COMPUTER-ASSISTED ^{13}C NMR IDENTIFICATION OF COMPONENTS OF COMPLEX ORGANIC MIXTURES: BYPRODUCTS IN THE MANUFACTURE OF CYCLOHEXANONE

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Carbon-13 nuclear magnetic resonance is used to identify components of the distillation residue from the manufacture of cyclohexanone. ^{13}C NMR spectra of rectification fractions provide the data utilized in an algorithm to extract subspectrum resonances specific to each component of the mixture. The subspectra are then subjected to search in ^{13}C NMR library of potential components. A number of components were unambiguously identified in original sample even if moderate peak overlaps occured. Generated subspectra made also possible identification of substances which are not present in ^{13}C NMR libraries.

In spite of some information about the nature of byproducts in manufacture of cyclohexanone available in literature sources, the heaviest distillation cuts are still characterized insufficiently.

Although gas chromatography combined with mass spectrometry is presently a method of choice for separation and characterization of complex mixtures, it suffers from a number of shortcomings. GC separation is not always possible because of sample nonvolatility or lack of sufficient chromatographic selectivity. Furthermore, present spectral libraries are incomplete and often contain spectra obtained under nonstandard conditions. In some cases, ^{13}C NMR spectrometry can be used to improve the reliability of GC/MS search, as clearly indicated in the work of Laude and coworkers[1].

However, unlike GC/MS applications, the use of NMR data does not necessarily require chromatographic separation. This is possible because the line widths of decoupled ^{13}C NMR resonance signals are narrow relative to the frequency range of ^{13}C NMR spectra. Reasonable resolution can be achieved especially at high magnetic fields. If quantitative conditions are ensured, it becomes possible to extract resonance signals specific to each compound in a mixture without prior separation[1 - 4]. In addition, the well-defined relationship between a ^{13}C NMR spectrum and chemical structure permits the implementation of elaborate computer-aided identification methods for the unknowns.

In this paper an alternative approach to analysis of complex mixtures is described. Unlike in quantitative ^{13}C NMR mixture analysis algorithm[1 - 4], identification is accomplished by comparing a set of ^{13}C NMR spectra of the unknowns which leads to generation of subspectra comprising lines with equivalent intensity ratios within the set. Algorithm logic is based upon the fact that, on varying concentration of a component in a set of samples, relative intensities of peaks pertaining to the component change in comparison with remaining peaks in the spectrum. Relative intensity ratios of peaks specific to a compound remain constant through the spectra within a tolerance unless peak overlap occurs. The subspectrum generated on the basis of this assumption is then subjected to a library search procedure. As an unambiguous match can be constrained because of insufficient resolution of the subspectrum and/or peak overlap, the analyst's evaluation of peak assignment as well as the possibility of intervention were implemented. In this way, moderate peak overlaps are amenable to resolution. The proposed computer-assisted method was described in more detail elsewhere[5].

Originally, the procedure was aimed at identification of mixture components in a set of distillation fractions: distillation of a complex mixture can ensure repeated occurrence of a compound as well as the changeability of its concentration in successive fractions. This is why the procedure seems to be suitable for analysis of distillation residue from the manufacture of cyclohexanone.

EXPERIMENTAL

The sample to be analysed was a distillation residue from the production of cyclohexanone by oxidation of cyclohexane in Chemko plant of Strážske. As capillary GC chromatogram revealed a complex mixture of more than 150 components, the sample was separated into 10 fractions on a packed rectification column (1 m long, 26 mm in diameter) at 1 666 Pa (five fractions) and subsequently at 1 200 – 1 300 Pa (five fractions). The operating reflux ratio was 20 : 1 and number of theoretical plates 25.

For GC separations a Hewlett–Packard 5880A chromatograph with a flame ionization detector was used. The operating conditions were as follows: 90 m × 0.53 mm i.d. fused silica column, coated with HP-1 and HP-FFAP, carrier gas – helium at 4.5 ml/min, column temperature 60 to 200 °C programmed at 5 °C/min, injector block temperature 200 °C.

The proton decoupled ^{13}C NMR spectra in $CDCl_3$ were run with a Varian XL-300 spectrometer at 75.426 MHz under conditions ensuring sufficient relaxation of quaternary carbon atoms. Multiplicity data were obtained from conventional APT and DEPT experiments.

A 165-compound library was created including potential byproducts in the production of cyclohexanone such as alkanes and alkenes, aliphatic and alicyclic alcohols, aldehydes, ketones, ethers and some aromatic-alicyclic hydrocarbons.

Each compound was characterized by ^{13}C NMR chemical shifts and theoretical relative intensities and multiplicities. Identification was accomplished using a SM 4-20 computer and a program written in FORTRAN IV PLUS.

RESULTS AND DISCUSSION

Ten rectification fractions were grouped into two sets comprising five fractions each. This subdivision was applied because the two sets of GC chromatograms indicated the presence of different components. Both sets were analysed separately. The results are summarized in Tables I and II.

In the fractions, only the GC peaks with relative peak area higher than about 1% are listed. GC peak assignment was accomplished by correlating ^{13}C NMR results with GC chromatograms. The compounds found by the computer procedure are indicated. In some cases identification was possible, even if their ^{13}C NMR data were not found in the existing libraries, due to successful resolution of extracted subspectra. This was also the case of tetrahydrofurfuryl alcohol and phenol which, not having been assumed as potential components, were not originally included in the library. On identifying them in the extracted subspectra their standard spectra were entered into the library and an unambiguous assignment was made in the subsequent run.

TABLE I
Chemical compounds found in the distillation residue from the manufacture of cyclohexanone

Compound [a]	Retention time, min	Relative peak area (%) in the fraction (b.p., °C/1 666 Pa)					
		[b]	50 – 72	72 – 80	80 – 91	91	95 – 97
I [c]	22.08	10.3	55.2 [d]	63.0 [d]	36.0 [d]	1.6	–
II [c]	23.43	0.2	–	–	4.0	–	–
III [c]	23.93	0.8	–	–	20.5 [d]	12.2 [d]	–
IV	24.08	0.2	0.9	4.2 [d]	[d,e]	3.0	–
V	26.77	0.6	–	–	–	20.0 [d]	10.8 [d]
VI	27.33	0.2	–	–	–	2.7	5.2
VII	27.63	0.4	–	–	–	2.9	8.5
VIII [c]	27.81	0.9	12.1 [d]	10.3 [d]	21.4 [d]	–	–
IX [c]	28.90	0.5	4.0 [d]	3.5 [d]	–	–	–
X	31.44	2.9	–	–	1.6	13.3 [d]	29.0 [d]
XI [c]	35.36	3.0	–	–	–	7.8 [d]	32.0 [d]

[a] Meaning of numbers: *I* cyclohexanol, *II* *trans*-2-methylcyclohexanol, *III* *cis*-3-methylcyclohexanol, *IV* tetrahydrofurfuryl alcohol, *V* cyclohexanemethanol, *VI* *trans*-2-ethylcyclohexanol, *VII* 2-methylcycloheptanol, *VIII* 1-butoxycyclohexane, *IX* 1-pentylcyclohexane, *X* 1-pentyloxycyclohexane, *XI* phenol; [b] in original mixture; [c] identification proved by GC standard; [d] compound found by the computer-assisted method; [e] peak overlap in GC.

The components not identified by the computer procedure and still listed in Tables I and II represent the most probable chemical structures found by a conventional ^{13}C NMR analysis which was carried out after the results of the computer-assisted procedure had been implemented. The assignments are based on characteristic chemical shifts and multiplicities of carbon atoms; some of them were confirmed using GC standards.

Even though a reasonably high magnetic field was used, peak overlaps in the spectra could not be eliminated. However, in some cases they were "resolved" by evaluating preliminary results during the procedure. This approach was discussed elsewhere[5].

Distilling a complex mixture and running spectra of its fractions might be considered a labour- and time-consuming process. Nevertheless, considering the fact that this made possible the identification of minor components as well as brought a piece of evidence by finding repeating sets of signals specific to a component, we believe the extra operations are worth doing. Moreover, when a component is a major constituent of a mixture, its unambiguous and correct identification is very likely. Actually, the more efficient the separation, the more successful interpretation can be expected.

TABLE II
Chemical compounds found in the distillation residue from the manufacture of cyclohexanone

Compound [a]	Retention time, min	Relative peak area (%) in the fraction (b.p., °C/1 200 –1 300 Pa)					
		[b]	126.5	127 – 128	128 – 133	133 – 134	>134
	33.54	1.3	9.3	–	–	–	–
	33.84	1.5	6.5	–	–	–	–
XII [c]	35.69	3.6	47.0 [d]	65.0 [d]	45.3 [d]	5.2 [d]	–
XIII [c]	37.14	10.9	–	7.2 [d]	29.5 [d]	75.0 [d]	–
XIV [c]	37.42	1.0	0.5	2.1	3.7	–	–
XV [c]	37.58	1.2	1.9	6.6 [d]	9.5 [d]	15.0 [d]	1.2
	38.28	1.6	–	–	–	–	3.2
	39.95	3.1	–	–	–	–	6.1
	43.12	1.1	–	–	–	–	2.3
	43.67	4.7	–	–	–	–	9.2
XVI	50.86	6.1	–	–	–	–	12.4
XVII [c]	53.48	20.3	–	–	–	–	40.7 [d]
XVIII	54.19	2.8	–	–	–	–	5.3

[a] Meaning of numbers: *XII* 1,1'-bicyclohexane, *XIII* 1,1'-oxybiscyclohexane, *XIV* 2-pentylcyclohexanone, *XV* cyclohexylbenzene, *XVI* (1-cyclohexenyloxy)cyclohexane, *XVII* 2-(1-cyclohexen-1-yl)cyclohexanone, *XVIII* 2-cyclohexylidenecyclohexanone. For explanation of other notes see Table I.

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