^2J_{P,P'}$ = 25.2 Hz); δ(**B**) 41.1 (*d*, $^2J_{P,P'}$ = 25.3 Hz), 34.8 (*d*, $^2J_{P,P'}$ = 25.4 Hz)). Although no NOESY contacts were detected between the sp^2 diazoester proton ($N_2{}^{13}$C-*H*) and any other signal, the diazoester complex **9** was identified

unambiguously by (^{31}P,^{1}H)-HMQC and by the use of ^{15}N labeled EDA (see **Experiment 3** below). The (^{31}P,^{1}H)-HMQC spectrum showed cross peaks between the ^{31}P signals and the $N_2{}^{13}$C-*H* proton of the coordinated diazoester in **A** and **B**, which had been previously identified by a (^{13}C,^{1}H)-HMQC experiment. Furthermore, (^{1}H-^{1}H)-NOESY and (^{31}P,^{1}H)-HMQC experiments indicate that **A** and **B** are exchanging with each other even at –40 °C. Again, we attribute this observation to the interconversion between the *s-cis* and *s-trans* isomers of the C(H)COOEt moiety (see above). Upon raising the temperature in 20 K-steps, the ^{31}P NMR signals of **9** coalesced at 253 K and then gave a single well-resolved AB system at 293 K (**A**+**B**, δ 42.1 (*d*, $^{2}J_{P,P'}$ = 24.2 Hz), 36.9 (*d*, $^{2}J_{P,P'}$ = 24.2 Hz)) (Figure S8). In the temperature interval between 253 K and 293 K, imine **5** was fully converted to aziridine **6**, and the signals of free ^{13}C-EDA disappeared in the ^{1}H and ^{13}C NMR spectra.

After few minutes at 293 K, the ^{13}C-EDA complex **9** was converted to the previously reported[6] carbene complex *trans*-[RuCl(^{13}C(H)COOEt)(PNNP)]$^{+}$ (**8**) (Figure S9). The ^{31}P and ^{13}C NMR spectra indicated that the conversion of **9** to **8** begins after the disappearance of free ^{13}C-EDA from the reaction solution and is quantitative after 15 minutes. Then, the *trans*-carbene complex **8** decomposes within 4 h to [RuCl($^{13}CH_2$COOEt)(PNNP)] (**11**). The main signals in the ^{31}P NMR spectrum after 10 h at 293 K are those of the dinitrogen complex **10** (signal **D**, 55%) at δ 49.2 and of alkyl complex **11** at ca. δ 47.9 (signal **E**, 45%, AB part of an ABX system, where X is ^{13}C) (Figure S10). As previously observed in **Experiment 1**, the alkyl complex **11** (signal **E**) was detected as the main product after 3 days at 298 K. At present, we have no explanation for its formation from *trans*-carbene **8**.

Experiment 2 was repeated three times with essentially the same results. In the last run, the ^{13}C NMR signals of the coordinated diazoester of **9** at δ 58.0 were irradiated at 273 K, which left the intensity of the signal of free $N_2{}^{13}C$(H)COOEt unchanged, indicating that the exchange between free and coordinated EDA is slow on the NMR time scale at this temperature.

Figure S5. (^{13}C,^{1}H)-HMQC after EDA addition at 195 K (500 MHz (^{1}H), CD_2Cl_2).

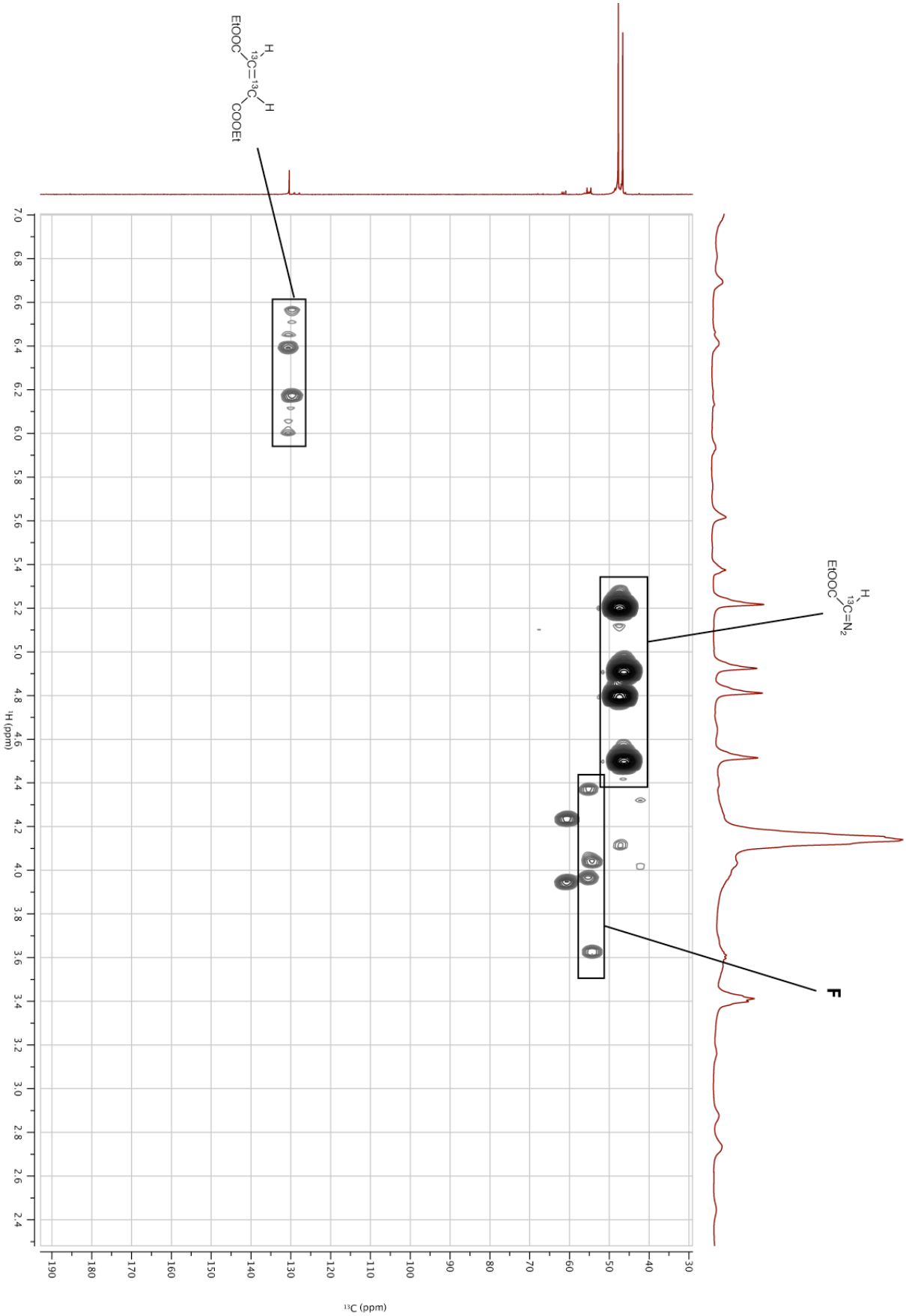


Figure S6. (^{13}C,^{1}H)-HMQC after EDA addition after warming up to 253 K and recooling to 213 K (500 MHz (^{1}H), CD_2Cl_2). (The poor quality is caused by the large excess of ^{13}C-EDA vs. aziridine.)

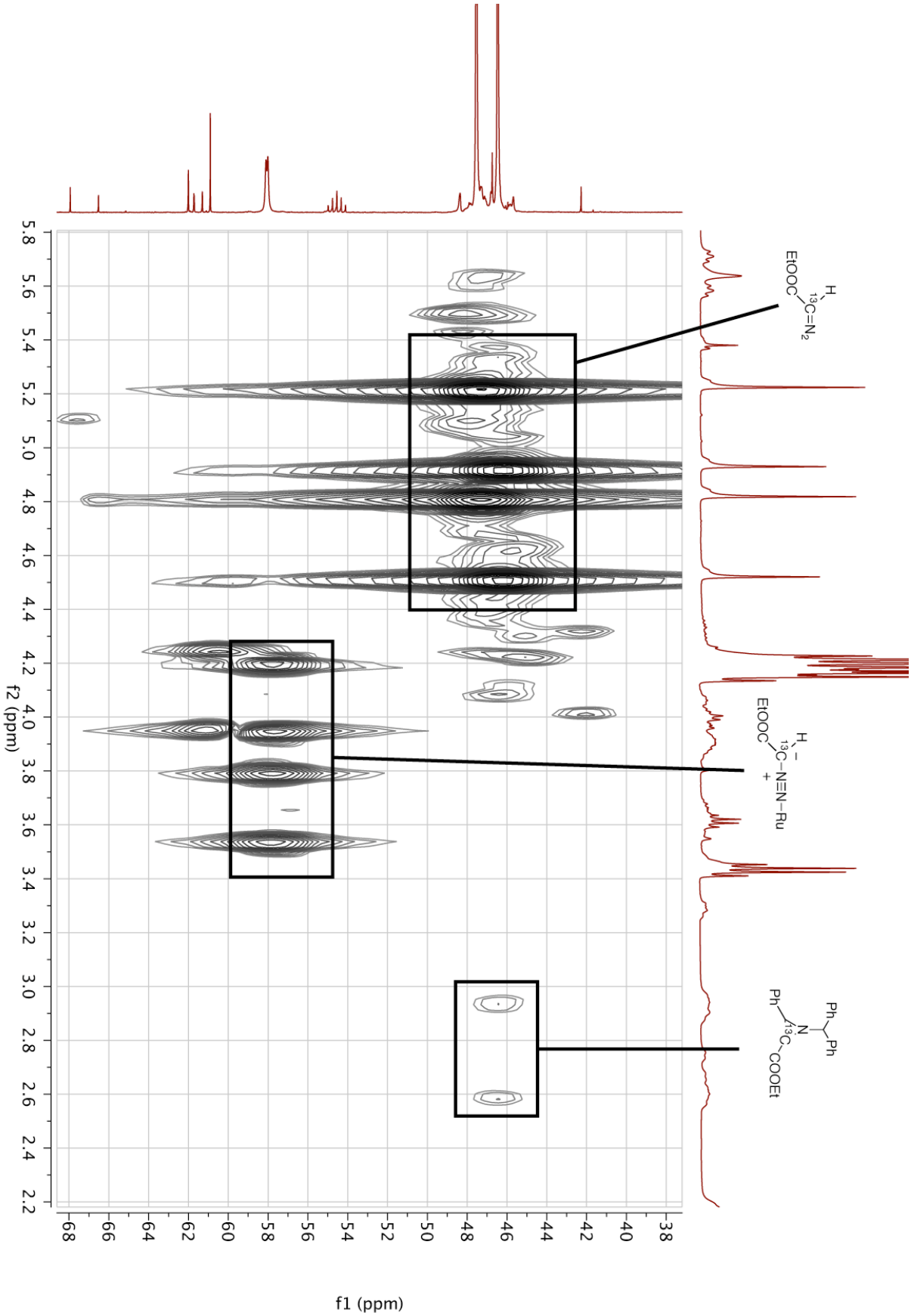


Figure S7. ^{31}P (202 MHz) and (^{31}P,^{1}H)-HMQC (500 MHz for ^{1}H) NMR spectra after EDA addition, warming up to 253 K, and re-cooling to 213 K in CD_2Cl_2.

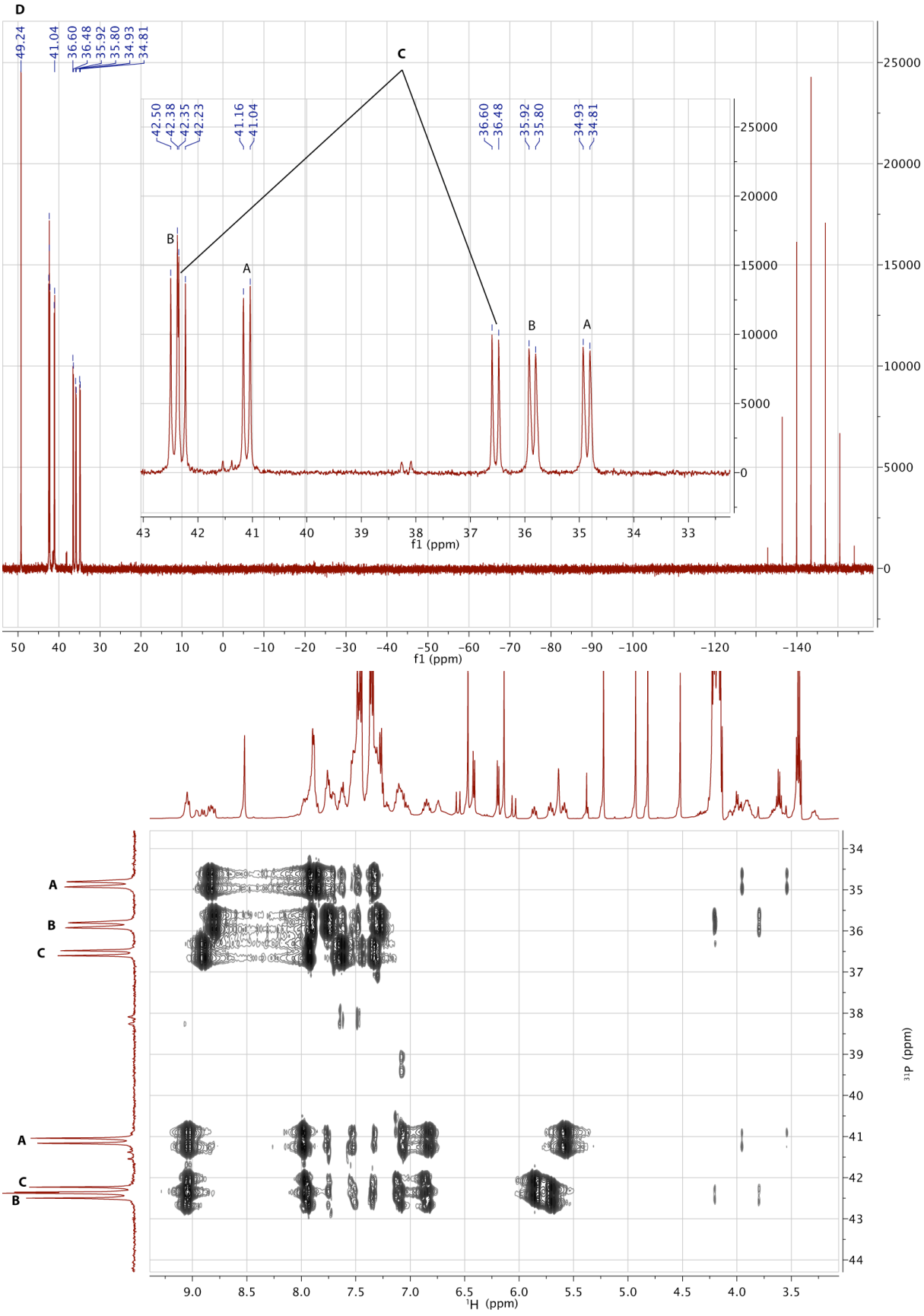


Figure S8. ^{31}P NMR spectrum of the CD_2Cl_2 reaction solution between 213 and 293 K (202 MHz). The signals undergoing coalescence (**A** and **B**) are those of the carbene complex *trans*-$[RuCl(N_2{}^{13}C(H)COOEt)(PNNP)]^+$ (**9**).

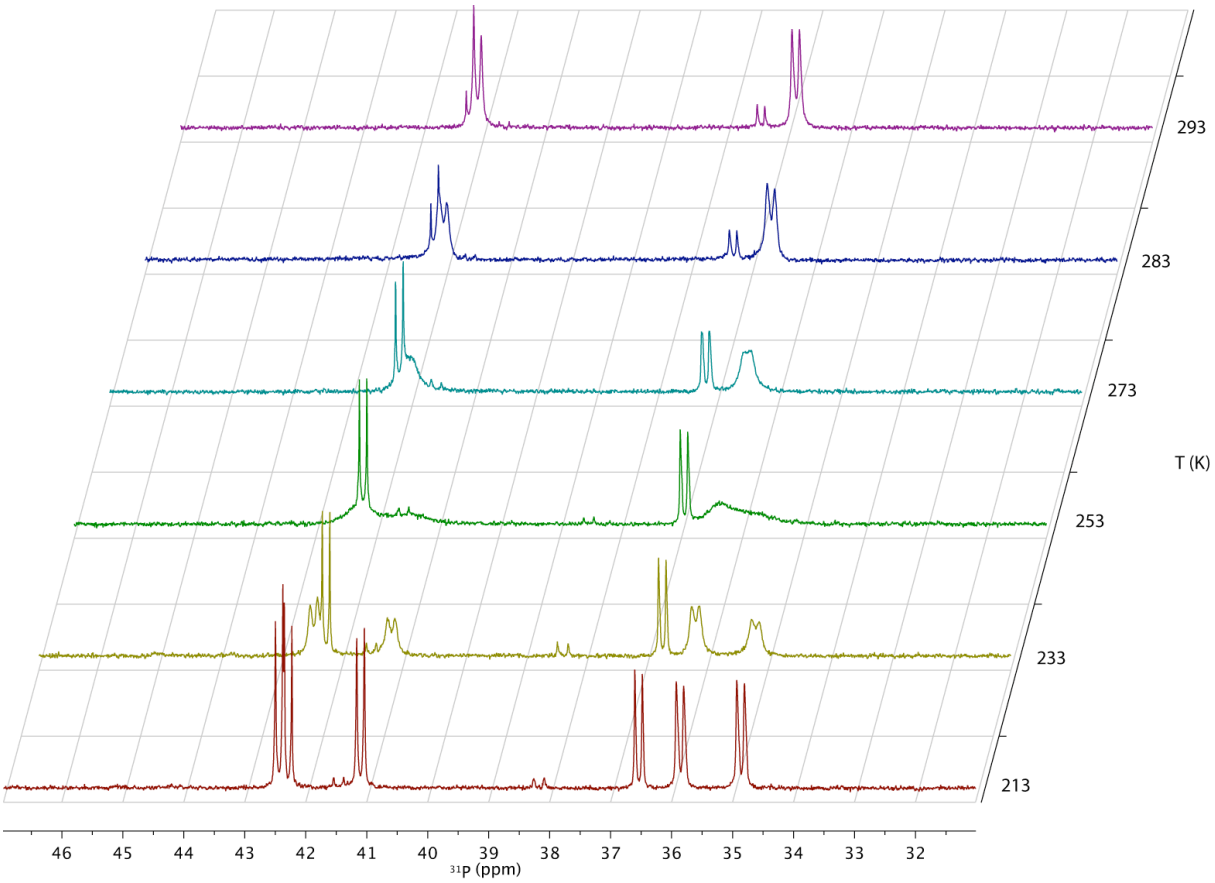


Figure S9. ^{31}P NMR spectrum just after heating to 293 K (202 MHz, CD_2Cl_2).

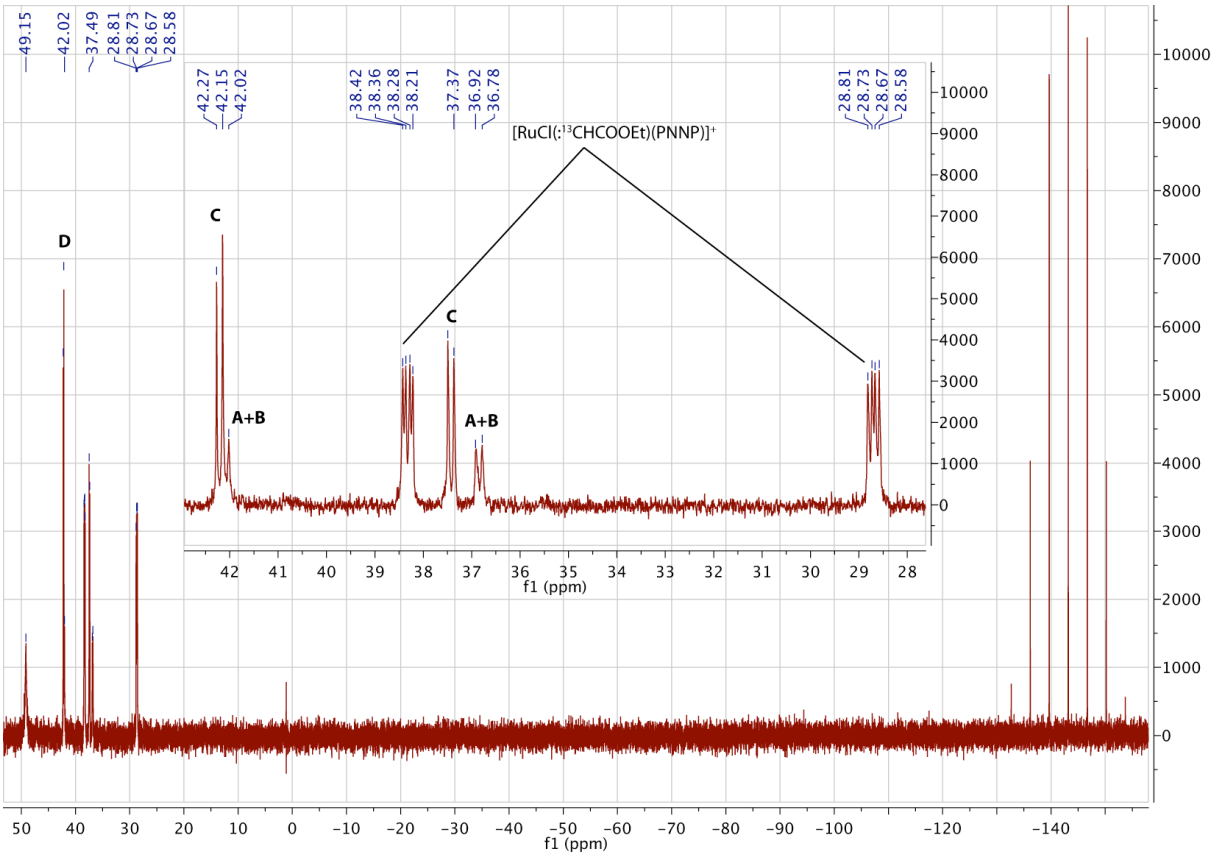
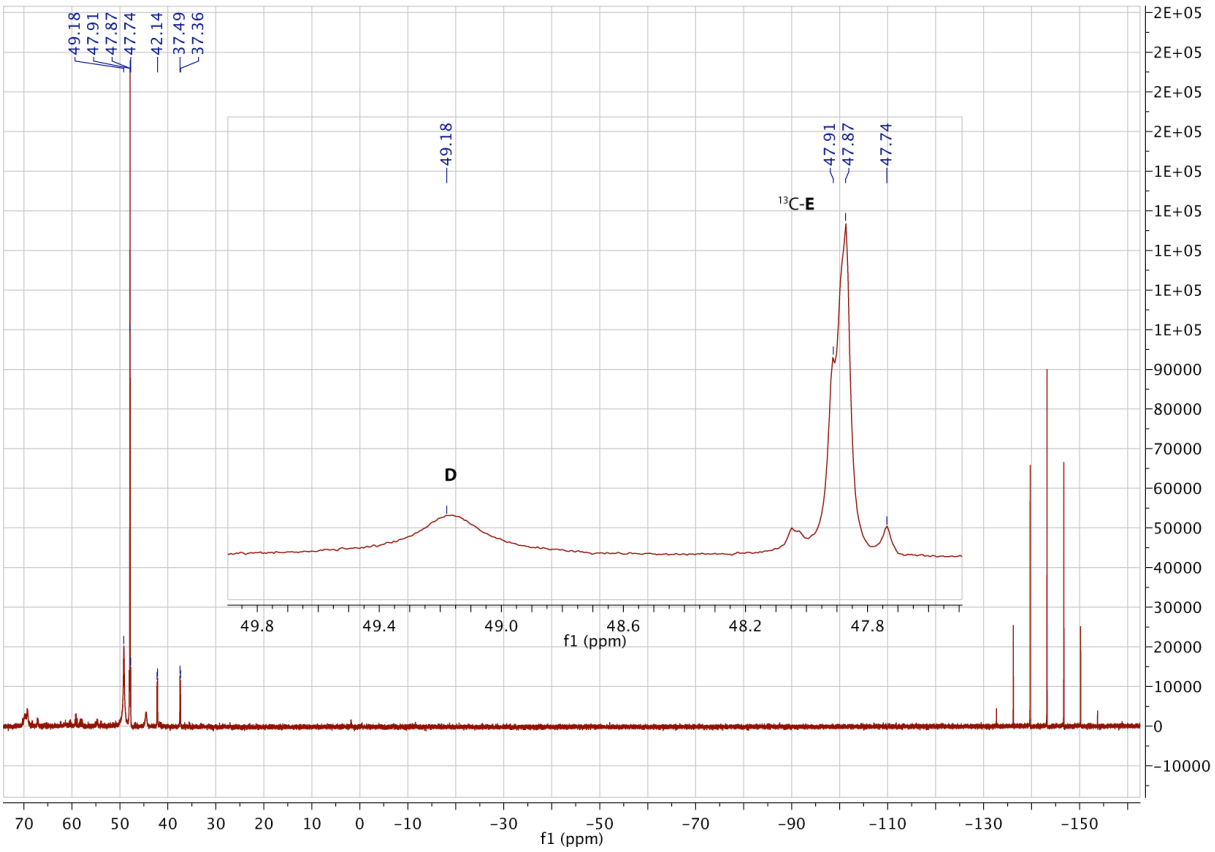


Figure S10. ^{31}P NMR spectrum after 10 h at 293 K (202 MHz, CD_2Cl_2).



Experiment 3 (**with ^{15}N-EDA).** The former experiment 2 was repeated with ^{15}N-EDA (10 equiv) instead of ^{13}C-EDA. The Ru:imine:^{15}N-EDA ration was 1:1:10. [$RuCl_2$(PNNP)] (21.5 mg, 0.026 mmol) and $(Et_3O)PF_6$ (6.4 mg, 0.026 mmol) were dissolved in CD_2Cl_2 (0.5 mL) and stirred overnight at room temperature, and ^{31}P and ^{1}H NMR spectra were recorded at 298 K and 195 K. Imine **5** (7.0 mg, 0.026 mmol) was added to the solution at room temperature.

Then, after cooling the sample to 195 K, ^{15}N-EDA (28.4 μL, 0.259 mmol) was added at 195 K, and the sample was transferred to the precooled NMR spectrometer. After warming to 253 K for 15 minutes to assure aziridine formation, the sample was cooled at 213 K. A (^{13}C,^{1}H)-HMQC experiment confirmed the formation of the aziridine. The ^{31}P NMR spectrum at the same temperature (213 K) showed that **4** was quantitatively converted to the diazoester complex **9** (signals **A**+**B**), the impurity (**C**), and to the dinitrogen complex **10** (signal **D**) with the same pattern observed in **Experiment 2** (Figure S11). As no P,N coupling was detected, the sample was further cooled down to 193 K. At this temperature, two of the four ^{31}P NMR signals of *trans*-[RuCl($^{15}N_2$C(H)COOEt)(PNNP)]$^+$ showed coupling to ^{15}N (δ 42.4 and 41.1, $^2J_{P,P'}$ = 25.3, $^2J_{P,N}$ = 2.4 Hz for both signals) (Figure S13). Additionally, the ^{15}N NMR spectrum at 213 K shows two broad signals corresponding to the two isomers of *trans*-[RuCl($^{15}N_2$C(H)COOEt)(PNNP)]$^+$ along with free ^{15}N-EDA, ^{15}NN, and coordinated ^{15}NN (Figure S12).

Figure S11. ^{31}P NMR spectrum at 213 K (202 MHz, CD_2Cl_2).

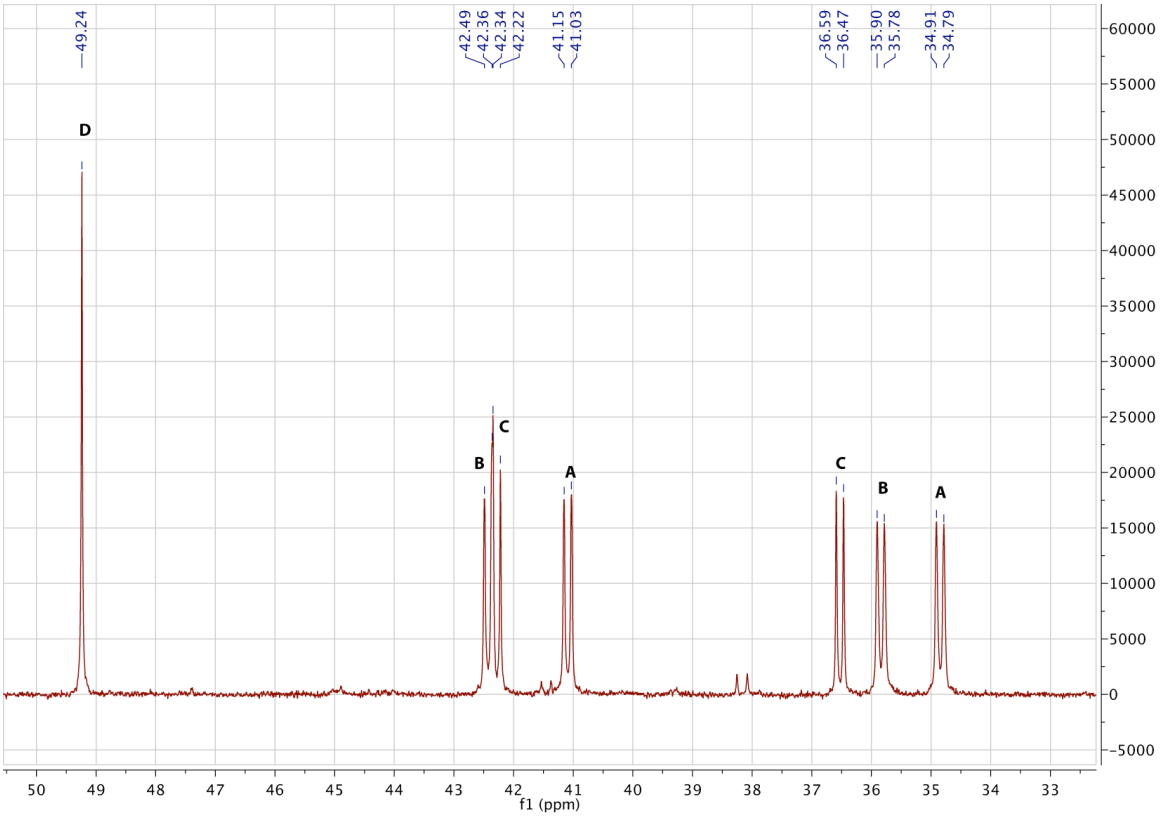


Figure S12. ^{15}N NMR spectrum at 213 K (50.7 MHz, CD_2Cl_2).

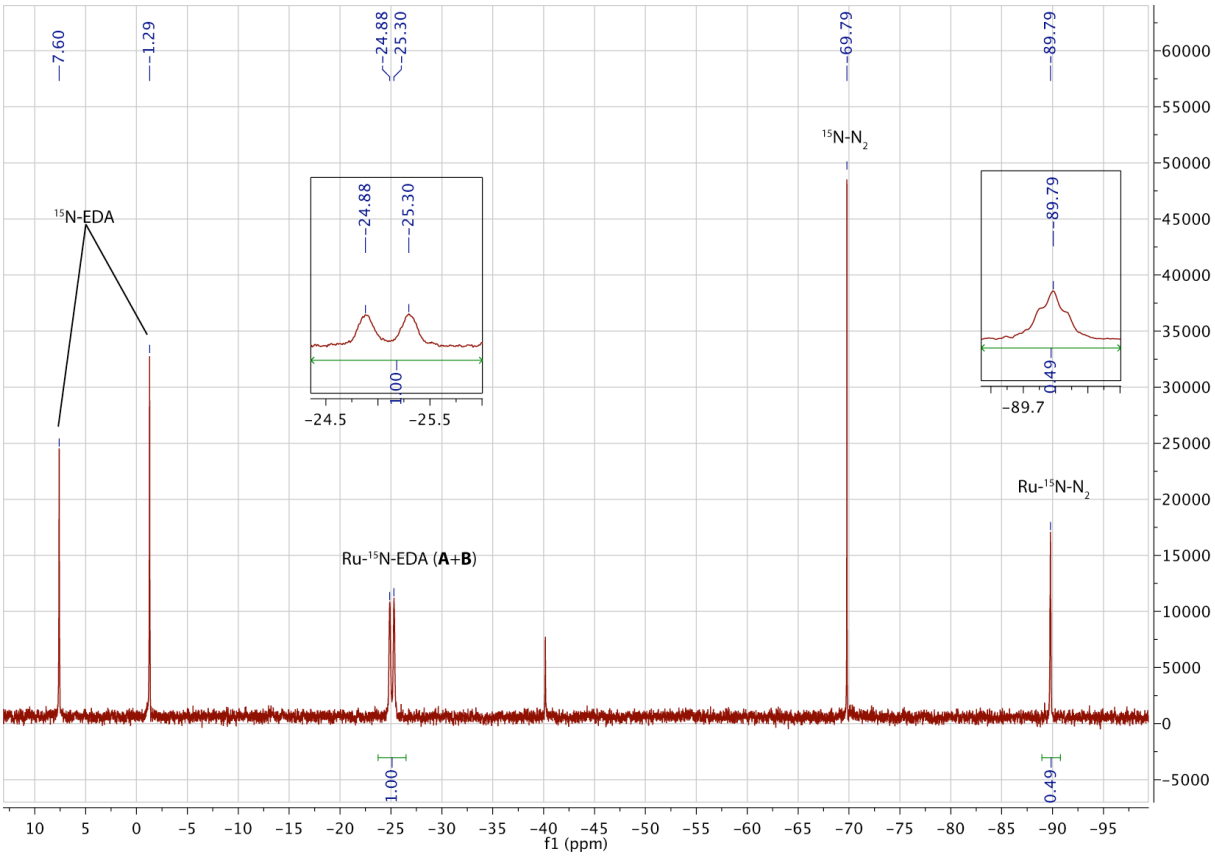
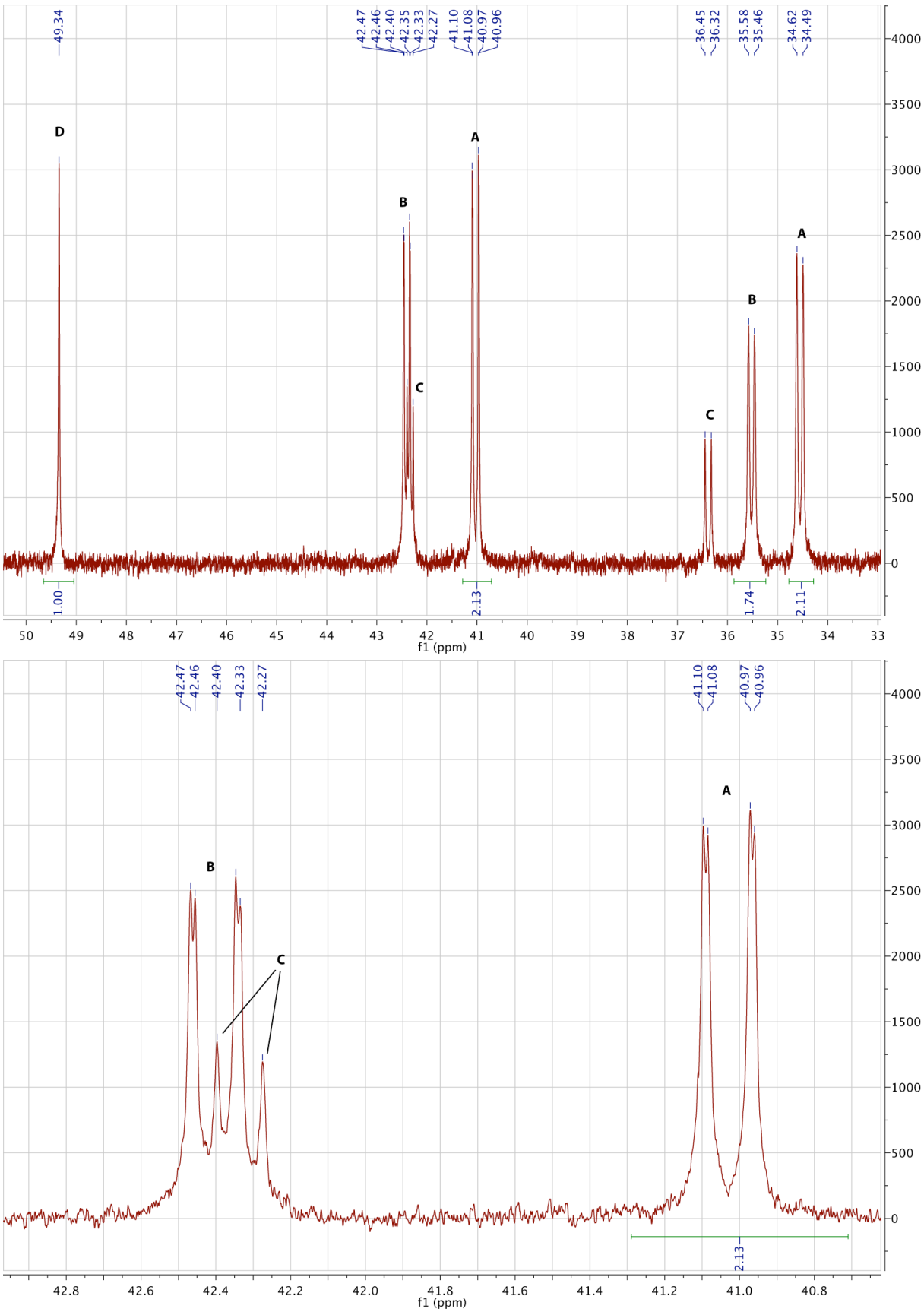


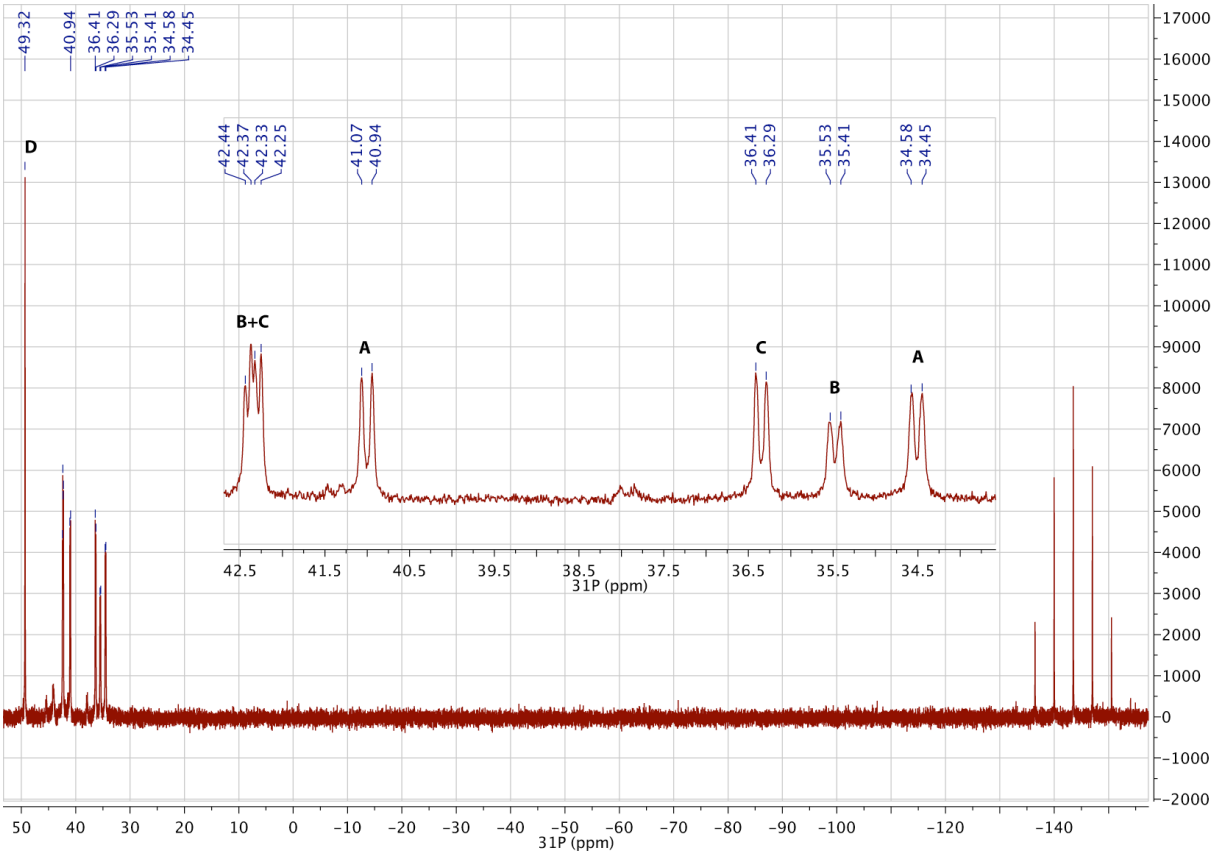
Figure S13. ^{31}P NMR spectrum at 193 K (202 MHz, CD_2Cl_2), with an expansion of the signals (**A**, **B**) of the *s-cis* and *s-trans* isomers of complex **9** showing the P,N-coupling of 2.4 Hz (signal **C** results from an unknown impurity).



Experiment 4. The goal of this control experiment was to check whether aziridine **6** is formed in the presence of diazoester complex **9** *after quantitative consumption of EDA*. The initial Ru:imine:^{13}C-EDA ratio was 1:1:10 and imine **5** was added to the solution at 195 K after the signals of ^{13}C-EDA had disappeared as described in detail below.

[$RuCl_2$(PNNP)] (21.8 mg, 0.026 mmol) and $(Et_3O)PF_6$ (6.5 mg, 0.026 mmol) were dissolved in CD_2Cl_2 (0.5 mL) and stirred at room temperature overnight. The formation of **4** was confirmed by ^{31}P and ^{1}H NMR spectroscopy at 298 K and 195 K. Then, ^{13}C-EDA (28.8 µL, 0.262 mmol) was added at 195 K, and the mixture was warmed to 273 K. After 30 minutes, the ^{1}H and ^{13}C NMR signals of free EDA had disappeared. Then, the mixture was cooled to 195 K, and ^{31}P NMR spectrum showed the signals of **A**+**B**, **C**, and **D** (Figure S14), which the same pattern observed in the presence of imine **5** (see Experiment 2).

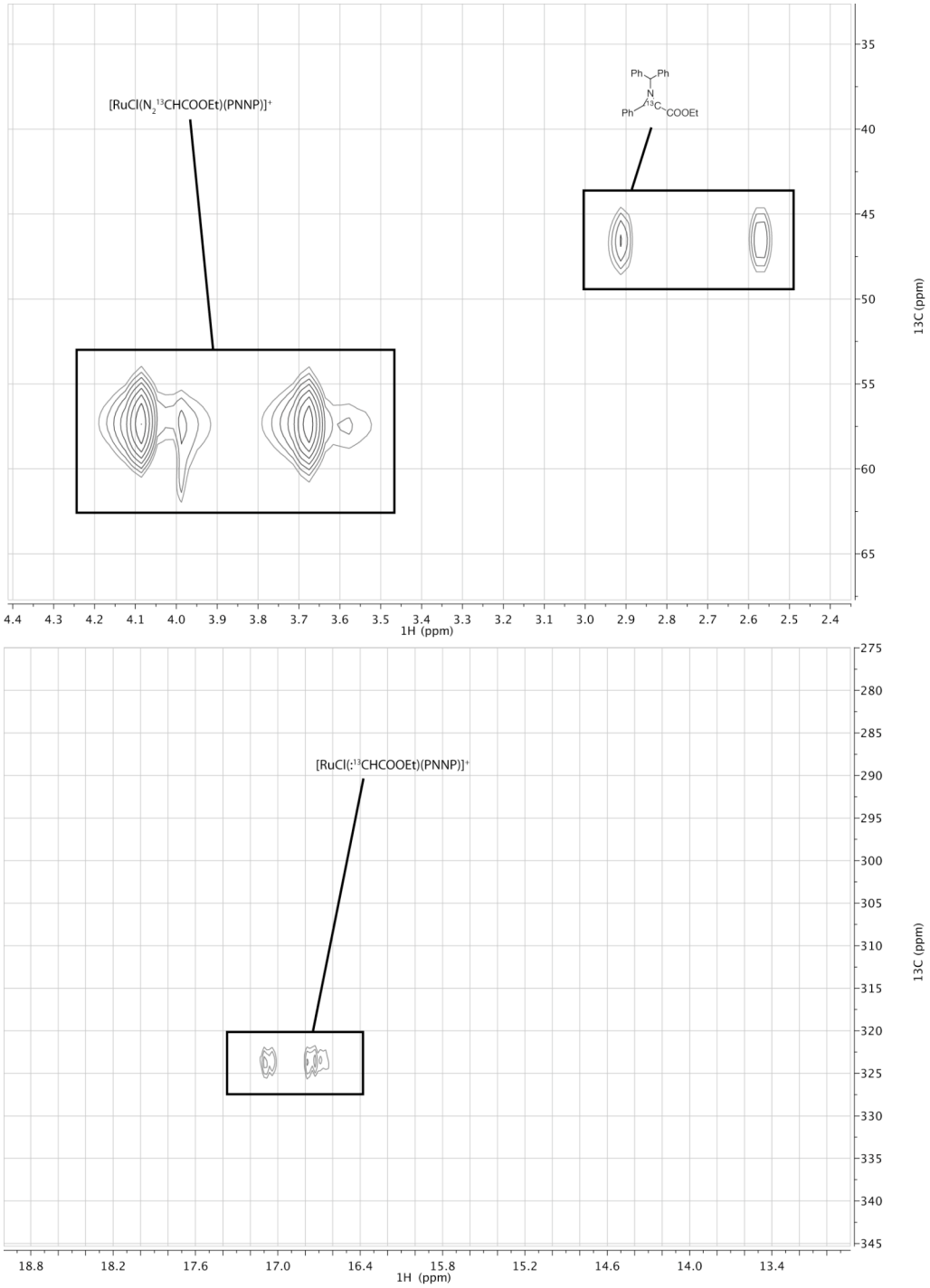
Figure S14. ^{31}P NMR spectrum at 193 K (202 MHz, CD_2Cl_2).



Then, imine **5** (7.1 mg, 0.026 mmol) was added to the solution at 195 K. The sample temperature was increased in 20 K-steps. At 253 K, a (^{13}C,^{1}H)-HMQC experiment (Figure

S15) indicated the formation of aziridine **6** and the decomposition of the diazoester complex **9** to the carbene complex **8**, as usually observed after the consumption of free EDA. It should be noted that, at this temperature, free and coordinated EDA are not exchanging with each other (see Experiment 3), indicating that the dissociation of EDA is slow. Therefore, we conclude that carbene transfer does not take place from uncoordinated EDA.

Figure S15. Sections of a (^{13}C,^{1}H)-HMQC experiment (195 K, 500 MHz (^{1}H), CD_2Cl_2) with the signals of aziridine, **9**, and **8**.



Experiment 5. The goal of this experiment was to establish whether carbene complex [RuCl(C(H)COOEt)(PNNP)]$^+$ (**8**) reacts with free EDA to give diethyl maleate **7**. To assess this unambiguously, preformed **8** was treated with ^{13}C-EDA (2 equiv).

[$RuCl_2$(PNNP)] (19.8 mg, 0.024 mmol) and $TlPF_6$ (8.3 mg, 0.024 mmol) were dissolved in CD_2Cl_2 (0.5 mL) and stirred overnight at room temperature, The ^{31}P and ^{1}H NMR spectra at 298 K showed the formation of the five-coordinate complex [RuCl(PNNP)]$^+$ (**2**). Then, EDA (5.2 μL, 0.024 mmol) was added at room temperature, and the mixture was cooled down to 195 K. The ^{31}P and ^{1}H NMR spectra showed full conversion of [RuCl(PNNP)]$^+$ (**2**) to [RuCl(C(H)COOEt)(PNNP)]$^+$ (**8**) (85%) and to the putative dinitrogen complex **10** having signal **D** (15%).

Upon addition of ^{13}C-EDA (10.4 μL, 0.048 mmol) at 195 K, the (^{13}C,^{1}H)-HMQC and ^{1}H NMR spectra showed the signals of the diazoester complex [RuCl(N_2^{13}C(H)COOEt)-(PNNP)]$^+$ (**9**), traces of [RuCl(^{13}C(H)COOEt)(PNNP)]$^+$ (**8**), and the signals of different isotopomers of diethyl maleate. The isotopic distribution, as determined by integration of the ^{1}H NMR spectrum, is 41% 2-(^{13}C)-ethylmaleate, 52% 2,3-bis(^{13}C)-ethylmaleate, and 7% diethyl maleate. The formation of the monolabeled 2-(^{13}C)-ethylmaleate (41%) is diagnostic of the reaction of ^{13}C-EDA with non-labeled [RuCl(^{13}C(H)COOEt)(PNNP)]$^+$ (**8**), whereas 2,3-bis(^{13}C)-ethylmaleate (52%) is formed by successive carbene formation. Accordingly, upon increasing the temperature, the ratio between [RuCl(C(H)COOEt)(PNNP)]$^+$ and [RuCl(^{13}C(H)COOEt)(PNNP)]$^+$ gradually decreased. Finally, the small amount of nonlabeled diethyl maleate (7%) can result from residual ^{12}C in the labeled compounds.

Summary of NMR Spectroscopic Data

(*cis*-β)-[RuCl(OEt_2)(PNNP)]$^+$ (**4**)
^{31}P NMR data (202 MHz, CD_2Cl_2, 195 K): δ 55.5 (*d*, $^2J_{P,P'}$ = 29.5 Hz), 36.9 (*d*, $^2J_{P,P'}$= 29.5 Hz).

A+B (^13C-labeled): *trans*-[RuCl(N_2^{13}C(H)COOEt)(PNNP)]$^+$ (^{13}C-**9**):
^{31}P NMR data (202 MHz, CD_2Cl_2, 213 K): δ 42.4 (*d*, $^2J_{P,P'}$ = 25.3 Hz), 41.1 (*d*, $^2J_{P,P'}$ = 25.3 Hz), 35.8 (*d*, $^2J_{P,P'}$ = 25.2 Hz), 34.8 (*d*, $^2J_{P,P'}$ = 25.4 Hz). At 298 K: δ 42.1 (*d*, $^2J_{P,P'}$ = 24.2 Hz), 36.9 (*d*, $^2J_{P,P'}$ = 24.2 Hz).
^{1}H NMR data (500 MHz, CD_2Cl_2, 213 K): δ 3.97 (*d*, 1H, $^1J_{C,H}$ = 203 Hz, RuN_2C*H*COOEt) 3.72 (*d*, 1H, $^1J_{C,H}$ = 205 Hz, RuN_2C*H*COOEt).
^{13}C NMR data (126 MHz, CD_2Cl_2, 213 K): δ 58.1 (*s*, RuN_2*C*HCOOEt), 58.0 (*s*, RuN_2*C*HCOOEt).

A+B (^15N-labeled): *trans*-[RuCl(^{15}NNC(H)COOEt)(PNNP)]$^+$ (^{15}N-**9**):
^{15}N NMR data (50.7 MHz, CD_2Cl_2, 213 K): δ –24.9 (*s*, 1N, ^{15}*N*NC), –25.3 (*s*, 1N, ^{15}*N*NC).
^{31}P NMR data (202 MHz, CD_2Cl_2, 193 K): δ 42.4 (*dd*, $^2J_{P,P'}$ = 25.3 Hz, $^2J_{P,N}$ = 2.4 Hz), 41.1 ($^2J_{P,P'}$ = 25.3 Hz, $^2J_{P,N}$ = 2.4 Hz), 35.8 (*d*, $^2J_{P,P'}$ = 25.2 Hz), 34.8 (*d*, $^2J_{P,P'}$ = 25.4 Hz).

C: Unknown Impurity
^{31}P NMR data (202 MHz, CD_2Cl_2, 195 K): δ 42.3 (*d*, $^2J_{P,P'}$ = 24.8 Hz), 36.3 (*d*, $^2J_{P,P'}$ = 24.8 Hz).

D: Dinitrogen Complex **10**
^{31}P NMR data (202 MHz, CD_2Cl_2, 195 K): δ 49.2 (*s*). 293 K: δ 49.2 (*br s*).

E: *trans*-[RuCl(CH_2COOEt)(PNNP)] (**11**)
^{31}P NMR data (202 MHz, CD_2Cl_2, 298 K): 47.9 (*d*, $^2J_{P,P'}$ = 28.2 Hz), 47.8 (*d*, $^2J_{P,P'}$ = 28.2 Hz).
^{1}H NMR data (500 MHz, CD_2Cl_2, 298 K): δ 3.79 (*d*, 1H, $^2J_{H,H'}$ = 11.2 Hz, RuC*H*H'COOEt), 3.36 (*d*, 1H, $^2J_{H,H'}$ = 11.2 Hz, RuCH*H'*COOEt).

F (^13C-labeled): Unknown Species containing a X=C(H)Y moiety observed below –20 °C.
^{1}H NMR data (500 MHz, CD_2Cl_2, 195 K): δ 4.21 (*d*, 1H, $^1J_{C,H}$ = 206 Hz), 4.21 (*d*, 1H, $^1J_{C,H}$ = 213 Hz).
^{13}C NMR data (126 MHz, CD_2Cl_2, 195 K): δ 55.4 (*s*), 54.6 (s).

G (^13C-labeled): *trans*-[RuCl(^{13}C(H)COOEt)(PNNP)] (**8**)
^{31}P NMR data (202 MHz, CD_2Cl_2, 298 K): 38.3 (*dd*, $^2J_{P,C}$ = 13.9 Hz, $^2J_{P,P'}$ = 30.4 Hz), 47.8 (*dd*, $^2J_{P,C}$ = 13.9 Hz, $^2J_{P,P'}$ = 30.4 Hz).

Diethylmaleate
^{1}H NMR data (500 MHz, CD_2Cl_2, 195 K): δ 6.29 (*s*, 2H).

2-^13C-diethylmaleate
^{1}H NMR data (500 MHz, CD_2Cl_2, 195 K): δ 6.29 (*dd*, 1H, $^2J_{C,H}$ = 2.0 Hz, $^2J_{H,H'}$ = 11.9 Hz, *H*C), 6.29 (*dd*, 1H, $^1J_{C,H}$ = 167 Hz, $^2J_{H,H'}$ = 11.9 Hz, *H*^{13}C).

2,3-bis(^13C)-diethylmaleate
^{1}H NMR data (500 MHz, CD_2Cl_2, 195 K): δ 6.29 (AA' of an AA'XX' system, 2H, $^1J_{C,H}$ = 166 Hz, $^2J_{C,H}$ = 16.7 Hz, $^3J_{C,H}$ = 6.81).

References

1 The aqua complex **3** is formed as a mixture of diastereoisomers in 5:1 ratio when H_2O (4.8 equiv) is added to the five-coordinate complex $[RuCl(PNNP)]^+$ (**2**). The major isomer gives an AX pattern at δ 67.0 and 46.3 ($^2J_{P,P'}$ = 31.6 Hz), whereas the signals of the minor isomer are at δ 50.8 and 44.1 ($^2J_{P,P'}$ = 27.2 Hz).

2 Antilla, J. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 5099.

3 Gerlach, M.; Putz, C.; Enders, D.; Gaube, G.; Patent Nr. WO 02/22569, 2002.

4 Searle, N. E. *Organic Syntheses Coll. Vol. 4* **1963**, 424.

5 (a) We have previously reported that $[RuCl_2(PNNP)]$ reacts quantitatively with $(Et_3O)PF_6$ (1 equiv) in CD_2Cl_2 within 15 min to give the elusive adduct $[RuCl(OEt_2)(\mathbf{1a})]^+$ (**4**).[5b] However, we discovered during the present study that the ^{31}P NMR spectroscopic data in reference 5b are incorrect. In all the experiments reported in this paper, the only product of the above reaction was a species featuring one broad ^{31}P NMR signals at δ 40.9 at room temperature, which progressively sharpened into an AX pattern at –80 °C (δ 55.5 and 36.9, $^2J_{P,P'}$ = 29.5 Hz). Addition of Et_2O (carefully dried by distillation and molecular sieves) to CD_2Cl_2 solutions does not change this spectral pattern either at room temperature or at –80 °C. We conclude that the ^{31}P NMR data previously reported[5b] for **4** (δ 66.8 and 45.9, $^2J_{P,P'}$ = 30.6 Hz, 300 K) were affected by adventitious water, as they are very similar to those of one isomer of the aqua complex $[RuCl(OH_2)(PNNP)]^+$ (δ 67.0 and 46.3, $^2J_{P,P'}$ = 31.6 Hz, 298 K). (b) Bonaccorsi, C; Bachmann, S.; Mezzetti, A. *Tetrahedron: Asymmetry* **2003**, *14*, 845.

6 Bachmann, S.; Furler, M.; Mezzetti, A. *Organometallics* **2001**, *20*, 2102.