BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 218—221 (1973)

Syntheses of Isoprenoids by Telomerizations. VIII.[1,2] Anionic Telomerizations of Isoprene with Secondary Amines

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(Received January 11, 1972)

The anionic telomerizations of isoprene with secondary amines in the presence of alkali-metal catalysts were investigated under several conditions. The $n=2$ telomers were found to contain *N,N*-dialkyl(3,7-dimethyl-2,6-octadienyl)amine (**2A**) and *N,N*-dialkyl(2-isopropenyl-5-methyl-4-hexenyl)amine (**2B**) as the main components, $n=1$ and $n=3$ telomers were also identified. On the basis of these results, the mechanism of this anionic telomerization and the reactivity of the carbanions connected with this reaction were discussed.

It has been known that the naturally-occurring monoterpenes have 4,1-(geranyl-, neryl-, linalyl-, and terpinyl-) mainly and 4,3-(lavandulyl) coupled skeletons of isoprene. Many investigations have been made of the syntheses of these terpenes by means of the telomerizations of isoprene, but the C_{10} telomers obtained by cationic[3-5] or radical-initiated[6] telomerizations contain many products, and the yield of acyclic monoterpenes is low.

No studies of the synthesis of the terpenoids by anionic telomerization[7] have been carried out. Therefore, the anionic telomerizations[8] of isoprene with secondary amines were studied in detail. In this paper, we wish to report on the structures of the telomers, the reaction scheme, and the reactivity of the carbanions connected with this reaction.

Results and Discussion

The Structure of the Telomers. The structures of the telomers obtained were identified by means of IR, NMR, and the mass spectra; they are summarized in Tables 1 and 2.

Reaction Scheme. The yields of the telomers and the ratios of **1A**/**1B** obtained under various conditions are shown in Table 3. When the molar ratio of isoprene to diethylamine was 1/2, the $n=2$ telomers were not formed. The order of the catalytic activity was K>Na>Li, but the ratio of **1A**/**1B** was the reverse. Table 4 shows that the ratio of **1A**/**1B** was not influenced by the reaction time, and was nearly constant.

Therefore, the mechanism of this reaction is similar to that of alkali metal-catalyzed reactions of isoprene with alkylaromatics[9] and can be formulated as follows;

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[1] A part of this work was presented at the Annual Meeting of the Chemical Society of Japan, Osaka, April, 1971.

[2] Part VII of this series: K. Takabe, T. Katagiri, and J. Tanaka, This Bulletin, **45**, 2662 (1972).

[3] J. Tanaka, T. Katagiri, and T. Takeshita, *Nippon Kagaku Zasshi*, **89**, 65 (1968).

[4] T. Asahara, M. Toyoda, and H. Kise, *Kogyo Kagaku Zasshi*, **72**, 1530 (1969).

[5] K. Takabe, T. Katagiri, and J. Tanaka, *ibid.*, **74**, 1162 (1971).

[6] T. Katagiri, K. Takabe, K. Ono, and J. Tanaka, *Nippon Kagaku Zasshi*, **91**, 393 (1970).

[7] The anionic telomerizations of styrene with some *sec*-amines have been investigated in detail by Asahara *et al.* [T. Asahara, M. Seno, S. Tanaka, and N. Den, This Bulletin, **42**, 1996, 2337 (1969).]

[8] The addition reactions of isoprene with some secondary amines have already been reported by Martirosyan *et al.* [G. T. Martirosyan, E. A. Grigoryan, and A. T. Bahayan, *Arm. Khim. Zh.*, **20**, 423 (1967); *Chem. Abstr.*, **68**, 48940 (1968).]

[9] H. Pines and N. C. Shi, *J. Org. Chem.*, **30**, 280 (1965); W. M. Stalic and H. Pines, *ibid.*, **35**, 422 (1970).

Table 1. The structural formulas of the telomers

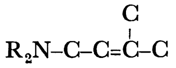
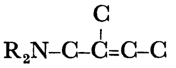
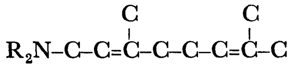
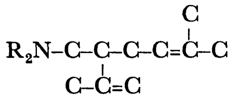
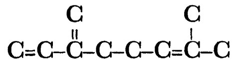
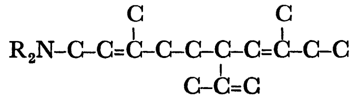
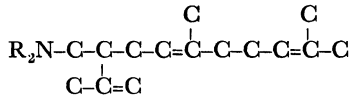
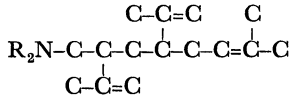
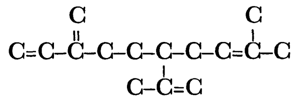
$n=1$	 $R_2N{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C$	(**1A**) *N*,*N*-dialkyl(3-methyl-2-butenyl)amine
	 $R_2N{-}C{-}\overset{\substack{C\\ \vert}}{C}{=}C{-}C$	(**1B**) *N*,*N*-dialkyl(2-methyl-2-butenyl)amine
$n=2$	 $R_2N{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C$	(**2A**) *N*,*N*-dialkyl(3,7-dimethyl-2,6-octadienyl)amine
	 $R_2N{-}C{-}\underset{\substack{\vert\\ C{-}C{=}C}}{C}{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C$	(**2B**) *N*,*N*-dialkyl(2-isopropenyl-5-methyl-4-hexenyl)-amine
	 $C{=}C{-}\overset{\substack{C\\ \Vert}}{C}{-}C{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C$	(**2H**) myrcene
$n=3$	 $R_2N{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C{-}C{-}\underset{\substack{\vert\\ C{-}C{=}C}}{C}{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C{-}C$	(**3B**) *N*,*N*-dialkyl(6-isopropenyl-3,9-dimethyl-2,8-decadienyl)amine
	 $R_2N{-}C{-}\underset{\substack{\vert\\ C{-}C{=}C}}{C}{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C$	(**3C**) *N*,*N*-dialkyl(2-isopropenyl-5,9-dimethyl-4,8-decadienyl)amine
	 $R_2N{-}C{-}\underset{\substack{\vert\\ C{-}C{=}C}}{C}{-}C{-}\overset{\substack{C{-}C{=}C\\ \vert}}{C}{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C$	(**3D**) *N*,*N*-dialkyl(2,4-diisopropenyl-7-methyl-6-octenyl)amine
	 $C{=}C{-}\overset{\substack{C\\ \Vert}}{C}{-}C{-}C{-}\underset{\substack{\vert\\ C{-}C{=}C}}{C}{-}C{-}C{=}\overset{\substack{C\\ \vert}}{C}{-}C$	(**3H**) 6-isopropenyl-9-methyl-3-methylene-1,8-decadiene

Table 2. Characterization of the telomers

Telogen	Products (Mass; M+)	IR (cm^{-1})	NMR (τ)
Me_2NH	**1A** (113)	1680, 817 (a trisubstituted double bond), 1020, 1040, (C–N), 2810, 2765, 2725 ($R{-}NMe_2$).	8.37(3H, s, $-(\mathbf{CH_3})C{=}$), 8.28 (3H, s, $-(\mathbf{CH_3})C{=}$), 7.90 (6H, s, $\mathbf{CH_3}{-}N\langle$), 7.23(2H, d, $J=7.2$ Hz, $=CH{-}\mathbf{CH_2}{-}N\langle$), 4.80 (1H, t, $J=7.2$ Hz, $\rangle C{=}\mathbf{CH}{-}$).
	1B (113)	1680, 817 (a trisubstituted double bond), 1020, 1040(C–N), 2810, 2765, 2725($R{-}NMe_2$).	8.21—8.54 (6H, m, $-(\mathbf{CH_3})C{=}$), 7.96(6H, s, $\mathbf{CH_3}{-}N\langle$), 7.36(2H, s, $=C{-}\mathbf{CH_2}{-}N\langle$), 4.50—5.01 (1H, m, $\rangle C{=}\mathbf{CH}{-}$).
	2A (181)	1665, 818 (trisubstituted double bonds), 1015, 1040(C–N), 2815, 2760, 2720($R{-}NMe_2$).	8.23—8.48(9H, m, $-(\mathbf{CH_3})C{=}$), 7.92(6H, s, $\mathbf{CH_3}{-}N\langle$), 7.90—8.13(4H, m, $=C{-}\mathbf{CH_2}{-}\mathbf{CH_2}{-}C{=}$), 7.24 (2H, d, $J=7.0$ Hz, $=CH{-}\mathbf{CH_2}\ {-}N\langle$), 4.70—5.15 (2H, m, $\rangle C{=}\mathbf{CH}{-}$).
	2B (181)	1645, 883 (an end methylene group), 1670, 840 (a trisubstituted double bond), 1040 (C–N), 2815, 2760, 2720($R{-}NMe_2$).	8.25—8.50(9H, bs, $-(\mathbf{CH_3})C{=}$), 7.91(6H, s, $\mathbf{CH_3}{-}N\langle$), 7.69—8.08(5H, m, $-\mathbf{CH_2}{-}$, $\rangle\mathbf{CH}{-}$), 5.38 (2H, bs, $\rangle C{=}\mathbf{CH_2}$), 5.03(1H, t, $J=7.0$ Hz, $\rangle C{=}\mathbf{CH}{-}$).
	3B (249)	1645, 886 (an end methylene group), 1670, 830 (trisubstituted double bonds), 1040, 1015(C–N), 2815, 2760, 2725($R{-}NMe_2$).	8.25—8.51(12H, m, $-(\mathbf{CH_3})C{=}$), 7.92(6H, s, $\mathbf{CH_3}{-}N\langle$), 8.20—8.70(2H, m, $-\mathbf{CH_2}{-}$), 7.75—8.12 (5H, m, $=C{-}\mathbf{CH_2}{-}$, $=C{-}\mathbf{CH}\langle$), 7.25(2H, d, $J=7.0$ Hz, $=CH\ {-}\mathbf{CH_2}{-}N\langle$), 5.35(2H, bs, $\rangle C{=}\mathbf{CH_2}$), 4.76—5.10 (2H, m, $\rangle C{=}\mathbf{CH}{-}$).
	3C (249)	1645, 886 (an end methylene group), 1675, 840 (trisubstituted double bonds), 1040(C–N), 2815, 2765, 2725($R{-}NMe_2$).	8.20—8.53 (12H, bs, $-(\mathbf{CH_3})C{=}$), 7.90(6H, s, $\mathbf{CH_3}\ {-}N\langle$), 7.70—8.18 (9H, m, $-\mathbf{CH_2}{-}N$, $=C{-}\mathbf{CH_2}{-}$, $=C\ {-}\mathbf{CH}\langle$), 5.35(2H, bs, $\rangle C{=}\mathbf{CH_2}$), 4.75—5.10(2H, m, $\rangle C{=}\mathbf{CH}{-}$).
	3D (249)	1645, 885(end methylene groups), 1670, 843 (trisubstituted double bonds), 1040 (C–N), 2810. 2775, 2725($R{-}NMe_2$).	8.25—8.52 (12H, bs, $-(\mathbf{CH_3})C{=}$), 7.92(6H, s, $\mathbf{CH_3}\ {-}N\langle$), 8.50—8.80 (2H, m, $-\mathbf{CH_2}{-}$), 7.80—8.12 (6H, m, $-\mathbf{CH_2}{-}N\langle$, $=C{-}\mathbf{CH_2}{-}$, $=C{-}\mathbf{CH}\langle$), 5.38(4H, bs, $\rangle C\ {=}\mathbf{CH_2}$), 4.90—5.10(1H, m, $\rangle C{=}\mathbf{CH}{-}$).
Et_2NH	**1A** (141)	1670, 835 (a trisubstituted double bond), 1055, 1170, 1200 (C–N).	9.04(6H, t, $J=7.1$ Hz, $\mathbf{CH_3}{-}CH_2{-}N\langle$), 8.39 (3H, s, $-(\mathbf{CH_3})C{=}$), 8.29(3H, s, $-(\mathbf{CH_3})C{=}$), 7.61 (4H, q, $J=7.1$ Hz, $CH_3{-}\mathbf{CH_2}{-}N\langle$), 7.09 (2H, d, $J=6.8$Hz, $=CH{-}\mathbf{CH_2}{-}N\langle$), 4.86(1H, t, $J=6.8$Hz, $\rangle C{=}\mathbf{CH}{-}$).
	1B (141)	1670, 850 (a trisubstituted double bond), 1050, 1170, 1195(C–N).	9.03(6H, t, $J=7.0$ Hz, $\mathbf{CH_3}{-}CH_2{-}N\langle$), 8.25—8.60 (6H, m,$-(\mathbf{CH_3})C{=}$), 7.61(4H, q, $J=7.0$ Hz, $CH_3{-}\mathbf{CH_2}\ {-}N\langle$), 7.18(2H, s, $=C{-}\mathbf{CH_2}N\langle$), 4.50—4.90 (1H, m, $\rangle C{=}\mathbf{CH}{-}$).

TABLE 3. REACTIONS OF ISOPRENE WITH DIETHYLAMINES[a)]

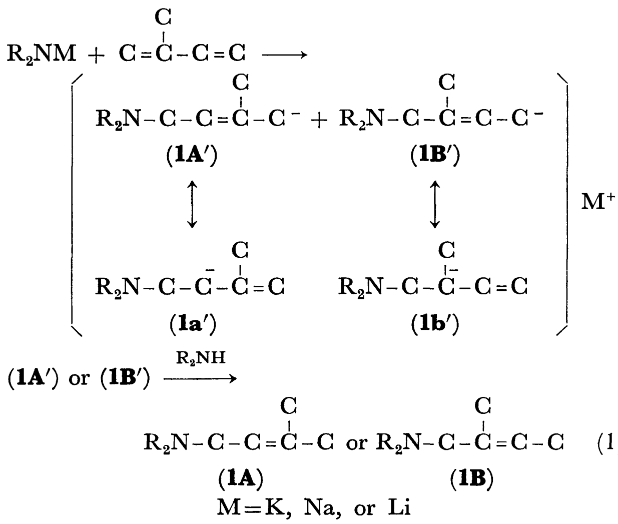
Cation	(g)	Temperature (°C)	Yield[b)] of $n=1$ telomer (%)	Composition (%)		(**1A**)/(**1B**)
				(**1A**)	(**1B**)	
Na	(0.2)	0—3	33	88	12	7.1
		40	64	84	16	5.4
		70	72	79	20	3.9
K	(0.3)	0—3	62	75	25	3.0
		40	80	71	18	3.9
Li	(0.1)	0—3	2	78	3	26
		40	12	95	5	20

a) Reaction condition; isoprene 6.8 g, isoprene/$Et_2NH=1/2$ (molar ratio), reaction time 1 hr.
b) Yields were calulated on the basis of isoprene added.

TABLE 4. REACTIONS OF ISOPRENE WITH DIETHYLAMINE[a)]

Time (min)	Cat. Na		Cat. K	
	Yield (%)[b)]	(**1A**)/(**1B**)	Yield (%)[b)]	(**1A**)/(**1B**)
15	2	6.5	51	2.7
30	43	6.8	85	2.8
60	59	6.5	89	2.9
120	82	6.4		
150	91	6.1	91	2.5

a) Reaction condition; isoprene 6.8 g, isoprene/$Et_2NH=1/2$ (molar ratio), cat. 0.2 g, reaction temperature 0—2°C.
b) Yields of $n=1$ telomers were calculated on the basis of isoprene.



$$R_2NM + C{=}\overset{C}{C}{-}C{=}C \longrightarrow \left[\begin{array}{ccc} R_2N{-}C{-}C{=}\overset{C}{C}{-}C^- & + & R_2N{-}C{-}\overset{C}{C}{=}C{-}C^- \\ (\mathbf{1A'}) & & (\mathbf{1B'}) \\ \updownarrow & & \updownarrow \\ R_2N{-}C{-}\overset{C}{\bar{C}}{-}C{=}C & & R_2N{-}C{-}\overset{C}{C}{}^{-}{-}C{=}C \\ (\mathbf{1a'}) & & (\mathbf{1b'}) \end{array}\right] M^+$$

$$(\mathbf{1A'})\text{ or }(\mathbf{1B'}) \xrightarrow{R_2NH} R_2N{-}C{-}C{=}\overset{C}{C}{-}C \text{ or } R_2N{-}C{-}\overset{C}{C}{=}C{-}C \quad (1)$$

$$(\mathbf{1A}) \qquad (\mathbf{1B})$$

$$M = K, Na, \text{ or } Li$$

The preferential formation of **1A** over **1B** is likely to be due mainly to the difference in the stabilities of the carbanions **1A′** and **1B′** (*prim↔sec vs. prim↔tert*) and only a small extent to a steric interaction between the R group of R_2NM and the methyl group of isoprene on addition.

The effect of the molar ratio of isoprene to dimethylamine is shown in Table 5. The $n \geq 2$ telomers and a small amount of **2H** and **3H**[10)] were formed as the reaction proceeded, as is shown in Table 6.

From these results, the schemes of the formation of the $n=2$ and 3 telomers are considered to be as is shown in Fig. 1.

Reactivity of Carbanions. It seems that such organosodium compounds (a) as **1A′**, **1a′**, **2A′**, **2a′**, **2B′**, **2b′**, **3A′**, **3B′**, **3C′**, and **3D′** react with isoprene or secondary amine; that is, propagation and transmetalation reactions occur competitively as follows:

$$R_2N(C_5H_8)_nNa \begin{array}{l} \xrightarrow[C_5H_8]{k_{np}} R_2N(C_5H_8)_{n+1}Na \quad \text{propagation} \\ \xrightarrow[R_2NH]{k_{nt}} R_2N(C_5H_8)_nH \quad \text{transmetalation} \end{array} \qquad (2)$$

As is shown in Fig. 1 and Eq. (1), the telomers (**1A**, **1B**, **2A**, **2B**, **3A**, **3B**, **3C**, and **3D**) confirmed in this telomerization might be formed by the transmetalation of the primary carbanions (**1A′**, **1B′**, **2A′**, **2B′**, **3A′**, **3B′**, **3C′**, and **3D′**), the telomers formed by the transmetalation of the secondary carbanions (**1a′**, **2a′**, and **2b′**) were not confirmed, but it seems that these secondary carbanions react with isoprene to give the primary carbanions (**2B′**, **3B′**, and **3D′**) *i.e.*, propagation occurs.

From these results, the reactivity of the carbanions in this telomerization is considered to be as follows:

$k_{nt}[R_2NH] \approx k_{np}[C_5H_8]$ for the primary carbanions

$k'_{nt}[R_2NH] < k'_{np}[C_5H_8]$ for the secondary carbanions

TABLE 5. EFFECT OF MOLAR RATIO (ISOPRENE/Me_2NH) ON COMPOSITIONS OF TELOMERS

Molar ratio	$n=1$ telomer (g)	Composition (%) of $n=1$ telomer		$n=2$ telomer (g)	Composition (%) of $n=2$ telomer			$n=3$ telomer (g)	Composition (%) of $n=3$ telomer				$n \geq 4$ telomer (g)
		(**1A**)	(**1B**)		(**2A**)	(**2B**)	(**2H**)		(**3B**)	(**3C**)	(**3D**)	(**3H**)	
1	2.0	76	24	t									0.2
2	2.0	54	46	2.1	12	87	t	0.3	18	18	50	t	0.6
3	1.5	16	84	2.6	14	84	2	1.6	24	26	40	t	1.0
5	0.3	6	94	3.0	32	62	4	3.0	22	34	31	2	4.7

a) Reaction condition; Me_2NH 1.8 g, Na 0.1 g, 40°C, 3 hr.

[10)] It is considered that these compounds have been formed by the anionic oligomerization of isoprene.[2)]

Table 6. Effect of reaction time[a)]

Time (hr)	$n=1$ telomer (g)	Composition (%) of $n=1$ telomer		$n=2$ telomer (g)	Composition (%) of $n=2$ telomer			$n=3$ telomer (g)	Composition (%) of $n=3$ telomer				$n\geq 4$ telomer (g)
		(1A)	**(1B)**		**(2A)**	**(2B)**	**(2H)**		**(3B)**	**(3C)**	**(3D)**	**(3H)**	
0.5	2.3	68	32	0.2	9	85	3	t					0.3
1	1.0	51	49	1.5	8	83	5	0.7	23	14	51	2	1.4
3	0.4	31	69	2.5	11	77	6	1.5	23	22	43	2	2.9
5	0.1	6	94	2.7	17	67	9	2.3	20	29	35	3	5.8

a) Reaction condition; isoprene 13.6 g, isoprene/Me_2NH=5(molar ratio), reaction temperature 15°C.

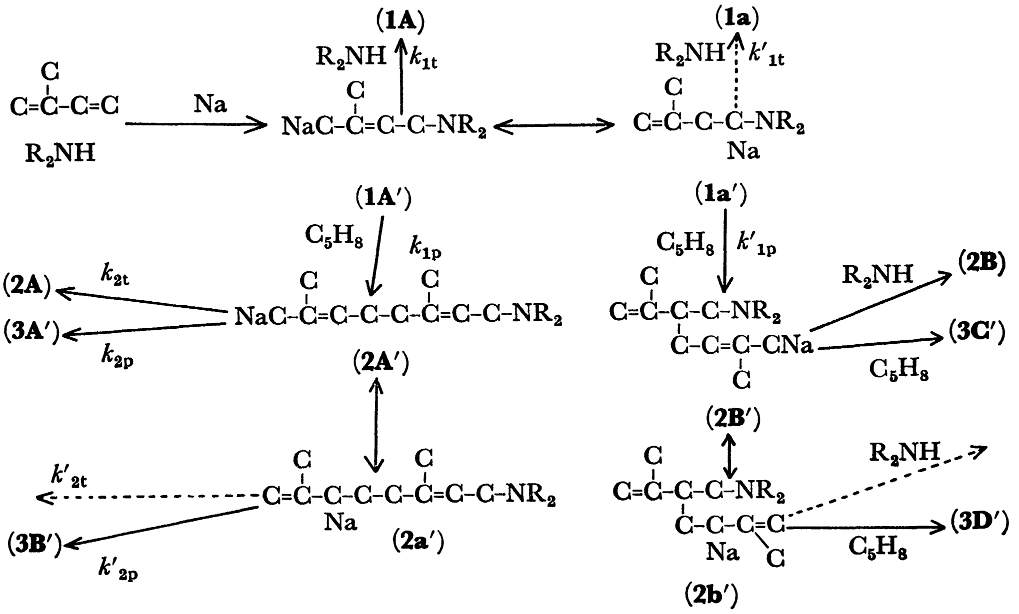


Fig. 1. Anionic telomerizations of isoprene with *sec*-amines.

Experimental

Materials. The secondary amines were commercial products of the purest grade, they were distilled and checked by glc. The isoprene was dried over anhydrous sodium sulfate and distilled in the presence of hydroquinone. The inorganic compounds were also commercial materials.

The Anionic Telomerization of Isoprene with Secondary Amine. For example, a mixture of dimethylamine (1.8 g) and isoprene (13.6 g) was placed in a pressure bottle. Then lumps of sodium (0.1 g) were added, and the mixture was allowed to react at 40°C for 3 hr while being stirring under a nitrogen atmosphere. After the reaction, the reaction mixture was cooled and treated with 10 ml of ethanol to decompose the sodium and organosodium compounds. Then the mixture was washed three times with a saturated sodium sulfate aqueous solution, and the organic layer was dried over anhydrous sodium sulfate. After the removal of the unreacted isoprene and dimethylamine under reduced pressure, the products were obtained (11.0 g). They included the $n=1$ telomer (0.3 g, bp 55—58°C/86 mmHg), and the $n=2$ telomer (3.0 g, bp 80—86°C/10 mmHg), the $n=3$ telomer (3.0 g, bp 80—90°C/1.5 mmHg), and the $n\geq 4$ telomers (4.7 g, residue), each telomer was analyzed by IR, NMR, and mass spectra after glc fractionation.

Measurements. All the products were analyzed after glc fractionation (15% Apiezone grease L/Celite 455, 4 mm$\phi\times$ 2.5 m, H_2: 50 ml/min). The IR spectra were recorded with a Perkin Elmer Model 337 spectrometer in a liquid film. The mass spectra were determined on a Hitachi RMU-7L spectrometer, and the NMR data, on a Hitachi-Perkin Elmer Model R-20 (60 MHz) spectrometer in carbon tetrachloride. The product ratios were determined by glc.