DETERMINATION OF ALCOHOLS IN MIXTURES BY ^{19}F NMR SPECTROSCOPY USING HEXAFLUOROACETONE REAGENT

Jiří KARHAN[a], Zbyněk KSANDR[a], Jiřina VLKOVÁ[b] and Věra ŠPATNÁ[c]

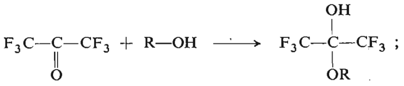
[a] *Department of Analytical Chemistry and*
[b] *Laboratory of Synthetic Fuels,*
Prague Institute of Chemical Technology, 166 28 Prague 6 and
[c] *J. Heyrovský Institute of Physical Chemistry and Electrochemistry,*
Czechoslovak Academy of Sciences, 110 00 Prague 1

Received December 15th, 1980

Dedicated to Professor J. Zýka on the occasion of his 60th birthday.

The determination of alcohols by ^{19}F NMR spectroscopy making use of their reaction with hexafluoroacetone giving rise to hemiacetals was studied on butanols. The calibration curve method and the internal standard method were used and the results were mutually compared. The effects of some experimental conditions, *viz.* the sample preparation procedure, concentration, spectrometer setting, and electronic integration, were investigated; the conditions, particularly the concentrations, proved to have a statistically significant effect on the results of determination. For the internal standard method, the standard deviation was 0·061 in the concentration region 0·032—0·74 mol l^{-1}. The method was applied to a determination of alcohols in the distillation residue from an oxo synthesis.

Several methods have been suggested for the determination of alcohols by NMR spectroscopy. The method based on the ^{1}H NMR signal of the OH group proton has not found wide application because the chemical shift and the shape of the signal are highly dependent on the experimental conditions — the temperature, concentration, and presence of other substances containing active hydrogen. Practically used are particularly methods employing reagents, such as dichloroacetic anhydride[1] or triacetyl isocyanate[2], which react with alcohols to give defined products whose ^{1}H NMR spectra are then evaluated for a determination or identification of the alcohols. Use has been made also of fluorinated reagents, such as trifluoroacetic acid[3] or hexafluoroacetone[4-6], the signals of their reaction products being monitored in the ^{19}F NMR spectra. The reaction of hexafluoroacetone with alcohols results in the formation of stable hemiacetals, in this manner a fairly high sensitivity is achieved with this reagent, as six fluorine atoms are monitored instead of a hydrogen atom.



$$\mathrm{F_3C{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}CF_3 + R{-}OH \longrightarrow F_3C{-}\overset{\overset{\displaystyle OH}{|}}{\underset{\underset{\displaystyle OR}{|}}{C}}{-}CF_3}\;; \qquad (1)$$

In addition to the signals from the hemiacetals, characteristic of the alcohol type involved, the ^{19}F NMR spectra exhibit also signals of the free (nonreacted) hexafluoroacetone and of the hexafluoroacetone–water adduct, $HFA(H_2O)$. A majority of signals of hemiacetals lie between the latter signals (their chemical shift difference is 7·35 ppm), which thus may serve also as internal standards for the determination of chemical shifts of the various hemiacetals[4].

Downfields of the $HFA(H_2O)$ internal standard signal lie the signals of hemiacetals of primary, secondary, and tertiary alcohols; their Δ_{H_2O} chemical shifts fall in the ranges 2·45–2·70, 1·75 to 1·95, and 1·2–1·4 ppm, respectively[4,6]. The ^{19}F NMR chemical shifts of hexafluoroacetone hemiacetals with amines, amides and other compounds containing active hydrogen can be established likewise[6].

By the hexafluoroacetone method, alcohols can be determined also in mixtures provided that the components afford well-resolved resonance signals and the reaction of hexafluoroacetone with the alcohols to be determined proceeds quantitatively. The reaction is conducted *in situ*, *i.e.* directly in the NMR cell. Owing to the high sensitivity, alcohols can be determined in milligram quantities per 0·5 ml solution.

Water and primary and secondary alcohols react with hexafluoroacetone instantaneously and quantitatively at ambient temperature, and the hemiacetals formed are sufficiently stable. In the case of branched alcohols the reaction is slower, steric hindrance playing here a role[4]. The equilibrium constants of the reactions with hexafluoroacetone have been published by Floyd and Ho for selected *o*-alkyl phenols[7] and by Pellisier for carboxylic acids[8].

The purpose of the present work was to examine the possibilities of determination of alcohol mixtures in distillation residue from oxo synthesis by ^{19}F NMR spectroscopy making use of the reaction with hexafluoroacetone. The analytical aspects were studied on selected butanols as model samples.

EXPERIMENTAL

1-Butanol, 2-butanol, 2-methyl-1-propanol, and 2-methyl-2-propanol were reagent grade chemicals of Lachema, Brno. The alcohols were redistilled and dried over Nalsit 4A molecular sieve, and their solutions were prepared in ethyl acetate (Lachema, Brno) dried in the same manner. The content of the alcohols in the distillation residue was determined after their treatment[9].

The reagent, approximately 0·5 mol l^{-1} solution of hexafluoroacetone in ethyl acetate, was prepared by absorbing hexafluoroacetone gas (Fluka, Switzerland) in the solvent at 0°C, and stored at −30°C.

1,1-Difluoro-1,2,2,2-tetrachloroethane, serving as the standard in the internal standard method, was checked for impurities by ^{19}F NMR spectroscopy. It was either directly weighed in the cells (about 50 mg) or added in the form of a standard solution by using a calibrated Hamilton syringe.

The ^{19}F NMR spectra were measured on a Varian XL-100 *cw* NMR spectrometer with the working frequency of 94·1 MHz (^{19}F) and external proton stabilization. The measuring temperature was 37°C. The resonance frequencies of the signals were read on a Tesla BM 445 counter with the precision of 0·1 Hz. Two spectral widths were used, *viz.* 2 500 Hz and 500 Hz; the integral scan rates were 100 and 50 Hz s^{-1}, respectively. Each integral scan was five times repeated.

The results were subjected to statistical processing by the variance analysis employing the FAKTOR program in which the AVDAT, AVCAL, and MEANQ standard subroutines[10] are implemented. The FAKTOR program was set up in the BASIC FORTRAN language as an interactive program for the ADT 4316 computer (ZPA, Čakovice).

RESULTS AND DISCUSSION

The reaction was found to proceed quantitatively with primary and secondary butanols. The course of the reaction of hexafluoroacetone with 2-methyl-2-propanol

TABLE I

Effect of the way of adding the standard on the determination of 1-butanol by the internal standard method

Weighing[a]		Pipetting[b]	
Added mmol l^{-1}	found %	Added mmol l^{-1}	found %
21·4	106·1	17·9	103·9
55·7	91·6	31·1	107·7
68·4	92·0	47·0	99·6
80·1	95·5	56·9	100·0
89·9	88·8	59·4	115·0
98·5	92·1	83·4	102·2
106·4	103·2	86·0	107·8
119·4	102·5	105·0	100·0

[a] Approximately 50 mg of standard weighed directly in the cell; [b] volume of standard solution (2·5 mol l^{-1}) containing approximately 50 mg of the substance added by means of a Hamilton microsyringe.

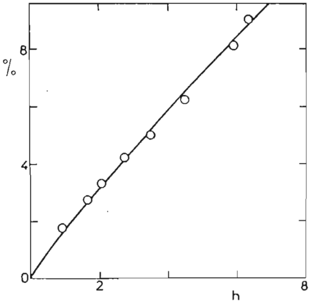


FIG. 1

Dependence of the reacted amount (with respect to the initial concentration) of 2-methyl-2-propanol with hexafluoroacetone on time. Initial concentration of the alcohol 0·3 mol l^{-1}, temperature 37°C

(Fig. 1), on the other hand, demonstrates that the method is unsuitable for a quantitative determination of tertiary alcohols.

The calibration curve method and the internal standard method were tested on 1-butanol and 2-butanol. The regression straight line equations obtained for the two alcohols by the former method are $h_x = 266{\cdot}3c + 1{\cdot}5$ and $h_x = 241{\cdot}5c + 1{\cdot}5$, respectively, in the concentration region $0{\cdot}0 - 0{\cdot}12$ mol l^{-1}; here h_x is the average value of the integral ^{19}F signal and c is the molar concentration of the alcohol in question. The correlation coefficient for both straight lines (10 points) was 0·990.

Because of the stringent requirement of constant experimental conditions (setting of the NMR spectrometer), the calibration curve method is not commonly used in spectroscopy. In the internal standard method the effect of the experimental conditions is considerably less pronounced. For this method, the effect of the way of adding the standard was examined: either the substance was weighed in the cell or its stock solution was added. The results of determination of 1-butanol for the two cases are given in Table I. The average relative error of the determination was lower when the solution was added, amounting to 4·4%.

The determination of primary and secondary alcohols in a mixture applying the internal standard method was tested on model mixtures of 1-butanol with 2-butanol over the mole fraction region 0 to 1. The results for the 500 and 2 500 Hz modes

TABLE II

Effect of the ^{19}F NMR spectral width on the analysis of mixture of 1-butanol and 2-butanol by the internal standard method

Added R^a	Found, %	
	500 Hz mode	2 500 Hz mode
^{b}	105·0	102·0
8·68	96·1	95·0
4·02	95·6	90·0
2·35	95·3	95·7
1·53	92·2	83·0
1·02	97·1	96·1
0·674	103·7	105·2
0·439	85·6	96·6
0·256	88·3	89·6
0·118	94·9	106·8
0·00^c	102·5	98·0

^{a} $R = x_{1\text{-butanol}}/x_{2\text{-butanol}}$, where x is the mole fraction; ^{b} pure 1-butanol; ^{c} pure 2-butanol.

are given in Table II. The average relative error of the determination was 6·23%, the standard deviation for the determination of 1-butanol in the mixtures, obtained by triplicate measurements over the concentration region $0{\cdot}032-0{\cdot}74 \text{ mol l}^{-1}$, was 0·061.

For assessing the effect of the experimental conditions, the statistical method of factor analysis of the variance was applied. The sample concentration and the number of measurements were treated as the factors affecting the results of determination, the number of integrations was the repetition factor. From a comparison of the calculated and tabulated values of the F-criterion for the level of significance $\alpha = 0{\cdot}95$, the absolute value of the concentration emerges as the decisive factor (experimental value ${}_{60}^{2}F = 33{\cdot}2$ as against the tabuled value 3·15). The effect of the number or repetition of measurements is considerably less significant, still the calculated F-criterion value, 3·71, is higher than the tabulated value (2·52); so the results cannot be claimed to differ only within the limits of random error.

The conclusions derived from the treatment of model mixtures of butanols were applied to the analysis of an industrial sample, *viz.* the distillation residue from an oxo synthesis. The sample contained a variety of oxygen compounds such as aldehydes, esters, ethers, acetals, and alcohols[9,13]. After the reaction with hexafluoroacetone, the system displayed a single, broad ^{19}F NMR signal in the range of 2·5 – 2·7 ppm, due probably to an overlap of the unresolved signals of the alcohol hemiacetals; the chemical shift value points to the occurrence of primary alcohols.

By the internal standard method, 1·4 to 1·7 wt.% primary alcohols (expressed as n-octanol) was found in the sample; the standard deviation estimate for five determinations amounted to 0·13.

The results can be compared with those obtained by Floyd and Ho[11], who determined with hexafluoroacetone the content of the hydroxy groups in polymers. The accuracy of determination was 2% rel.; carboxylic acids, amides and amines did not interfere. Konishi, Mori and Kaniguchi[12] transformed *o*- and *p*-allyl phenols in binary mixtures into esters of trifluoroacetic acid to determine them with the accuracy of 1·5% rel.

Quantitative NMR analysis is influenced by a number of factors, determining thus the quality of the results[13]. With regard to the complexity of the matrix, the results attained in the present work can be regarded as very good and complying with the standard of the spectrometer used. It should be mentioned that there is no other method available enabling so fast and simple analysis to match the method suggested.

REFERENCES

1. Babiac J. S., Barrante J. R., Wickers G. C.: Anal. Chem. *50*, 610 (1968).
2. Goodlet V. W.: Anal. Chem. *37*, 431 (1965).
3. Manatt S. L.: J. Amer. Chem. Soc. *88*, 1323 (1966).

4. Leader G. R.: Anal. Chem. *42*, 16 (1970).
5. Leader G. R.: Appl. Spectrosc. Rev. *11*, 287 (1976).
6. Leader G. R.: Anal. Chem. *45*, 1700 (1973).
7. Floyd F., Ho L.: Anal. Chem. *46*, 496 (1974).
8. Pellisier N.: Org. Magn. Resonance *9*, 563 (1977).
9. Hájek M., Vodička L., Vlková J.: Chem. Listy *75*, 870 (1981).
10. *Sbornik Nauchnykh Programm na FORTRANE* (translation from the English). Vilenkina, Statistika, Moscow 1974.
11. Floyd F., Ho L.: Anal. Chem. *45*, 603 (1973).
12. Konishi K., Mori Y., Kaniguchi M.: Analyst (London) *94*, 1002 (1969).
13. Vodička L., Vlková J., Hájek M.: Chem. Prům. *31/56*, 295 (1981).

Translated by P. Adámek.