Table II. Hydroboration-Isomerization-Oxidation of 15-Triacontene[a]

solvent (amt, mL)	reagent (amt, mmol)	t_H, h[c]	T,[d] °C (t_R,[d] h)	product yield, %[b] $C_{30}H_{60}$	sec-$C_{30}H_{61}OH$	1-$C_{30}H_{61}OH$
diglyme (30)	BH_3 (0.37)	4	160 (9)	45	36	15
diglyme (20)	BH_3 (0.5)	4	160 (9)	36	34	30
diglyme (30)	BH_3 (0.5)	5	160 (13)	20	32	47
diglyme (20)	BH_3 (0.6)	4	160 (12)	32	17	51
triglyme (20)	BH_3 (1.5)	12	216 (19)	44	39	17
diglyme (100)	Sia_2BH (2.5)	6	160 (5)	13	56	31
diglyme (1)	9-BBN (2)		160 (16)	45	55	

[a] 15-Triacontene (1 mmol). [b] By GLC analysis. [c] Time for hydroboration. [d] Reflux temperature (T) and time (t_R).

olefins at the second stage than that of 15-triacontene, which leads to the $C_{30}BR'_2$ instead of the $(C_{30})_3B$ compound. However, the problem of this improved procedure is contamination of the alcohols arising from the 1-olefins added, making the separation of the desired product difficult. The hydrosilylation method was not examined, since the addition of the Si–H bond to olefins requires high temperature and long reaction times. In conclusion, it is now clear that the metathesis of 1-olefins–hydroboration–isomerization–oxidation procedure is generally applicable to the synthesis of fatty alcohols with extremely long chain lengths.

Experimental Section

^1H NMR spectra were recorded on a JEOL JNM-MH-100 instrument; chemical shifts (δ) are expressed in parts per million relative to Me_4Si. IR spectra were recorded on a JASCO IRA-1 spectrophotometer. All temperatures are uncorrected. Reagent-grade solvents were purified by standard techniques and kept over a drying agent. The chemicals, such as WCl_6 and Bu_4Sn, were purchased from Nakarai Chemical Co. Ltd. and purified by standard procedures.

Metathesis of 1-Hexadecene. Into a 50-mL flask, equipped with a magnetic stirrer and a reflux condenser and maintained under Ar, were injected 1-hexadecene (30 mmol, 8.6 mL), a trichloroethylene solution of WCl_6 (22 mL, 1.4 mmol), CH_3CN (0.96 mmol, 0.05 mL), and a trichloroethylene solution of Bu_4Sn (6 mL, 2.8 mmol) in this order by means of hypodermic syringes. The mixture was heated at 80 °C for 5 h and filtered through a short column of alumina to remove tungsten derivatives. Distillation of the filtrate gave 2.5–3.8 g of 15-triacontene [40–60%, bp 172–174 °C (0.015 mmHg)] and hexadecene [bp 81 °C (0.015 mmHg)]. Recrystallization of 15-triacontene from benzene gave white crystals: mp 53–55 °C; IR (KBr) 960 cm^{-1}; NMR ($CDCl_3$) δ 5.24 (t, 3 H), 1.92 (m, 4 H), 1.24 (m, 48 H), 0.87 (t, 3 H); mass spectrum, m/e 420 (parent) (calcd 420). Anal. Calcd for $C_{30}H_{60}$: C, 85.63; H, 14.37. Found: C, 85.65; H, 14.47. Ozonolysis of 15-triacontene was carried out by the known procedure,[11] and the alcohol thus obtained was identified by comparison with an authentic sample (Tokyo Kasei Co. Ltd.) as 1-pentadecanol by various spectroscopic methods.

Conversion of 15-Triacontene into 1-Triacontanol. Into a 100-mL flask, equipped with a magnetic stirrer and reflux condenser and maintained under Ar, were placed 15-triacontene (10 mmol, 4.21 g) and diglyme (60 mL). A BH_3–THF solution (5 mmol, 2.2 mL) was added at room temperature. The mixture was stirred at this temperature for 1 h and then maintained at 70 °C for 3 h. The resulting mixture was refluxed for 11 h and cooled to room temperature. Oxidation was accomplished with large excess amounts of H_2O_2–NaOH. Since separation of secondary alcohol $C_{30}H_{61}OH$ and primary alcohol $C_{30}H_{61}OH$ is quite difficult, the reaction products were acetylated with acetic anhydride in pyridine. Separation by column chromatography on silica gel with benzene–hexane as an eluent gave the primary acetate. Treatment with KOH in EtOH–H_2O produced 1-triacontanol in 47% overall yield: mp 87–88.5 °C (lit.[12] 86.5 °C); IR (KBr) 3300, 1068 cm^{-1}; NMR ($CDCl_3$) δ 3.62 (m, 2 H), 1.24 (m, 56 H), 0.88 (t, 3 H).

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Registry No. 1-Hexadecene, 629-73-2; 15-triacontene, 72443-19-7; 1-triacontanol, 593-50-0; 1-heptene, 592-76-7; 1-nonene, 124-11-8; 1-decene, 872-05-9; 1-undecene, 821-95-4; 1-dodecene, 112-41-4; 6-dodecene, 29493-00-3; 8-hexadecene, 18899-20-2; 9-octadecene, 5557-31-3; 10-eicosene, 66587-45-9; 11-docosene, 62978-77-2; sec-triacontanol, 28351-05-5.

Synthetic Furocoumarins. 10. Synthesis of α-Methylbenzo[*b*]furano Compounds[1]

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Phenols can be converted to α-methylbenzofurans by a five-step process which involves O-allylation, Claisen rearrangement to an *o*-allylphenol, acetylation of the phenolic hydroxyl group, addition of halogen to the allylic double bond, and cyclization in an alkaline alcoholic medium.[2] That approach has been successfully utilized to convert 7-hydroxycoumarins to α-methylfurocoumarins,[3] including 4,5′,8-trimethylpsoralene (**5**) which was obtained from 4,8-dimethyl-7-hydroxycoumarin (**1a**) in 28% overall yield. Trimethylpsoralen, under the generic name Trioxsalen, has been extensively used with ultraviolet radiation in the treatment of vitiligo[4] and has been recommended[5] in psoriasis therapy. Recently, its 4′-aminomethyl derivative has been recommended for the study of nucleic acids because it can form cross-linking diadducts[6] or, with short-pulse laser radiation, monoadducts.[7] Thus, a convenient and efficient synthesis of α-methylfurocoumarins is of contemporary practical interest.

Such a synthesis was sought through the conversion of hydroxycoumarins (**1**) to β-haloallyl ethers (**2**) which, it was hoped, would undergo Claisen rearrangement to *o*-(β-haloallyl)umbelliferones (**3** or **4**) that could subsequently

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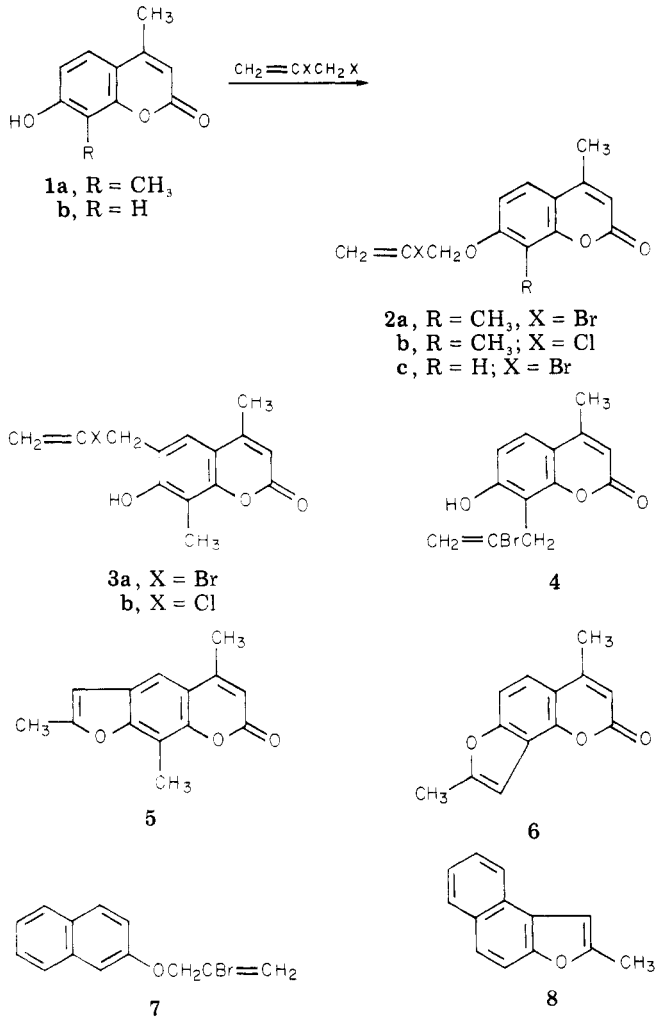
Chart I



be cyclized to methylated furocoumarins (**5** or **6**).[8] The first step proceeded smoothly when either 2,3-dichloropropene or 2,3-dibromopropene was used, providing the latter was redistilled at reduced pressure shortly before use. Thus, 4,8-dimethylumbelliferone (**1a**) was converted to its β-bromoallyl ether (**2a**) in 91% yield or to its β-chloroallyl ether (**2b**) in 77% yield. Similarly, 4-methylumbelliferone (**1b**) afforded β-bromoallyl ether **2c** in 89% yield.

The Claisen rearrangement of β-haloallyl ethers is of the type that has been described[9] as "abnormal" and that usually proceeds in poor yield. Thus, the rearrangement of β-bromoallyl phenyl ether has been reported[10] to proceed in 30% yield in boiling decalin. Hurd and Webb[11] were unable to obtain a pure product from the same rearrangement in decalin or fluorene or by heating without a solvent but isolated 24% of *o*-(β-chloroallyl)phenol and 19% of the cyclized product α-methylbenzofuran by heating β-chloroallyl phenyl ether. Anderson and LaVoie,[12] on the other hand, reported the Claisen rearrangement of the latter compound in refluxing *N,N*-diethylaniline yields *o*-(β-chloroallyl)phenol almost quantitatively but no α-methylbenzofuran.

Dramatically different results were obtained when the [(β-haloallyl)oxy]coumarins **2** of the present study were heated in a basic medium such as refluxing *N,N*-dimethylaniline or *N,N*-diethylaniline. The β-bromoallyl ethers **2a,c**, after 3–5 h, gave small yields of *o*-(β-bromoallyl)umbelliferones **3a** or **4**, but extension of the reaction time gave acceptable yields of cyclized furocoumarins **5** or **6**. Thus, 4,8-dimethyl-7-[(β-bromoallyl)oxy]coumarin (**2a**) was converted directly into pure 4,5′,8-trimethylpsoralen (**5**) in 60% yield after 24 h in refluxing *N,N*-diethylaniline. Similarly, 4,5′-dimethylisopsoralen (**6**) was obtained in 45% yield from 4-methyl-7-[(β-bromoallyl)oxy]coumarin (**2c**) in boiling *N,N*-dimethylaniline. As expected, the β-chloroallyl ether **2b** was less reactive toward cyclization. After 19 h in refluxing *N,N*-diethylaniline, **2b** was converted to the simple rearrangement product (**3b**), which was isolated in 37% yield. 4,5′,8-Trimethylpsoralen (**5**) was obtained from **2b** after a 24-h reflux period, but the yield was only 14%.

The results suggest a general approach to the synthesis of an α-methylfuran ring fused to an aromatic system. In two steps, a phenol can be converted to such a system by treatment with 2,3-dihalopropene followed by prolonged heating in a high-boiling basic medium. The scope of this new synthesis was explored with a simpler phenol without a lactone ring. Treatment of 2-naphthol with 2,3-dibromopropene gave 2-[(β-bromoallyl)oxy]naphthalene (**7**) in excellent yield. Cyclization in boiling *N,N*-diethylaniline proceeded smoothly to give a 58% yield of a 2-methylnaphthofuran, which is formulated as 2-methylnaphtho[2,1-*b*]furan (**8**) rather than its linear isomer because the Claisen rearrangement of (β-allyloxy)naphthalenes is known[13] to occur exclusively to the adjacent α position. Thus, the approach appears to have general applicability. Further studies are in progress.

Experimental Section

Melting points were determined in glass capillary tubes and are corrected. Columns for chromatography were packed in hexane with 95% of the Florisil to be used. The remaining 5% of the Florisil was stirred vigorously with a solution of the sample in methylene chloride while heat from a steam bath was applied. When dry, the Florisil with the adsorbed sample was added to the top of the column. The total weight of Florisil used was 40 times the weight of the sample. Elution was with hexane or solutions of acetone in hexane.

4,8-Dimethyl-7-[(β-bromoallyl)oxy]coumarin (2a). A mixture of 4,8-dimethyl-7-hydroxycoumarin (2.00 g, 10.5 mmol), anhydrous potassium carbonate (2.9 g, 21 mmol), freshly distilled 2,3-dibromopropene [2.50 g, 12.6 mmol, bp 42–44 °C (11 torr)], and acetone (75 mL) was stirred and heated under reflux for 6 h. Inorganic salts were filtered from the cooled solution and washed with acetone. Evaporation of the combined filtrate and washes under reduced pressure left a nearly colorless residue (3.52 g, mp 128.5–131 °C) that smelled faintly of 2,3-dibromopropene. Recrystallization of a sample (1.00 g) from methanol gave colorless needles (0.84 g, 91% yield), mp 130–132 °C. Another recrystallization gave an analytical sample, mp 131–131.5 °C.

Anal. Calcd for $C_{14}H_{13}O_3Br$: C, 54.39; H, 4.24; Br, 25.85. Found: C, 54.32; H, 4.24; Br, 26.07.

4,8-Dimethyl-7-[(β-chloroallyl)oxy]coumarin (2b). A mixture of 4,8-dimethyl-7-hydroxycoumarin (8.00 g, 42.1 mmol), anhydrous potassium carbonate (18.1 g, 130 mmol), 2,3-dichloropropene (33.6 g, 302 mmol), and acetone (600 mL) was stirred and heated under reflux for 24 h. The reaction mixture was concentrated to ca. 200 mL and filtered, and the inorganic

(8) While this paper was awaiting clearance by the sponsor, D. R. Bender, J. E. Hearst, and H. Rapoport, *J. Org. Chem.*, **44**, 2176 (1979), reported the synthesis of 4,5′,8-trimethylpsoralen in 70% yield from 4,8-dimethylumbelliferone (**1a**) via its β-chloroallyl ether (**2a**). Their procedure differs from that reported below in that they accomplish Claisen rearrangement and cyclization in separate steps under different conditions.

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salts were washed with acetone. Evaporation of the combined filtrate and washes under reduced pressure left a tan residue (11.30 g). Recrystallization from aqueous methanol gave small, off-white, needles (8.55 g, 77% yield), mp 117.5–120 °C. Another recrystallization did not change the melting point but gave an analytical sample.

Anal. Calcd for $C_{14}H_{13}O_3Cl$: C, 63.52; H, 4.95; Cl, 13.39. Found: C, 63.39; H, 5.12; Cl, 13.52.

4,5′,8-Trimethylpsoralen (5). Method A. A mixture of 4,8-dimethyl-7-[(β-bromoallyl)oxy]coumarin (200 mg, 0.65 mmol, mp 130–132 °C) and freshly distilled *N,N*-diethylaniline (5.0 mL) was stirred under a nitrogen atmosphere and heated under reflux for 24 h at an oil bath temperature of 225 ± 2 °C. An ether solution of the dark brown reaction mixture was filtered, and the filtrate was washed with several portions of 5% aqueous sodium hydroxide and one portion of 6 M hydrochloric acid. After drying ($MgSO_4$), the ether solution was concentrated under reduced pressure to a tan residue (131 mg, 88% yield, mp 222–228 °C). Recrystallization of 120 mg from 95% ethanol gave fine needles (82 mg, 60% yield), mp 232.5–233.5 °C (lit.[3] mp 234 °C). The melting point of a commercial sample[14] was 230–232 °C when determined simultaneously. The infrared spectra of the two samples were identical.

Method B. A mixture of 4,8-dimethyl-7-[(β-chloroallyl)-oxy]coumarin (500 mg, 1.89 mmol) and *N,N*-diethylaniline (5.0 mL) was protected by an Aquasorb tube while being heated under reflux for 24 h at an oil bath temperature of 220–225 °C. Treatment of the reaction mixture as described in method A gave some black, ether-insoluble material which was discarded. The desired product was obtained as a tan solid (154 mg, 41.6% yield), which was recrystallized from 95% ethanol to obtain light tan needles (53 mg, 14% yield), mp 233 °C (lit.[3] mp 234 °C). Its infrared spectrum was identical with that of a commercial sample.[14]

4,8-Dimethyl-6-(β-bromoallyl)-7-hydroxycoumarin (3a). A mixture of 4,8-dimethyl-7-[(β-bromoallyl)oxy]coumarin (1.00 g, 3.24 mmol) and freshly distilled *N,N*-diethylaniline (5.0 mL) was protected by an Aquasorb tube while being stirred and heated under reflux for 3 h at an oil bath temperature of 225 ± 3 °C. An ether solution of the dark brown reaction mixture was filtered to remove a black solid (ca. 10 mg), extracted with several portions of 5% aqueous sodium hydroxide, washed several times with 6 M hydrochloric acid, dried ($MgSO_4$), and concentrated to a tan solid (0.43 g, mp 114–125 °C) which was probably impure starting material. The alkaline extracts were acidified with concentrated hydrochloric acid to obtain an off-white solid (0.53 g, 53% yield, mp 154–161 °C) that was collected by ether extraction. Recrystallization from aqueous ethanol, followed by another recrystallization from benzene, gave an analytical sample, mp 175–176 °C.

Anal. Calcd for $C_{14}H_{13}O_3Br$: C, 54.39; H, 4.24; Br, 25.85. Found: C, 54.83; H, 4.39; Br, 25.87.

4,8-Dimethyl-6-(β-chloroallyl)-7-hydroxycoumarin (3b). A mixture of 4,8-dimethyl-7-[(β-chloroallyl)oxy]coumarin (500 mg, 1.89 mmol) and *N,N*-diethylaniline (5.0 mL) was protected by an Aquasorb tube while refluxing for 19 h at an oil bath temperature of 220–225 °C. The cooled mixture was treated as described above to obtain a tan solid (307 mg, 61% yield, mp 135–163 °C) from the acidified alkaline extracts. Recrystallization from benzene and Norit gave small yellow needles (183 mg, 37% yield, mp 172–175 °C).

Anal. Calcd for $C_{14}H_{13}O_3Cl$: C, 63.52; H, 4.95; Cl, 13.39. Found: C, 63.62; H, 4.75; Cl, 13.42.

4-Methyl-7-[(β-bromoallyl)oxy]coumarin (2c). 4-Methyl-7-hydroxycoumarin (2.00 g, 11.4 mmol) was refluxed with freshly distilled 2,3-dibromopropene (2.72 g, 13.6 mmol), anhydrous potassium carbonate (3.15 g, 22.8 mmol), and acetone (80 mL) for 4 h. The reaction mixture was treated as described for the preparation of **2a** to obtain an off-white solid (3.70 g) that contained some excess 2,3-dibromopropene. Recrystallization of a portion (500 mg) from ligroin (bp 100–120 °C) gave needles (394 mg, 89% yield), mp 109.5–110.5 °C. An analytical sample melting at 110–111 °C was obtained by recrystallization from methanol.

Anal. Calcd for $C_{13}H_{11}O_3Br$: C, 52.97; H, 3.75; Br, 27.08. Found: C, 52.98; H, 3.80; Br, 27.18.

4,5′-Dimethylisopsoralen (6). Rearrangement and cyclization of 4-methyl-7-[(β-bromoallyl)oxy]coumarin (500 mg, 1.69 mmol) was carried out as described in method A of the preparation of 4,5′,8-trimethylpsoralen except that *N,N*-dimethylaniline (12.5 mL) was used instead of the diethyl homologue. The same purification procedure gave a tan solid (289 mg, 80% yield), mp 173–179.5 °C. Recrystallization from methanol and Norit afforded light tan needles (161 mg, 45% yield), mp 182.5–184 °C (lit.[3] mp 182–183 °C). The infrared spectra of this sample and that of an authentic sample[3] were identical.

4-Methyl-8-(β-bromoallyl)-7-hydroxycoumarin (4). A mixture of 4-methyl-7-[(β-bromoallyl)oxy]coumarin (500 mg) and freshly distilled *N,N*-diethylaniline (12.5 mL) was stirred under a nitrogen atmosphere and heated under a reflux for 5 h at an oil bath temperature of ca. 225 °C. An ether solution of the reaction mixture was extracted with several portions of 5% aqueous sodium hydroxide, which were acidified and reextracted with ether to obtain an off-white solid (206 mg). Recrystallization from 95% ethanol gave fine, off-white needles (102 mg, 20% yield), mp 201–202 °C. Another recrystallization gave an analytical sample, mp 204.5–205 °C.

Anal. Calcd for $C_{13}H_{11}O_3Br$: C, 52.97; H, 3.75; Br, 27.08. Found: C, 52.97; H, 3.75; Br, 26.56.

2-[(β-Bromoallyl)oxy]naphthalene (7). A mixture of 2-naphthol (2.00 g, 13.9 mmol), anhydrous potassium carbonate (3.78 g, 27.8 mmol), freshly distilled 2,3-dibromopropene (3.24 g, 16.7 mmol), and acetone (90 mL) was stirred and heated under reflux for 4.5 h. Inorganic salts were filtered from the cooled solution and washed with acetone. Evaporation of the combined filtrate and washes left a yellow oil (3.81 g). Chromatography of a portion (300 mg) on a Florisil column, eluted with 5% acetone in hexane, gave a colorless solid (266 mg, 93% yield), mp 39–41.5 °C (Fisher-Johns apparatus).

Anal. Calcd for $C_{13}H_{11}OBr$: C, 59.37; H, 4.22; Br, 30.37. Found: C, 59.54; H, 4.48; Br, 29.93.

2-Methylnaphtho[2,1-*b*]furan (8). Rearrangement and cyclization of 2-[(β-bromoallyl)oxy]naphthalene (500 mg, 1.90 mmol) in freshly distilled *N,N*-diethylaniline (12.5 mL) was accomplished as described in method A of the preparation of 4,5′,8-trimethylpsoralen to obtain a dark oil that eventually solidified. Chromatography on a Florisil column (hexane eluant) gave a colorless solid (200 mg, 58% yield): mp 56.5–57.5 °C (Fisher-Johns apparatus); NMR ($CDCl_3$) δ 2.52 (3 H, s, CH_3), 6.85 (1 H, s, C_3-H), 7.2–7.6 (4 H, m, C_{4-7}-H), 7.83–8.14 (2 H, m, C_8-H and C_9-H).

Anal. Calcd for $C_{13}H_{10}O$: C, 85.69; H, 5.53. Found: C, 85.54; H, 5.97.

Acknowledgment. Grateful acknowledgment is made of financial support for this project from the Elder Pharmaceutical Co.

Registry No. **1a**, 4115-76-8; **1b**, 90-33-5; **2a**, 72478-66-1; **2b**, 69897-63-8; **2c**, 72478-67-2; **3a**, 72478-68-3; **3b**, 72478-69-4; **4**, 72478-70-7; **5**, 3902-71-4; **6**, 4063-41-6; **7**, 72478-71-8; **8**, 18747-04-1; 2,3-dibromopropene, 513-31-5; 2,3-dichloropropene, 78-88-6; 2-naphthol, 135-19-3.

(14) Supplied by the Paul B. Elder Co.

A Novel Synthesis of Aryl Orthoesters: Trimethyl *m*-Iodoorthobenzoate

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For some applications of our procedure of remote template-directed halogenation[1] to specific steroid problems, we required an orthoester of *m*-iodobenzoic acid. Unfortunately, the standard method for preparation of

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