SNa³⁾ in refluxing diglyme to the benzylthioether (IX), IR $\nu_{\max}^{\text{liquid}}$ cm^{-1}: 3070, 3040, 1603, 1495, 699 (phenyl), 2674, 1418 cm^{-1} (methylene adjacent to sulfur), which on desulfurization with Raney nickel yielded the ketal (X), $C_{17}H_{30}O_2$, n_D^{25} 1.497, $[\alpha]_D$ +23.2°, IR $\nu_{\max}^{\text{liquid}}$ cm^{-1}: 1198, 1078 (ketal). Acid-catalyzed hydrolysis of X produced the corresponding ketone (XI), $C_{15}H_{26}O$, d_4^{25} 0.963, n_D^{25} 1.491, $[\alpha]_D$ −49.0°, IR $\nu_{\max}^{\text{liquid}}$ 1702 cm^{-1} (carbonyl), NMR: singlet (3H) at 9.21 τ ($\underline{CH_3}$-C<), doublet (6H) at 9.13 τ (J=7.1, $\underline{CH_3}$-CH〈), singlet (3H) at 9.02 τ ($\underline{CH_3}$-C<CO-), which was identified with authentic valeranone by means of gas chromatogram, infrared spectrum, and 2,4-dinitrophenylhydrazone, $C_{21}H_{30}O_4N_4$, m.p. 101.5~102°.

The stereochemistry of valeranone as shown in formula (XI) has been rigorously established by the authors.⁴⁾ Whereupon it follows that kanokonol is correctly presented as 15-hydroxyvaleranone.

The authors indebted to Research Laboratories, Takeda Chemical Industries, Ltd., for NMR spectra, to Research Laboratory, Shionogi & Co., Ltd., for ORD curves, and to Hitachi, Ltd. for mass spectra.

Pharmaceutical Institute,
Faculty of Medicine,
Tohoku University,
Kita-4-bancho, Sendai.

Hiroshi Hikino (ヒキノヒロシ)
Yasuko Hikino (曳野靖子)
Tsunematsu Takemoto (竹本常松)

Received May 21, 1963
Revised June 17, 1963

---

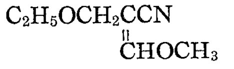
3) F.G. Bordwell, B. Pitt, M. Knell: J. Amer. Chem. Soc., **73**, 5004 (1951).
4) H. Hikino, Y. Hikino, Y. Takeshita, K. Meguro, T. Takemoto: This Bulletin, **11**, 1207 (1963) and references cited therein.

(Chem. Pharm. Bull.
11 (9) 1212 ~ 1214)

UDC 547.339.2.05

Isolation of *cis*- and *trans*-2-Methoxymethylene-3-ethoxypropionitrile

As had been reported previously,¹⁾ infrared spectrum of 2-methoxymethylene-3-ethoxypropionitrile (I) which was used as a starting material for pyrimidine derivatives has suggested that I is a mixture of its geometrical isomers. However, the determination of the *cis*- and *trans*-isomers has not yet been made completely.



$$\begin{array}{l} C_2H_5OCH_2\underset{\parallel}{C}CN \\ \qquad\quad\ \ CHOCH_3 \end{array}$$

I

The product prepared from 3-ethoxypropionitrile as cited in the previous paper¹⁾ gives two peaks at the retention times of 9.6 and 11.7 minutes by a gas chromatographic analysis.*¹ᵃ Further, the nuclear magnetic resonance (NMR) spectrum*² of this product

---

*1 Gas chromatography was carried out under the following conditions: Apparatus, Shimadzu GC-1B. *a*) Column, 4 mm.×1.5 m.; 0.75% N.G.S. on Anackrom A; column temp., 106°; N_2 23 ml./min. *b*) Column, 6 mm.×3 m.; 5% KF-54 on Chromosorb W; column temp. 120.5°; H_2 100 ml./min.

*2 The NMR spectra were taken with a Varian A-60 analytical spectraometer system on about 10% solutions in carbon tetrachloride containing about 1% tetramethylsilane as an internal reference. Chemical shifts are expressed in τ-units and coupling constants are in c.p.s. Accuracy limits are about ±0.02 τ and ±0.3 c.p.s.

1) A. Takamizawa, K. Ikawa, M. Narisada: Yakugaku Zasshi, **78**, 622 (1958).

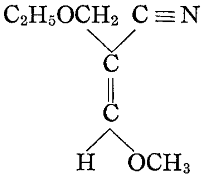
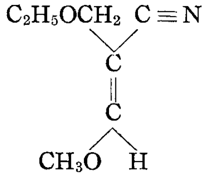
shows two triplet signal peaks (J=0.8 c.p.s.) assigned to methylidyne proton at 3.10 and 3.22 τ,[*3] and these relative area was about 1:1.5. Thus, it becomes evident that this product is a mixture containing *cis*- and *trans*-isomers in a ratio of 1.5:1.

This mixture was purified by fractional distillation under reduced pressure. Each fraction was checked by NMR spectroscopy. The fraction of b.p$_{1.0}$ 91.0° (α-compound) showed only one signal for the methylidyne proton at 3.22 τ. Gas chromatography also showed this fraction has only one peak at a retention time of 16.5 minutes.[*1b] The liquid of lower boiling point was not easily separated from the fraction of higher boiling point. However, after continuous distillation, the fraction of 6.p$_{2.0}$ 91.5° (β-compound) which shows only one signal for the methylidyne proton at 3.10 τ was obtained. Gas chromatogram of this fraction also shows one peak at 14.8 minutes.[*1b] Accordingly, it was recognized that the mixture was completely separated.

NMR studies of acrylonitrile and its derivatives2) have shown that the signal of the *cis*-proton to the CN group appears at a lower field than that of *trans*-proton. Therefore, also in the present case, the β-compound showing the signal of the methylidyne proton at the lower field is believed to have the structure in which the CN group and the proton are at the same side (*trans*-isomer), and accordingly, the α-compound is the *cis*-isomer. This consideration was confirmed by measurements of the dipole moment of these two isomers. The dipole moments observed for the α- and β-compounds are 5.47 D and 4.58 D, respectively. Thus, the α-compound is evidently the *cis*-isomer, because the dipole moment expected for the *cis*-isomer is considerably larger than that expected for the *trans*-isomer.

The physical constants of these two isomers are listed in Table I.

TABLE I. Physical Constants of *cis*- and *trans*-2-Methoxymethylene-3-ethoxypropinitrile

Compound		
	Iα (*cis*)	Iβ (*trans*)
b.p. (°C/mm. Hg)	91.0/1.0	91.5/2.0
n_D^{23}	1.4591	1.4478
NMR (τ, in 10% CCl_4), =CH	3.22 (triplet)	3.10 (triplet)
=C-CH_2	6.03 (doublet)	6.13 (doublet)
=C-OCH_3	6.12 (singlet)	6.12 (singlet)
J_{CH, CH_2} (c.p.s.)	0.8	0.8
Gas chromatography (min.)	16.5	14.8
Dipole moment (D)	5.47	4.58
IR (cm^{-1}), characteristic	716	808
UV λ_{max}^{EtOH} mμ (log ε)	231.7 (4.17)	228.9 (4.12)

The authors express their gratitude to Prof. Emeritus E. Ochiai of the University of Tokyo, Prof. M. Tomita and Prof. S. Uyeo of Kyoto University, Prof. S. Nagakura of the University of Tokyo, and Dr. K. Takeda, Director of this laboratory, for their kind encouragement, and their appreciation to Dr. H. Watanabe and Mr. T. Yoshizaki for the dipole moment measurements and discussion, to Dr. N. Ikekawa of Institute of Physical and Chemical Research, Mr. I. Ishizuka and Miss Y. Sato for carrying out the gas chromatography, and to Drs. T. Kubota and Y. Matsui and Messrs. I. Tanaka

---

[*3] Effects of solvents and concentrations on the NMR spectrum of I were ascertained. For example, in pyridine or in pure liquid, the positions of two signal peaks for the methylidyne protons of each isomer are almost coincided.

2) G.S. Reddy, J.H. Goldstein, L. Mandell: J. Am. Chem. Soc., **83**, 1300 (1961), and references cited therein.