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A Novel Method for the Preparation of Acid-Sensitive Epoxides from Olefins with the Combined Use of Molecular Oxygen and Aldoacetal Catalyzed by a Cobalt(II) Complex

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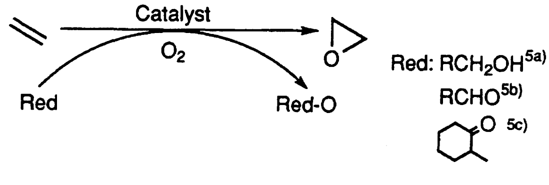
An efficient synthesis of acid-sensitive epoxides, such as chromene oxide or epoxide of γ,δ-unsaturated alcohol, was successfully achieved by the oxygenation of corresponding olefins with the combined use of an atmospheric pressure of molecular oxygen and aldoacetal catalyzed by a cobalt(II) complex coordinated with the 1,3-diketone ligand. The reactions proceeded under mild and neutral conditions, and the desired epoxides were obtained in good yields. Neither overoxidation nor decomposition of the formed epoxide was observed under the present reaction conditions. Furthermore, various silyl enol ethers and silyl ketene acetals, acid-sensitive compounds, were also smoothly monooxygenated into the corresponding α-hydroxy ketones and α-hydroxy carboxylic acid esters, respectively.

The epoxidation of olefins is one of the most important reactions in organic synthesis, because epoxides are useful synthetic intermediates, which can be regio- and stereoselectively converted into various oxygen-containing compounds.[1)] Peroxy acids are often employed as convenient oxidants[2a)] in the epoxidation of olefins. In these reactions, acid-sensitive epoxides often undergo decomposition caused by the co-produced carboxylic acids;[2b)] accordingly, much effort has been dedicated to developing the epoxidation of olefins under neutral conditions. Concerning this problem, the vanadium-catalyzed epoxidation of allylic alcohols with *t*-butyl hydroperoxide was performed under acid-free conditions, since only *t*-butyl alcohol was produced as a co-product of the oxidant.[3)] It was recently reported that dimethyldioxirane and its derivatives, prepared from ketones and potassium peroxomonosulfate, were also useful reagents for this purpose, because nonacidic compounds were formed during the epoxidation.[4)]

Our continuous study on the development of a useful and practical method for monooxygenation of olefinic compounds with molecular oxygen has been focused on finding a suitable reductant which would accept one oxygen atom from molecular oxygen to perform the reaction. It had already been reported from our laboratory that primary alcohols,[5a)] aldehydes,[5b)] or cyclic ketones[5c)] could be utilized as efficient reductants in the aerobic epoxidation of olefins catalyzed by transition-metal complexes (Scheme 1).

All of these reductants were converted into undesirable acidic compounds as the result of accepting one oxygen atom during the epoxidation reaction. Here, in place of the reductants mentioned above, aldoacetal, such as propionaldehyde diethyl acetal (**1**), was found to be a novel reductant in the aerobic epoxidation of olefins (Scheme 2).[6a)] It was confirmed that the acetal **1** was converted into the corresponding ester and alcohol, a nonacidic compound; the present epoxidation was therefore expected to proceed under neutral conditions.



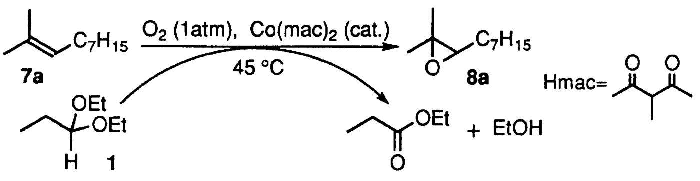
Scheme 1.

In this paper we disclose our full results concerning a practical procedure for synthesizing acid-sensitive epoxides by using molecular oxygen and propionaldehyde diethyl acetal (**1**) catalyzed by a cobalt(II) complex.[6b)] The present epoxidation procedure was also applied to the oxygenation of acid-sensitive compounds, such as silyl enol ethers[7a)] and silyl ketene acetals,[7b)] to afford α-hydroxy carbonyl compounds in good yields.

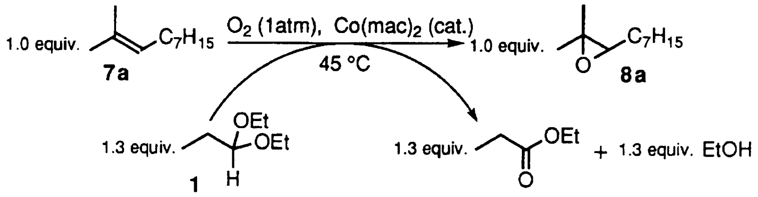
Results and Discussion

Aldoacetal as a Novel Reductant in the Aerobic Epoxidation of Olefins. In the first place, several aldoacetals were screened by taking the oxygenation of 2-methyl-2-decene (**7a**) with molecular oxygen in the presence of a catalytic amount of bis(2,4-pentanedionato)cobalt(II) (Co(acac)$_2$, **5a**) as a model reaction. When the reaction was carried out in a propionaldehyde diethyl acetal (**1**) solvent, it was found that the corresponding epoxide, 2,3-epoxy-2-methyldecane (**8a**), was obtained in 48% yield (Entry 1 in Table 1), while isobutyraldehyde diethyl acetal (**2**) or pivalaldehyde diethyl acetal (**3**) was a less effective solvent to promote the present aerobic epoxidation (Entries 2 and 3).

Next, the amount of consumed acetal **1** was measured in the epoxidation of 2-methyl-2-decene (**7a**) catalyzed by bis(3-methyl-2,4-pentanedionato)cobalt(II) (Co(mac)$_2$, **6a**). When the conversion of olefin **7a** was 55%, the corresponding epoxide **8a** was obtained in 53% yield by a GC analysis. It was found that a 1.3 molar

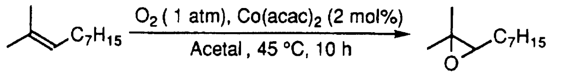


Scheme 2.



Scheme 3.

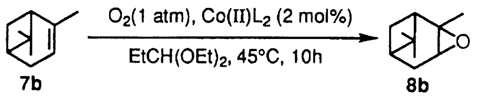
Table 1. Epoxidation of 2-Methyl-2-decene (**7a**) in Several Acetal[a)]



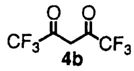
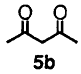
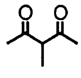
Entry	Acetal	Conversion/%[b)]	Yield/%[b)]
1	$\mathrm{EtCH(OEt)_2}$ **1**	52	48
2	*i*-$\mathrm{PrCH(OEt)_2}$ **2**	36	25
3	*t*-$\mathrm{BuCH(OEt)_2}$ **3**	25	18

a) Reaction conditions; 2-methyl-2-decene (**7a**) 3.2 mmol in 5.0 ml of acetal. b) Determined by GC analysis.

Table 2. Effect of Various Ligands on Yield of Epoxide[a)]



7b **8b**

Entry	Ligand(LH)	Conv./%[b)]	Yield/%[b)]
1	 **4b**	19	14
2	 **5b**	48	35
3	 **6b**	45	41

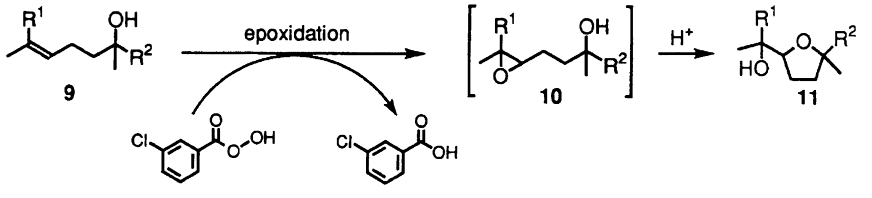
a) Reaction conditions; α-pinene (**7b**) 3.2 mmol in 20 ml of acetal **1**. b) Determined by GC analysis.

equivalent of acetal **1** was converted into the same molar equivalents of ethyl propionate and ethanol against the consumed olefin **7a**. The present epoxidation is illustrated in the following Scheme 3.[6c)] Thus, the acetal **1** was expected to act as a reductant to accept one oxygen atom from molecular oxygen; the acetal **1** is then converted into the corresponding ester and alcohol stoichiometrically. Because no further oxidation of the resulting ester and alcohol was observed, it is reasonable to assume that the present epoxidation proceeded under neutral conditions.

Further, various cobalt(II) complex catalysts were examined for the epoxidation of α-pinene (**7b**) with molecular oxygen propionaldehyde diethyl acetal (**1**) solvent. When the bis(1,1,1,5,5,5-hexafluoro-2,4-pentanedionato)cobalt(II) complex ($\mathrm{Co(hfa)_2}$, **4a**) was employed, the conversion of olefin **7a** was low (Entry 1 in Table 2). In contrast with cobalt(II) complex **4a**, when $\mathrm{Co(acac)_2}$ (**5a**) or $\mathrm{Co(mac)_2}$ (**6a**) was used as a catalyst, the corresponding epoxides were obtained in 35 or 41% yields (Entries 2 and 3). This difference in the catalytic activities between $\mathrm{Co(hfa)_2}$ (**4a**) and $\mathrm{Co(mac)_2}$ (**6a**) is explained as follows: Cobalt(II) complexes coordinated by 1,3-diketone ligands with electron-donating groups, such as $\mathrm{Co(mac)_2}$ (**6a**), were reported to show lower oxidation potentials compared with that of $\mathrm{Co(hfa)_2}$ (**4a**), which has an electron-withdrawing group in the ligand.[8)] It is therefore reasonable to consider that $\mathrm{Co(mac)_2}$ (**6a**) is quite easily oxidized into an active cobalt(III) complex by accepting molecular oxygen; the thus-formed active species behaves as an excellent oxidant to form the epoxides in good yields.

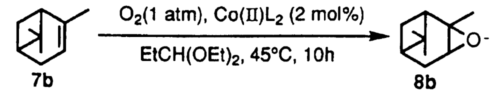
In the case of employing $\mathrm{Co(mac)_2}$ (**6a**) as a catalyst, the above-mentioned epoxidation reaction stopped halfway (Entry 1 in Table 3). Then, several additives were examined to improve the yield of epoxide; when Molecular Sieves 4A (MS4A) was used together, the yield of α-pinene oxide **8b** increased up to 93% (Entry 2).

Epoxidation of Various Olefins. According to the above-mentioned procedure for the combined use of the acetal **1** and molecular oxygen catalyzed by $\mathrm{Co(mac)_2}$ (**6a**), various trisubstituted olefins were smoothly monooxygenated into the corresponding epoxides in high yields (Entries 1, 2, and 4, Table 4). Similarly, tetracyclododecene **7c** was converted into the corresponding epoxide **8c** in high yield (Entry 3). Trisubstituted carbon-carbon double bonds in linalyl acetate (**7e**) and linalool methyl ether (**7f**) were also chemoselectively oxygenated into the corresponding monoepoxides **8e**, **f** in high to quantitative yields (Entries 5 and



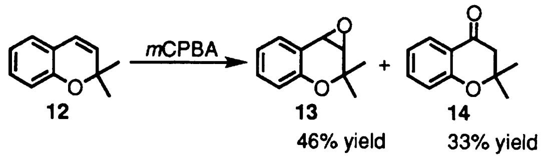
Scheme 4.

Table 3. Effect of Molecular Sieves 4A on Yield of Epoxide[a)]



Entry	Additive	Conv./%[b)]	Yield/%[b)]
1	None	45	41
2	MS4A[c)]	96	93

a) Reaction conditions; α-pinene (**7b**) 3.2 mmol in 20 ml of acetal **1**. b) Determined by GC analysis. c) Molecular Sieves 4A (500 mg) was added.



Scheme 5.

6). Olefins having an ester or silyloxy group were converted into the corresponding epoxides in good to high yields without any accompanying undesirable decomposition of these functional groups (Entries 7 and 8). The epoxidation of the olefinic alcohols, α-ionol (**7k**) and α-ionone (**7l**), proceeded smoothly to afford the corresponding epoxides **8k**, **l** in good yields (Entries 9—12). Other olefins, such as 2-methyl-1-decene (*exo*-terminal olefin) and cyclooctene (1,2-disubstituted olefin) were converted into the corresponding epoxides in 54 and 58% yields, respectively.

Preparation of Acid-Sensitive Epoxides. It was reported that when the epoxidation of γ,δ-unsaturated alcohol **9** was tried by using *m*-chloroperbenzoic acid (*m*CPBA), 2-(hydroxymethyl)tetrahydrofuran **11** was obtained in 84% yield as a major product via an acid-catalyzed intramolecular cyclization of the initially formed epoxide **10** (Scheme 4).[9a)] On the other hand, when γ,δ-unsaturated alcohol **9** was treated under the present reaction conditions together with a catalytic amount of 2,6-lutidine, the corresponding epoxide **10** was obtained in 76% yield and no cyclized product was detected.[9b)] It is thus expected that the present reaction can be applied to the preparation of various acid-sensitive epoxides, such as epoxide **10**.

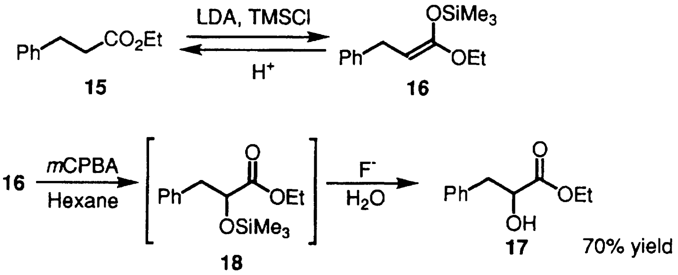
The above-mentioned procedure was successfully applied to various γ,δ-unsaturated alcohols, as expected. As shown in Table 5, acid-sensitive epoxides were obtained in good yields; however, no cyclized product via acid-catalyzed intramolecular cyclization of the initially generated epoxide was detected.

Since much interest has recently been focused on 3,4-epoxy-2,2-dimethylchroman derivatives having cytotoxic activity, the epoxidation of 2,2-dimethyl-2*H*-chromene (**12**) was attempted. However, the conventional preparative method using *m*CPBA was not suitable for this purpose.[11a)] For example, when *m*CPBA was employed, even under buffered conditions by sodium hydrogencarbonate, the corresponding epoxide **13** was obtained in only 46% yield along with ketone **14** (33% yield) (Scheme 5).

However, chromene oxide **13a** was obtained selectively in 77% yield without any accompanying ketone **14**[11b)] when chromene **12a** was oxygenated under the present reaction conditions using propionaldehyde diethyl acetal (**1**) as a reductant. According to the above-mentioned procedure, various chromene oxides were successfully prepared from the corresponding chromenes, as shown in Table 6. The epoxidation of 2,2-dialkyl-2*H*-chromenes **12a**—**c** proceeded smoothly to afford the corresponding epoxides in good yields (Entries 1—3). 2,2-Dimethyl-2*H*-chromenes having an ester or nitrile group **12d**—**f** were converted into the corresponding epoxides in good yields (Entries 4—6); no undesirable decomposition of epoxides was observed. Thus, an efficient method for the preparation of various types of acid-sensitive epoxides, such as the epoxide of γ,δ-unsaturated alcohol or chromene oxides, was established.

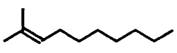
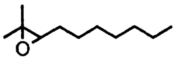
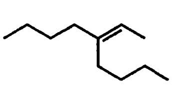
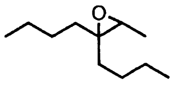
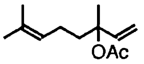
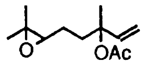
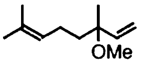
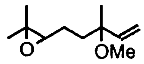
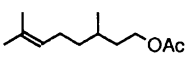
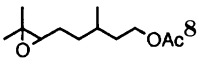
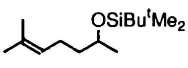
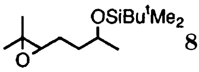
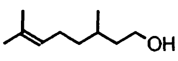
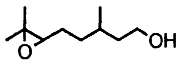
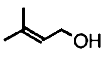
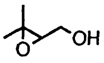
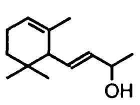
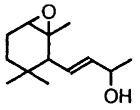
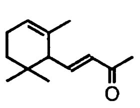
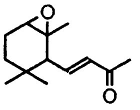
Oxygenation of Acid-Sensitive Enolates. It was reported that monooxygenation of silyl enol ethers or silyl ketene acetals, derived from the corresponding ketones or carboxylic acid esters and successive desilylation, afforded α-hydroxy carbonyl compounds,[12a)] which are useful intermediates for the synthesis of biologically active natural products.[12b)] Silyl ketene acetal is very sensitive, and is easily decomposed to the starting carboxylic acid ester; for example, the desired α-hydroxy carboxylic ester **17** was obtained in 70% yield,[12c,13)] when only *m*CPBA was employed as an oxidant in a hexane solution (Scheme 6).

On the other hand, silyl ketene acetal **16** was smoothly consumed under the present reaction conditions; after a treatment of the reaction mixture with tetrabutylammonium fluoride in THF solution, the corresponding α-hydroxy carbonyl compound **17** was obtained in 96% yield. It is reasonable to assume that the undesirable decomposition of the starting enolate **16**



Scheme 6.

Table 4. Epoxidation of Various Olefins Catalyzed by Co(mac)$_2^{a)}$

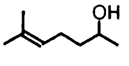
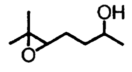
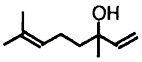
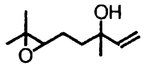
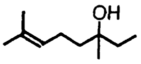
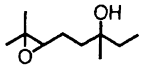
Entry	Olefin		Time/h	Epoxide		Conv./%$^{c)}$	Yield/%$^{c)}$
1$^{b)}$		7a	12		8a	99	97
2		7b	20		8b	96	93
3$^{b)}$		7c	10		8c	96	87
4$^{b)}$		7d	20		8d	98	88
5		7e	20		8e	100	82
6		7f	20		8f	100	Quant
7		7g	20		8g	100	82
8		7h	14		8h	100	91
9		7i	10		8i	100	82$^{d)}$
10		7j	10		8j	100	85$^{d)}$
11		7k	10		8k	100	60$^{e)}$
12		7l	21		8l	93	71

a) Reaction conditions; olefin 3.2 mmol, propionaldehyde diethyl acetal (**1**) 20 ml, Co(mac)$_2$ (**6a**) 0.065 mmol (2 mol%), and MS4A 500 mg. b) Propionaldehyde diethyl acetal (**1**) 5 ml. c) Determined by GC. d) Isolated yield. e) By-product was a complex mixture and not identified.

into carboxylic acid ester **15** did not take place under the present reaction conditions.

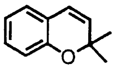
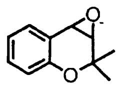
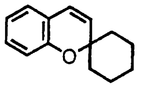
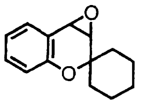
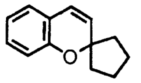
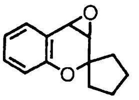
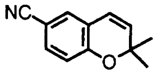
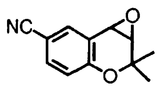
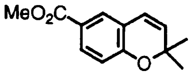
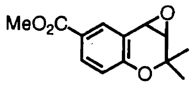
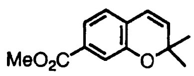
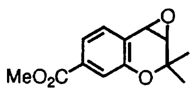
It is thus expected that the above-mentioned procedure can be applied to the oxygenation of various enolates, acid-sensitive compounds, into the corresponding α-hydroxy carbonyl compounds. As shown in Table 7, various enolates were oxygenated into the corresponding α-hydroxy carbonyl compounds by the combined use of molecular oxygen and aldoacetals **1**. Silyl enol ethers **16a**, **b** were smoothly oxygenated into the corresponding α-hydroxy ketones **17a**, **b** in good to high yields (Entries 1 and 2). Similarly, α'-hydroxy α,β-unsaturated ketone **17c** was selectively prepared in 87% yield from the silyl enol ether of α,β-unsaturated ketone

Table 5. Epoxidation of γ,δ-Unsaturated Alcohols[a)]

Entry	Olefin	Time/h	Epoxide	Yield/%[b)]
1	 **9a**	8	 **10a**	76[c)]
2	 **9b**	8	 **10b**	78
3	 **9c**	8	 **10c**	62

a) Reaction conditions; olefin 3.2 mmol, propionaldehyde diethyl acetal (**1**) 20 ml, Co(mac)$_2$ (**6a**) 0.065 mmol (2 mol%), MS4A 500 mg, 2,6-lutidine 1.28 mmol (Reference 10), 45 °C, and purified by column chromatography on aluminum oxide. b) Isolated yield. c) Diastereomer ratio 76 : 24.

Table 6. Preparation of Various Chromene Oxides[a)]

Entry	Olefin	Time/h	Epoxide	Yield/%[b)]
1	 **12a**	11	 **13a**	77
2	 **12b**	14	 **13b**	70
3	 **12c**	16	 **13c**	69
4	 **12d**	18	 **13d**	81
5	 **12e**	19	 **13e**	78
6	 **12f**	19	 **13f**	78

a) Reaction conditions; olefin 3.2 mmol, propionaldehyde diethyl acetal (**1**) 20 ml, Co(mac)$_2$ (**6a**) 0.065 mmol (2 mol%), MS4A 500 mg, 2,6-lutidine 1.28 mmol 45 °C, and purified by column chromatography on aluminum oxide. b) Isolated yield.

16c having two carbon-carbon double bonds (Entry 3).[12d)] Silyl ketene acetals **16d**, **e** were also smoothly oxygenated into the corresponding α-hydroxy or α-silyloxy carboxylic acid esters **17d**, **e** in high yields, respectively (Entries 4 and 5). The monooxygenation of enol ester, such as 1-acetoxy-1-cyclohexene (**16f**), also proceeded smoothly to afford the corresponding acetate of α-hydroxy ketone **17f** in 89% yield (Entry 6).

Conclusion

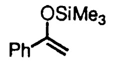
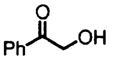
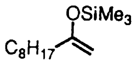
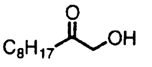
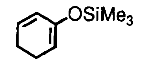
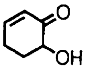
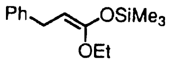
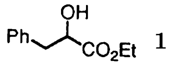
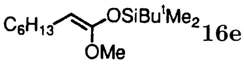
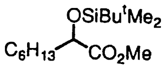
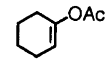
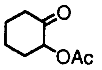
A convenient method for preparing acid-sensitive epoxides, such as chromene oxides or epoxides of γ,δ-unsaturated alcohols, was demonstrated by the aerobic oxygenation of the corresponding olefins using propionaldehyde diethyl acetal (**1**) as a reductant in the presence of a catalytic amount of bis(3-methyl-2,4-pentanedionato)cobalt(II) (Co(mac)$_2$, **6a**). The present procedure is also effective for the oxygenation of various acid-sensitive enolates into the corresponding α-hydroxy carbonyl compounds.

Experimental

General. (a) Spectrometers: The IR spectra were obtained by using a JASCO Model IR-700 infrared spectrometer on a liquid film on KBr. The ^{1}H NMR spectra were recorded with a JEOL Model FX270 spectrometer using CDCl$_3$ as solvent and with tetramethylsilane used as an internal standard.

(b) Chromatography: Column chromatography was conducted under silica gel (Daiso gel IR-60). Preparative TLC was carried out on silica gel (E. Merck, 13895). GC-analysis was performed on a Shimadzu GC-14A or GC-15A chromatograph using a glass capillary column (Shimadzu

Table 7. Oxygenation of Various Enolates[a]

Entry	Enolate		Time/h	Product		Yield/%[b,c]
1		**16a**	9		**17a**	83[d]
2		**16b**	10		**17b**	77[d]
3		**16c**	10		**17c**	87[d]
4		**16d**	10		**17d**	96[d]
5		**16e**	14		**17e**	95
6		**16f**	14		**17f**	89

a) Reaction conditions; olefin 3.2 mmol, propionaldehyde diethyl acetal (**1**) 20 ml, Co(mac)$_2$ (**6a**) 0.065 mmol (2 mol%), MS4A 500 mg, 45 °C. b) Isolated yield. c) Yield was based on starting enolates. d) After the oxygenation, tetrabutylammonium fluoride treatment was carried out.

CBP-10, 25 m); the peak areas were obtained with a Shimadzu chromatopack CR-5A.

(c) Reagent: Propionaldehyde diethyl acetal (**1**) was purchased from TCI (Tokyo Kasei Kogyo, Co., Ltd.) and used without further purification. Isobutyraldehyde diethyl acetal (**2**) and pivalaldehyde diethyl acetal (**3**) were prepared from the corresponding aldehydes and alcohols,[14] and purified by distillation.

Preparation of Cobalt(II) Complexes. Bis(2,4-pentanedionato)cobalt(II) (Co(acac)$_2$, **5a**) and bis(trifluoroacetylacetonato)cobalt(II) (Co(hfa)$_2$, **4a**) were purchased from TCI and dried under reduced pressure (1 mmHg, 1 mmHg=133.322 Pa) at 90 °C.

Bis(3-methyl-2,4-pentanedionato)cobalt(II) Complex (Co(mac)$_2$, 6a): A solution of 3-methyl-2,4-pentanedione (**6b**, 42.0 mmol, 4.80 g) in methanol (30 ml) was added to a solution of cobalt dichloride (21.0 mmol, 5.00 g) in water (80 ml) under a nitrogen atmosphere at room temperature. After stirring for 15 min, an aqueous solution of ammonia (25 ml) was added; mixture stirring was continued for 0.5 h at room temperature. Orange precipitates were collected by filtration under a nitrogen atmosphere, and dried in vacuo at 90 °C for 2 h to afford Co(mac)$_2$ (**6a**, 4.01 g, 67%).

General Procedure for Epoxidation of Olefins. Epoxidation of Citronellol (see Entry 9 in Table 4): Citronellol (**7i**, 512 mg, 3.2 mmol), Co(mac)$_2$ (**6a**, 19 mg, 0.065 mmol, 2.0 mol%) and Molecular Sieves 4A (500 mg) in propionaldehyde diethyl acetal (**1**, 20.0 ml) was stirred at 45 °C under an atmospheric pressure of oxygen. After stirring for 10 h the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica-gel (Hexane/AcOEt=1/1) to afford the corresponding epoxide (**8i**, 465 mg, 82% yield).

3,7-Dimethyl-6,7-epoxy-1-octanol (8i): ^{1}H NMR (CDCl$_3$) δ=0.93 (3H, d, J=6.26 Hz), 1.27 (3H, s), 1.30 (3H, s), 1.40—1.50 (2H, m), 1.51—1.80 (5H, m), 1.90 (1H, s), 2.70 (1H, t, J=6.10 Hz), 3.70 (2H, m); IR (neat) 3420, 2960, 2932, 2872, 1463 cm^{-1}.

2,3-Epoxy-2-methyldecane (8a): ^{1}H NMR (CDCl$_3$) δ=0.88 (3H, t, J=6.92 Hz), 1.26 (3H, s), 1.28 (10H, m), 1.31 (3H, s), 1.50 (2H, m), 2.71 (1H, t, J=6.27 Hz); IR (neat) 2925, 2850, 1465 cm^{-1}.

2,3-Epoxy-2,6,6-trimethylbicyclo[3.1.1.]heptane (8b): ^{1}H NMR (CDCl$_3$) δ=0.94 (3H, s), 1.29 (3H, s), 1.35 (3H, s), 1.62 (1H, d, J=12.0 Hz), 1.72 (1H, m), 1.85—2.05 (4H, m), 3.07 (1H, d, J=3.90 Hz); IR (neat) 2976, 2916, 2870, 1468, 1447, 1432, 1377 cm^{-1}.

2,3-Epoxy-(1α, 4α, 4aα, 5β, 8β, 8aα)-decahydro-1, 4:5,8-dimethanonaphthalene (8c): ^{1}H NMR (CDCl$_3$) δ=0.94 (3H, s), 1.29 (3H, s), 1.35 (3H, s), 1.62 (1H, d, J=12.0 Hz), 1.72 (1H, m), 1.85—2.05 (4H, m), 3.07 (1H, d, J=3.90 Hz); IR (neat) 2976, 2916, 2870, 1468, 1447, 1432, 1377 cm^{-1}.

3-Butyl-2,3-epoxyheptane (8d): ^{1}H NMR (CDCl$_3$) δ=0.88—0.95 (6H, m), 1.27 (3H, d, J=5.61 Hz), 1.26—1.67 (12H, m), 2.83 (1H, q, J=5.61 Hz); IR (neat) 2956, 2930, 2870, 1466 cm^{-1}.

1-(3,4-Epoxy-4-methylpentyl)-1-methylallyl Acetate (8e): ^{1}H NMR (CDCl$_3$) δ=1.20 (3H, d, J=6.92 Hz), 1.26 (3H, s), 1.30 (3H, s), 1.50—1.60 (4H, m), 2.00 (3H, s), 2.71 (1H, t, J=6.26 Hz), 5.15 (2H, m), 5.95 (1H, m); IR (neat) 2974, 2932, 1738, 1461, 1372, 1249 cm^{-1}.

6,7-Epoxy-3,7-dimethyl-3-methoxy-1-octene (8f): ^{1}H NMR (CDCl$_3$) δ=1.24 (3H, s), 1.26 (3H, s), 1.30 (3H, s), 1.50—1.60 (4H, m), 2.71 (1H, t, J=5.80 Hz), 3.15 (3H, s), 5.10—5.30 (2H, m), 5.70—5.80 (1H, m); IR (neat) 2976, 2934, 1644, 1462, 1078 cm^{-1}.

6,7-Epoxy-3,7-dimethyloctyl Acetate (8g): ^{1}H NMR (CDCl$_3$) δ=0.94 (3H, d, J=6.27 Hz), 1.27 (3H, s), 1.31 (3H, s), 1.40—1.60 (7H, m), 2.05 (3H, s), 2.70 (1H, t, J=6.06 Hz), 4.11 (2H, m); IR (neat) 2960, 2924, 2872, 1741, 1461, 1379, 1367, 1241 cm^{-1}.

2,3-Epoxy-6-(*t*-butyldimethylsilyloxy)-2-methyl-

heptane (8h): ^{1}H NMR ($CDCl_3$) δ=0.05 (6H, m), 0.89 (9H, s), 1.12 (3H, d, J=6.27 Hz), 1.27 (3H, s), 1.32 (3H, s), 1.45—1.68 (4H, m), 2.72 (1H, m), 3.86 (1H, m); IR (neat) 2960, 2932, 2872, 1463 cm^{-1}.

2,3-Epoxy-3-methyl-1-butanol (8j): ^{1}H NMR ($CDCl_3$) δ=1.27 (3H, s), 1.30 (3H, s), 2.10 (1H, br), 2.92 (2H, m), 3.13 (1H, m); IR (neat) 3420, 2960, 2875, 1460 cm^{-1}.

α-Ionol Oxide (8k): ^{1}H NMR ($CDCl_3$) δ=0.71 (1.5H, s), 0.74 (1.5H, s), 0.88 (3H, s), 0.95 (1H, m), 1.23 (3H, s), 1.26—1.30 (3H, m), 1.30—1.40 (1H, m), 1.79—1.98 (2H, m), 2.10 (1H, br), 3.06 (1H, m), 4.33 (1H, m), 5.53—5.64 (2H, m); IR (neat) 3420, 2976, 2935, 1644, 1460, 1078 cm^{-1}.

α-Ionoe Oxide (8l): ^{1}H NMR ($CDCl_3$) δ=0.75 (3H, s), 0.93 (3H, s), 1.02 (1H, m), 1.26 (3H, s), 1.41 (1H, m), 1.74—2.00 (2H, m), 2.10 (1H, d, J=9.89 Hz), 2.30 (3H, s), 3.11 (1H, m), 6.10 (1H, d, J=15.83 Hz), 6.73 (1H, dd, J=15.83 Hz, J=9.89 Hz); IR (neat) 2976, 2935, 1715, 1644, 1460, 1078 cm^{-1}.

General Procedure of Epoxidation of γ,δ-Unsaturated Alcohols and Chromene Derivatives. Epoxidation of 6-Methyl-5-hepten-2-ol (see Entry 1 in Table 5): 6-Methyl-5-hepten-2-ol (**9a**, 410 mg, 3.2 mmol), Co(mac)$_2$ (**6a**, 19 mg, 0.065 mmol, 2.0 mol%), 2,6-lutidine (137 mg, 1.28 mmol) and Molecular Sieves 4A (500 mg) in propionaldehyde diethyl acetal (**1**, 20.0 ml) was stirred at 45 °C under an atmospheric pressure of oxygen. After stirring for 8 h the solvent was removed under reduced pressure. The residue was purified by column chromatography on aluminum oxide (Hexane/AcOEt=2/1) to afford the corresponding epoxide (**10a**, 351 mg, 76% yield).

5,6-Epoxy-6-methyl-2-heptanol (10a): ^{1}H NMR ($CDCl_3$) δ=1.20 (1.5H, s), 1.22 (1.5H, s), 1.29 (3H, s), 1.32 (3H, s), 1.50—1.80 (4H, m), 2.28 (1H, br), 2.75 (1H, m), 3.84 (1H, m); IR (neat) 3420, 2960, 2933, 2875, 1460 cm^{-1}.

6,7-Epoxy-3,7-dimethyl-1-octen-3-ol (10b): ^{1}H NMR ($CDCl_3$) δ=1.27 (3H, s), 1.296 (3H, s), 1.305 (3H, s), 1.46—1.90 (4H, m), 2.73 (1H, m), 3.84 (1H, m), 5.06 (1H, d, J=10.88 Hz), 5.22 (1H, d, J=16.16 Hz), 5.90 (1H, m); IR (neat) 3420, 2976, 2934, 1644, 1462, 1078 cm^{-1}.

6,7-Epoxy-3,7-dimethyl-3-octanol (10c): ^{1}H NMR ($CDCl_3$) δ=0.90 (3H, t, δ=7.59 Hz), 1.16 (3H, s), 1.50 (2H, q, J=7.59 Hz), 1.55—1.71 (4H, m), 2.10 (1H, br), 2.74 (1H, m); IR (neat) 3420, 2962, 2932, 2874, 1461 cm^{-1}.

3,4-Epoxy-2,2-dimethylchroman (13a): ^{1}H NMR ($CDCl_3$) δ=1.25 (3H, s), 1.58 (3H, s), 3.50 (1H, d, J=4.29 Hz), 3.90 (1H, d, J=4.29 Hz), 6.79—6.95 (2H, m), 7.20—7.35 (2H, m); IR (neat) 2928, 2852, 1236, 752 cm^{-1}.

2,2-Cyclohexylidene-3,4-eopxychroman (13b): ^{1}H NMR ($CDCl_3$) δ=1.10—2.15 (10H, m), 3.48 (1H, d, J=4.28 Hz), 3.86 (1H, d, J=4.28 Hz), 6.38—6.94 (2H, m), 7.20—7.33 (2H, m); IR (neat) 2930, 2854, 1238, 752 cm^{-1}.

2,2-Cyclopentylidene-3,4-eopxychroman (13c): ^{1}H NMR ($CDCl_3$) δ=1.10—2.15 (8H, m), 3.46 (1H, d, J=3.95 Hz), 3.80 (1H, d, J=3.95 Hz), 6.74 (1H, d, J=8.57 Hz), 7.32 (1H, dd, J=8.57, 2.63 Hz), 7.44 (1H, d, J=2.63 Hz); IR (neat) 2928, 2854, 1481, 1241 cm^{-1}.

6-Cyano-3,4-epoxy-2,2-dimethylchroman (13d): ^{1}H NMR ($CDCl_3$) δ=1.25 (3H, s), 1.59 (3H, s), 3.54 (1H, d, J=4.29 Hz), 3.91 (1H, d, J=4.29 Hz), 6.86 (1H, d, J=8.24 Hz), 7.52 (1H, d, J=8.24 Hz), 7.65 (1H, s); IR (neat) 2922, 2852, 2226, 1462 cm^{-1}.

3,4-Epoxy-6-methoxycarbonyl-2,2-dimethylchroman (13e): ^{1}H NMR ($CDCl_3$) δ=1.28 (3H, s), 1.60 (3H, s), 3.52 (1H, d, J=4.28 Hz), 3.89 (3H, s), 3.95 (1H, d, J=4.28 Hz), 6.83 (1H, d, J=8.57 Hz), 7.93 (1H, dd, J=8.57, 2.31 Hz), 8.07 (1H, d, J=2.31 Hz); IR (neat) 2922, 2852, 1725, 1462 cm^{-1}.

3,4-Epoxy-7-methoxycarbonyl-2,2-dimethylchroman (13f): ^{1}H NMR ($CDCl_3$) δ=1.26 (3H, s), 1.59 (3H, s), 3.52 (1H, d, J=4.29 Hz), 3.89 (3H, s), 3.92 (1H, d, J=4.29 Hz), 7.41 (1H, d, J=7.91 Hz), 7.48 (1H, d, J=1.32 Hz), 7.61 (1H, dd, J=7.59, 1.32 Hz); IR (neat) 2922, 2852, 1730, 1463 cm^{-1}.

General Procedure of Oxygenation of Enolates. Oxygenation of 1-(Trimethylsilyloxy)styrene (see Entry 1 in Table 7): 1-(Trimethylsilyloxy)styrene (**16a**, 615 mg, 3.2 mmol), Co(mac)$_2$ (**6a**, 19 mg, 0.065 mmol, 2.0 mol%) and Molecular Sieves 4A (500 mg) in propionaldehyde diethyl acetal (**1**, 20.0 ml) was stirred at 45 °C under an atmospheric pressure of oxygen. After stirring for 9 h the solvent was removed under reduced pressure. To a solution of crude product in aqueous THF was successively added 1 M-tetrabutylammonium fluoride (1 M=1 mol dm^{-3}) in a THF solution (5.0 ml, 5.0 mmol) at room temperature. After stirring for 3 h the reaction mixture was extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate. Subsequently, the solvent was removed and the crude product was purified by silica-gel TLC (Hexane/AcOEt=1/1) to give 2-hydroxyacetophenone (**17a**) (362 mg, 83% yield).

2-Hydroxyacetophenone (17a): Mp 87—89 °C; ^{1}H NMR ($CDCl_3$) δ=4.88 (2H, s), 7.51 (2H, m), 7.64 (1H, m), 7.95 (2H, m); IR (KBr) 3064, 2932, 2898, 1686, 1599, 1450 cm^{-1}.

1-Hydroxy-2-decanone (17b): ^{1}H NMR ($CDCl_3$) δ=0.90—1.10 (14H, m), 2.48 (2H, m), 3.88 (2H, m); IR (neat) 1740, 1454, 1218 cm^{-1}.

6-Hydroxy-2-cyclohexen-1-one (17c): ^{1}H NMR ($CDCl_3$) δ=1.71—2.63 (4H, m), 4.19 (1H, m), 6.02 (1H, m), 7.00 (1H, m); IR (neat) 2951, 1686, 1390, 1218 cm^{-1}.

Ethyl 2-Hydroxy-3-phenylpropanoate (17d): ^{1}H NMR ($CDCl_3$) δ=1.30 (3H, t, J=7.00 Hz), 1.90—2.00 (1H, m), 2.10—2.20 (1H, m), 2.35 (2H, q, J=7.00 Hz), 2.80 (2H, m), 4.22 (1H, m), 7.15—7.30 (5H, m); IR (neat) 1737, 1454, 1218 cm^{-1}.

Methyl 2-(*t*-Butyldimethylsilyloxy)octanoate (17e): ^{1}H NMR ($CDCl_3$) δ=0.40 (6H, s), 0.70 (9H, s), 0.89 (3H, t, J=7.00 Hz), 1.20—1.83 (10H, m), 3.79 (3H, s), 4.21 (1H, m); IR (neat) 1740, 1454, 1218 cm^{-1}.

2-Acetoxycyclohexanone (17f): ^{1}H NMR ($CDCl_3$) δ=1.54—2.56 (6H, m), 2.15 (3H, s), 5.19 (1H, m); IR (neat) 1738, 1460, 1371, 1218 cm^{-1}.

References

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