

Supporting Information

Hydroxyapatite-Bound Cationic Ruthenium Complexes as Novel Heterogeneous Lewis Acid Catalysts for Diels-Alder and Aldol Reactions

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The synthesis of hydroxyapatite-bound cationic Ru complexes: Hydroxyapatite was synthesized by the precipitation method according to the literature procedure (See: Sugiyama, S.; Minami, T.; Hayashi, H.; Tanaka, M.; Shigemoto, N.; Moffat, J. B. *J. Chem Soc., Faraday Trans.* **1996**, 92, 293). $(\text{NH}_4)_2\text{HPO}_4$ (40.0 mmol) was dissolved in deionized water (150 mL) and pH was adjusted to 11 with aqueous NH_3 solution. To a solution of $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ (66.7 mmol) in deionized water (120 mL) adjusted to pH 11 with aqueous NH_3 solution was added drop-wise over 30 min into the above solution with vigorous stirring at room temperature, and then the obtained milky solution was heated at 90 °C for 10 min. The precipitate was filtered, washed with deionized water and dried at 110 °C, giving $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ (HAP, Ca/P=1.67). The HAP (1.0 g) was stirred with a 1.34×10^{-2} M aqueous $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ solution (75 mL) at room temperature for 24 h. The obtained slurry was filtered, washed with water and dried under vacuum, yielding the RuHAP ($\text{RuCa}_9(\text{PO}_4)_6(\text{OH})_2$) as a dark brown powder (Ru content: 0.97 mmol·g⁻¹). From the elemental analysis, the (Ru+Ca)/P ratio of the RuHAP were estimated to

1.67, which shows the occurrence of an equimolar substitution of the Ru for Ca on hydroxyapatite surface. The cationic RuHAP-(I) and -(II) were synthesized *in situ* by treatment of the RuHAP (0.05 g) with aqueous solution of AgX (1.1 equiv. of Ru, $X = \text{SbF}_6^-$, TfO^-) at room temperature under argon atmosphere. After 5 h, the solution was removed, dried under vacuum and the solvent was added prior to the reaction. The complete exchange of the Cl by SbF_6 was confirmed by elemental analysis: the atomic ratio of Ru to Sb was ca 1:1.

A typical example for the Diels-Alder reaction: Into a reaction vessel with the cationic RuHAP-(I) (0.05 g, Ru: 0.05 mmol) and nitromethane (5 mL) were placed cyclopentadiene (1 mmol) and methyl vinyl ketone (1.2 mmol) under Ar atmosphere, and then the resulting mixture was stirred at room temperature. The progress of the reaction was monitored by GC analysis. After 4 h, 92 % of 5-norbornene-2-carboxaldehyde (*endo:exo*=90:10) was obtained. The *endo:exo* ratio was determined by ^1H NMR spectroscopy.

The procedure of the subsequent three Diels-Alder reaction: Into a reaction vessel were placed the cationic RuHAP (I) (0.05 g, Ru: 0.05 mmol), cyclopentadiene (1 mmol), methyl acrylate (1.2 mmol), and nitromethane (5 mL) under Ar atmosphere, and then the resulting mixture was stirred at room temperature. The progress of the reaction was monitored by GC analysis. When the above reaction was completed, two substrates were added and a new mixture was allowed to further react. The subsequent three reactions gave the corresponding cycloadduct over 92 % yields at essentially the same rates, as shown in Figure 1S.

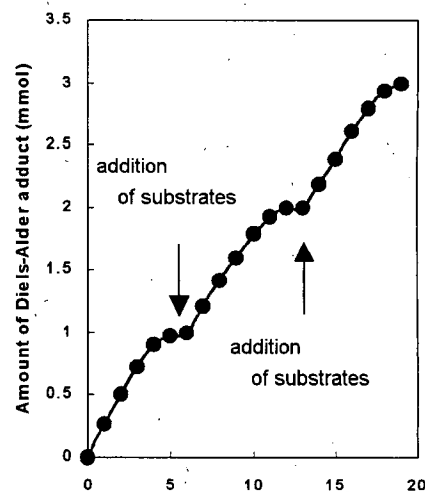


Figure 1S. Time profile of the Diels-Alder reaction

A typical example for the aldol reaction of nitriles: Into a reaction vessel with the cationic RuHAP-(II) (0.05 g, Ru: 0.05 mmol) and water (5 mL) were placed ethylcyanoacetate (1 mmol) and benzaldehyde (1.2 mmol) under Ar atmosphere, and then the resulting mixture was stirred at room temperature. The progress of the reaction was monitored by GC analysis. After 4 h, 99 % of (*E*)-ethyl 2-cyano-3-phenyl-2-propenoate was obtained. For the recycling experiment, the reaction mixture was centrifuged after the fresh run, and the liquid phase was decanted. The residual solid catalyst was again added to water and substrates, and reacted under identical conditions. The first, the second, and the third runs gave (*E*)-ethyl 2-cyano-3-phenyl-2-propenoate in 99, 97, and 97 % yields, respectively.

A procedure of the large-scale aldol reaction of nitriles: Into a reaction vessel with the cationic RuHAP-(II) (0.2 g, Ru: 0.2 mmol) and water (50 mL) were placed ethylcyanoacetate (100 mmol) and benzaldehyde (120 mmol) under Ar atmosphere, and then the resulting mixture was stirred at 50 °C. After 24 h, the catalyst was separated by filtration and the GC analysis of the filtrate showed a 94 % yield of (*E*)-ethyl 2-cyano-3-phenyl-2-propenoate. The filtrate was extracted with diethylether (30 mL x 3), and the organic layer was concentrated under reduced pressure to afford the 18.1 g of a pure product (90 % isolated yield).

The procedure for the aldol reaction of nitriles with α , β -unsaturated carbonyl compounds: Into a reaction vessel were placed the cationic RuHAP (II) (0.05 g, Ru: 0.05 mmol), malononitrile (1 mmol), 2-cyclohexene-1-one (1.2 mmol), and water (5 mL) under Ar atmosphere, and then the resulting mixture was stirred at 80°C. After 8 h, the catalyst was separated by a filtration and the GC analysis of the filtrate showed a 89 % yield of aldol product. The filtrate was extracted with diethylether (10 mL x 3), and the organic layer was concentrated under reduced pressure to afford the 0.12 g of pure products (85 % isolated yield).

2-cyclohexene-1-ylidene-propanedinitrile: ^1H NMR (400 MHz, CD_3Cl), δ/ppm 1.87 (m, 2H); 2.46 (m, 2H), 2.56 (t, 2.0 Hz, 2H), 6.15 (m, 1H), 6.71 (d, $J = 10.3$ Hz, 1H). ^{13}C NMR (400 MHz, CD_3Cl), δ/ppm 199.2, 141.6, 131.1, 118.0, 78.3, 30.5, 25.6, 24.3.

2-cyclopentene-1-ylidene-propanedinitrile ^1H NMR (400 MHz, CD_3Cl), δ/ppm 1.63 (m, 2H), 2.09 (t, 2.2 Hz, 2H), 5.12 (m, 1H), 5.87 (d, $J = 5.7$ Hz, 1H). ^{13}C NMR (400 MHz, CD_3Cl), δ/ppm 190.3, 145.3, 133.7, 117.6, 78.9, 30.2, 26.1.

Characterization by Ru K-edge X-ray absorption fine structure (XAFS): X-ray absorption spectra were recorded using at the beam line 01B1 station with attached Si (111) monochromator at SPring-8, JASRI, Harima, Japan. Details of data analysis are referred to the reported procedure (See: Tanaka, T.; Yamashita, H.; Tsuchitani, R.; Funabiki, T.; Yoshida, S. *J. Chem. Soc., Faraday Trans.* **1988**, *84*, 2987). Fourier-transforms (FT) and Inverse FT of k^3 -weighted Ru K-edge EXAFS experimental data for the RuHAP, cationic RuHAP-(I), and cationic RuHAP-(II) after treatment with **3a** are shown in Figure 1S. Inverse FT were performed for the regions of 0.8-2.8 Å in Figure. 1S(A), 0.8-2.9 Å in Figure. 2S(B), and 0.8-2.8 Å in Figure. 1S(C). The results of curve-fitting analysis are summarized in Table 1S.

Table 1S. Curve-fitting analysis for RuHAP

Sample	Shell	C.N. ^a	R (Å) ^b	$\Delta\sigma$ (Å ²) ^c
RuHAP	Ru-O(1)	4.1	1.97	0.0067
	Ru-O(2)	2.1	2.28	0.0008
	Ru-O(3)	1.7	2.62	-0.0054
	Ru-Cl	1.2	2.32	0.0010
Cationic RuHAP	Ru-O(1)	4.1	1.98	-0.0013
	Ru-O(2)	2.2	2.28	-0.0029
	Ru-O(3)	1.7	2.68	-0.0007
	Ru-O(4)	1.0	2.10	0.0093
Cationic RuHAP after treatment with 3a	Ru-O(1)	3.2	1.97	-0.0052
	Ru-O(2)	3.0	2.28	0.0088
	Ru-O(3)	1.7	2.61	-0.0040
	Ru-N(O)	1.1	2.10	0.0114

^a Coordination number. ^b Interatomic distance. ^c Difference between Debye-Waller factor of the RuHAP and that of the reference sample.

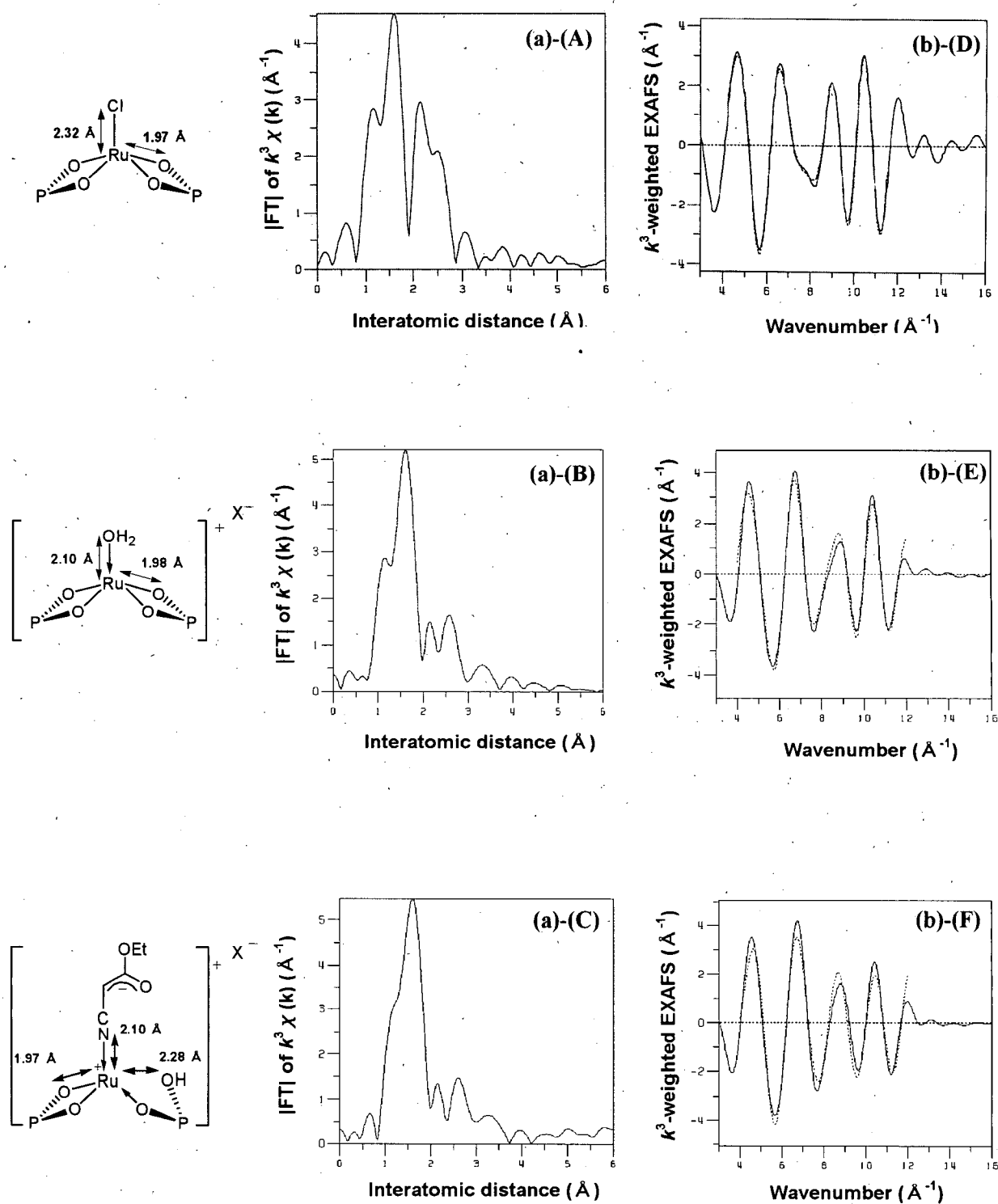


Figure 2S. (a) Fourier-transforms (FT) of k^3 -weighted Ru K-edge EXAFS experimental data for (A) RuHAP, (B) cationic RuHAP-(I), and (C) cationic RuHAP-(II) after treatment with 3a. (b) Inverse FT for (D) RuHAP, (E) cationic RuHAP-(I), and (F) cationic RuHAP-(II) after treatment with 3a. The dotted line shows the results of curve fitting analysis in the range 4-12 \AA^{-1} .

IR measurement: IR spectra of (A) ethylcyanoacetate (**3a**), (B) fresh cationic RuHAP (**II**), (C) after treatment of (B) with **3a** at 80 °C and desorbed under vacuum, and (D) after treatment of (C) with benzaldehyde and desorbed under vacuum were shown in Figure 3S. The signal derived from $\nu(\text{CN})$ band at 2260 cm^{-1} shifted to 2093 cm^{-1} after treatment with **3a** (A vs. C), showing the formation of an adduct between **3b** and the cationic Ru species. In the case of hydride(enolato)ruthenium(II) complex, the $\nu(\text{CN})$ band was observed at 2185 cm^{-1} (See: Hirano, M.; Takenaka, A.; Mizuho, Y.; Hiraoka, M.; Komiya, S. *J. Chem. Soc., Dalton Trans.*, **1999**, 3209). In contrast, no interaction was observed in either parent RuHAP or HAP, which were inactive for the Diels-Alder and aldol reactions. Furthermore, the additional peak, which is assigned to the P-OH group of HPO_4^{2-} ion on hydroxyapatite surface, was observed at 870 cm^{-1} in the spectrum of (C). Treatment of (C) with benzaldehyde resulted in the disappearance of these two bands, as shown in the spectrum of (D). On the basis of these results, the aldol reaction of nitriles is thought to proceed via bifunctional-catalysis by cationic Ru species and basic phosphate ligand; the former acts as Lewis acid to increase the acidity of α C-H bond, while the latter abstracts a proton of the Ru-coordinated nitriles to generate enolate species. A possible reaction mechanism is illustrated in Scheme 1S.

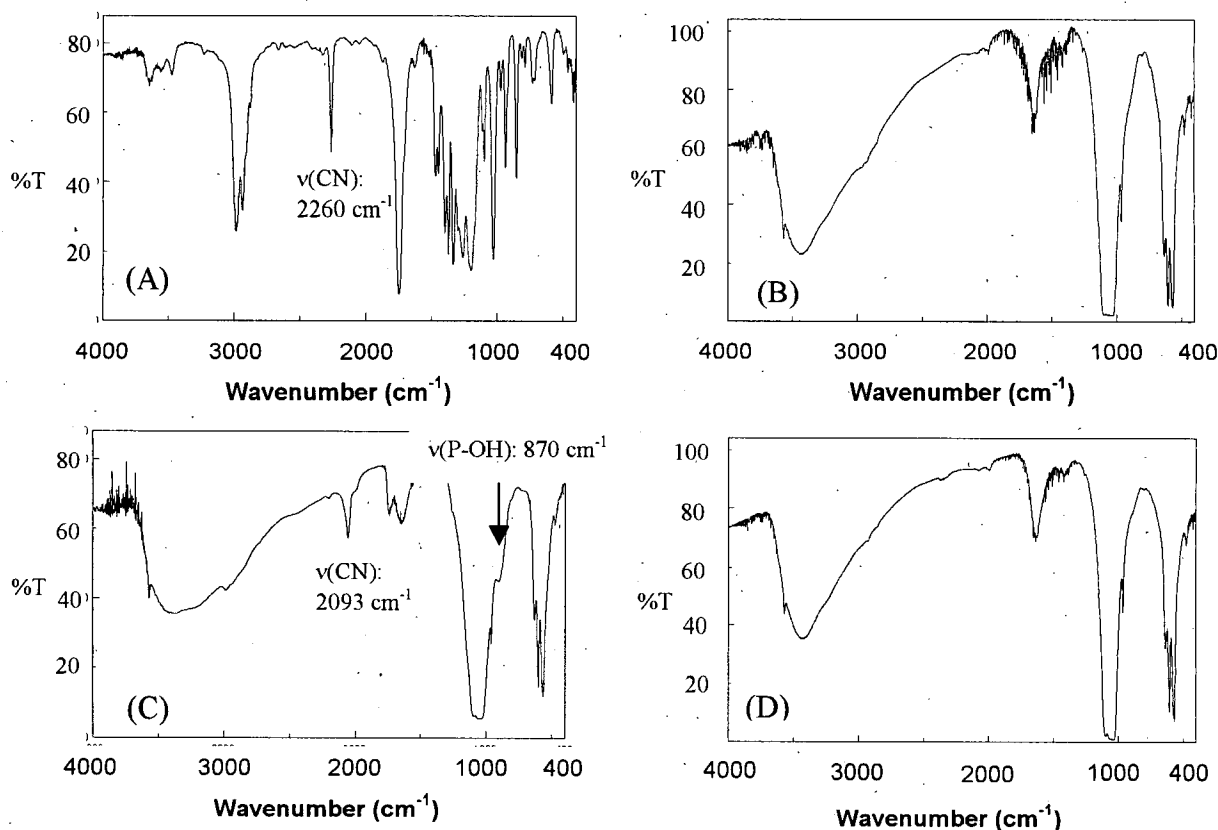
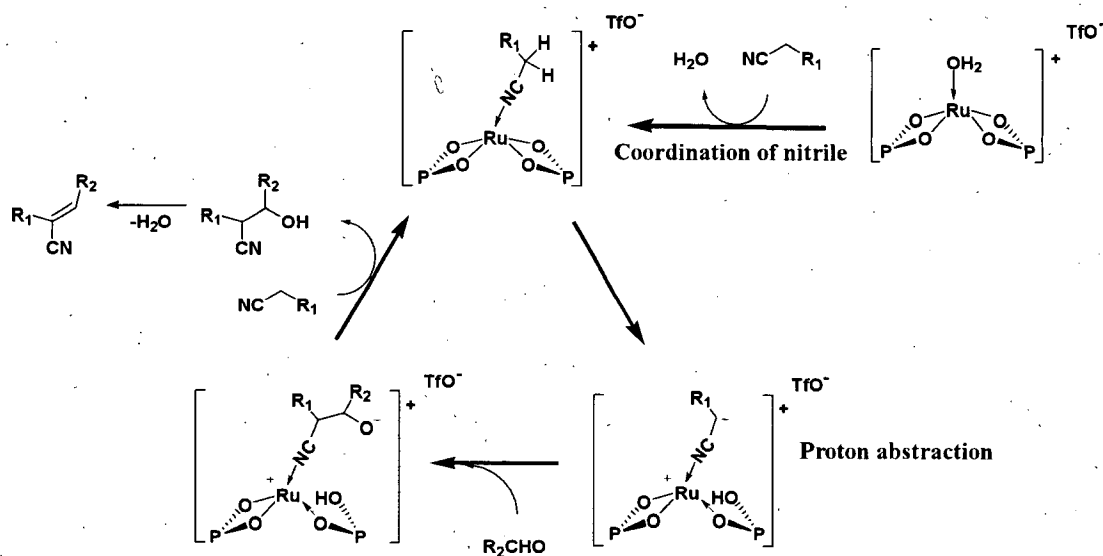


Figure 3S. IR spectra of the samples (A)-(D)



Scheme 1S. A possible mechanism for the aldol reaction of nitriles with carbonyl compounds catalyzed by the cationic RuHAP-(II)