Aldol Reaction and Robinson-Type Annelation Catalyzed by Lanthanoid Triisopropoxides

Tamon Okano,* Yoshikazu Satou, Motoshi Tamura, and Jitsuo Kiji

Department of Materials Science, Faculty of Engineering, Tottori University, Koyama, Tottori 680

(Received January 27, 1997)

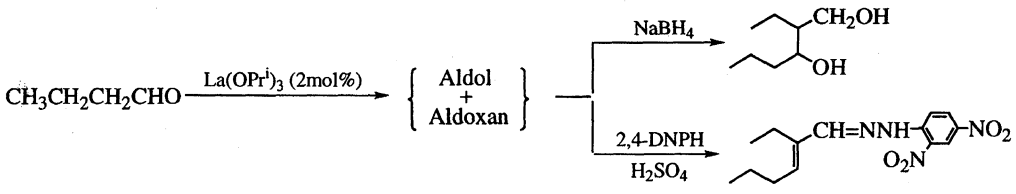
Lanthanoid triisopropoxides are active catalysts for aldol reactions. Aldehydes give the corresponding β-hydroxyaldehydes at low temperatures in good yields, whereas ketones are less reactive, but form condensation products at high temperatures. Exceptionally, γ- or δ-diketones easily undergo condensation to give five- and six-membered unsaturated ketones in high yields. The lanthanoid propoxides, catalyzing the Michael addition of ketones to α,β-unsaturated ketones, which give δ-diketones, are also good catalysts for the Robinson-type annelation. In these reactions, the catalytic activity of the lanthanum propoxide is higher than those of the heavy lanthanoid propoxides, and is almost comparable to that of sodium isopropoxide. Since aluminum triisopropoxide shows poor activity, the lanthanoid propoxides are considerably basic for trivalent metal alkoxides.

Organic synthesis using lanthanoid compounds is one of the most developing areas.[1] Among the lanthanoid reagents, so far the trivalent compounds have been exclusively used as Lewis acids.[2] Even the metal center of 1,1′-bi-2-binaphthoxy[3] and alkyl[4] compounds is reported to act as a Lewis acid. However, since the lanthanoids are highly positive metals, their compounds seem to be fit to use as bases. Previously, Kagen et al. and we found the aldol condensation to be a side reaction of the Meerwein–Ponndorf–Verley–Oppenauer reaction with lanthanoid triisoproxides.[5,6] However, even now, only a few studies on the reactions using basic lanthanoid compounds have been reported,[7] and little is known about the properties of the alkoxides as base catalysts. Here, we describe the aldol reaction and the Robinson-type annelation catalyzed by lanthanoid triisopropoxides.

Results and Discussion

The present work started with the aldol reaction of aldehydes, because we had known that aldehydes form unidentified oily products in the presence of lanthanoid triisopropoxides under the conditions of the Meerwein–Ponndorf–Verley reduction.[5,8] The reaction of butanal in the presence of La(OPr^i)$_3$ in THF gave an oily product. The reduction of the oily product with $NaBH_4$ afforded 2-ethyl-1,3-hexanediol in good yield (Scheme 1). A treatment with 2,4-dinitrophenylhydrazine under acidic conditions gave the hydrazone of 2-ethyl-2-hexenal. Though the ^{13}C NMR of the oily product showed many peaks, the GC spectrum of the product showed two dominant peaks assigned to the diastereomers of the aldol adduct and a small peak assigned to 2-ethyl-2-hexenal. These results indicate that the oily product was mostly a mixture of the aldol adduct and the aldoxan (5-ethyl-4-hydroxy-2,6-dipropyl-1,3-dioxane) decomposing to the aldol adduct under GC conditions. Therefore, the total of the aldol adduct and the aldoxan was used as the yield of the aldol.

The solvent effect and the catalytic activity of Ln(OPr^i)$_3$ are summarized in Table 1. The reaction of butanal with La(OPr^i)$_3$ in nonpolar solvents, such as toluene and THF, was slow, and formed a considerable amount of the condensation product. The reaction was fast in 2-propanol, and gave the aldol with better selectivity than those in THF and toluene (Scheme 2). Surprisingly, butanol was not formed in spite of the same reaction conditions for a Meerwein–Ponndorf–Verley reduction, though the reaction with Gd(OPr^i)$_3$ or Yb(OPr^i)$_3$ formed a small amount of butanal. This reactivity of the trialkoxides is different from that of the lanthanoids alkoxide dihalides, which act as catalysts for the Meerwein–Ponndorf–Verley–Oppenauer reaction.[9] It is known that the heavy lantanoid alkoxides, which are more Lewis-acidic than the light ones, show catalytically higher activities than do the light lanthanoids in the Meerwein–Ponndorf–Verley reduction,[8,10] whereas in

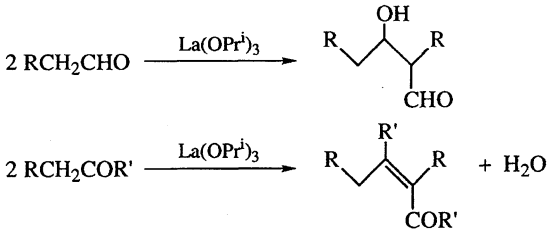


Scheme 1.

Table 1. $Ln(OPr^i)_3$-Catalyzed Aldol Addition of Aldehydes[a)]

Aldehyde	Catalyst	Solvent	Temp	Time	Products[b)]/%	
			°C	min	**1**	**2**
Butanal	$NaOPr^i$	*i*-PrOH	0	60	15	40
Butanal	$Al(OPr^i)_3$	*i*-PrOH	0	60	10	15
Butanal	$La(OPr^i)_3$	*i*-PrOH	−20	120	71	2
Butanal	$La(OPr^i)_3$	*i*-PrOH	0	20	82 (73 : 27)[c)]	1
Butanal	$Gd(OPr^i)_3$	*i*-PrOH	0	20	76	1
Butanal	$Yb(OPr^i)_3$	*i*-PrOH	0	20	67 (77 : 23)[c)]	1
Butanal	$La(OPr^i)_3$	THF	0	60	67	7
Butanal	$La(OPr^i)_3$	Toluene	0	60	38	16
Butanal	$La(OPr^i)_3$	THF	60	30	73 (55 : 45)[c)]	7
2-Methylpropanal	$La(OPr^i)_3$	*i*-PrOH	0	60	48	
3-Methylbutanal	$La(OPr^i)_3$	*i*-PrOH	0	60	64	7
Hexanal	$La(OPr^i)_3$	*i*-PrOH	0	60	77	4
	$La(OPr^i)_3$	THF	60	30	80	12
3,5,5-Trimethylhexanal	$La(OPr^i)_3$	*i*-PrOH	0	60	54	13
Heptanal	$La(OPr^i)_3$	*i*-PrOH	0	60	72 (59 : 41)[c)]	5
	$La(OPr^i)_3$	THF	60	30	70	17
Octanal	$La(OPr^i)_3$	*i*-PrOH	0	60	67	7
Nonanal	$La(OPr^i)_3$	*i*-PrOH	0	60	62	10
Decanal	$La(OPr^i)_3$	THF	60	60	59	15
Undecanal	$La(OPr^i)_3$	*i*-PrOH	0	120	53	19
$PhCH_2CH_2CHO$	$La(OPr^i)_3$	*i*-PrOH	0	60	55	8

a) The reaction was carried out using a mixture of the catalyst (0.1 mmol) and an aldehyde (5 mmol) in a solvent (5 cm^3), and the yield based on the starting aldehyde was determined by GLC using an internal standards. b) **1**; Aldol, **2**; α,β-Unsaturated aldehyde. c) The value shows the *threo–erythro* isomer ratio.



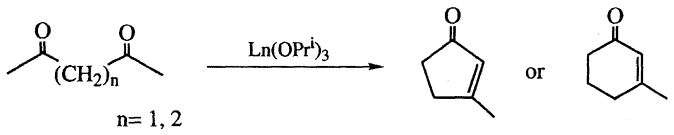
Scheme 2.

this aldol reaction the catalytic activity of $La(OPr^i)_3$ was higher than those of $Gd(OPr^i)_3$ and $Yb(OPr^i)_3$. Therefore, the high selectivity of $La(OPr^i)_3$ is ascribed to the high activity to the aldol reaction as well as to the low activity to the Meerwein–Ponndorf–Verley reduction. While aldol reactions are catalyzed by bases or acids, the lanthanoid propoxides are considered to be base catalysts in the above reactions. The basicity depends on the lanthanoid ion size[11] as well as the electronic effect of the ligands. Therefore, it is explainable that $La(OPr^i)_3$ shows higher activity than do the heavy lanthanoid triisopropoxides or than do the alkoxide dihalides. Interestingly, the reaction with $Ln(OPr^i)_3$ was much faster than that with $Al(OPr^i)_3$. This fact suggests that the basicity of $Ln(OPr^i)_3$ is much stronger than that of $Al(OPr^i)_3$. The reaction with $NaOPr^i$, which is a strong base, gave aldol adducts in unsatisfactory yields under these conditions in spite of the high conversion of butanal. Consequently, the basicity of $Ln(OPr^i)_3$ is considered to be suitable for the aldol addition reaction.

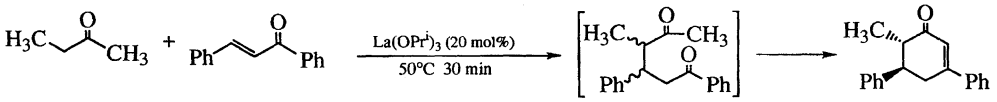
Generally, it is difficult to obtain the β-hydroxy aldehydes in good yields in the aldol reaction of aldehydes having a long alkyl chain, because they are liable to form condensation products in the presence of common bases.[12] On the other hand, the La catalyst exhibited good applicability to the aldol reaction of these aldehydes, which gave aldols in considerable yields under mild conditions (see Table 1).

Although ketones were less reactive than aldehydes in the aldol reaction with $Ln(OPr^i)_3$, the ketones susceptible to enolization gave dehydrated products of the aldols.[13] Cyclopentanone gave an α,β-unsaturated ketone in good yield under reflux in benzene (see Table 2 and Scheme 3). A similar reaction of cyclohexanone formed a β,γ-unsaturated ketone in good yield. The β,γ-unsaturated ketone is known to be a product of the aldol condensation with KOH.[14] The intramolecular aldol condensation of 2,5-hexanedione and 2,6-heptanedione also occurred to give cyclic unsaturated ketones in good yields (Scheme 4). Unfortunately, acyclic mono ketones, such as acetophenone, 3-pentanone, and 2-hexanone, gave the corresponding α,β-unsaturated ketones in low yields. The La catalyst in the course of these reactions turned into inorganic precipitates, which seemed to be $La(OH)_3$. The lanthanum hydroxide prepared from $LaCl_3$ with NaOH was inactive for the aldol reaction of cyclohexanone.

The catalytic activity of $Ln(OPr^i)_3$ in the reaction of cyclohexanone increased in the following order: La > Nd≥Gd≥Er≈Yb, suggesting that the isopropoxides act as



Scheme 3.



Scheme 4.

Table 2. Ln(OPr^i)$_3$-Catalyzed Aldol Condensation of Ketones[a]

Ketone	Ln(OPr^i)$_3$ Ln=	Solvent	Time h	Condensation product/%[b]
Cyclopentanone[c]	La	Benzene	5	72
Cyclohexanone[d]	La	Benzene[e]	1	12
	La	THF	1	29
	La	Benzene	1	65
	La	Benzene	5	79
	La	Toluene	1	60
	Nd	Benzene	1	54
	Gd	Benzene	1	50
	Er	Benzene	1	48
	Yb	Benzene	1	48
2,5-Hexanedione[f]	Nd	Benzene	4	63
2,6-Heptanedione[g]	Nd	Benzene	5	85
PhCOCH$_3$[h]	La	Benzene	2	19
	La[i]	Benzene	2	27

a) A mixture of Ln(OPr^i)$_3$ (0.1 mmol) and ketone (5 mmol) in a solvent (5 cm^3) was refluxed. b) The yield based on the starting ketone was determined by GLC using internal calibration standards. c) The product was 2-cyclopentylidenecyclopentanone. d) The product was 2-(2′-cyclohexenyl)cyclohexanone. e) At 60 °C. f) 3-Methyl-2-cyclopentenone was formed. g) 3-Methyl-2-cyclohexenone was formed. h) The product was 1,3-diphenyl-2-buten-1-one. i) MS 4A 1/16 (0.2 g) was added.

a base catalyst. This is consistent with the high reactivity of the cyclic- and di-ketones, which are easily enolizable.[15] The fast condensation reaction of these ketones results in the high yields, because the catalytic reaction precedes the above-mentioned deactivation of the catalyst.

The lanthanum catalyst is active for the intermolecular aldol condensation of 2,6-heptanedione, whose derivatives may be prepared by a Michael addition of ketones to α,β-unsaturated ketones. Since basic lanthanoid catalysts are known to be efficient for Michael additions of nitromethane and malonates,[16] we attempted Robinson-type annelation using Ln(OPr^i)$_3$. The reaction of chalcone with an excess of 2-butanone in the presence of La(OPr^i)$_3$ successfully proceeded at 50 °C, and gave *trans*-6-methyl-3,5-diphenyl-2-cyclohexen-1-one selectively (Scheme 5). However, this reaction did not form a detectable amount of the *cis*-isomer. This can possibly be ascribed to an isomerization of the *cis*-isomer in the presence of the lanthanum catalyst.[17] Since no Michael adduct was detected either, the intramolecular aldol condensation step seems to be far faster than the Michael reaction step.

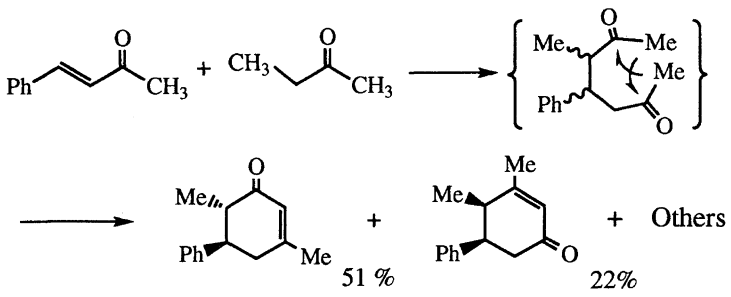
The catalytic activity of La(OPr^i)$_3$ was higher than those of the heavy lanthanoid propoxides as in the above-mentioned aldol reaction (see Table 3). The phenoxy lanthanum complex, Na$_3$[La(BINOL)$_3$]·H$_2$O·6THF (BINOLH$_2$ = 1,1′-bi-2-naphthol), and Al(OPr^i)$_3$, however, were catalytically inactive under these conditions. This fact suggests that the basicity of these compounds is insufficient to mediate the Robinson-type annelation. Interestingly, La(OPr^i)$_3$ was more effective than sodium isopropoxide, which is a strong base. The superiority of La(OPr^i)$_3$ to NaOPr^i was also found in the annelation reactions of other substrates (see Table 4). The catalytic superiority of La(OPr^i)$_3$ is possibly due to a cooperative effect of the Lewis acidity of the lanthanum cation, as suggested before.[3,4]

The catalytic activity of La(OPr^i)$_3$ was somewhat enhanced by the addition of a proper amount of Molecular Sieves 4A (MS 4A), and an almost quantitative yield (96% GC yield using *o*-terphenyl as internal standard and 77% isolated yield) was attained at 50 °C for 30 min. An analogous effect of MS 4A has been observed in the Oppenauer oxidation with La(OPr^i)$_3$.[6] One of the effects of MS4A is probably due to the removal of the water formed from the aldol condensation. However, the promotive effect was not

Table 3. Robinson Annelation of Chalcone with 2-Butanone[a]

Catalyst	Yield/%[b]
La(OPr^i)$_3$	82
Gd(OPr^i)$_3$	71
Yb(OPr^i)$_3$	67
Al(OPr^i)$_3$	< 1
NaOPr^i	69
Na$_3$La(BINOL)$_3$·H$_2$O·6THF[c]	< 1
La(OPr^i)$_3$–TBBP[d]	35
La(OPr^i)$_3$–MS4A[e]	95 (80)[f]
La(OPr^i)$_3$–MS4A[g]	85
La(OPr^i)$_3$–MS4A[h]	44
NaOPr^i–MS4A[e]	70

a) The reaction was carried out by heating a mixture of a metal alkoxide (0.2 mmol), chalcone (1 mmol) and 2-butanone (20 mmol) in toluene (5 cm^3) at 50 °C for 30 min. b) Determined by GLC using *o*-terphenyl as internal standard. c) BINOLH$_2$ = [1,1′ − binaphthyl]-2,2′-diol. d) 3,3′,5,5′-tetra-*t*-Butylbiphenyl-2,2′-diol (0.2 mmol) was added. e) MS 4A 1/16 (0.2 g) was used. f) Isolated yield. g) MS 4A (0.5 g) was used. h) MS 4A (0.2 g) and 2-butanone (2 mmol) were used.

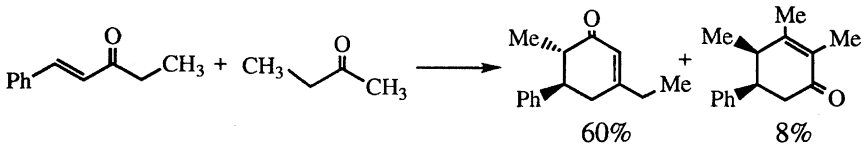


Scheme 5.

Table 4. Robinson-Type Annelation of α,β-Unsaturated Ketones with Saturated Ketones in the Presence of $La(OPr^i)_3$[a]

α,β-Unsaturated ketone	Saturated ketone	Catalyst	Substituted 2-cyclohexen-1-one	Yield/%[b]
PhCH=CHCOPh	$(CH_3)_2CHCOCH_3$	$La(OPr^i)_3$–MS4A	6,6-Dimethyl-3,5-diphenyl-	85 (72)[c]
	Acetone[d]	$La(OPr^i)_3$–MS4A	3,5-Diphenyl-	77
$PhCH=CHCOCH_3$	$PhCOCH_3$	$La(OPr^i)_3$–MS4A	3,5-Diphenyl-	68
	Acetone[d]	$La(OPr^i)_3$–MS4A	3-Methyl-5-phenyl-	63
		$NaOPr^i$		30
	Cyclohexanone	$La(OPr^i)_3$–MS4A	*trans*-4-Phenyl-4,4a,5,6,7,8-hexa-	83 (74)[c]
		$La(OPr^i)_3$	hydronaphthalen-2(3*H*)-one	71
$CH_3CH_2CH_2CH=CHCOCH_3$	$PhCOCH_3$	$La(OPr^i)_3$–MS4A	3-Phenyl-5-propyl-	89
		$La(OPr^i)_3$		82
		$NaOPr^i$		62
	Acetone[d]	$La(OPr^i)_3$–MS4A	3-Methyl-5-propyl-	60
$(CH_3)_2CHCH=CHCOCH_3$	$PhCOCH_3$	$La(OPr^i)_3$–MS4A	3-Phenyl-5-isopropyl-	81
$(CH_3)_2C=CHCOCH_3$	$PhCOCH_3$	$La(OPr^i)_3$–MS4A	5,5-Dimethyl-3-phenyl-	25
$CH_2=CHCOCH_3$	Cyclohexanone	$La(OPr^i)_3$–MS4A	4,4a,5,6,7,8-Hexahydro-	65
			naphthalen-2(3*H*)-one	
	$PhCOCH_3$	$La(OPr^i)_3$–MS4A	3-Phenyl-	35
		$La(OPr^i)_3$		23

a) The reaction was carried out by heating a mixture of an α,β-unsaturated ketone (1 mmol), saturated ketone (20 mmol), $La(OPr^i)_3$ (0.2 mmol) and MS 4A 1/16 (0.2 g) in toluene (5 cm^3) at 50 °C for 2 h. b) Determined by GLC using internal standard. c) Isolated yield. d) Acetone (5 cm^3)was used instead of toluene.



Scheme 6.

observed in the reaction with $NaOPr^i$.

The excess use of saturated ketones was important for the Robinson-type annelation. A decrease in the amount of 2-butanone resulted in the formation of nonvolatile oily products, which seemed to be oligomers of chalcone. The lanthanoid compounds are known to be active catalysts for the oligomerization of enones.[18] α,β-Unsaturated ketones having alkyl substituents underwent other type of side-reactions, such as cyclodimerization and self-Robinson annelation. The former reaction has been reported separately.[17] Concerning the latter reaction, *cis*-5-isopropyl-3-methyl-4-(2-methyl-1-propenyl)-2-cyclohexen-1-one was isolated from the reaction of 5-methyl-3-hexen-2-one in 18% yield.

The Robinson-type annelation was applicable to several α,β-unsaturated ketones in the presence of an excess of saturated ketones, and gave the corresponding 2-cyclohexen-1-ones in considerable yields (see Table 4). The reactions were completed in 2 h at 50 °C, though the prolonged reaction time reduced the yield. Chalcone reacted with 3-methyl-2-butanone to give 6,6-dimethyl-3,5-diphenyl-2-cyclohexen-1-one in good yield (Scheme 6). The annelation of 4-phenyl-3-buten-2-one with 2-butanone formed *trans*-3,6- and *cis*-3,4dimethyl-5-phenyl-2-cyclohexen-1-ones. A similar reaction of 1-phenyl-1-penten-3-one mostly formed *trans*-3-ethyl-6-methyl-5-phenyl-2-cyclohexen-1-one. These results indicate that the methylene carbon of 2-butanone selectively attacks at the β-carbon of the unsaturated ketones in the stage of Michael addition, and that in the next stage the methyl group is more susceptible to aldol addition than the methylene group.

Experimental

General Comments. All operations were performed using Schlenk-tube techniques under an argon atmosphere. 2-Propanol was distilled from a mixture of aluminum triisoproxide and calcium hydride. Benzene, toluene and THF were distilled from sodium benzophenone ketyl. The lanthanoid tri-isopropoxides,[8] $La(OH)_3$,[19] and $Na_3[La(BINOL)_3]\cdot H_2O\cdot 6THF$,[3] were prepared according to the published procedures. Though it has been reported that the propoxides prepared from the metals with the alcohol are oxide isopropoxides,[20] a disproof has also been reported.[21] Therefore, we write the compounds as triisopropoxides. Molecular Sieves 4A 1/16 (nakarai tesque Inc.) were dried at 300 °C for 2 h before use. Other solid chemicals were used as received. The other liquid organic chemicals were dried with an appropriate drying agent and purified by distillation before use. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-GX 270 spectrometer at 270 and 67.8 MHz, respectively. Gaschromatographic analyses were performed on a Yanagimoto G-2800 or a Shimadzu GC-14B with a flame-ionization detector using durene, naphthalene or *o*-terphenyl as an internal standard. Infrared spectra were recorded on a Perkin–Elmer 1600. Column chromatographic purifications were performed with ICN silica gel using ICN nylon-foil tubing.

Aldol Reaction of Aldehydes. The following example provides a general procedure for the aldol reaction of aldehydes. A solution of $La(OPr^i)_3$ (63 mg, 0.2 mmol) in 5 cm^3 of THF was cooled to 0 °C. Butanal (0.72 g, 10 mmol) was added to the mixture, and the mixture was stirred at 0 °C for 1 h. The solution was treated with 0.2 M HCl (10 cm^3, 1 M = 1 mol dm^{-3}) at 0 °C, and then extracted with ether (15 $cm^3 \times 3$). After the addition of a small amount of durene as an internal calibrant, the combined ether layers were washed with 2% $NaHCO_3$ (5 cm^3) and brine (5 cm^3). After drying with Na_2SO_4 and filtration, the ether solution was analyzed by GC using a capillary column (J & W Fused Silica Capillary Column, DB-17, 30 m×0.254 mm, 0.25 μm). For the purpose of reduction, a solution without durene was prepared. After concentration in a vacuum, the resulting viscous oil (0.7 g) was dissolved in ethanol (5 cm^3). The mixture was added dropwise to a stirring solution of $NaBH_4$ (0.57 g, 15 mmol) in ethanol (5 cm^3) at 0 °C. After stirring for 20 h at room temperature, the mixture was treated with 3 M HCl (5 cm^3) and then extracted with ether (15 $cm^3 \times 3$). The extracts were combined and washed with brine (5 $cm^3 \times 2$). After drying with Na_2SO_4 and filtration, the extract was concentrated under vacuum to give a viscous oil. The oil was distilled under vacuum to give 0.45 g of 2-ethyl-1,3-hexanediol,[22] (Yield 62%) as a colorless oil: Bp 100—105 °C/3×10^2 Pa; ^1H NMR ($CDCl_3$) δ = 0.94 (6H, m), 1.3—1.5 (7H, m), 3.1 (2H, bs), 3.6—3.9 (5H, m); ^{13}C NMR ($CDCl_3$) δ = 11.6, 12.2, 13.9, 14.0, 18.3, 18.9, 19.4, 21.5, 35.6, 37.9, 46.3, 46.5, 63.5, 64.2, 74.6, 76.0; IR (neat) 3350 (OH), 1160, and 1036 cm^{-1}. The derivatization of the aldol product with 2,4-dinitrophenylhydazine was carried out as follows. A mixture of the oily product (0.7 g), 2,4-dinitrophenylhydazine (0.99 g, 5 mmol) and concd H_2SO_4 (4 cm^3) in ethanol (40 cm^3), was heated at 60 °C for 1 h. Concentration of the mixture to ca. 20 cm^3 and standing for 40 h at room temperature afforded the hydrazone of (*E*)-2-ethyl-2-hexenal as orange crystals (0.47 g, 31%): Mp 122—124 °C; ^1H NMR ($CDCl_3$) δ = 0.97 (3H, t, *J* = 7.3 Hz, CH_3), 1.12 (3H, t, *J* = 7.3 Hz, CH_3), 1.50 (2H, tq, *J* = 7.3 and 7.2 Hz, CH_2), 2.28 (2H, dq, *J* = 7.4 and 7.2 Hz, CH_2), 2.49 (2H, q, *J* = 7.3 Hz, CH_2), 5.91 (1H, t, *J* = 7.4 Hz, =C*H*), 7.66 (1H, s, N=C*H*), 7.92 (1H, d, *J* = 9.8 Hz), 8.30 (1H, dd, *J* = 9.8 and 2.6 Hz), 9.13 (1H, d, *J* = 2.6 Hz), 11.1 (1H, s, N*H*); ^{13}C NMR ($CDCl_3$) δ = 13.5, 13.8, 19.3, 22.4, 30.5, 116.5, 123.6, 129.1, 129.9, 137.8, 139.1, 142.8, 145.1, 152.5; IR (KBr) 1620, 1330, 1220 cm^{-1}.

Aldol Reaction of Hexanal. The reaction of hexanal (1.0 g, 10 mmol) was carried out in a similar way. The reduction of the oily product with $NaBH_4$ (0.57 g, 15 mmol) gave 0.53 g (53%) of 2-butyl-1,3-octanediol as a viscous oil: Bp 110—114 °C / 2×10^2 Pa; ^{13}C NMR ($CDCl_3$) δ = 13.9, 14.0, 22.3, 22.6, 22.9, 24.9, 25.4, 26.0, 28.3, 29.5, 30.8, 31.3, 31.8, 33.2, 34.0, 35.6, 48.8, 48.9, 64.2, 64.9, 75.6, 76.0.

Aldol Condensation of Ketones. The following example provides a general procedure for the aldol condensation of ketones. A mixture of cyclohexanone (0.49 g, 5 mmol) and $La(OPr^i)_3$ (32 mg, 0.1 mmol) in benzene (5 cm^3) was refluxed for 5 h. The mixture was treated with 2 M HCl (5 cm^3), and then extracted with ether (10 $cm^3 \times 2$). After the addition of a small amount of durene as an internal calibrant, the combined extracts were washed with 5% $NaHCO_3$ (5 cm^3) and an brine (5 cm^3). After drying with Na_2SO_4 and filtration, the ether solution was analyzed by GC using a capillary column (Chrompack Fused Silica Capillary Column, CP-Sil 8 CB, 60 m×0.25 mm, 0.25 μm). The solution was concentrated under vacuum. The residue was distilled under vacuum to give 0.27 g (61%) of 2-(1-cyclohexenyl)cyclohexanone:[23,24] Bp 115—120 °C / 2×10^2 Pa; ^1H NMR ($CDCl_3$) δ = 1.5—2.6 (16H, m), 2.88 (1H, dd, *J* = 10.5 and 5.1 Hz), 5.43 (1H, s); ^{13}C NMR ($CDCl_3$) δ = 22.3, 22.7, 24.7, 25.2, 27.2, 27.5, 31.7, 41.9, 58.6, 123.5, 135.8, 211.2; IR (neat) 1712 cm^{-1} (CO).

2-Cyclopentylidenecyclopentanone.[24] The title compound was isolated from the reaction of cyclopentanone by distillation in 55% yield. Bp 100—105 °C / 2×10^2 Pa; ^1H NMR ($CDCl_3$) δ = 1.55—1.65 (4H, m), 1.8—1.9 (2H, m), 2.2—2.3 (4H, m), 2.45—2.5 (2H, m), 2.7 (2H, m); ^{13}C NMR ($CDCl_3$) δ = 19.1, 24.2, 25.9, 28.5, 31.5, 33.3, 38.8, 126.9, 157.5, 206.2.

Robinson Annelation of Chalcone with 2-Butanone. This reaction provides a general procedure for the Robinson annelation. To a mixture of $La(OPr^i)_3$ (63 mg, 0.2 mmol), Molecular Sieves 4A 1/16 (0.2 g) and *o*-terphenyl as internal calibrant in toluene (5 cm^3) was added successively chalcone (0.21 g, 1 mmol) and 2-butanone (1.44 g, 20 mmol). After being stirred for 0.5 h at 50 °C, the mixture was treated with 1 M HCl (10 cm^3). The solution was extracted with either (10 $cm^3 \times 2$). The combined organic layers were washed with 5% $NaHCO_3$ (5 cm^3) and brine (5 cm^3), and then dried over Na_2SO_4. A small portion of the solution was analyzed by GC using a capillary column (Chrompack Fused Silica Capillary Column, CP-Sil 8 CB, 60 m×0.25 mm, 0.25 μm). The remainder was concentrated under vacuum, and the residue was chromatographed on a dry silica column (CH_2Cl_2) to afford colorless crystals (0.21 g, 80%) of *trans*-6-methyl-3,5-diphenyl-2-cyclohexen-1-one: Mp 75—79 °C; ^1H NMR ($CDCl_3$) δ = 6.50 (1H, s, =C*H*), 2.9—3.1 (3H, m, C^4H_2 and C^5H), 2.64 (1H, dq, *J* = 12.3 and 6.5 Hz, C^6H), 0.99 (3H, d, *J* = 6.5 Hz, CH_3), 7.2—7.5 (10H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 12.8, 37.0, 46.0, 48.6, 124.6, 127.0, 126.0, 127.5, 128.8, 129.9, 138.2, 142.9,156.9, 200.8; IR (KBr) 1668 cm^{-1} (C=O). Anal. Found: C, 87.28; H, 7.49%. Calcd for $C_{19}H_{18}O$: C, 87.02; H, 7.25%.

3,5-Diphenyl-2-cyclohexen-1-one.[25] The title compound was prepared by the reaction of chalcone (0.21 g, 1 mmol) in acetone (5 cm^3) in the presence of a mixture of $La(OPr^i)_3$ (63 mg, 0.2 mmol) and MS 4A 1/16 (0.2 g) at 50 °C for 2 h. The GC and isolated yields were 77 and 63%, respectively. This compound was also obtained from the reaction of $PhCH{=}CHCOCH_3$ (0.15 g, 1 mmol) with acetophenone (1.2 g, 10 mmol) in toluene (5 cm^3) in 52% isolated yield. Mp 89—90 °C; ^1H NMR ($CDCl_3$) δ = 6.57 (1H, d,

J = 2.2 Hz, =C*H*), 2.70 (1H, dd, J = 16.2 and 12.1 Hz, C^4H^a), 2.79 (1H, dd, J = 16.2 and 4.9 Hz, C^4H^e), 3.46 (1H, m, C^5H), 2.91 (1H, ddd, J = 17.6, 10.4, and 2.2 Hz, C^6H^a), 3.08 (1H, dd, J = 17.6 and 4.8 Hz, C^6H^e), 7.2—7.5 (10H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 36.3, 41.0, 44.0, 125.1, 126.1, 126.8, 127.1, 128.8, 130.1, 138.4, 143.2, 158.6, 199.0; IR (KBr) 1652 cm^{-1} (C=O).

6,6-Dimethyl-3,5-diphenyl-2-cyclohexen-1-one. This compound was prepared in a similar manner as described for the reaction of chalcone with 2-butanone, and isolated by recrystallization of the reaction mixture from methanol as colorless crystals (72%): Mp 111—112 °C; ^{1}H NMR ($CDCl_3$) δ = 6.48 (1H, s, =C*H*), 2.95 (1H, m, C^4H^a), 3.16—3.3 (2H, m, C^4H^e and C^5H), 1.06 (3H, s, CH_3), 1.08 (3H, s, CH_3), 7.2—7.6 (10H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 19.5, 23.1, 31.8, 44.8, 50.8, 123.7, 126.1, 127.1, 128.2, 128.8, 129.1, 130.0, 138.2, 140.5, 156.8, 204.3; IR (KBr) 1649 cm^{-1} (C=O). Anal. Found; C, 87.11; H, 7.42%. Calcd for $C_{20}H_{20}O$: C, 86.96; H, 7.25%.

3-Methyl-5-phenyl-2-cyclohexen-1-one.[26] Mp 20—22 °C; ^{1}H NMR ($CDCl_3$) δ = 5.94 (1H, s, =C*H*), 2.4—2.7 (4H, m, C^4H_2 and C^6H_2), 3.46 (1H, m, C^5H), 1.96 (3H, s, CH_3), 7.2—7.4 (5H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 24.2, 38.8, 40.6, 43.7, 126.4, 126.6, 126.8, 128.6, 143.2, 161.5, 198.7; IR (neat) 1660 cm^{-1} (C=O).

3-Phenyl-2-cyclohexen-1-one.[27] Mp 64—65 °C; ^{1}H NMR ($CDCl_3$) δ = 6.36 (1H, s, =C*H*), 2.46 (2H, t, J = 6.5 Hz, C^4H_2), 2.12 (2H, tt, J = 6.5 and 6.0 Hz, C^5H_2), 2.74 (2H, t, J = 6.0 Hz, C^6H_2), 7.35 (3H, m, *m*- and *p*-*Ph*), 7.47 (2H, m, *o*-*Ph*); ^{13}C NMR ($CDCl_3$) δ = 22.5, 27.7, 36.9, 125.0, 125.7, 128.4, 129.6, 138.4, 159.3, 199.1; IR (KBr) 1653 cm^{-1} (C=O).

3-Phenyl-5-propyl-2-cyclohexen-1-one.[26] Liquid; ^{1}H NMR ($CDCl_3$) δ = 6.38 (1H, d, J = 1.8 Hz, =C*H*), 2.1—2.2 (2H, m), 2.43 (1H, m, C^5H), 2.57 (1H, m), 2.82 (1H, m), 1.3—1.5 (4H, m, CH_2CH_2), 0.93 (3H, t, J = 6.9 Hz, CH_3), 7.25—7.60 (5H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 14.1, 19.7, 34.8, 34.9, 38.0, 43.6, 125.2, 126.1, 128.7, 129.9, 138.9, 159.1, 200.0; IR (neat) 1661 cm^{-1} (C=O).

3-Methyl-5-propyl-2-cyclohexen-1-one.[26] Liquid; ^{1}H NMR ($CDCl_3$) δ = 5.86 (1H, s, =C*H*), 2.0—2.5 (5H, m, C^4H_2, C^5H, and C^6H_2), 1.3—1.4 (4H, m, *propyl* CH_2CH_2), 1.96 (3H, s, CH_3), 0.91 (3H, t, J = 7.3 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ = 14.1, 19.6, 24.4, 34.7, 37.7, 38.0, 43.4, 126.5, 161.9, 200.0; IR (neat) 1668 (C=O), 1625 cm^{-1} (C=C).

5,5-Dimethyl-3-phenyl-2-cyclohexen-1-one.[26,28] Liquid; ^{1}H NMR ($CDCl_3$) δ = 6.39 (1H, s, =C*H*), 2.31 (2H, s, C^4H_2), 2.6 (2H, s, C^6H_2), 1.11 (6H, s, CH_3), 7.3—7.5 (5H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 28.3, 33.6, 42.2, 50.9, 124.3, 126.6, 128.7, 129.9, 139.0, 157.5, 199.7; IR (neat) 1660 cm^{-1} (C=O).

4,4a,5,6,7,8-Hexahydronaphthalen-2(3*H*)-one.[29] Liquid; ^{1}H NMR ($CDCl_3$) δ = 5.82 (1H, s, =C*H*), 1.2—2.5 (13H, m); ^{13}C NMR ($CDCl_3$) δ = 25.6, 27.0, 29.2, 34.5, 35.6, 36.5, 38.0, 124.8, 167.5, 200.2; IR (neat) 1665 cm^{-1} (C=O).

***trans*-4-Phenyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one.**[26,30] Mp 82—83 °C; ^{1}H NMR ($CDCl_3$) δ = 5.92 (1H, s, =C*H*), 2.90 (1H, ddd, J = 13.5, 9.6, and 4.3 Hz), 2.64 (1H, dd, J = 15.9 and 13.5 Hz, C^6H^a), 2.49 (1H, dd, J = 15.9 and 4.3 Hz, C^6H^e), 2.5 (2H, m), 2.23 (1H, m), 1.7—1.9 (3H, m), 1.3—1.5 (2H, m), 1.05 (1H, m), 7.1—7.4 (5H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 25.4, 26.5, 32.3, 35.7, 44.0, 44.8, 47.7, 124.6, 126.9, 127.5, 128.7, 142.6, 166.0, 198.9; IR (KBr) 1664 cm^{-1} (C=O).

***cis*-5-Isopropyl-3-methyl-4-(2-methyl-1-propenyl)-2-cyclohexen-1-one.**[31] Liquid; ^{1}H NMR ($CDCl_3$) δ = 5.75 (1H, s, =C^2H), 3.37 (1H, dd, J = 9.6 and 4.0 Hz, C^4H), 1.5—1.6 (1H, m, C^5H), 2.18 (1H, dd, J = 18.7 and 10.3 Hz, C^6H^a), 2.31 (1H, dd, J = 18.7 and 5.4 Hz, C^6H^e), 1.92 (3H, s, CH_3), 5.06 (1H, d, J = 9.5 Hz, *proenyl* =C*H*), 1.78 (3H, s, CH_3), 1.69 (3H, s, CH_3), 1.5—1.6 (1H, m, $CHMe_2$) 0.92 (3H, d, J = 6.4 Hz, CH_3), 0.87 (3H, d, J = 6.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ = 18.6, 20.5, 20.6, 26.2, 24.1, 29.6, 32.6, 44.4, 48.2, 116.4, 125.5, 136.8, 160.2, 199.4; IR (neat) 1661 cm^{-1} (C=O).

***trans*-3,6-Dimethyl-5-phenyl-2-cyclohexen-1-one.**[32] Liquid; ^{1}H NMR ($CDCl_3$) δ = 5.96 (1H, s, =C*H*), 2.43 (1H, dd, J = 18.4 and 4.7 Hz, C^4H^e), 2.5—2.6 (2H, m, C^4H^a and C^6H), 2.91 (1H, ddd, J = 11.5, 11.5, and 4.7 Hz, C^5H), 1.95 (1H, s, CH_3), 0.93 (3H, d, J = 7.0 Hz, CH_3), 7.2—7.4 (5H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 12.5, 23.7, 39.9, 45.5, 48.3, 126.0, 126.7, 127.2. 128.5, 142.8, 159.6, 200.6; IR (neat) 1663 cm^{-1} (C=O).

***cis*-3,4-Dimethyl-5-phenyl-2-cyclohexen-1-one.** Liquid; ^{1}H NMR ($CDCl_3$) δ = 5.91 (1H, s, =C*H*), 3.53 (1H, ddd, J = 14.5, 4.2, and 4.2 Hz, C^5H), 2.84 (1H, dd, J = 16.7 and 4.2 Hz, C^6H^a), 2.45—2.55 (2H, m, C^4H and C^6H^e), 2.03 (3H, s, CH_3), 0.85 (3H, d, J = 7.3 Hz, CH_3), 7.2—7.4 (5H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 12.0, 23.0, 36.1, 43.5, 41.2, 125.8, 126.8, 127.4, 128.5, 141.6, 167.6, 199.2; IR (neat) 1664 cm^{-1} (C=O).

***trans*-3-Ethyl-6-methyl-5-phenyl-2-cyclohexen-1-one.** Liquid; ^{1}H NMR ($CDCl_3$) δ = 5.96 (1H, s, =C*H*), 2.44 (1H, dd, J = 18.1 and 4.9 Hz, C^4H^e), 2.55—2.6 (2H, m, C^4H^a and C^6H), 2.91 (1H, ddd, J = 11.5, 11.3, and 4.9 Hz, C^5H), 2.23 (2H, q, J = 7.4 Hz, CH_2CH_3), 1.10 (3H, t, J = 7.4 Hz, CH_2CH_3), 0.94 (3H, d, J = 7.0 Hz), 7.2—7.4 (5H, m, *Ph*); ^{13}C NMR ($CDCl_3$) δ = 11.2, 12.7, 30.4, 38.8, 46.0, 48.6, 124.0, 126.8, 127.4, 128.6, 143.0, 164.8, 201.0; IR (neat) 1667 cm^{-1} (C=O).

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas "New Development of Rare Earth Complexes" No. 06241108 from The Ministry of Education, Science and Culture.

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