Cation-Exchanged Montmorillonite-Catalyzed Facile Friedel–Crafts Alkylation of Hydroxy and Methoxy Aromatics with 4-Hydroxybutan-2-one To Produce Raspberry Ketone and Some Pharmaceutically Active Compounds

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Received May 2, 1994®

The Friedel–Crafts alkylation of hydroxy and methoxy aromatics with 4-hydroxybutan-2-one (γ-KB) in the presence of a cation-exchanged montmorillonite (M^{n+}-mont; $M^{n+} = Zr^{4+}$, Al^{3+}, Fe^{3+}, and Zn^{2+}) was investigated. Phenol was C-alkylated regiospecifically with γ-KB in the presence of Zr^{4+}-, Al^{3+}-, or Fe^{3+}-mont to produce 4-(4-hydroxyphenyl)butan-2-one (raspberry ketone) in 31–35% GLC yield. Anisole, 2-methoxynaphthalene, and 1-methoxynaphthalene were regiospecifically C-alkylated to produce 4-(4-methoxyphenyl)butan-2-one, 4-(2-methoxy-1-naphthyl)butan-2-one (pharmaceutically active), and 4-(4-methoxy-1-naphthyl)butan-2-one, respectively. Al^{3+}- and Fe^{3+}-mont were the most effective catalysts in these cases (13–58% isolated yield). γ-KB could be used as an alkylating agent instead of the highly toxic 3-buten-2-one (MVK) which also polymerizes easily.

Introduction

Friedel–Crafts alkylations of aromatic substrates with alkenes, alcohols, and alkyl halides are catalyzed by various clays, both natural and acid-activated.[1] However, many of these reactions require relatively high temperature and pressure and the products are often isomeric mixtures. The results have usually been published in patents such that some of the detailed experimental procedures are not readily available.[2,3] We are interested in the catalytic applications of cation-exchanged montmorillonite (M^{n+}-mont), a modified natural clay, to organic synthesis under mild conditions. These catalysts have attractive features such as ease of handling, noncorrosiveness, low cost, regeneration, and easy modification of acidity by exchange of cations in the interlayer space.[1,4] They are environmentally-friendly catalysts, in that they circumvent the production of aluminum waste.[3]

We have attempted the alkylation of phenol with commercially-available, inexpensive 4-hydroxybutan-2-one (γ-KB) using various M^{n+}-mont as catalysts to produce the target 4-(4-hydroxyphenyl)butan-2-one (**1a**). This compound is the odor source of raspberry and is called raspberry ketone. Until now, this ketone has been prepared industrially by the use of an acid catalyst such as concentrated H_2SO_4, H_3PO_4, aqueous HCl,[5] or the cation-exchange resin Dowex-50W.[6] We report here the successful result of a highly *para*-selective alkylation of phenol with a facile workup procedure. The application of this method to anisole and 2-methoxy- and 1-methoxynaphthalene is also reported. Some of the products of this alkylation are pharmaceutically active compounds. For example, 4-(4-methoxyphenyl)butan-2-one (**1b**) is the insect attractant for the scarabaeid subfamily, Rutelinae,[7] and 4-(2-methoxyphenyl)butan-2-one (**2b**) is a key intermediate en route to the bronchospasmolytically active (aralkylamino)(hydroxyphenyl)ethanols.[8] 4-(2-Methoxy-1-naphthyl)butan-2-one (**4**) is known to be pharmaceutically active, though slightly less effective than 4-(2-methoxy-6-naphthyl)butan-2-one (Nabumeton), a nonsteroidal antiinflammatory compound.[9]

Results and Discussion

Friedel–Crafts Alkylation of Phenol with 4-Hydroxybutan-2-one (γ-KB). In the presence of Zr^{4+}-mont or Fe^{3+}-mont as an acid catalyst, 4-(4-hydroxyphenyl)-butan-2-one (**1a**) was obtained regioselectively in 35% GLC yield by alkylation of phenol, which served as the reactant as well as the solvent, with 4-hydroxybutan-2-one (γ-KB) at 100 °C for 48 h (Scheme 1; Table 1, runs 1 and 3). The formation of a small amount of 4-phenoxybutan-2-one (**3**) was observed, but no *ortho*-alkylation products, 4-(2-hydroxyphenyl)butan-2-one (**2a**), or polyalkylated compounds were produced. The time course of this reaction is illustrated in Figure 1.

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® Abstract published in *Advance ACS Abstracts,* September 1, 1994.

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Scheme 1

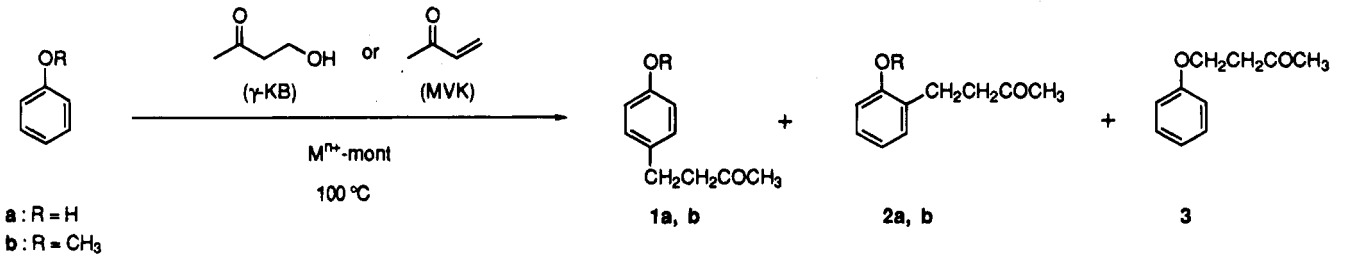

Table 1. M^{n+}-Mont-Catalyzed Alkylation of Phenol or Anisole with 4-Hydroxybutan-2-one (γ-KB)[a]

			product and GLC yield (%)[b]	
run	reactant	catalyst	**1a**	**3**
1	phenol	Zr^{4+}-mont	35 (28)[c]	1 (0.4)[c]
2	phenol	Al^{3+}-mont	31	1
3	phenol	Fe^{3+}-mont	35	<1
4	phenol	Zn^{2+}-mont	4	3
5	phenol	Zr^{4+}-mont[d]	16	13
6	phenol	Zr^{4+}-mont[e]	34	3
7	phenol	Zr^{4+}-mont[d,e]	27	7
8	phenol	Zr^{4+}-mont[f]	11[g]	2[g]
9	phenol	$ZrOCl_2 \cdot 8H_2O$[h]	3	0
			1b	**2b**
10	anisole	Zr^{4+}-mont	3	1
11	anisole	Al^{3+}-mont	22	2
12	anisole	Fe^{3+}-mont	25 (10)[c]	2 (0.3)[c]
13	anisole	Zn^{2+}-mont	9	1
14	anisole	Fe^{3+}-mont[d]	3	<1
15	anisole	Fe^{3+}-mont[e]	41	5
16	anisole	Fe^{3+}-mont[d,e]	34	6
17	anisole	Fe^{3+}-mont[f]	<1[g]	<1[g]

[a] Phenol or anisole (56.7 mmol), γ-KB (1.00 g, 11.3 mmol), M^{n+}-mont (1.00g) at 100 °C for 48 h. [b] Based on γ-KB. [c] Isolated yield. [d] 3-Buten-2-one (MVK, 0.792 g, 11.3 mmol) was used as an alkylating agent. [e] γ-KB or MVK was added using a microfeeder during 24 h. [f] Phenol or anisole (6.32 mmol), γ-KB (2.00 g, 22.6 mmol), M^{n+}-mont (0.50 g) at 100 °C for 48 h. [g] Based on phenol or anisole. [h] 5 mmol.

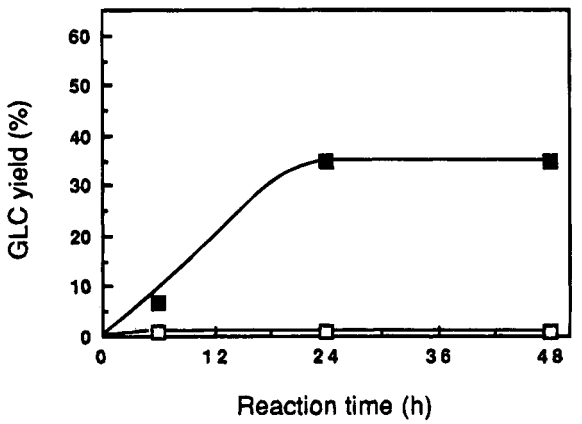

Figure 1. Time course of the alkylation of phenol (56.7 mmol) with 4-hydroxybutan-2-one (γ-KB, 11.3 mmol) in the presence of Zr^{4+}-mont (1.00 g) at 100 °C. Yield of the compounds **1a** (■) and **3** (□).

The yields of the products were influenced by the nature of the exchanged cation in M^{n+}-mont, the structure of the alkylating agent, and the drying procedure used during catalyst preparation. In the alkylation with γ-KB, Zr^{4+}-, Al^{3+}-, and Fe^{3+}-mont gave the expected products in relatively good yields, but Zn^{2+}-mont proved ineffective (Table 1, runs 1–4). The yield did not relate to the number of acid sites present in the M^{n+}-mont, since Fe^{3+}- and Zn^{2+}-mont are similar in this regard (see Experimental Section). Although the number of acid sites in the M^{n+}-mont determined by the temperature-programmed desorption of ammonia gas (NH_3-TPD) may not accurately represent the active acid sites available to this alkylation, it provides a reference for M^{n+}-mont acidity. Upon using 3-buten-2-one (MVK) as an alkylating agent instead of γ-KB, low product selectivity was observed (Table 1, run 5). A comparison of catalyst drying procedures was made with Zr^{4+}-mont. In alkylations conducted at half scale with γ-KB in the presence of Zr^{4+}-mont catalyst dried at 120 °C for 24 h, the compounds **1a** and **3** were produced in 26 and 9% GLC yield, respectively. These products were not obtained when catalyst, dried first at 120 °C for 24 h and then at 100 °C *in vacuo* for 1 h, was used. The interlayered Zr^{4+}-mont probably deactivated during the drying procedure at reduced pressure by collapsing or for other reasons. Use of Zr^{4+}-mont dried by azeotropic distillation with toluene or air-dried Zr^{4+}-mont gave the compounds **1a** and **3** in relatively low yields of 19 and 8%, and 24 and 3%, respectively. In the presence of added water (0.2 mL), the reaction with Zr^{4+}-mont dried at 120 °C for 24 h proceeded smoothly to produce **1a** and **3** in 28 and 4% yield, respectively. Since no Zr cations were detected in the reaction supernatant by X-ray fluorescence (XRF) analysis, it is clear that Zr cations were not removed from the surface of Zr^{4+}-mont. This suggests that the active catalytic site for the alkylation was not the cation, but an acid site induced by the cation exchange. In connection with this, it is worth noting that $ZrOCl_2 \cdot 8H_2O$ itself was almost ineffective in this alkylation (Table 1, run 9). With excess γ-KB (Table 1, runs 8 and 17), the yield of **1a** was poor and some polymeric compounds such as the MVK dimer (*m*/*z*, M^+: 140), the MVK trimer (*m*/*z*, M^+: 228), and higher molecular weight products were detected by GC/MS analyses.

Although a small amount of **3** was always observed in the alkylation of phenol with γ-KB, the product distribution versus time (Figure 1) did not indicate the sequential rearrangement of **3** to **1a**, but suggested the competitive formation of both **1a** and **3**. Although we cannot exclude the possibility of transformation of **3** to **1a** completely, the main reaction course seems to be that 3-oxobutyl cation produced from γ-KB or MVK (its very strong odor was detected) attacks an aromatic carbon of phenol electrophilically to give **1a**. MVK may be produced by dehydration of γ-KB in the presence of M^{n+}-mont.

Friedel–Crafts Alkylation of Anisole, 2-Methoxynaphthalene, and 1-Methoxynaphthalene with 4-Hydroxybutan-2-one (γ-KB). Similar alkylations of anisole, 2-methoxynaphthalene, and 1-methoxynaphthalene with γ-KB also proceeded regioselectively in the presence of M^{n+}-mont catalyst. Anisole was monoalkylated to produce 4-(4-methoxyphenyl)butan-2-one (**1b**) (major) and 4-(2-methoxyphenyl)butan-2-one (**2b**) (Scheme 1,

Scheme 2

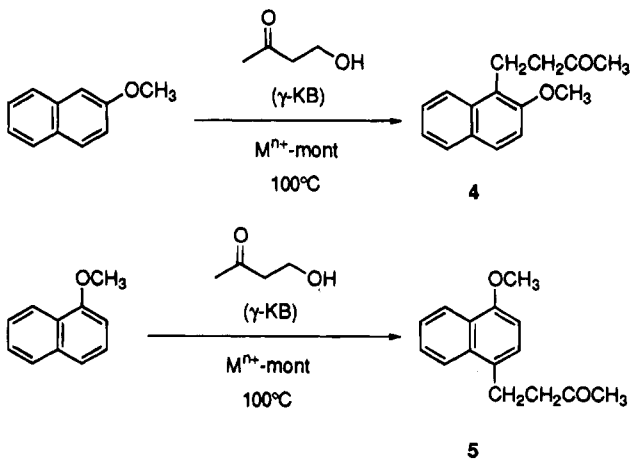

Table 2. M^{n+}-Mont-Catalyzed Alkylation of Methoxynaphthalene with 4-Hydroxybutan-2-one (γ-KB)[a]

run	reactant	catalyst	product	isolated yield (%)[b]
1	2-methoxynaphthalene	Zr^{4+}-mont[c]	**4**	10
2	2-methoxynaphthalene	Al^{3+}-mont[c]	**4**	18
3	2-methoxynaphthalene	Al^{3+}-mont	**4**	10
4	2-methoxynaphthalene	Fe^{3+}-mont[c]	**4**	13
5	2-methoxynaphthalene	Zn^{2+}-mont[c]	**4**	3
6	1-methoxynaphthalene	Zr^{4+}-mont	**5**	29
7	1-methoxynaphthalene	Al^{3+}-mont[c]	**5**	51
8	1-methoxynaphthalene	Al^{3+}-mont	**5**	58
9	1-methoxynaphthalene	Fe^{3+}-mont	**5**	31
10	1-methoxynaphthalene	Zn^{2+}-mont	**5**	25

[a] Methoxynaphthalene (1.00 g, 6.32 mmol), γ-KB (2.00 g, 22.6 mmol), M^{n+}-mont (0.50 g) at 100 °C for 48 h. [b] Based on methoxynaphthalene. [c] Carried out with a half amount of γ-KB for 24 h.

Table 1). Fe^{3+}- and Al^{3+}-mont were effective catalysts. Unlike with phenol, Zr^{4+}-mont was not effective in this case (Table 1, runs 10–12). When γ-KB or MVK was added very slowly to the reaction mixture by use of a microfeeder, the yield of compounds **1b** and **2b** increased appreciably in both cases (Table 1, runs 15 and 16).

Only one regioisomer was produced in alkylations of 2-methoxynaphthalene and 1-methoxynaphthalene (Scheme 2, Table 2). Thus, in the presence of Al^{3+}-mont, 4-(2-methoxy-1-naphthyl)butan-2-one (**4**) (18% isolated yield) was obtained from 2-methoxynaphthalene. 4-(4-Methoxy-1-naphthyl)butan-2-one (**5**) was obtained in 58% isolated yield from 1-methoxynaphthalene (Table 2, runs 2 and 7). All of these reactions were carried out in the presence of excess γ-KB to facilitate the isolation of the products from the starting methoxynaphthalenes. Unfortunately, some polymeric compounds such as the MVK dimer, the MVK trimer, and higher molecular weight compounds were formed.

Conclusion

We have accomplished the Friedel–Crafts alkylations of phenol, anisole, and methoxynaphthalenes with γ-KB or MVK in the presence of Zr^{4+}-, Al^{3+}-, or Fe^{3+}-mont to produce raspberry ketone and several pharmaceutically active compounds, in moderate yields. In the presence of the usual Friedel–Crafts catalysts, $AlCl_3$ and concentrated H_2SO_4, many side reactions such as isomerization, transalkylation, polymerization, and polyalkylation are known to occur. Workup procedures are sometimes troublesome. In contrast, these undesired side reactions did not occur using M^{n+}-mont as a catalyst. Furthermore, workup of the reaction mixture was quite simple. Additionally, γ-KB could be used as an alkylation agent instead of MVK, which is toxic and polymerizes easily.

Experimental Section

^1H NMR spectra were recorded on a JEOL GSX-270 (270 MHz) instrument for solutions in $CDCl_3$ with TMS as an internal standard. ^{13}C NMR spectra were obtained with JEOL GSX-270 (67.8 MHz) and JEOL FX-100 (25.0 MHz) instruments for solutions in $CDCl_3$ with TMS as an internal standard. Coupling constants J are given in hertz. Mass spectra were measured on a Shimadzu QP-2000 mass spectrometer equipped with a Shimadzu GC-14A gas-liquid chromatography (25 m × 0.20 mm, 2.5 μm film thickness, Shimadzu fused silica capillary column HiCap CBP10-M25-025). The ionizing voltage was 70 eV for all compounds. GLC analyses were performed on a Hitachi 163 instrument (2 m × 3 mm stainless steel column packed with 3% OV-17 on Chromosorb W) and a Shimadzu GC-14A instrument (25 m × 0.33 mm, 5.0 μm film thickness, Shimadzu fused silica capillary column HiCap CBP10-S25-050) with flame-ionization detectors and N_2 as carrier gas with di-*n*-butyl phthalate as an internal standard. Mps were determined on a Yanaco MP-S3 micro melting point apparatus and uncorrected. X-ray powder diffraction (XRD) data were obtained on a Shimadzu XD-D1 diffractometer using Cu Kα radiation and an energy dispersive detector. Column chromatography on SiO_2 was performed with Wakogel C-200 and C-300 [hexane and hexane–ethyl acetate as eluents]. Combustion analyses were performed at the Microanalytical Center of Kyoto University. X-ray fluorescence (XRF) analyses were carried out at the Environment Preservation Center of Kyoto University.

All commercially available organic and inorganic compounds were used without further purification except for the solvent, which was dried and distilled by the known method before use. Kunipia G, namely Na^+-mont, was obtained from Kunimine Industries Co., Ltd. The compound **1a** was identified by comparison of ^1H NMR, ^{13}C NMR, mass spectrum, and GLC retention time with those of commercial product.[10] The compounds **1b**, **2b**, **3**, **4**, and **5** are known compounds and characterized by their spectral data after their isolation.

General Procedure for the Preparation of Cation-Exchanged Montmorillonite (M^{n+}-Mont). By following and slightly modifying the reported preparative method,[11] M^{n+}-mont was prepared as follows. Na^+-Mont (Kunipia G, Kunimine Industries Co., Ltd., <100 mesh, 6 g) was dispersed to 50% aqueous acetone (400 mL) under vigorous magnetic stirring at 25 °C for 24 h. The resulting suspension was heated to 50 °C and then added with an aqueous solution (600 mL) of 100 mM of a particular metal salt [namely, $ZrOCl_2 \cdot 8H_2O$, $Al(NO_3)_3 \cdot 9H_2O$, $Fe(NO_3)_3 \cdot 9H_2O$, or $Zn(NO_3)_2 \cdot 6H_2O$]. The mixture was stirred at 50 °C for 24 h. After it had been stood for a while, the resulting wet clay was collected by filtration (Whatman, qualitative filter paper no. 5) or decantation which was washed with pure water several times (1 × 500 mL and then 5–8 × 200 mL) under magnetic stirring, and the solid clay was collected by filtration when the presence of the cation in a washing was not confirmed by quantitative analysis of respective ions.[12] It was dried at 80 °C in an oven for 24 h and then ground and passed through a 100 mesh screen. The obtained solid was again dried at 120 °C for 24 h and in a hot state it was stored in a desiccator. The color of Zr^{4+}-, Al^{3+}-, and Zn^{2+}-mont is white, while that of Fe^{3+}-mont is reddish brown.

The amount of acid sites (Brönsted and Lewis acid sites) of Zr^{4+}-, Al^{3+}-, Fe^{3+}-, and Zn^{2+}-mont was estimated by the

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temperature-programmed desorption of ammonia gas (NH_3-TPD) analyses to be 0.734, 0.531, 0.349, and 0.371 mmol g^{-1}, respectively. Thus, the glass vessel containing M^{n+}-mont (ca. 70–80 mg) was evacuated at 300 °C for 2 h. After it had been cooled to 100 °C, ammonia gas was introduced to the glass vessel for 1.5 h. After evacuation at 100 °C for 2 h, the amount of adsorbed ammonia gas was measured gravimetrically or volumetrically.

The basal spacings (d_{001}) of Al^{3+}- and Zn^{2+}-mont were estimated by a sharp peak obtained on XRD analyses to be 12.5 and 14.9 Å, respectively, showing clearly that the catalysts have an interlayer structure. On the other hand, those of Zr^{4+}- and Fe^{3+}-mont were estimated by a broad peak to be >18 Å indicating that the catalysts might have either an interlayer structure or a random structure.

Regioselective Alkylation of Phenol with 4-Hydroxybutan-2-one (γ-KB) in the Presence of Zr^{4+}-Mont To Form 4-(4-Hydroxyphenyl)butan-2-one (1a) (Table 1, run 1). To phenol (5.34 g, 56.7 mmol) was added Zr^{4+}-mont (1.00 g, 0.73 mmol as an acid site) at ca. 40 °C with magnetic stirring. The temperature of the mixture was raised to 100 °C during ca. 30 min with stirring and then stirred at 100 °C for 15 min. To the mixture was added γ-KB (1.00 g, 11.3 mmol) dropwise in 5 min at the temperature and the mixture was stirred for 48 h. After it had been cooled, the catalyst was filtered and washed with diethyl ether (20 mL). A mixture of the filtrate and ether washings was treated with 10% aqueous NaOH (3 × 20 mL). After acidification of the alkaline extract with 17% aqueous HCl (25 mL), it was extracted with diethyl ether (4 × 20 mL), and the extract was washed with brine and dried over $MgSO_4$. Removal of the organic solvent including phenol by a rotary evaporator left a brown oil which was subjected to column chromatography several times for purification [Wakogel C-200, eluents: hexane and then hexane–ethyl acetate (95:5 to 80:20)]. Evaporation of the solvent from the fractions including an expected compound left a pale yellow oil which was dissolved in a mixture of diethyl ether and hexane (1:9), and the solution was allowed to stand for a while at room temperature to afford a colorless needle-like crystal of the compound **1a** (560.9 mg, 3.42 mmol, 28% yield, GLC yield 35%. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.10; H, 7.30. Found: C, 73.17; H, 7.37). Washing with water (20 mL), drying with $MgSO_4$, and evaporation of the first ethereal solution which was treated with 10% aqueous NaOH left a brown oil which was subjected to column chromatography [Wakogel C-200, eluent: hexane–ethyl acetate (95:5)]. Removal of the solvent from the fraction including an expected compound left a colorless liquid of 4-phenoxybutan-2-one (**3**) (9.0 mg, 0.05 mmol, 0.4% yield, GLC yield 1%): ^1H NMR δ 2.24 (s, 3H, CH_3), 2.90 (t, 2H, J = 6.4, CH_2CO), 4.23 (t, J = 6.4, 2H, CH_2O), 6.87–7.31 (m, 5H, ArH); ^{13}C NMR δ 30.5 (q), 43.0 (t), 62.8 (t), 114.5 (d), 121.0 (d), 129.5 (d), 158.5 (s), 206.4 (s); MS, m/z (relative intensity) 164 (M^+, 17), 94 (46), 71 (24), 43 (100). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.10; H, 7.30. Found: C, 72.93; H, 7.15. In the cases of reactions using other M^{n+}-mont as catalysts, the ether extract was analyzed by GLC which showed the presence of both **1a** and **3** (Table 1).

Alkylation of Anisole with 4-Hydroxybutan-2-one (γ-KB) in the Presence of M^{n+}-Mont To Form 4-(4-Methoxyphenyl)butan-2-one (1b) and 4-(2-Methoxyphenyl)butan-2-one (2b) (Table 1, run 12). The reaction was similarly carried out as above using anisole in place of phenol, and **1b** (203.0 mg, 1.14 mmol, 10% yield, GLC yield 25%) and **2b** (5.3 mg, 0.03 mmol, 0.3% yield, GLC yield 2%) were isolated as a colorless oil, respectively. 4-(4-Methoxyphenyl)butan-2-one (**1b**): ^1H NMR δ 2.11 (s, 3H, CH_3), 2.67–2.86 (m, 4H, CH_2-CH_2, AA'BB' type), 3.75 (s, 3H, CH_3O), 6.81 (d, J = 8.8, 2H, ArH), 7.09 (d, J = 8.8, 2H, ArH); ^{13}C NMR δ 28.8 (t), 30.0 (q), 45.3 (t), 55.1 (q), 129.1 (d), 132.9 (s), 157.8 (s), 207.8 (s); MS, m/z (relative intensity) 178 (M^+, 35), 121 (100), 43 (23). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.21; H, 7.86. 4-(2-Methoxyphenyl)butan-2-one (**2b**): ^1H NMR δ 2.13 (s, 3H, CH_3), 2.68–2.91 (m, 4H, CH_2CH_2, AA'BB' type), 3.81 (s, 3H, CH_3O), 6.82–6.90 (m, 2H, ArH), 7.10–7.22 (m, 2H, ArH); ^{13}C NMR δ 24.9 (t), 29.8 (q), 43.6 (t), 55.1 (q), 110.2 (d), 120.4 (d), 127.4 (d), 129.2 (s), 129.9 (d), 157.4 (s), 208.6(s); MS, m/z (relative intensity) 178 (M^+, 71), 121 (97), 108 (69), 91 (93), 79 (37), 43 (100). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.21; H, 7.86. For reactions under other conditions, a mixture of the filtrate and the ether washings was analyzed by GLC which showed the presence of **1b** and **2b**.

Alkylation of 2-Methoxynaphthalene and 1-Methoxynaphthalene with 4-Hydroxybutan-2-one (γ-KB) in the Presence of M^{n+}-Mont To Produce 4-(2-Methoxy-1-naphthyl)butan-2-one (4) and 4-(4-Methoxy-1-naphthyl)butan-2-one (5) (Table 2). A mixture of 2-methoxynaphthalene (1.00 g, 6.32 mmol) and γ-KB (1.00 g, 11.3 mmol) was stirred for 10 min with a slight heating and heated until 100 °C during ca. 30 min under magnetic stirring and then kept at 100 °C for 15 min. To the mixture was added Zr^{4+}-mont (500 mg) portionwise in 5 min at the temperature and the mixture was stirred for 48 h. After it had been cooled, the catalyst was filtered and washed with diethyl ether (20 mL). Removal of the organic solvent from a mixture of the filtrate and ether washings left a brown oil which was subjected to flash column chromatography [Wakogel C-300, eluents: hexane and then hexane–ethyl acetate (99:1 to 98:2)]. Evaporation of the solvent from fractions including an expected product left a colorless oil. A mixture of diethyl ether–hexane (1:9) was added and the solution was allowed to stand for a while to produce a colorless needle-like crystal of 4-(2-methoxy-1-naphthyl)butan-2-one (**4**) (257.6 mg, 1.13 mmol, 18% yield): mp 52.5–53.0 °C (lit.[9] 51–52 °C); ^1H NMR δ 2.18 (s, 3H, CH_3), 2.72 (t, J = 8.1, 2H, CH_2CO), 3.34 (t, J = 8.1, 2H, $ArCH_2$), 3.94 (s, 3H, CH_3O), 7.26 (d, J = 8.8, 1H, ArH), 7.30–7.37(m, 1H, ArH), 7.44–7.51 (m, 1H, ArH), 7.74 (d, J = 8.8, 1H, ArH), 7.79 (d, J = 8.8, 1H, ArH), 7.91 (d, J = 8.8, 1H, ArH); ^{13}C NMR δ 18.9 (t), 29.4 (q), 43.2 (t), 55.9 (q), 112.6 (d), 121.5 (s), 122.2 (d), 122.8 (d), 126.1 (d), 127.5 (d), 128.1 (d), 128.8 (s), 132.2 (s), 153.8 (s), 208.2 (s); MS, m/z (relative intensity) 228 (M^+, 50), 171 (100), 141 (61), 43 (37). Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.91; H, 7.05.

4-(4-Methoxy-1-naphthyl)butan-2-one (5). The reaction was similarly carried out as above using 1-methoxynaphthalene and a colorless needle-like crystal of the compound **5** (833.7 mg, 3.65 mmol, 58% yield) was isolated: mp 66.0–67.0 °C (lit.[9] 67–69 °C); ^1H NMR δ 2.09 (s, 3H, CH_3), 2.79 (t, J = 7.9, 2H, CH_2CO), 3.24 (t, J = 7.9, 2H, $ArCH_2$), 3.93 (s, 3H, CH_3O), 6.68 (d, J = 8.1, 1H, ArH), 7.18 (d, J = 8.1, 1H, ArH), 7.41–7.54 (m, 2H, ArH), 7.86–7.91 (m, 1H, ArH), 8.28–8.32 (m, 1H, ArH); ^{13}C NMR δ 26.3 (t), 30.0 (q), 44.5 (t), 55.4 (q), 103.4 (d), 122.7 (d), 123.2 (d), 124.9 (d), 125.8 (d), 126.0 (s), 126.5 (d), 128.7 (s), 132.3 (s), 154.3 (s), 208.2(s); MS, m/z (relative intensity) 228 (M^+, 30), 171 (100), 43 (34). Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.15; H, 7.16.

Acknowledgment. The authors wish to thank Professor Hiroshi Takatsuki and Mr. Yoshiji Honda of the Environment Preservation Center of Kyoto University for XRF analyses. They also thank Kunimine Industries Co., Ltd. for the gift of Kunipia G.