Solvent Assisted Oxy-Cope Rearrangement of Diastereomeric 1,5-Hexadien-3-ols. A New Industrial Process for Polyprenyl Ketones

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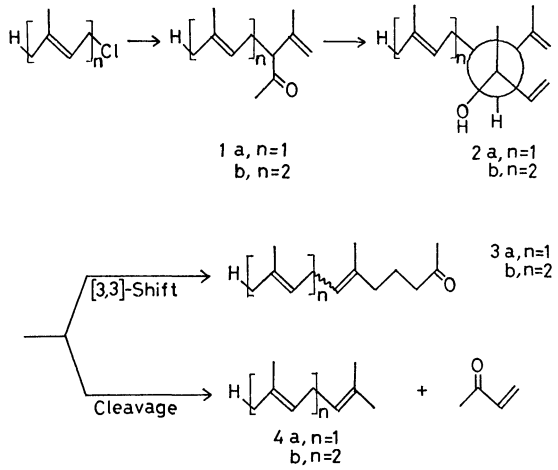
Oxy-Cope rearrangement of diastereomeric 1,5-hexadien-3-ols, new key intermediates for terpenoids production in industrial scale, were investigated in neat systems and solvent assisted systems. Various solvents affecting the selectivity of [3,3]-shift were classified by means of NMR studies on hydroxyl proton exchange time.

The carbon-carbon elongation reactions based on [3,3]-sigmatropic rearrangement, such as the Carroll reaction[1] as well as Saucy-Marbet method[2] (C-3 extension) or Thomas[3] and Faulkner-Petersen[4] methods (C-5 extension), proceed after the loss of eliminating groups (*e.g.* CO_2, ROH) which decrease the efficiency of chain extenders particularly in lower molecules. Recently, mesityl oxide has been utilized in full as a C-6 chain extender *via* synthetically equivalent transpositions of Cope[5,6] and oxy-Cope[7] reactions.

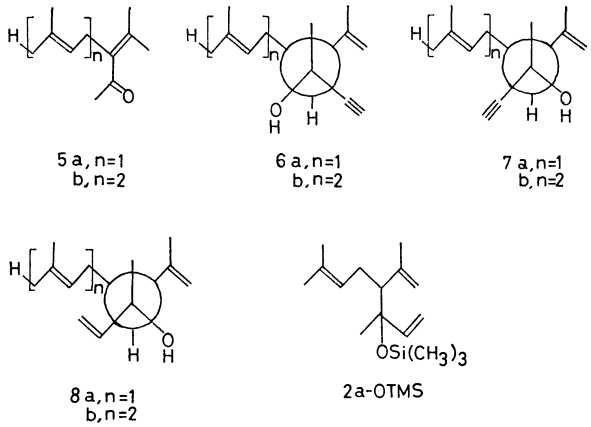
Synthetic utility of oxy-Cope rearrangement is considerably reduced owing to the β-hydroxyolefin cleavage reaction. In order to avoid the cleavage, several modifications such as siloxy-Cope processes[8] or anionic processes[9] have been developed. On the other hand, no attention has been paid to solvent effects in oxy-Cope processes although such effects have been studied in the case of other [3,3]-sigmatropic rearrangement.[10] A report was given on a convenient solvent assisted method to increase the selectivity of [3,3]-shift of some 1,5-hexadien-3-ol systems.[7,11] We have further elaborated this method by comparing the behavior of diastereomeric dienols (**2** and **8**), and various solvents affecting the selectivity of this reaction were classified by means of NMR studies on hydroxy proton exchange time. A new process for polyprenyl ketones (**3**) useful for squalane and isophytol, which may be manufactured in the near future together with pseudoionone from intermediates **6** and **7** *via* acetylenic oxy-Cope reaction,[12] is presented in this paper.



Results and Discussion

Preparation of Diastereomeric 1,5-Hexadien-3-ols and Siloxy Compound. The condensation reaction of prenyl or geranyl chloride with mesityl oxide gave the desired ketone (**1**) together with α,β-unsaturated isomer (**5**).[13,14] Reaction of **1** with vinylmagnesium bromide in tetrahydrofuran and subsequent hydrolysis afforded the only product **2** in *ca.* 80% yield. Diastereomer **2** is also obtainable by partial hydrogenation of the stoichiometric sodium acetylide ethynylation product of **1** [**1**/**5**/**6**/**7**=5/15/78/2].[13]

Semicatalytic potassium hydroxide ethynylation of **1** or **5** in liquid ammonia under pressure gave two diastereomeric alcohols in the composition **1**/**5**/**6**/**7**= 6/16/45/33. However, fractional distillation and silica gel column chromatography were ineffective for the separation of **6** and **7**. After partial hydrogenation of the mixture, careful fractional distillation gave pure dienol **8a** (50 g) from 1500 g of **2a**/**8a**=55/45.



Treatment of **2a** with dry pyridine/trimethylchlorosilane in ether gave **2a**-OTMS (OTMS=trimethylsiloxy) in 78% yield.

Thermolysis of 2, 8a, and 2a-OTMS. Thermolysis of **2a** in the temperature range 160—190 °C in neat system gave **3a** (E/Z=59.5/40.5; 170 °C) in applroximately 55% yield, along with cleavage products (**4a**, methyl vinyl ketone, and polymer). Below this temperature range, the reaction was too slow for synthesis and above it the cleavage reaction occurred predominantly. The selectivity of [3,3]-shift decreased to a small extent with progress of the reaction (Fig. 3). The result of thermolysis of **2b** is similar to that of **2a**. However, dienol **8a**, in comparison to its diastereomer **2a**, shows interesting behavior: No appreciable difference in yield of **3a** was observed, but the ratio of stereoisomer of **3a** inclined to the *E*-form (E/Z=65.8/34.2; 170 °C).[15] The reaction of **8a** occurred slightly faster than **2a** [k=0.404 and 0.858 s^{-1} at 170 and 180 °C, respectively].

Table 1. Results of thermolyses of **2**, **8a**, and **2a**-OTMS

Compound	Reaction temp (°C)	E/Z ratio of **3**[a]	k[b] (s^{-1})	E_a (kcal/mol)	log A (s^{-1})
2a	160	60.0/40.0	0.107	30.34+1.78	14.35+0.87
	170	59.5/40.5	0.241		
	180	58.9/41.1	0.476		
	190	58.4/41.6	1.060		
2a/NMP=1/1[c]	160	66.8/33.2	0.192	29.45+0.55	14.16+0.27
	170	66.5/33.5	0.431		
	180	66.3/33.7	0.874		
	190	66.0/34.0	1.740		
2b/NMP=1/1[c]	170	66.2/33.8	0.494	32.59+2.53	15.78+1.21
	180	66.0/34.0	1.155		
	190	——	2.196		
	200	65.6/34.4	5.449		
8a/NMP=1/1[c]	170	60.1/39.9	0.470	——	——
	180	61.7/38.3	1.092		
	190	62.6/37.4	2.022		
2a-OTMS	150	64.0/36.0	0.120	30.86+2.38	15.06+1.18
	160	63.8/36.2	0.319		
	170	63.5/36.5	0.676		
	180	63.2/36.8	1.441		
	190	63.0/37.0	3.026		

a) E/Z ratio of **3** from **2a**-OTMS was obtained by GC analyses after the hydrolysis of **9**. b) First order rate constant [disappearance of **2**, **8a**, **2a**-OTMS]. c) By weight.

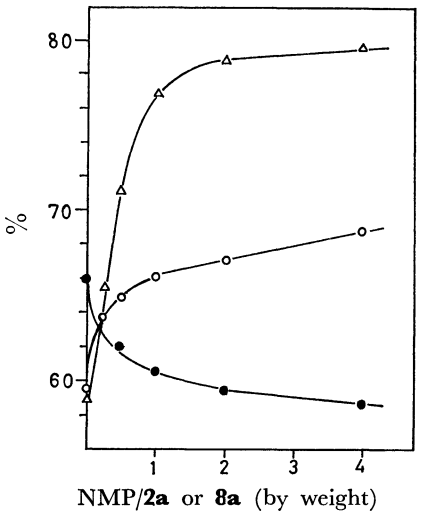


Fig. 1. Solvent effect on oxy-Cope rearrangement of **2a** and **8a** (180 °C) △: Selectivity of **3a**. ○: E-isomer of **3a** from **2a**. ●: E-isomer of **3a** from **8a**.

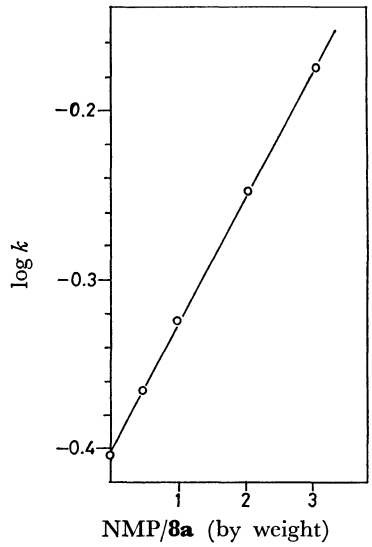


Fig. 2. Rate acceleration of **8a** by NMP (170 °C).

The siloxy-Cope rearrangement of **2a**-OTMS afforded **9** in *ca.* 97% yield, with a little rate acceleration owing to its steric factor. Hydrolysis of **9** with 1M-hydrochloric acid at 0 °C yielded **3a** quantitatively as a mixture of E/Z=63/37.

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Ozonolysis of **3a** gave mainly 4-methyl-3-pentenal and 2,6-heptanedione, and hydrogenation of **3a** with Pd/C afforded 6,10-dimethyl-2-undecanone.

Solvent Assisted Oxy-Cope Rearrangement of ***2*** *and* ***8a****.* Increase of the selectivity of [3,3]-shift without troublesome and costly handling is our essential problem. In this respect, the solvent assisted modification seems to be suitable for large scale production.

The use of *N*-methyl-2-pyrrolidone (NMP) as a solvent in various amounts, as shown in Fig. 1, increased the yield of **3a** to 80% with the amount of the E-isomer increasing from 59 to 71% in the case of **2a**, while with **8a** it decreased from 66 to 58%. A small acceleration in rate was observed (Fig. 2). Further addition of NMP, even as much as fifty-fold, caused neither increase in yield, variation in the E/Z ratio,

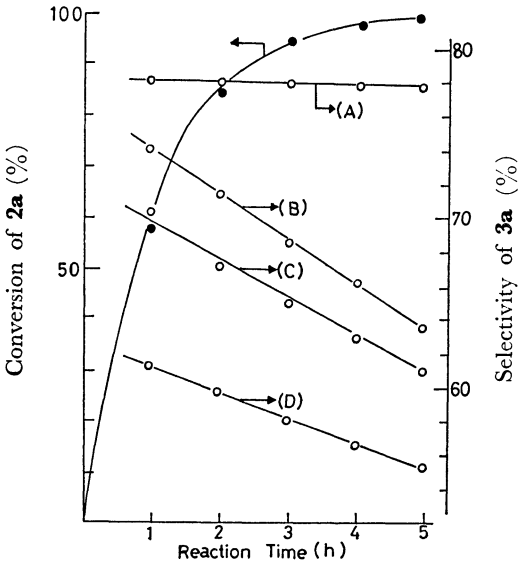
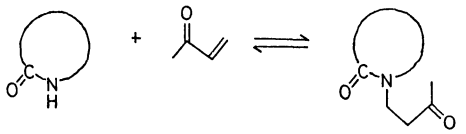


Fig. 3. Effect of the addition of *n*-decyl alcohol on selectivity of **3a** from **2a** (180 °C). ●: Conversion of **2a**. ○: Selectivity of **3a**; (A) NMP/**2a**=2/1. (B) NMP/**2a**/*n*-$C_{10}H_{21}OH$=2/1/1.5. (C) NMP/**2a**/*n*-$C_{10}H_{21}OH$=2/1/1. (D) NMP/**2a**=0 by weight.

or acceleration in rate. The decrease in the selectivity of the [3,3]-shift during the reaction observed in the neat system [initial stage 62%, end of reaction 53%] was not observed upon addition of NMP. This solvent effect was considerably reduced by the addition of primary alcohols (*e.g.* 1-decanol, ethylene glycol), even though there was no effect on the selectivity of [3,3]-shift in the neat system (Fig. 3).

A similar result was obtained by using ε-caprolactam (or 2-pyrrolidone) instead of NMP with some difference in the reaction rate and selectivity of [3,3]-shift. However, under the reaction conditions, ε-caprolactam reacted with methyl vinyl ketone derived from cleavage reaction to yield *N*-(3-oxobutyl)-ε-caprolactam which showed similar activity to that of ε-caprolactam.



Other solvents such as glycerol, triphenylamine, decane, diethylene glycol diethyl ether[17] *etc.*, were ineffective for increasing the yield of **3** (Table 2). In the case of hydrocarbon solvent, *E*/*Z* ratio of **3** changed to 54/46. Solvents such as istain and benzotriazole were effective contrariwise for cleavage reaction.

Classification of Solvents Affecting the Selectivity of [3,3]-Shift: NMR-studies on Proton Exchange Time. The fact that the effect changes with the amount of solvent and diminishes considerably by the addition of primary alcohols indicates that there is interaction between solvent and hydroxy proton. We have studied the effect of solvent on hydroxy proton exchange by NMR wherein 10 mg of solvent was added to 0.5 ml of a solution of **2** in dimethyl-d_6 sulfoxide (DMSO-d_6) of purity higher than 99.5% and containing water as a contaminant.

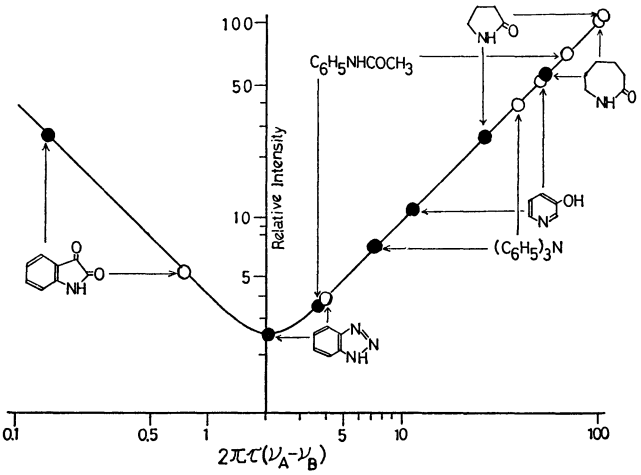


Fig. 4. Solvent effects on hydroxy proton exchange time of **2a**. ○: At 30 °C. ●: At 100 °C.

In calculating the proton exchange time (the time of exchange between the hydroxy proton of **2** and water in DMSO-d_6), the line shape [$g(\nu)$] of the NMR spectrum, chemical shift being taken into account, is theoretically a function of ν_A, ν_B, τ_A, and τ_B, where A is the change site on **2**, B is the exchange site on water; τ_A and τ_B are the times during which the protons are detained at each site, and ν_A and ν_B represent the chemical shifts. Assuming that $\tau_A=\tau_B=2\tau$ and that the line width has no broadening throughout the process except for the change, we get the following Bloch-equation.[18]

$$g(\nu) = K\frac{\tau(\nu_A-\nu_B)^2}{[1/2(\nu_A-\nu_B)-\nu]^2+4\pi^2\tau^2(\nu_A-\nu)^2(\nu_B-\nu)^2}$$

$$K = \int_{-\infty}^{\infty} g(\nu)d\nu$$

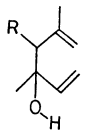
The equation was solved approximately with the assumption that proton exchange occurs mainly between the hydroxyl proton of **2** and water in DMSO-d_6. The line shape was calculated with $\nu_A=\nu_B=90$ Hz and on varying the value of $2\pi\tau(\nu_A-\nu_B)$ from 100 to 0.1. The proton exchange time can be obtained by comparing the values obtained by calculation with measured line shape values. By comparing the results of thermolysis of **2** in neat system and solvent assisted system (Table 2), solvents effective for [3,3]-shift can be defined to be those for which proton exchange time is not less than 10^{-1} s at 30 °C and not less than 10^{-2} s at 100 °C. Figure 4 shows some results in which the logarithm of the value of $2\pi\tau(\nu_A-\nu_B)$ is horizontally plotted and the logarithm value of signal height based 100 with $2\pi\tau(\nu_A-\nu_B)=100$ is vertically plotted to give the curve. The relative value of the measured line shape, based on the height of hydroxyl proton of **2a** in the presence of 2-pyrrolidone, is plotted on the curve. Solvent plotted on the right of the center line of Fig. 4 would be effective for increasing the selectivity of [3,3]-shift. On the contrary, solvent plotted on the left would decrease [3,3]-shift. Benzotriazole plotted near the center at 100 °C can not be a favorable solvent for [3,3]-shift in consideration of the fact that

Table 2. Solvent effect on oxy-Cope rearrangement and on hydroxyl proton exchange time

Compound	Solvents /2 or 8 (by weight)	Reaction conditions[a]	Conversion of 2 or 8; %[b]	Selectivity of 3; %[b] [E/Z of 3]	Proton exchange time τ_0(s) at 30 °C	Proton exchange time τ_0(s) at 100 °C
2a	None	A[c]	84	55 [58.9/41.1]	——	——
	Glycerol (1.0)	B	87	52		
	Triphenylamine (1.0)	C	40	53	1.3×10^{-1}	2.4×10^{-2}
	Decane (2.0)	B	89	51 [44/46]	——	——
	Acetanilide (1.0)	C	51	55	2.4×10^{-1}	1.3×10^{-2}
	Diethylene glycol diethyl ether (2.0)	A[c]	90	55 [59/41]	——	——
	Benzotriazole (1.0)	C	78	12	1.3×10^{-2}	$>7.0\times10^{-3}$
	Isatin (1.0)	C	58	8	4.2×10^{-3}	$<5.2\times10^{-4}$
	NMP (1.0)	A[c]	98	79 [66/34]	$>4.0\times10^{-1}$	1.8×10^{-1}
	2-Pyrrolidone (2.0)	A	96	77	3.6×10^{-1}	8.8×10^{-2}
	ε-Caprolactam (1.0)	A[c]	95	77 [66.5/33.5]	$>4.0\times10^{-1}$	1.9×10^{-1}
	N-(3-Oxobutyl)-ε-caprolactam (1.0)	A[c]	92	76	$>4.0\times10^{-1}$	1.8×10^{-1}
	3-Pyridinol (1.0)	C	40	70	1.8×10^{-1}	3.8×10^{-2}
	Benzimidazole (1.0)	C	45	70	1.9×10^{-1}	7.4×10^{-2}
2b	None	A[c]	87	60 [59/41]	——	——
	3-Pyridinol (1.0)	C	46	71	2.3×10^{-1}	8.8×10^{-2}
	NMP (1.0)	A[c]	100	82 [66/34]	4.0×10^{-1}	4.5×10^{-2}
8a	None	A	87	57 [66/34]	——	——
	NMP (2.0)	A	100	79 [59/41]	——	——
10	None	A	90	58	——	——
	NMP (2.0)	A[c]	100	83 [73.5/26.5]	$>4.0\times10^{-1}$	4.9×10^{-2}
11	None	A	92	51	——	——
	NMP (2.0)	A[c]	100	78 [70/30]	3.6×10^{-1}	6.6×10^{-2}
12	None	A	90	54 [60/40]	——	——
	NMP (2.0)	A[c]	100	78 [73.6/26.4]	1.9×10^{-1}	6.2×10^{-2}

a) A; 180 °C for 4 h. B; 175 °C for 6 h. C; 170 °C for 2 h. b) Determined by GC analyses: PEG-20 M 10% on Chromosorb W (AW) or Silicone DC-550 10% on Chromosorb W (AW). c) Results of GC analyses were confirmed by isolation in large scale experiments (50—500 g).

the reaction temperature is above 160 °C. Solvent in which the hydroxyl proton exchange time largely depends upon temperature, such as acetanilide or triphenylamine, would not be preferable for [3,3]-shift. This classification is applicable to the other systems **10**—**12**.[7]



10, R=p-$CH_3C_6H_4CH_2$-
11, R=furfuryl
12, R=2-thenyl

Despite the difference in the conditions between NMR measurement and oxy-Cope reaction, it might be postulated that the added solvents effective for increasing the selectivity of [3,3]-shift fix the hydroxyl proton, slowing down the rate of proton exchange.

Synthetic utility of the process was confirmed by large scale production (semi-commercial) of geranylacetone (**3a**), and application to other naturally occurring compounds is under investigation in our laboratory.

Experimental

Boiling points are uncorrected. Infrared spectra were determined on a JASCO (DC-403G) spectrometer. NMR spectra were taken with a Varian Associate HA-100 or Varian Model A-60 spectrometer and MS with a Finnigan 9500 instrument. GC analyses were made with a Shimadzu GC-4A using 3 mm×300 cm column. Separation of the reaction products was made with a Shimadzu GC-5A using 7 mm ×200 cm column of 10% Silicone DC-550 or 10% PEG-20M on Chromosorb W (AW). Rectification of the reaction products was carried out with a Shibata Automatic Packing Column, Model HPC-A-1500-B having 70 theoretical plates. Oxy-Cope rearrangements were carried out in nitrogen atmosphere.

*(3S)-4-Isopropenyl-3,7-dimethyl-1,6-octadien-3-ol (**2a**).* The compound was obtained according to the method reported previously[11b] by the reaction of **1a** (1 mol) with vinylmagnesium bromide (1.2 mol) in THF (1.5 l) at 40 °C for 3 h (yield 79%): bp 60—63 °C/0.5 mmHg.

*(3S)-4-Isopropenyl-3,7,11-trimethyl-1,6,10-dodecatrien-3-ol (**2b**).* The compound was obtained by the same procedure described above, from **2b** (0.5 mol) and vinylmagnesium bromide (0.6 mol): yield 81%; bp 104—106 °C 0.3 mmHg (*E*-form). IR (neat) 3480, 1640, 1450, 1375, 920, and 895 cm^{-1}. NMR (CCl_4) δ 1.15 (s, CH_3, 3H), 1.54, 1.62, 1.67 (s, CH_3, 12H), *ca.* 1.92—2.30 (m, CH_2CH and CH_2CH_2, 7H), *ca.* 4.75—5.10 (m, CH and CH_2, 4H), 5.00(dd, CH, 1H, J=2, 10 Hz), 5.18 (dd, CH, 1H, J=2, 18 Hz), and 5.90 (dd, CH, 1H, J=10, 18 Hz). MS (70 eV) *m/e* (rel intensity) 262 (M^+, 1.6), 244 (6.1), 191 (9.4), 149 (11.7),

123 (55.3), 81(41.5), and 71 (100).

Found: C, 82.62; H, 11.58%. Calcd for $C_{18}H_{30}O$: C, 82.38; H, 11.52%.

*4-Isopropenyl-3,8-dimethyl-6-octen-1-yn-3-ol (**6a**).* Acetylene gas was bubbled into a solution of sodium metal (69 g; 3 mol) in liquid ammonia (3 l) until the reaction mixture turned grey. Introduction of acetylene was then suspended and 517 g (3.1 mol) of **1a** was added over a period of 30 min. The reaction was continued for 3 h, acetylene being bubbled through the reaction system maintained at −33 °C. After removal of ammonia, the residue was neutralized with ammonium chloride, water was added, and then the mixture was extracted with ether. Distillation gave 519 g of a mixture of **1a**/**5a**/**6a**/**7a**=5/15/78/2 [analyzed by GC; PEG-20M, 160 °C], which was purified by careful fractional distillation to afford a mixture of **5a**/**6a**/**7a**=4/94/2. Pure **6a** was obtained by silica gel column chromatography (C_6H_6/*n*-C_6H_{14}=4/6; **6a**/**7a**=97/3) or preparative GC [PEG-20M, 170 °C]: bp 59—61 °C/0.5 mmHg.[13]

*4-Isopropenyl-3,7,11-trimethyl-6,10-dodecadien-1-yn-3-ol (**6b**).* The compound was obtained as a mixture of **1b**/**5b**/**6b**/**7b**=10/30/57/3 by the same procedure as described above, except for the use of **1b** (0.5 mol) in 500 ml of ether solution. Separation of **6b** by preparative GC [PEG-20M, 210 °C] was unsuccessful owing to the accompaniment of acetylenic oxy-Cope rearrangement. Pure **6b** was obtained by silica gel column chromatography (C_6H_6/*n*-C_6H_{14}=4/6): bp 120—125 °C/0.3 mmHg (**6a**/**7a**=95/5).[13]

General Procedure for Partial Hydrogenation. Hydrogen was bubbled into a mixture of **1a**/**5a**/**6a**/**7a**=5/15/78/2 (300 g) in hexane (900 ml), in the presence of 5 g of 2% Pd Lindlar catalyst at 35—40 °C for 7 h. After checking the completion of reaction by GC [PEG-20M, 160 °C], the catalyst was filtered and mother liquid evaporated under reduced pressure. Distillation gave 294 g of a mixture of **1a**/**5a**/**2a**/**8a**=6/14/78/2.

*(3R)-4-Isopropenyl-3,7-dimethyl-1,6-octadien-3-ol (**8a**).* In a 5 l autoclave, 335 g (2 mol) of **1a** was added to liquid ammonia (3.3 l) in contact with 20 wt% of aqueous KOH (45 g; 0.16 mol) as a catalyst, acetylene gas (*ca.* 260 g) being introduced with stirring at −33 °C. The reaction temperature was raised to 5 °C, stirring being continued for 32 h. The reaction mixture was cooled to −33 °C and neutralized with ammonium chloride. After removal of ammonia, water was added, and the mixture was extracted with ether. Distillation gave 319 g of a mixture of **1a**/**5a**/**6a**/**7a**=6/16/45/33: bp 59—63 °C/0.5 mmHg. Pure **7a** was obtained only by preparative GC.[13] After partial hydrogenation of the mixture (315 g) by the same method as described above, distillation [bp 82—91 °C/1.5—2 mmHg] afforded 310 g of a mixture of **1a**/**5a**/**2a**/**8a**=7/15/44/34. Careful rectification of 1500 g of a mixture [bottom temp, 128—134 °C; top temp, 94—95 °C; pess., 4 mmHg; reflux ratio=25] afforded 52 g of pure **8a**. IR (neat) 3480, 1639, 1450, 1375, 1110, 1000, 922, and 897 cm^{-1}. NMR (CCl_4) δ 1.18 (s, CH_3, 3H), 1.55, 1.60, 1.63 (s, CH_3, 9H), *ca.* 2.02—2.17 (m, CH_2CH, 3H), *ca.* 4.73—5.00 (m, CH and CH_2, 3H), 5.00 (dd, CH, 1H, J=2,10 Hz), 5.15 (dd, CH, 1H, J=2, 18 Hz), and 5.98 (dd, CH, 1H, J=10, 18 Hz). MS fragmentation pattern of **8a** was analogous to that of **2a**.

Found: C, 80.07; H, 11.18%. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41%.

*(3R)-4-Isopropenyl-3,7,11-trimethyl-1,6,10-dodecatrien-3-ol (**8b**).* The compound was obtained as a mixture of **1b**/**5b**/**2b**/**8b**=8/18/42/32 by the same procedure as described above. Separation and purification of **8b** by preparative GC [PEG-20 M, 210 °C] or by fractional distillation was unsuccessful owing to the occurrence of oxy-Cope rearrangement.

*3-Trimethylsiloxy-4-isopropenyl-3,7-dimethyl-1,6-octadiene (**2a**-OTMS).* The compound was obtained according to the method reported previously[11b] by the reaction of **2a** (58.2 g; 0.3 mol) with dry pyridine (28.4 g; 0.36 mol)/trimethylchlorosilane (38.9 g; 0.36 mol) in ether (200 ml) at 35 °C for 4 h; yield 78%; bp 68—70 °C/0.5 mmHg.

*6,-10Dimethyl-6,9-undecadien-2-one (**3a**). General Procedure of Oxy-Cope Rearrangement in Neat System.* 800 g of **2a** (purity 93%) was placed in a 1 litre 3-necked flask and heated to 185—187 °C for 4 h in nitrogen atmosphere. The reaction mixture was cooled and distilled *in vacuo* to remove 305 g of a mixture of 2,6-dimethyl-2,5-heptadiene (**4a**)/methyl vinyl ketone, and 47 g of **5a** (impurity in the starting material, as the low-boiling fraction). As a higher boiling product [bp 77—79 °C/0.5 mmHg], 394 g (53%) of **3a** was obtained. GC analysis of **3a** [Silicone DC-550, 160 °C] showed two peaks (11.5 and 13.0 min) in the ratio 41.1 : 58.9. Separation of these compounds by fractional distillation [bottom temp, 143—147 °C; top temp, 77—83 °C; press., 0.3 mmHg; reflux ratio=30] and spectral analyses showed that the former peak is *Z*-isomer and the latter *E*-isomer.[11b]

*6,10,14-Trimethyl-6,9,13-pentadecatrien-2-one (**3b**).* The compound was obtained by the same procedure described above in 52% yield (180 °C for 3.5 h): bp 123—128 °C/0.1 mmHg (*E*/*Z*=57.5/42.5). IR (neat) 1715, 1672, 1440, 1158, 985, 970, 890, and 830 cm^{-1}. NMR (CCl_4) δ 1.50, 1.56 (s, CH_3, 12H), *ca.* 1.70—2.05 (m, CH_2CH_2, 8H), 1.92 (s, CH_3, 3H), 2.13—2.30 (m, CH_2, 2H), 2.55 (t, CH_2, 2H, J=7 Hz), and *ca.* 4.94 (broad t, CH, 3H).

Found: C, 81.99; H, 11.71%. Calcd for $C_{18}H_{30}O$: C, 82.38; H, 11.52%.

General Procedure of Oxy-Cope Rearrangement in Solvent Assisted System. A solution of 350 g of **2a** (purity 92%) in 700 g of NMP was subjected to reaction at 180 °C for 5 h with stirring. The reaction mixture was poured into water (1500 ml) and extracted with ether (500 ml×4). Distillation of the products gave 245 g (76%) of **3a** (*E*/*Z*=67/33). Quantitative analyses were carried out with gas chromatography: In the case of **2a** and **8a**, *n*-decyl alcohol was used as an internal standard to obtain the calibration curve [PEG-20M, 160 °C]. Reactions of **2b** in NMP solvent were monitored by using NMP itself as an internal standard.

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