

Syntheses of ω -Methylalkanols

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Abstract

As the first step of preparing branched alkane compounds, ω -methylalkanols were synthesized as purely as possible. 10-Methylundecanol was prepared by Cason's procedure as follows. Diisohexylcadmium, derived from isohexyl bromide, was condensed with 5-carbethoxyvaleroyl chloride to produce 6-oxo-10-methylundecanoic acid, which was converted into 10-methylundecanoic acid by the Clemmensen reduction, and then 10-methylundecanol was produced by reduction of the latter compound with lithium aluminum hydride. At every stage in these reactions, it was estimated on gas and thin-layer chromatography (GLC and TLC, respectively) that each intermediate product was sufficiently pure, and moreover structures of 6-oxo-10-methylundecanoic acid and 10-methylundecanol were determined with NMR and mass spectra. Consequently, it was recognized that, if the refining of each intermediate product was carried out carefully, ω -methylalkanols could be prepared by this procedure with high purity.

Recently, *n*-alkanes have been used as starting materials for preparing soft-style synthetic detergents, and petroproteins. Usually, these *n*-alkanes are separated selectively from the kerosine fraction of petroleum, but, at present, the raffinates have been scarcely utilized in preparing industrial products.

Now, according to the search on constituents of the gasoline fraction from the Ponca crude oil (Oklahoma, U. S. A.), made by Rossini¹⁾ (API Research Project 6), it was observed that the most abundant isomers in branched alkanes are usually 2-methyl isomers, and the other isomers present in only a small amount.

As a attempt to utilize such branched alkanes, this work was carried out to synthesize ω -methylalkanol (isoalkanol), one of their derivatives, as purely as

possible. It has been well-known that branched fatty acid esters are prepared by reducing branched oxo-fatty acid esters, which are synthesized by the reaction between ω -carbethoxyacyl chloride and isoalkyl metal compound. Fordyce *et al.*²⁾ and Cason³⁾ prepared intended long-chain isoalkyl compounds by using isoalkylmagnesium bromide and diisoalkylcadmium, respectively, as alkyl metal compounds, but they did not use analytical instruments to determine the properties of intermediate and final products at all.

In this paper, the authors prepared 10-methylundecanol (isolauryl alcohol) and 8-methylnonanol (isodecyl alcohol) by partly modifying the Cason's procedure³⁾. The syntheses of these compounds were carried out such as cited in Figure 1, and the applicability of the Cason's procedure to prepare pure long-chain branched paraffinic compounds were evaluated by ascertaining the purity of intermediate products at every stage of reaction on GLC and TLC, and by determining the molecular structure with NMR and mass spectrometry.

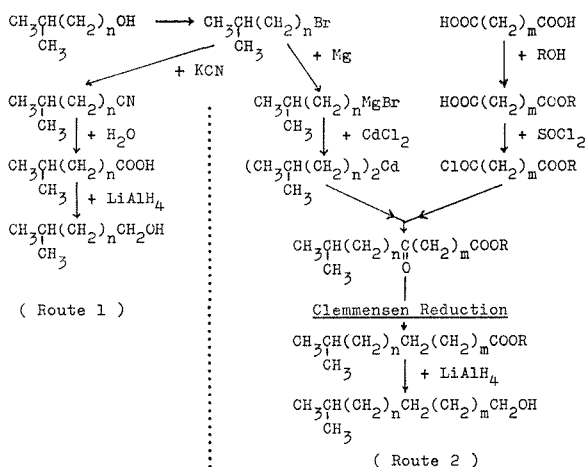


Fig. 1 Synthetic scheme of ω -methylalkanols.

Results and Discussion

10-Methylundecanol. Fieser *et al.*⁴⁾ prepared isolauroic acid by the Wolff-Kischner reduction from 5-oxo-isolauroic acid, which was synthesized from 1-isoheptyl bromide and γ -carbethoxybutyryl chloride by Cason's method³⁾. Milburn *et al.*⁵⁾ prepared isolauroic acid by electrolyzing the mixture of isovaleric acid and monomethyl pimelate.

The authors prepared 10-methylundecanol *via* 6-oxo-10-methylundecanoic acid, which was prepared from 1-isoheptyl bromide (I) and 5-carbethoxyvaleroyl chloride (II) (Fig. 1, Route 2). I was obtained *via* Route 1. All the intermediate

products, such as 1-isoamyl bromide (III), isocaproic acid (IV) and isohexanol (V), and I were ascertained as single component on GLC.

The other starting material, II, was prepared in good yield *via* Route 2. In this preparation, it was recognized that ethyl hydrogen adipate (VI), which is a intermediate product, contained only a trace of diethyl adipate (VII), but the latter could be removed during the purification of II.

It was found that ethyl 6-oxo-10-methylundecanoate, prepared by condensation of II with diisohexylcadmium (VIII), contained at least three components on GLC. One of them was identified as VII, while the others were difficult to separate each other by usual operations. Then, this product was saponified and acidified subsequently to make produce as free acid. After recrystallization of free acid from petroleum ether, a white crystal was obtained. This was estimated as single component on GLC. Analytical data on this compound agreed well with calculated values for 6-oxo-10-methylundecanoic acid (IX).

As IX has not been reported in the literatures within the limits of the authors' examination, the molecular structure of this compound was discussed on the basis of IR, NMR, and mass spectra.

The IR spectrum shows doublet peaks at 1380 and 1390 cm^{-1} , and a strong peak at *ca.* 1700 cm^{-1} due to isopropyl and carbonyl groups, respectively. Generally, two carbonyl groups are present in keto-acid, but only one peak was found in this spectrum. IR bands at 1600–1800 cm^{-1} region of 4-oxo-6-methylheptanoic acid and 6-oxo-8-methylnonanoic acid, prepared by the same procedures as IX, and IX (Fig. 2) show a tendency to appear in only one peak at this region, when the two carbonyl groups exist in a distance separating each other.

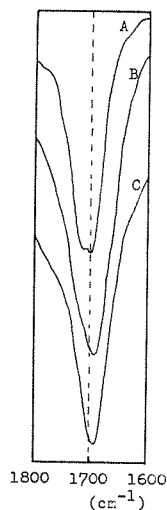


Fig. 2 IR Spectra of carbonyl groups in the keto-acids in the 1800 to 1600 cm^{-1} region. (KBr disk)

- A: 4-Oxo-6-methylheptanoic acid.
- B: 6-Oxo-8-methylnonanoic acid.
- C: 6-Oxo-10-methylundecanoic acid.

NMR spectrum (Fig. 3) shows the presence of isopropyl methyl (doublet at 0.83 and 0.93 ppm, 6H), methylene adjacent to carbonyl and carboxyl groups (multiplet at 2.1–2.5 ppm, 6H), the other methylene and isopropyl methine (multiplet at 1.1–1.9 ppm, 9H), and carboxyl (singlet at 11.35 ppm, 1H). Peaks between 1.0 and 2.0 ppm are seemed to be divisible in two parts, that is, peaks near 1.26 ppm (2H) and near 1.60 ppm (7H). As the latter contains isopropyl methine proton (*ca.* 1.7 ppm), the remained six protons including in this peak may be ascribed to β -methylene groups against carbonyl and carboxyl groups behaving in a same character. If this assumption is permissible, peak near 1.26 ppm will be due to methylene group adjacent to isopropyl group. Consequently, these assignments seemed to support the structure of **IX**.

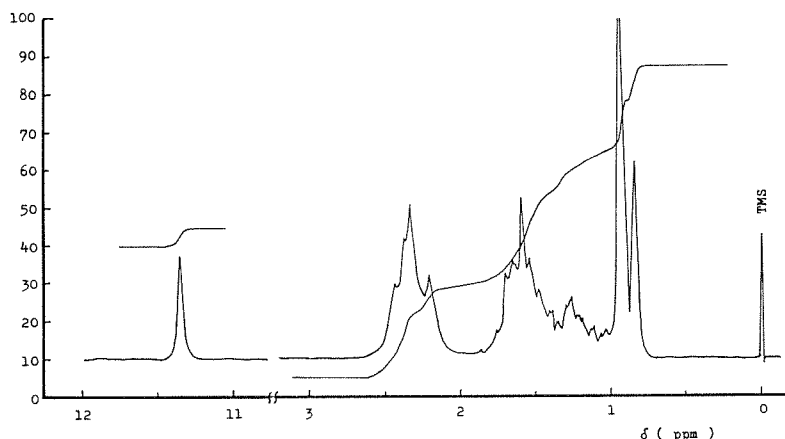


Fig. 3 NMR spectrum of 6-oxo-10-methylundecanoic acid, with sweep width 600 Hz and sweep time 500 sec.

Mass spectrum (Fig. 4) shows the molecular ion peak at m/e 214, and such ion peaks as m/e 129 [$\text{O}^+\equiv\text{C}-(\text{CH}_2)_4-\text{COOH}$], 113 [$(\text{CH}_3)_2\text{CH}-(\text{CH}_2)_3-\text{C}\equiv\text{O}^+$] which were generated by α -cleavages on either side of the carbonyl group, and isopropyl fragment ion peak at m/e 43. The ion peaks at m/e 60, 128 and 144 were owing to the so-called β -cleavages after the McLafferty rearrangement. These cleavages were shown to occur respectively between the carbons in the second and third, the fourth and fifth, and the seventh and eighth positions, and moreover the peaks at m/e 126 [m/e 144– H_2O] was observed. These ion peaks indicated that carbonyl and methyl groups were combined with the sixth and tenth carbons, respectively, in **IX**.

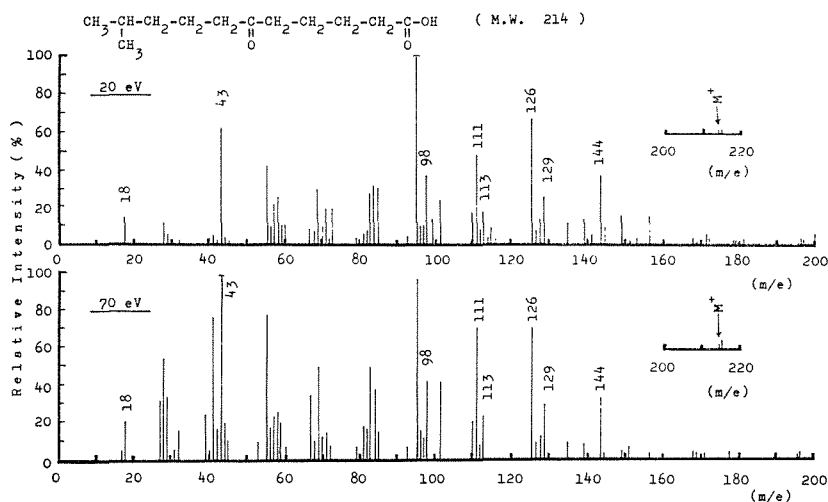


Fig. 4 Mass spectra of 6-oxo-10-methylundecanoic acid at ionization energies of 20 eV (A) and 70 eV (B).

Operating conditions: Total emission 80 μA ;

Chamber temperature 250°C; Evaporation

temperature (A) 140°C, (B) 150°C.

The meta-stable ion peaks observed at m^* 110.2 [calcd 110.25; m/e 144 \rightarrow 126 ($-\text{H}_2\text{O}$)] and m^* 95.5 [calcd 95.51; m/e 129 \rightarrow 111 ($-\text{H}_2\text{O}$)] support the fact that cleavages readily occur on the side of large alkyl group.

The intensity of a strong peak at m/e 95 scarcely changed even in the spectrum estimated at such a low electron ionizing voltage as 20 eV. This fact seemed to indicate that this peak was owing to the other volatile substance contained in only a small amount in this sample. The peak at this mass unit did not appear in the case of 10-methylundecanol at the electron ionizing voltage of both 15 and 70 eV.

The elemental analyses of the semicarbazone of **X** gave a good agreement with the calculated values.

The Clemmensen reduction of **X** was continued till the spot of **X** disappeared on TLC (about 13 hours). The melting points of the reduction product after recrystallization from petroleum ether and of the amide were agreed well with the referenced values of 10-methylundecanoic acid (**X**), and this crystal was determined as a single component on TLC and GLC.

The reduction of **X** to 10-methylundecanol (**XI**) was carried out by means of lithium aluminum hydride in good yield. The IR spectrum of **XI** shows the doublet peaks owing to the isopropyl group at 1380 and 1390 cm^{-1} , and a characteristic pattern of primary fatty alcohols. Both TLC and GLC show that this

product is composed of a single component.

NMR spectrum(Fig. 5), in which the presence of isopropyl methyl(doublet at 0.82 and 0.92 ppm, 6H), 1-methylene (triplet at 3.50 ppm, 2H), the other methylenes and isopropyl methine (singlet at 1.27 ppm, 17H), and hydroxyl proton (singlet at 2.56 ppm, 1H) is shown, supports the structure of XI.

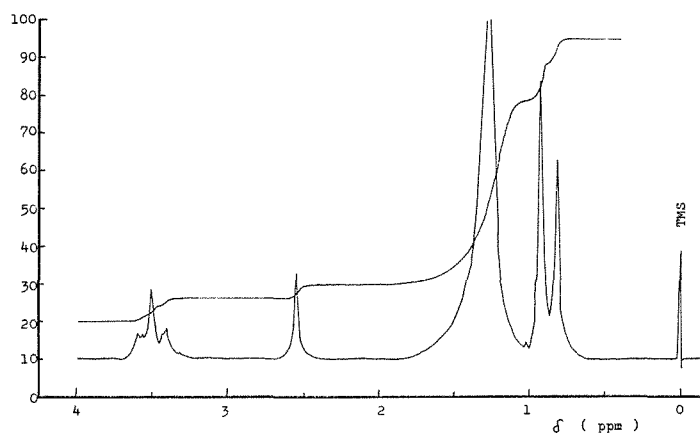


Fig. 5 NMR spectrum of 10-methylundecanol, with sweep width 600 Hz and sweep time 500 sec.

Mass spectrum (Fig. 6), which gave the following peaks at m/e 18 [H_2O^+], 31 [$\text{CH}_2=\text{OH}^+$], 43 [$\text{CH}_3-\text{CH}^+-\text{CH}_3$], and 168 [M^+-18], also supports this structure. In this spectrum, the molecular ion peak could not be found clearly, as generally known in the case of usual fatty alcohols.

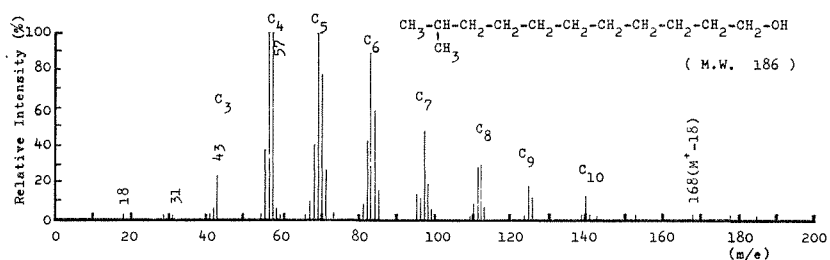


Fig. 6 Mass spectrum of 10-methylundecanol at ionization energy of 15 eV, with total emission 80 μA , chamber temperature 250°C, and evaporation temperature 100°C.

Consequently, it was confirmed that, if the refining of each intermediate product was carried out carefully, ω -methylalkanol could be prepared by the Cason's procedure with a satisfactory purity. Then, 8-methylnonanol was

synthesized according to this procedure.

Experimental

Measurements. All the melting and boiling points and reflux indexes were uncorrected. The IR spectra were recorded on a Hitachi EPI-S2 spectrometer (NaCl prism). The NMR spectra were determined at 60 MHz with a Hitachi R-20A High Resolution NMR spectrometer in carbon tetrachloride solutions using tetramethylsilane as an internal standard. Their chemical shifts were presented in terms of δ -values: s: singlet; d: doublet; t: triplet; m: multiplet. The mass spectra were obtained on a Hitachi RMU-6D mass spectrometer with a indirect inlet and an ionization energies of 20 (or 15) and 70 eV. The GLC were performed on a Hitachi Model KGL-2B gas chromatograph equipped with a flame-ionization detector at 190°C, with a flow-rate of nitrogen of 30 ml/min (in the case of C₆-derivatives, 90°C and 20 ml/min were used), and using a 4-mm \times 2-m stainless steel column packed with 5%PDEG succinate on Diasolid L(60/80 mesh).

The thin-layer chromatograms were prepared on silica gel (Wakogel B-10) and developed with a *n*-hexane—diethyl ether—glacial acetic acid (70:30:1, v/v) for adipic acid esters and oxo-fatty acids, petroleum ether (bp 35—50°C)—diethyl ether—glacial acetic acid (50:50:1, v/v) for ω -methyl fatty acids, and *n*-hexane—diethyl ether (1:1, v/v) for ω -methylalkanols, respectively. The spots were detected by charring with 50% sulfuric acid.

1-Isohexyl bromide (I). III was prepared from isoamyl alcohol (bp 127.5—129°C; purity: over 99% on GLC) applying the method of Kamm *et al.*⁸⁾ Yield 62.3%, bp 115—120°C (lit.⁷⁾, 121.3—121.7°C), n_D^{20} 1.4421(lit.⁸⁾, 1.44199), single peak on GLC. After III was converted to capronitrile, IV was obtained by successive hydrolysis. Yield 82.0%, bp 90—92°C/9 mmHg (lit.⁹⁾, 91—92°C/9mmHg), n_D^{20} 1.4145(lit.¹⁰⁾, 1.4144), single peak on GLC (ethyl ester). Mp of anilide 111.5—112°C (lit.¹¹⁾, 112.5—113.5°C). IV was reduced to V with lithium aluminum hydride in ether solution. Yield 91.0%, bp 150—151.5°C(lit.⁵⁾, 152°C), n_D^{20} 1.4143(lit.⁹⁾, 1.4142), single peak on GLC. Then, V was converted to I by the procedure previously described. Yield 78.8%, bp 146—148°C(lit.¹²⁾, 147—148°C), single peak on GLC.

Ethyl hydrogen adipate (VI). VI was prepared by modifying a method described by Swann *et al.*¹³⁾ in the preparation of ethyl hydrogen sebacate. Concentrated sulfuric acid (25 ml) was added into the mixture of adipic acid (1 mole) and VII (0.58 mole), and heated at 100—170°C in the oil bath to dissolve adipic acid. After the bath temperature was lowered to 130°C, ethanol (1 mole) was added and heated under reflux for four hours. The reaction

product was poured into a large amount of water and extracted with ether. The ether solution was washed with water, dried over anhydrous sodium sulfate, and evaporated to leave oily residue, from which VI was obtained by distillation under reduced pressure. Yield 52.4%, bp 159—160°C/7mmHg (lit.¹³), 155—157°C/7mmHg), mp 27—28.5°C (lit.¹⁴, 29°C). Amide of VI, mp 65—66°C. Found: C, 55.23%; H, 8.92%. Calcd for $C_8H_{16}O_3N$: C, 55.47%; H, 8.73%. It was found on TLC that VII contained a trace of VIII.

*5-Carbethoxyvaleroyl chloride*¹⁵ (II). A mixture of thionyl chloride (1.2 mole) and VI (1 mole) was heated under reflux for five hours. After removal of excess thionyl chloride, II was recovered as colorless liquid by distillation under reduced pressure. Yield 85.5%, bp 117—118°C/9mmHg (lit.¹⁶), 122—133°C/12mmHg), n_D^{25} 1.4462 (lit.¹⁷), 1.4460).

6-Oxo-10-methylundecanoic acid (IX). Dried cadmium chloride (0.12 mole) was added to the ether solution of Grignard reagent prepared from I (0.25 mole) in one portion. After stirring one hour under reflux, VIII was obtained by removing solvent. VIII was dissolved in 60 ml of dried benzene (thiophene free), and a dried benzene solution of II (0.2 mole) was added drop by drop under vigorous stirring. The reaction was carried out for one hour at room temperature, and subsequently for one hour under reflux. After the reaction was over, excess of 20% hydrochloric acid was added, and separated benzene layer was washed with water and dried over anhydrous sodium sulfate, then crude ethyl ester of IX was left in liquid by removing solvent (yield 56.2%).

This was saponified, and decomposed to free acid with diluted hydrochloric acid, and then extracted with ether. The ether solution was washed with water, dried over anhydrous sodium sulfate, and evaporated to leave a crystal, from which IX was recovered as a white crystal by recrystallization from petroleum ether (bp 35—50°C). IX was recognized as a single component on TLC and GLC (ethyl ester). Yield 40%, mp 54.0—54.5°C (no lit.). Found: C, 67.06%; H, 10.90%. Calcd for $C_{12}H_{22}O_3$: C, 67.25%; H, 10.35%. NMR (δ , in CCl_4): 0.83 and 0.93 ppm (isopropyl CH_3 , 6H, d), 1.26 ppm (CH_2 , 2H, m), 1.59 ppm (CH_2 and CH , 7H, m), 2.32 ppm (CH_2 adjacent to carbonyl and carboxyl groups, 6H, t), and 11.35 ppm (COOH, 1H, s). MS (70 eV): m/e 214 (M^+ ; relative intensity 4%), α -cleavage fragment ion peaks m/e 129(6, 7C; 29), 113(5, 6 C; 22), 111(m/e 129— H_2O ; 70), and 43 ($CH_3\overset{+}{C}$ —H— CH_3 ; 100), McLafferty rearrangement ion peaks m/e 144(7, 8 C; 34), 128(4, 5 C; 12), 126(m/e 144— H_2O ; 70), 98(m/e 144—(CO, H_2O); 42), and 60(2, 3 C; 4), meta-stable ion peaks m/e 95.5(calcd 95.51; m/e 129→111) and 110.2 (calcd 110.25; m/e 144→126). Semicarbazone of IX, mp 135.5—136.0°C (no lit.). Found: C, 57.65%; H, 9.41%; N, 15.01%. Calcd for $C_{13}H_{26}O_3N$: C, 57.54%; H, 9.29%; N, 15.49%.

10-Methylundecanoic acid (X). The Clemmensen reduction of IX was carried

out as follows. Amalgamated zinc sand (50 g) and concentrated hydrochloric acid (160 ml) were added to **IX** (7 g), and the reaction was continued under reflux for thirteen hours. Each 25 ml of concentrated hydrochloric acid was added to the reaction mixture at an interval of three hours, and the end point of the reaction was detected by the disappearance of **IX** on TLC. Reaction product was extracted with ether, and the ether solution was washed with water, dried over anhydrous sodium sulfate, and a crystal was recovered by removing solvent (yield 91.5%). A white crystal, obtained by recrystallization from petroleum ether (bp 35–50°C), was confirmed as a single component on TLC and GLC (ethyl ester). Mp 39–40°C (lit.⁴), 40°C). Amide of **X**: mp 105.0–105.5°C (lit.⁴), 105.7°C).

10-Methylundecanol (**XI**). Dried ethereal solution of **X** (10.5 g) was added drop by drop under vigorous stirring into a dispersion of lithium aluminum hydride (3 g) in dried ether. After the dropping was over, the mixture was stirred for thirty minutes at room temperature, and then the ethereal layer was separated by adding water and 20% sulfuric acid. The ether solution washed with 5% solution of sodium bicarbonate and water in due order, and a liquid reduction product, which was found as a single component on TLC and GLC, was recovered after the ether was removed (yield 84.5%).

IR spectrum (oil film): $\nu_{\text{O-H}}$ 3350 cm^{-1} , $\delta_{\text{C-H}}$ 1390 and 1370 cm^{-1} (isopropyl, doublet), $\nu_{\text{C-O}}$ 1050 cm^{-1} . NMR(δ , in CCl_4): 0.82 and 0.92 ppm (isopropyl CH_3 , 6H, d), 1.27 ppm (CH_2 and CH, 17H, s), 2.55 ppm (OH, 1H, s), and 3.50 ppm (CH_2 adjacent to hydroxyl group, 2H, t). MS (15 eV): m/e 18(H_2O^+ ; relative intensity 3%), 31($\text{CH}_2=\text{OH}^+$; 2), 43($\text{CH}_3-\text{CH}^+-\text{CH}_3$; 24), 57 (8, 9 C; 100), and 168 (M^+-18 ; 4).

8-Methylnonanol. Ethyl 6-oxo-8-methylnonanoate was prepared from 1-isobutyl bromide (0.1 mole) and **II** (0.08 mole) by means of the procedure previously described, and successively 6-oxo-8-methylnonanoic acid (**XII**) was obtained by hydrolysis of this product. After recrystallization from petroleum ether (bp 35–50°C), **XII** was obtained as a white crystal. Yield 12.4%, mp 39–40°C (lit.¹⁸), 39–40°C), single peak on GLC (methyl ester).

8-Methylnonanoic acid (**XIII**) was produced by the Clemmensen reduction of **XII** (yield 60.1%). **XIII** was recrystallized from petroleum ether (bp 35–50°C). White crystal, mp 22.5–23.5°C (no lit.), single peak on GLC (methyl ester).

8-Methylnonanol was obtained as a liquid substance by reduction of **XIII** with lithium aluminum hydride in dried ether. Yield 87%, single peak on GLC. IR spectrum (oil film): $\nu_{\text{O-H}}$ 3350 cm^{-1} , $\delta_{\text{C-H}}$ 1385–1370 cm^{-1} (isopropyl, doublet), $\nu_{\text{C-O}}$ 1050 cm^{-1} .

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ω -メチルアルカノールの合成

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分枝アルカン化合物合成の第一歩として、 ω -メチルアルカノールを、できるだけ純粋に合成することを試みた。Cason の方法により、下記のようにして10-メチルウンデカノールを合成した。臭化イソヘキシルより誘導したジイソヘキシルカドミウムと5-カルベトキシバレロイルクロリドの縮合により6-オキソ-10-メチルウンデカン酸を得、このもののクレメンゼン還元により10-メチルウンデカン酸とし、ついで水素化リチウムアルミニウムで還元して10-メチルウンデカノールとした。この合成に際しては、反応の各段階における生成物が充分純粋であることをガスクロマトグラフおよび薄層クロマトグラフで確かめながら反応を進め、また、主な生成物については、その構造を NMR または質量スペクトルで確かめた。以上の結果より、各中間生成物の精製に充分注意することにより、この方法で高純度の ω -メチルアルカノールを合成しうることを確かめることができた。