*NMR Spectra of Aliphatic Compounds Containing Oxygen Atoms and the Related Compounds**

By Kenkichi NUKADA

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Many works concerning the chemical shifts of functional groups in organic molecules[1-4] have been reported, but the systematic study for the chemical shifts of functional groups containing oxygen atoms has not yet been carried out in detail. In this paper, the author presents the NMR spectra of more than thirty aliphatic compounds containing the oxygen atom and the related compounds such as ethers, formals, acetals, ketal, orthoaliphatic acid esters, polyethylene glycol diethers and cyclic compounds. These compounds contain various types of functional groups such as CH_3–O, O–CH_2–O, HC(O)(O)O, etc. Comparing spectra with each other, the author obtained a table of chemical shifts of functional groups. It is also found that there exist some correlations between the chemical shifts of the same type of equivalent protons and the type of alkyl groups bonded to the oxygen atom. The origin of the correlation was considered.

Experimental

Measurement of NMR Spectra.—Spectra were obtained by means of a Varian 4300 B spectrometer (40 Mc). The spectra of both pure liquid benzene solution (volume ratio of solute to benzene equals to 4 : 1) for each sample were obtained and the chemical shifts with respect to proton resonance in benzene were calculated. As a field marker, the spectrum of pure propionic acid was used (Fig. 1). The absolute value of shift was calibrated by the displacement between proton resonances and cyclohexane (223 cps)[3]. Since it is necessary to maintain all the experimental conditions as stable as possible in the accurate chemical shift measurement, a sweep rate of $1p/10^7$ per second was used. When necessary to obtain higher resolved spectra, a smaller sweep rate ($0.4p/10^7$) was used. In the latter case, however, the error of chemical shift was considerably increased. The probable error of the measurement in case of rapid passage was within ±2%. Spectra of pure sample were obtained because sometimes it was necessary to check the solvent effect in benzene solution.

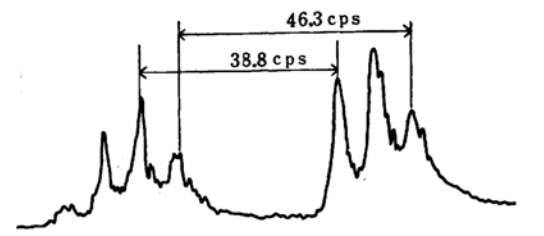

Fig. 1. NMR spectrum of pure propionic acid. This spectrum was used as a field marker, i. e., before and after every chemical shift measurement this spectrum was measured. The absolute values between peaks were calibrated by the displacement between proton resonances in benzene and cyclohexane (223 cps).

Samples. — Formals (dimethyl formal, methyl ethyl formal, diethyl formal and diisopropyl formal) and acetals (dimethyl acetal, methyl ethyl acetal and diethyl acetal) were synthesized in the author's laboratory[5]. All the other compounds are commercial products (Tokyo Kasei and Eastman Kodak Co.).

* This is essentially the extension of the work already reported in this Bulletin as a short communication. (K. Nukada and U. Maeda, This Bulletin, 32, 656 (1959)).

1) L. H. Meyer, A. Saika and H. S. Gutowsky, *J. Am. Chem. Soc.* 75, 4567 (1953).

2) V. D. Tiers, "Characteristic Nuclear Magnetic Resonance Shielding Values (Spectral Position) for Hydrogen in Organic Structures", Organic Section, Exploratory NMR Studies, Project 737602, Minnesota Mining and Manufacturing Co. U. S. A. (1958).

3) N. F. Chamberlain, *Anal. Chem.*, 31, 56 (1959).

4) B. L. Bothner-By, C. Naar-Colin and B. L. Shapiro "NMR Spectra and Structure Correlations", (Vol. II), Harvard University, (1958).

5) K. Nukada, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), 80, 976 (1959).

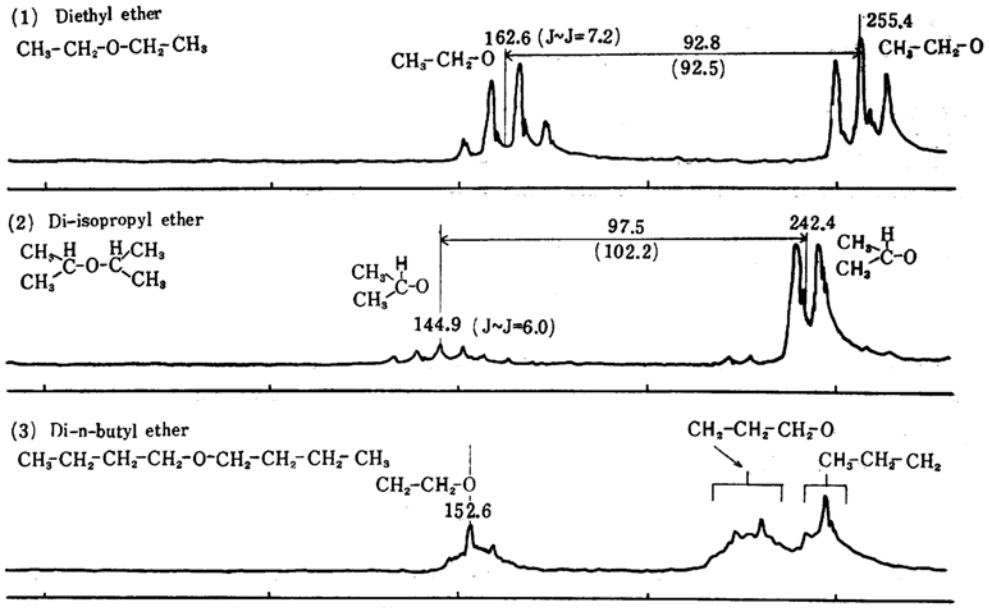
(1) Diethyl ether
CH3-CH2-O-CH2-CH3
162.6 (J~J=7.2)
92.8
(92.5)
255.4
(2) Di-isopropyl ether
97.5
(102.2)
242.4
144.9 (J~J=6.0)
(3) Di-n-butyl ether
CH3-CH2-CH2-CH2-O-CH2-CH2-CH2-CH3
152.6

Fig. 2-1.

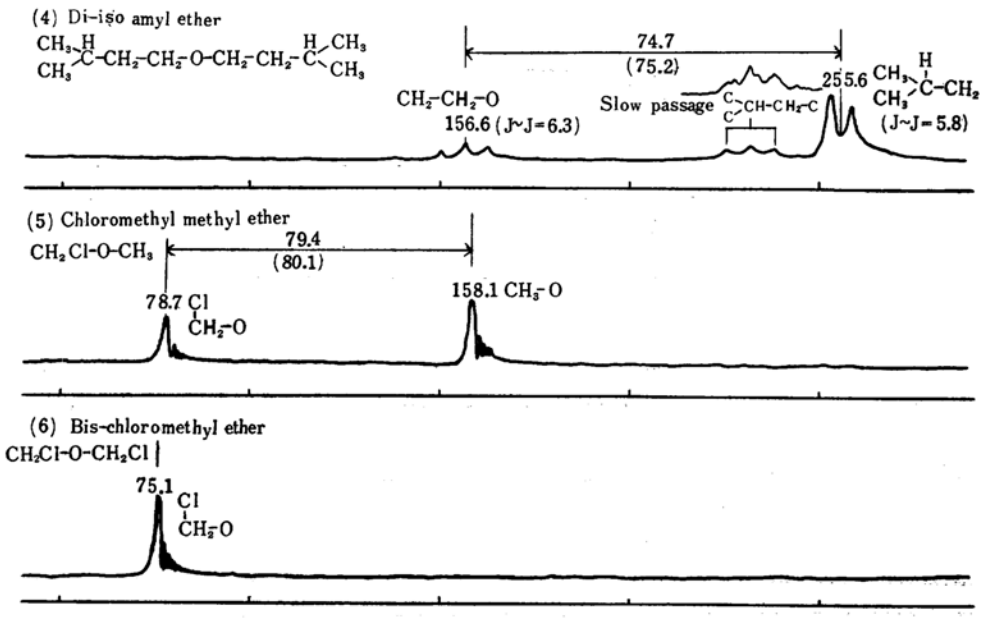
(4) Di-iso amyl ether
74.7
(75.2)
156.6 (J~J=6.3)
Slow passage
255.6
(J~J=5.8)
(5) Chloromethyl methyl ether
CH2Cl-O-CH3
79.4
(80.1)
78.7
158.1
(6) Bis-chloromethyl ether
CH2Cl-O-CH2Cl
75.1

Fig. 2-2.

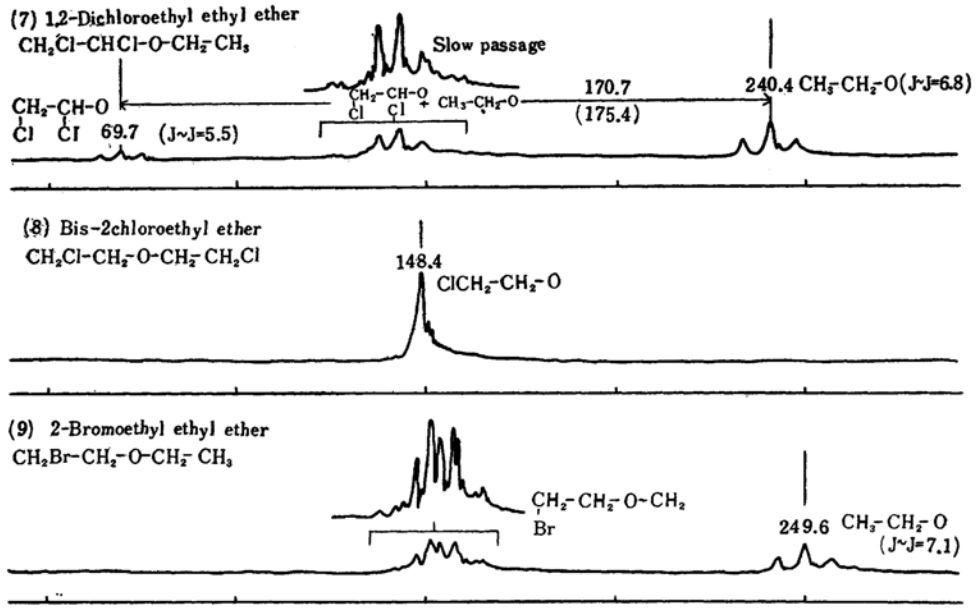
(7) 1,2-Dichloroethyl ethyl ether
CH2Cl-CHCl-O-CH2-CH3
Slow passage
CH2-CH-O
Cl Cl
69.7 (J~J=5.5)
CH2-CH-O + CH3-CH2-O
170.7
(175.4)
240.4 CH3-CH2-O(J~J=6.8)
(8) Bis-2chloroethyl ether
CH2Cl-CH2-O-CH2-CH2Cl
148.4
ClCH2-CH2-O
(9) 2-Bromoethyl ether
CH2Br-CH2-O-CH2-CH3
CH2-CH2-O-CH2
Br
249.6 CH3-CH2-O
(J~J=7.1)

Fig. 2-3.

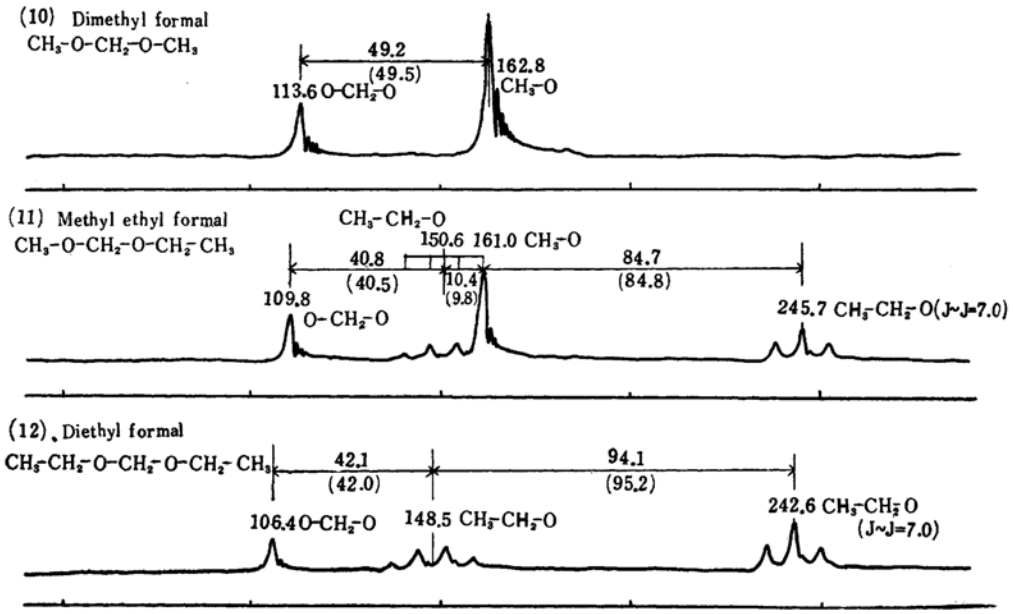
(10) Dimethyl formal
CH3-O-CH2-O-CH3
49.2
(49.5)
113.6 O-CH2-O
162.8
CH3-O
(11) Methyl ethyl formal
CH3-O-CH2-O-CH2-CH3
CH3-CH2-O
150.6 161.0 CH3-O
40.8
(40.5)
10.4
(9.8)
84.7
(84.8)
109.8
O-CH2-O
245.7 CH3-CH2-O(J~J=7.0)
(12) Diethyl formal
CH3-CH2-O-CH2-O-CH2-CH3
42.1
(42.0)
94.1
(95.2)
106.4 O-CH2-O
148.5 CH3-CH2-O
242.6 CH3-CH2-O
(J~J=7.0)

Fig. 2-4.

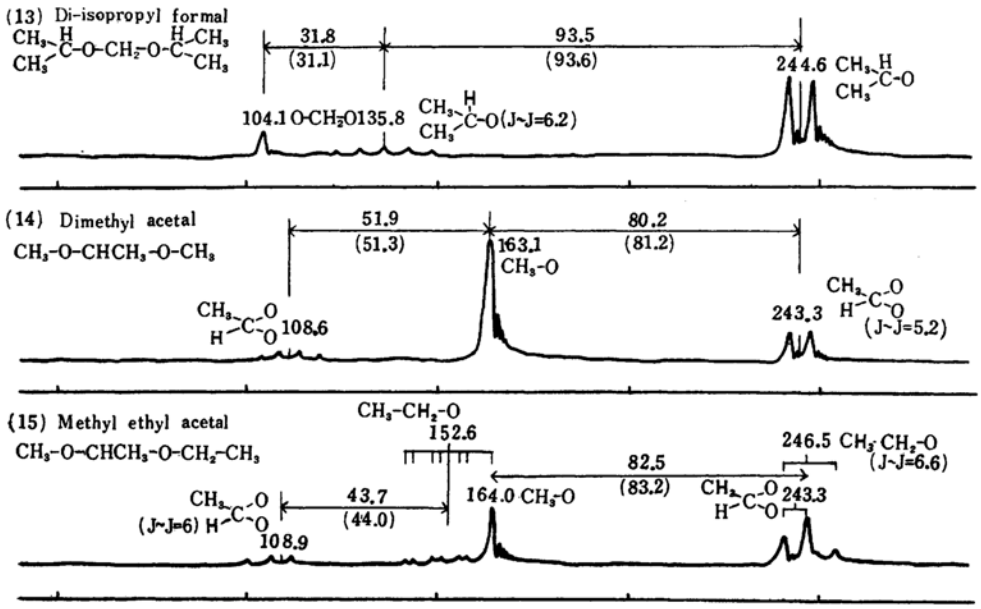
(13) Di-isopropyl formal
31.8
(31.1)
93.5
(93.6)
244.6
104.1 O-CH2-O 135.8
(J~J=6.2)
(14) Dimethyl acetal
CH3-O-CHCH3-O-CH3
51.9
(51.3)
80.2
(81.2)
163.1
CH3-O
108.6
243.3
(J~J=5.2)
(15) Methyl ethyl acetal
CH3-O-CHCH3-O-CH2-CH3
CH3-CH2-O
152.6
246.5
(J~J=6.6)
82.5
(83.2)
43.7
(44.0)
164.0 CH3-O
243.3
(J~J=6)
108.9

Fig. 2-5.

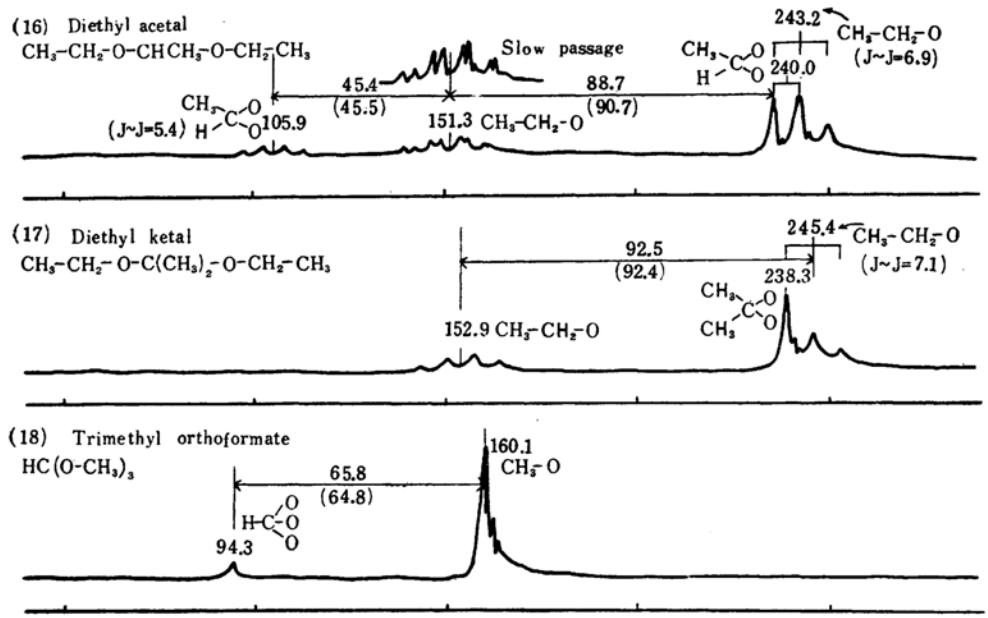
(16) Diethyl acetal
CH3-CH2-O-CHCH3-O-CH2-CH3
Slow passage
243.2
CH3-CH2-O
(J~J=6.9)
240.0
45.4
(45.5)
88.7
(90.7)
(J~J=5.4)
105.9
151.3 CH3-CH2-O
(17) Diethyl ketal
CH3-CH2-O-C(CH3)2-O-CH2-CH3
245.4
CH3-CH2-O
(J~J=7.1)
92.5
(92.4)
238.3
152.9 CH3-CH2-O
(18) Trimethyl orthoformate
HC(O-CH3)3
160.1
CH3-O
65.8
(64.8)
94.3

Fig. 2-6.

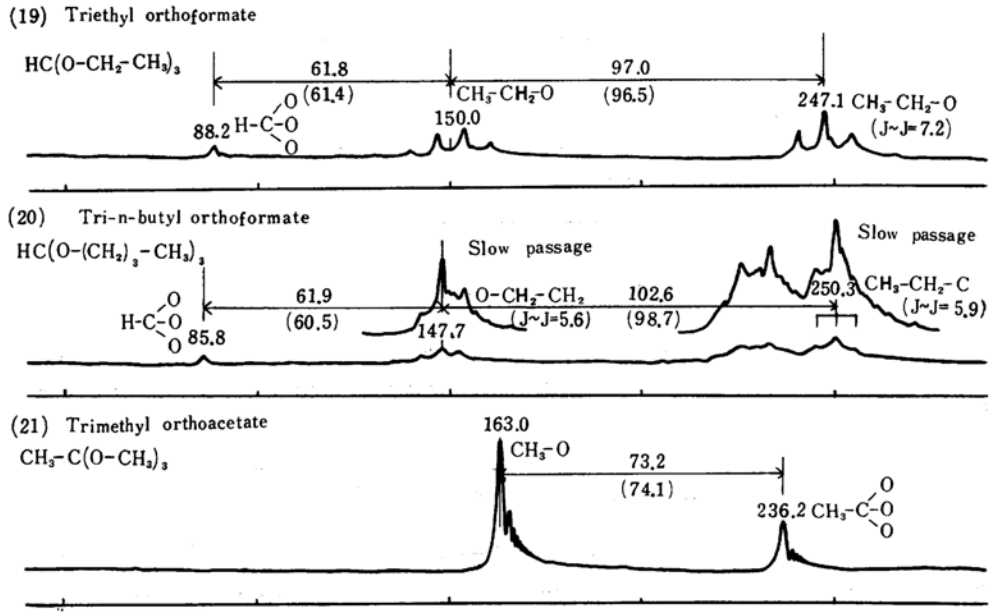
(19) Triethyl orthoformate
HC(O-CH2-CH3)3
61.8
(61.4)
97.0
(96.5)
CH3-CH2-O
88.2
150.0
247.1 CH3-CH2-O
(J~J=7.2)
(20) Tri-n-butyl orthoformate
HC(O-(CH2)3-CH3)3
Slow passage
Slow passage
61.9
(60.5)
O-CH2-CH2
(J~J=5.6)
102.6
(98.7)
250.3
CH3-CH2-C
(J~J=5.9)
85.8
147.7
(21) Trimethyl orthoacetate
CH3-C(O-CH3)3
163.0
CH3-O
73.2
(74.1)
236.2 CH3-C-O

Fig. 2-7.

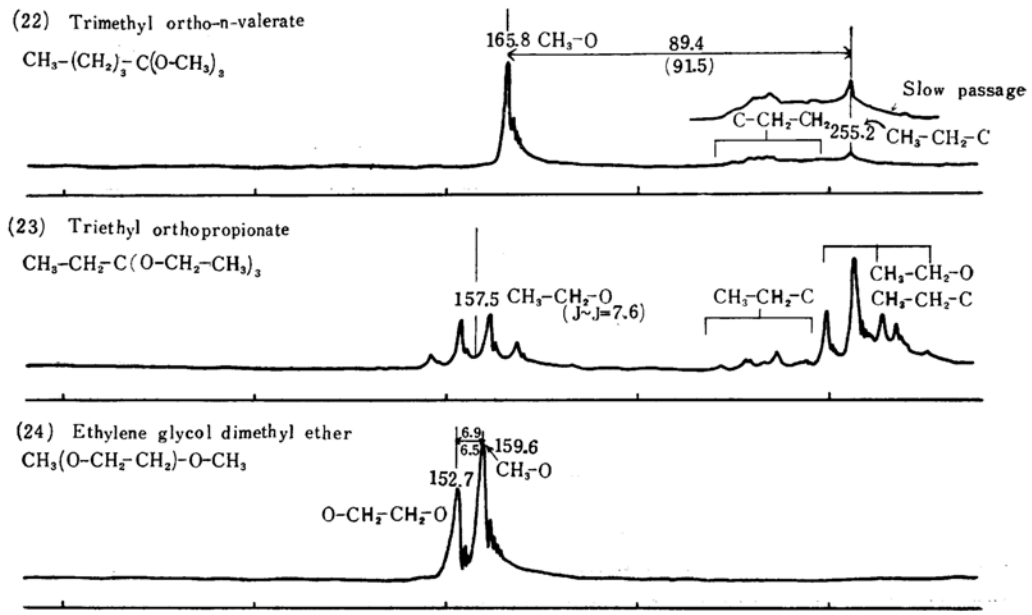
(22) Trimethyl ortho-n-valerate
CH3-(CH2)3-C(O-CH3)3
165.8 CH3-O
89.4
(91.5)
Slow passage
C-CH2-CH2
255.2
CH3-CH2-C
(23) Triethyl orthopropionate
CH3-CH2-C(O-CH2-CH3)3
157.5 CH3-CH2-O
(J~J=7.6)
CH3-CH2-C
CH3-CH2-O
CH3-CH2-C
(24) Ethylene glycol dimethyl ether
CH3(O-CH2-CH2)-O-CH3
6.9
6.5
159.6
CH3-O
152.7
O-CH2-CH2-O

Fig. 2-8.

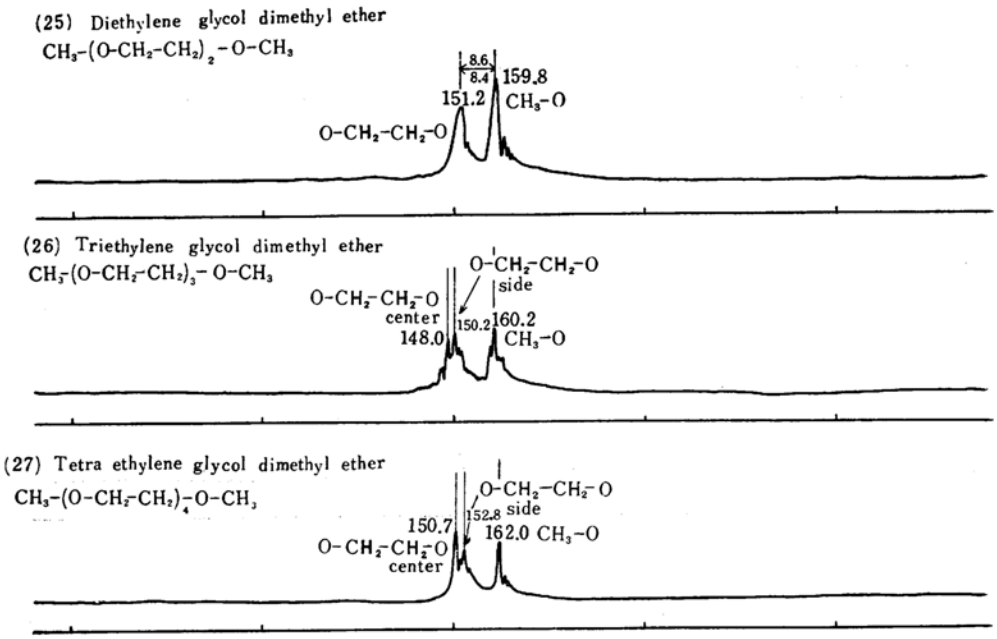

Fig. 2-9.

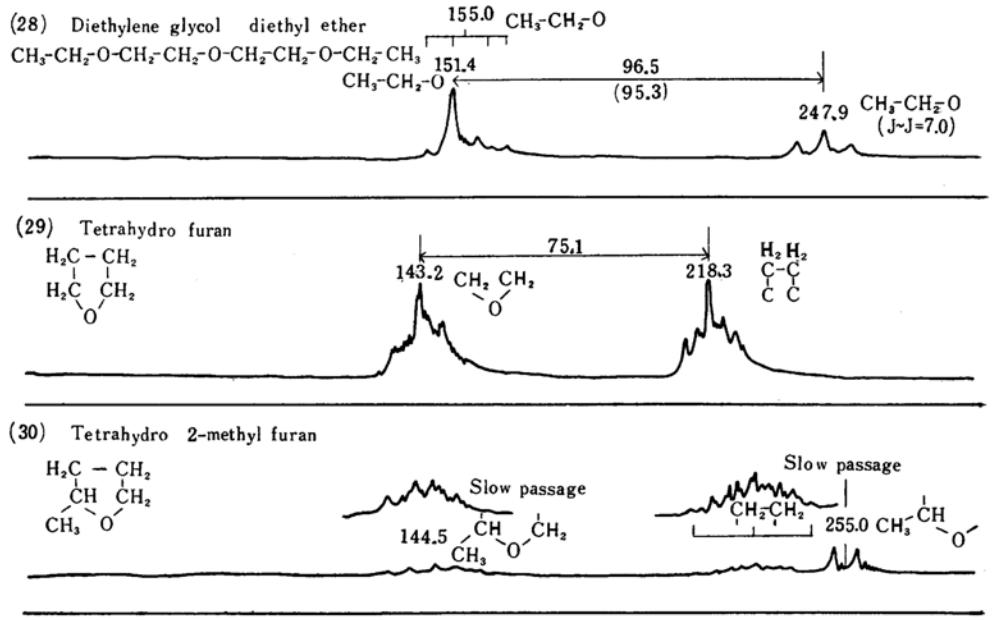

Fig. 2-10.

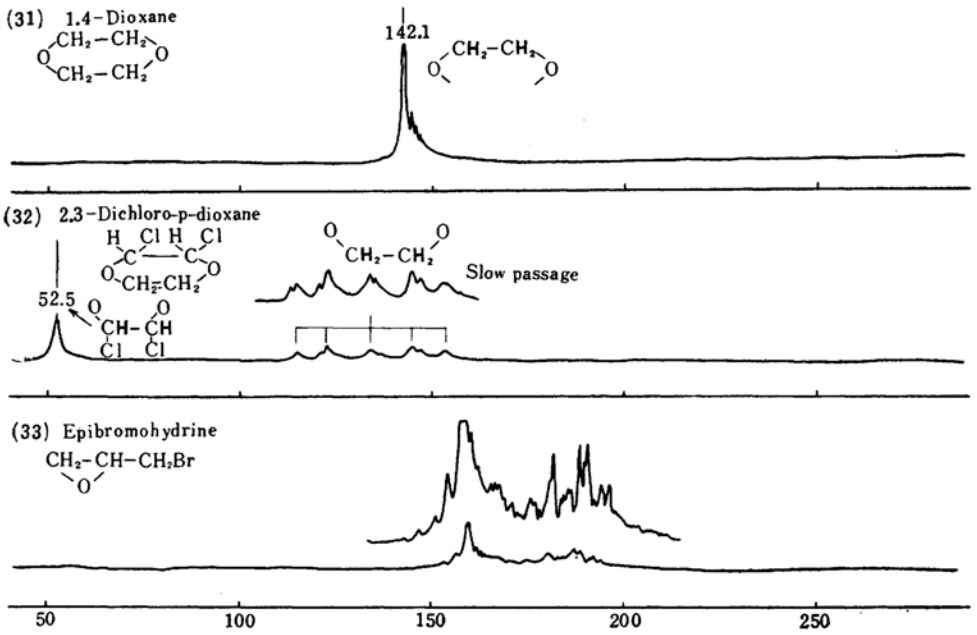

Fig. 2-11.

Fig. 2. NMR spectra of oxygen containing aliphatic compounds. Chemical shift (cps) from benzene protons and assignment are marked on each peak. J-J coupling constant and separation between peaks are also described.

TABLE I. CHEMICAL SHIFT OF FUNCTIONAL GROUP

Name of group	Type of group	Type of sub-group	Chemical shift cps	Number of samples
CH_3-C-C-C-		δ_{CH_3}	253.7±3.4	3
CH_3-CH_2-O-	B	β_{CH_3}	246.4±9.0	10
$\begin{matrix}CH_3\\CH_3\end{matrix}$>CH-O-	B	β_{CH_3}	243.5±1.1	2
$\begin{matrix}CH_3\\CH_3\end{matrix}$>C<$\begin{matrix}O-\\O-\end{matrix}$	B	$\beta^2{}_{CH_3}$	242.2±2.2	3
CH_3-C(O-)(O-)(O-)	B	$\beta^3{}_{CH_3}$	236.2	1
-CH_2-C-O- (Five members ring)	B	β_{CH_2} (ring)	218.3	1
CH_3-O-	A	α_{CH_3}	161.6±4.2	11
-C-CH_2-O-	A	α_{CH_2}	152.9±9.7	12
-O-CH_2-CH_2-O	A	$\alpha\beta_{CH_2}$	151.0±3.0	5
Cl-CH_2-CH_2-O-		$\alpha'\beta_{CH_2}$, $\alpha\beta'_{CH_2}$	148.4	1
-C-CH_2-O- (Five members ring)	A	α_{CH_2} (ring)	143.9±0.7	2
-O-CH_2-CH_2-O- (Six members ring)	A	$\alpha\beta_{CH_2}$ (ring)	142.1	1
$\begin{matrix}CH_3\\CH_3\end{matrix}$>CH-O-	A	α_{CH}	140.4±4.6	2
-O-CH_2-O-	A^2	$\alpha^2{}_{CH_2}$	108.5±5.1	4
$\begin{matrix}CH_3\\H\end{matrix}$>C<$\begin{matrix}O-\\O-\end{matrix}$	A^2	$\alpha^2{}_{CH}$	107.8±1.9	3
H-C(O-)(O-)(O-)	A^3	$\alpha^3{}_{CH}$	89.4±4.9	3
Cl-CH_2-O-		$\alpha\alpha'_{CH_2}$	76.9±1.8	2
$\begin{matrix}Cl\\Cl\end{matrix}$>CH-O-		$\alpha\alpha'^2{}_{CH}$	69.7	1
$\begin{matrix}-O\\Cl\end{matrix}$>CH-CH<$\begin{matrix}O-\\Cl\end{matrix}$ (Six members ring)		$\alpha\alpha'\beta\beta'_{CH}$	52.5	1

TABLE II. CORRELATION BETWEEN CHEMICAL SHIFT AND THE TYPE OF SUBSTITUENT ALKYL GROUP (I)

Type of molecule	Type of alkyl group	Equivalent proton group	Chemical shift
$HC(OR)_3$	CH_3-	$HC(O)_3$	94.3
	CH_3-CH_2-		88.2
	$CH_3-(CH_2)_3-$		85.8
$H_2C(OR_1)(OR_2)$	R_1, R_2: CH_3-	$H_2C(O)_2$	113.6
	R_1: CH_3-, R_2: CH_3-CH_2-		109.8
	R_1, R_2: CH_3-CH_2-		106.4
	R_1, R_2: $CH_3>CH$ CH_3		104.1
$CH_3-CH(OR_1)(OR_2)$	R_1, R_2: CH_3-	$CH_3-CH(O)_2$	108.6
	R_1: CH_3-, R_2: CH_3-CH_2-		108.9
	R_1, R_2: CH_3-CH_2-		105.9
$CH_3-CH(OR_1)(OR_2)$	R_1, R_2: CH_3-	$CH_3-CH(O)_2$	243.3
	R_1: CH_3-, R_2: CH_3-CH_2-		343.3
	R_1, R_2: CH_3-CH_2-		240.0

TABLE III. CORRELATION BETWEEN CHEMICAL SHIFT AND THE TYPE OF SUBSTITUENT ALKYL GROUP (II)

Type of molecule	Type of alkyl group	Equivalent proton group	Chemical shift
$RC(O-CH_3)_3$	H-	$-O-CH_3$	160.1
	CH_3-		163.0
	$CH_3-(CH_2)_3-$		165.8
$RC(O-C_2H_5)_3$	H-	$-O-CH_2-CH_3$	150.0
	CH_3-CH_2-		157.5
$H-CR(O-CH_3)_2$	H-	$-O-CH_3$	162.8
	CH_3-		163.1
$H-CR(O-CH_3)(O-C_2H_5)$	H-	$-O-CH_3$	161.0
	CH_3-		164.0
$H-CR(O-CH_3)(O-C_2H_5)$	H	$-O-CH_2-CH_3$	150.6
	CH_3-		152.6
$R_1R_2C(O-C_2H_5)_2$	R_1, R_2: H-	$-O-CH_2-CH_3$	148.5
	R_1: H-, R_2: CH_3-		151.3
	R_1, R_2: CH_3-		152.9
$R_1R_2C(O-C_2H_5)_2$	R_1, R_2: H-	$-O-CH_2-CH_3$	242.6
	R_1: H-, R_2: CH_3-		243.2
	R_1, R_2: CH_3-		245.4
$H-CR(O-CH_3)(O-C_2H_5)$	H-	$-O-CH_2-CH_3$	245.7
	CH_3-		246.5

The purity of some compounds (formals, dimethyl acetal, methyl ethyl acetal, ethers except 1, 2-dichloroethyl ethyl ether, polyethylene glycol diethers and cyclic compounds except tetrahydrofuran and epibromohydrin) was checked by gaschromatograph. The other compounds were found to decompose in the column of gaschromatograph, and in this case the purity was checked by the infrared spectra*. The detailed description of the purification was reported elswhere[5,6].

Results and Discussion

The spectra obtained may be classified into three types as follows:

a) No peaks overlap with each other, so it is quite easy to assign them from the relative intensity and the appearance of the multiplet structures.

b) Some peaks overlap with each other, but referring to the assignment of class a) it is not so difficult to assign them in most cases.

c) Separation of chemical shift is the same order as J-J splitting. In this paper, the assignment of this class is not given since it is impossible to assign them without exact calculation.

In Fig. 2, the assignment and the value of chemical shifts (in cycle per second) are marked on each peak. The separation between peaks is also shown together with that of pure liquid in parentheses.

* Since the infrared spectra of ketal and orthoaliphatic acid esters have not been reported in the literature, it is impossible to check the purity of these compounds merely by the infrared spectra. Since these compounds were known to decompose gradually to alcohols, esters or to aldehydes in air at room temperature, they were distilled (in vacuo) several times until bands at 3500 cm^{-1} and 1700 cm^{-1} completely disappeared.

6) K. Nukada, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 1028 (1960).

The average values of shifts of all functional groups are listed in Table I and these values are consistent with those listed by Chamberlain[3].

Except for halogenated ethers, all functional groups may be divided into four groups, B, A, A^2 and A^3 according to the approximate value of shift. These groups include sub-groups β, β^2 and β^3, $\alpha\beta$ and α, α^2 and α^3, respectively. The notation of "the type of sub-group" is defined as follows*: n equivalent protons bonded to α or β carbon atoms are designated as α_{CH_n} or β_{CH_n}. If carbon atoms are at α and/or β positions with respect to more than two oxygen atoms, several notations are used, i.e., $\alpha^2{}_{CH_n}$ or $\alpha\beta_{CH_n}$, etc. If the carbon atom is at α position with respect to the chlorine atom the notation α' is used. Practically, the chemical shifts of protons bonded to γ or far separated carbon atoms are not influenced by the electronegative atoms interested.

The order of shielding is $B > A > A^2 > A^3$ within the main groups. Further in each group, some correlations are recognized. In groups B and A, the order of shielding is $\beta > \beta^2 > \beta^3$ for CH_3 protons and $\alpha > \alpha\beta$ for CH_2 protons, respectively. In groups A and A^2, the order of shielding is $CH_3 > CH_2 > CH$ for α sub-group and $CH_2 > CH$ for α^2 sub-group, respectively.

The correlation between the chemical shift and electronegativity of the functional group being directly related to "the type of group" and "the type of sub-group" is quite reasonable.

Let us next consider the change in chemical shift within each sub-group in more detail. The chemical shift of equivalent protons in some functional groups changes, though very slightly, in homologue. The methyl proton shift of the methoxyl group in $R\text{-}C\langle^{O\text{-}Me}_{O\text{-}Me}_{O\text{-}Me}$, for example, goes to a higher field as the alkyl-group R becomes larger. In another example, the methylene proton shift in $CH_2\langle^{OR_1}_{OR_2}$, goes to a lower field as the alkyl groups R_1 and R_2 become larger. In Tables II and III, the correlations between the chemical shift and the type of attached alkyl group are shown in the former and the latter cases, respectively. Although the change of chemical shift is very slight and some correction of the solvent effect should be considered, surprisingly regular correlations are obtained.

* It is essentially the same as the notation given by Chamberlain. See Ref. 3.

If it is assumed that after a possible correction due to the solvent effect the order of the magnitude of the chemical shift does not change, the result obtained here will give some information concerning the molecular structure and electron density distribution in the molecule.

The possible explanation for the slight change of chemical shift is as follows:

1) **Steric Effect.**—By the steric repulsion between alxyl groups, the X-C-H bond angle changes slightly, following the slight change in hybridization of the carbon atom in C-H bond.

2) **Inductive Effect.** — As R goes from H through CH_3 to higher alkyl groups in R'-O-R, the electron affinity of oxygen atom for R' is lowered causing protons in R' to be more shielded*.

3) **Steric and Inductive Effect.**—As R goes from H to higher alkyl groups in R'-O-R, by the steric hindrance the C-O-C bond angle in R'-O-R increases slightly causing a slight change of hybridization of the oxygen atom and further the increase of electron affinity of the oxygen atom.

4) **Direct Effect.** — As R goes from H to higher alkyl groups, the bond angle in molecules change slightly, causing the slight change of magnetic anisotropy of atoms and then shielding for the protons interested.

At present, it is impossible to decide immediately which cause is predominant, since it is quite difficult to estimate the amounts of the influences of these effects on chemical shift quantitatively. The author could say, however, that at least two causes must be considered since opposite senses are obtained in the correlations shown in Tables II and III.

More detailed discussion concerning this problem will be reported in the near future.

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* Dewar described this as I effect of alkyl group in his text book. M. J. S. Dewar, "The Electronic Theory of Organic Chemistry", Oxford Univ. Press, London (1949), p. 52.