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SYNTHESIS OF CYCLOPENTADECANONE

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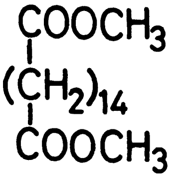
Ring contraction by the Favorskii-type rearrangement of α-sulfonyloxycyclohexadecanone (3) gave the corresponding cyclopentadecanecarboxylic acid (5) in a good yield. The acid (5) was converted to cyclopentadecanone (7) via α-phenylthio-(or α-methylthio-)cyclopentadecanecarboxylic acid (6).

In the previous report on macrocyclic ketone, we have described new synthesis of ß-methylcyclopentadecanone (dl-muscone).1) In this communication, we wish to report new synthesis of cyclopentadecanone (7) from α-hydroxycyclohexadecanone (2) via cyclopentadecanecarboxylic acid (5).2)

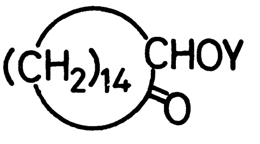
α-Hydroxycyclohexadecanone (2) was prepared by the acyloin condensation of dimethyl hexadecanedionate (1) in a good yield.3) Treatment of the α-hydroxyketone (2) with some sulfonyl chlorides in pyridine at 0°C gave the corresponding sulfonates (3) in 94-97% yields. Reaction of the sulfonate (3) with excess sodium methoxide in refluxing ether for 6 hours or in benzene at room temperature for 3 hours provided the mixture of cyclopentadecanecarboxylic acid (5) and the methyl ester (4) in a 70% yield.4) Cyclopentadecanecarboxylic acid (5) (mp 61°C) was sulfenylated by the treatment with 2 equiv of lithium diisopropyl amide and disulfide (PhSSPh or MeSSMe) in tetrahydrofuran to give the α-phenylthio-(or α-methylthio-)carboxylic acid (6).5) The α-thiocarboxylic acid (6) (R=Ph, mp 133°C; R=Me, mp 106°C) was converted to cyclopentadecanone (7) by anodic oxidation quantitatively. A typical procedure of this facile anodic oxidation reaction is as follows.

α-Phenylthiocarboxylic acid (6) (1 mmol) was dissolved in aqueous base (30 ml of water, 100 mg of NaOH, and 2 ml of ethanol). To this solution was added hexane (20 ml), and platinum electrodes (6 cm^2) were immersed in the aqueous layer.6) The mixture was electrolysed with stirring at a constant current of 0.05 A/cm^2, applied voltage ca. 5 V at 30°C for 2 hours. n-Hexane layer (uper layer) was separated and dried. Removal of the solvent afforded the mixture of cyclopentadecanone (7) and diphenyldisulfide. The yields of 6 and 7 are summarized in Table.

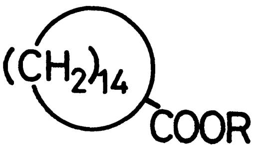


$COOCH_3-(CH_2)_{14}-COOCH_3$

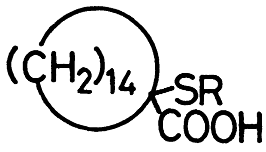
1



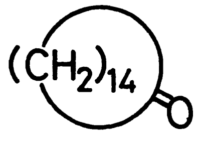
2 Y=H
3 Y=Ts,Bs,Ms



4 R=CH$_3$
5 R=H



6 R=Ph,CH$_3$



7

Table The Yields of α-Thiocarboxylic Acid (**6**) and Cyclopentadecanone (**7**)

R	**6** Yield (%)	**7** Yield (%)
Ph	85	97
CH_3	90	91

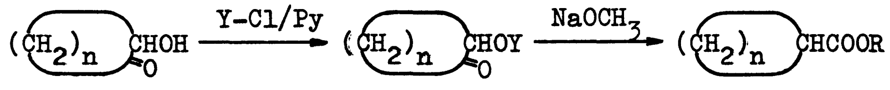
References and Notes

1) J. Nokami, Y. Kusumoto, K. Jinnai, and M. Kawada, Chem. Lett., 715(1977).

2) Synthesis of macrocyclic ketones by ring contraction has been reported; B. D. Mookherjee, R. W. Trenkle, and R. R. Patel, J. Org. Chem., **36**, 3266(1971). Conversion of cyclopentadecanecarboxylic acid (**5**) to cyclopentadecanone (**7**) via halocyclopentadecane has been patented; H. Nozaki, R. Noyori, and M. Mori, Japan 70 02,576, C. A., **72**, 100160g(1970).

3) The commercially available 1,16-hexadecanedioic acid (Okamura-seiyu Co., LTD.) was used. The reaction was as follows. To a suspension of sodium (10 g) in xylene (1000 ml) was added **1** (25 g in 100 ml of xylene) for 5 hours with vigorous stirring at 136 °C, and the stirring was continued for additional 2 hours. The reaction mixture was worked up according to the usual manner; yield 75% (15.2 g) 154 °C/2 mmHg.

4) This reaction seems to be useful for synthesis of alicyclic carboxylic acid. Some detailed results of the conversion of macrocyclic α-hydroxyketone to carboxylic acid are shown below.



ii **iii** **iv**

n	$Y^{a)}$	**iii** Yield (%)	**iv** Yield (%) in ether (in benzene)
12	Ts	83	72
	Bs	87	82
	Ms	91	84
14	Ts	97	55 (48)
	Bs	97	63 (65)
	Ms	94	70 (69)
18	Ts	90	52 (54)
	Bs	89	65 (70)
	Ms	93	69 (64)

a) Ts=p-$CH_3C_6H_4SO_2$, Bs=$C_6H_5SO_2$, Ms=CH_3SO_2.

5) B. M. Trost and Y. Tamaru, J. Amer. Chem. Soc., **99**, 3101(1977); α-methylthiocarboxylic acid was oxidatively decarboxylated to the corresponding ketone by using oxidizing agent such as N-chlorosuccinimide in organic solvent. Compared with the chemical method, the electrochemical method has some advantages.

6) The utility of the two-layer system of electrolysis solvents has been reported; S. Torii, H. Tanaka, and K. Misima, Bull. Chem. Soc. Jpn., **51**, 1575(1978).

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