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Carbon-13 NMR Spectra of Benzene Mono- and Di-Carboxylic Acids and Their Analytical Applications

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Carbon-13 NMR spectra of benzoic, and phthalic acids were compared both in D_2O with an excess of sodium hydroxide and in a mixture of DMSO-d_6 and H_2O (4:1). Tight ion pair forms of benzoate anion were considered. A simple additive rule for isomeric phthalic acids was employed to assign the spectral peaks. These carboxylic acids gave characteristic peaks and so can be distinguished from others in mixtures. Quantitative analyses of these carboxylic acids with calibration curves are also possible by a simple preparation of basic D_2O solutions. An example of the use of these data is the Henkel process (*cf.* Fig. 1) for the synthesis of terephthalic acid.

Better analyses of a mixture of benzoic acid (**1**) and isomeric phthalic acids (**6**—**8**) are highly desired not only in organic laboratories but also in polyester manufacturing industries. The most well-known method for the analyses of the benzenepolycarboxylic acids may be esterification, followed by gas-chromatographic separation. Ultraviolet spectroscopy is also of potential usefulness, but it is often interfered with by contamination.

Nuclear magnetic resonance (NMR) spectroscopic analysis is inferior to the gas-chromatographic method in accuracy and sensitivity, but it is still useful and of convenience in most cases when one needs to analyze a reaction mixture quickly or to follow its conversions as the reaction proceeds.

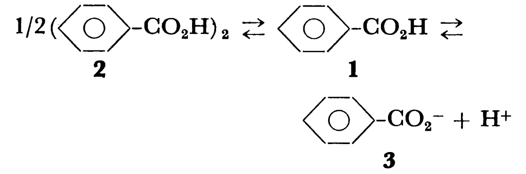
Unfortunately, the much more versatile ^1H NMR is often unsuitable for identifying structurally similar derivatives. On the other hand, the widely-ranging chemical shifts of ^{13}C NMR reflect a small difference in the structures.

Besides analytical purposes, the ^{13}C NMR data of aromatic carboxylic acids will be added to the data collections from which unambiguous empirical rules for the ^{13}C chemical shifts of substituted benzenes may be derived. The chemical shifts of carboxylic acids, however, often vary with the changes in solvent basicities, polarities, *etc.*, because the degrees of association and dissociation of carboxylic acids are solvent-dependent.[1)] More generalized values of the chemical shifts of aromatic carboxylic acids are desirable.

Herein we will report some attempts to use ^{13}C NMR for comparing the differences among benzoic and benzenedicarboxylic acids.

Results and Discussion

Benzoic Acid. A few data on the ^{13}C NMR chemical shifts (δ^C) of benzoic acid have appeared in the literature.[2—4)] The poor solubility of the acid in D_2O made it impossible to get a reasonable spectrum with an accumulation of 10000 transients at 26 °C. While no solubility problem is met with in aprotic polar solvents, such as DMSO-d_6, a small amount of water in the solvent often affects chemical shifts, especially when hydrogen bonding participates. Adding water in a 25 volume percentage to a DMSO-d_6 solution seems to be a successful way to eliminate the ill-defined effects of concentration changes and other factors which may vary the degrees of hydrogen bonding or dissociation of benzoic acid.[1)] Species **1** seemed to be dominant in the possible equilibrations.



(1)

The peaks of the spectra are assigned with reference to the literature values, the off-resonance decoupled spectra, the gradual shift in peaks with different ratios of a mixed solvent, and the virtual peak intensities. The data are summarized in Table 1.

A large solvent dependency of the chemical shifts is evident in Table 1. The resonance-field change in δ_{CO} (the chemical shift of the carboxyl carbon atom) reaches *ca.* 5 ppm, this shift is attributable to the change in the association degree of benzoic acid.[1)]

Benzoate Anion. Benzoic acid in a strong, basic heavy water shows a clean spectrum of the benzoate anion, the δ_{CO} of which shifts downfield by 11.4 ppm relative to δ_{CO} in DMSO-d_6, while the δ_{ipso} shifts by 8.8—10.1 ppm, compared to the values in DMSO-d_6 or $CDCl_3$ respectively. Essentially the same spectrum was obtained when sodium benzoate was dissolved in D_2O. This suggests that all the chemical shifts observed in a basic D_2O solution are attributable to the anion species, **3**. On the other hand, benzoic acid dissociated incompletely in the mixed solvent. The resulting chemical shifts were values between those of **1** and **3**. Similar chemical shifts were recorded when sodium benzoate was dissolved in the mixed solvent without adding sodium hydroxide (see

Table 1. Chemical shifts of benzoic acid in various solvents

δ^C a)	$CDCl_3$[1)]	CCl_4[b)]	DMSO-d_6[1)]	DMSO-d_6-H_2O(4 : 1)
Carboxyl	172.6	—	167.3	167.7
Ipso	129.4	130.6	130.7	130.3
Ortho	130.3	130.0	129.2	129.1
Meta	128.5	128.5	128.2	128.2
Para	133.8	133.6	132.5	132.7

a) Chemical shifts from TMS or DSS at a concentration of *ca.* 500 mg in a solvent of 3 ml (4 ml in the case of $CDCl_3$). b) Data from Ref. 3, in which data were converted using $\delta_C^{C_6H_6}$ 128.5.[3)] 10% solution.

TABLE 2. CHEMICAL SHIFTS OF BENZOATE ANION

	Solvent	D_2O[1]	Mixture[a]	$CDCl_3$	DMSO-d_6	D_2O	Mixture[a]
	Additive	NaOH	NaOH	Et_3N	Et_3N	b)	b)
δ^C	Carboxyl	178.7	171.4	172.2	170.2	178.7	171.2
	Ipso	139.5	138.2	136.7	135.6	139.7	138.3
	Ortho	132.1	129.0	129.2	129.0	132.2	129.6
	Meta	131.5	127.5	127.4	127.8	131.7	128.9
	Para	134.5	129.7	129.9	130.8	134.5	127.5

a) A mixture of DMSO-d_6 and H_2O in a ratio of 4 to 1. b) Sodium benzoate was used instead of benzoic acid.

TABLE 3. CHEMICAL SHIFTS OF BENZENEDICARBOXYLIC ACIDS IN TWO KINDS OF MEDIA

δ^C	In DMSO-d_6-H_2O (4 : 1)			In D_2O with *vs.* NaOH		
	6	**7**	**8**	**6**	**7**	**8**
Carboxyl	168.8	166.6	166.7	180.9	178.4	178.3
C_1	131.0	130.5	134.1	141.0	139.7	141.9
C_2	131.0	129.8	129.4	141.0	132.3	131.7
C_3	128.3	130.5	129.4	130.5	139.7	131.7
C_4	132.1	133.3	134.1	132.1	134.6	141.9
C_5	132.1	128.8	129.4	132.1	131.5	131.7
C_6	128.3	133.3	129.4	130.5	134.6	131.7

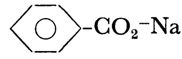
TABLE 4. CALCULATED CHEMICAL SHIFTS OF BENZENEDICARBOXYLIC ACIDS AND THEIR ANIONS

δ^C	Dicarboxylic acids[a]			Dicarboxylate anions[b]		
	6	**7**	**8**	**6**	**7**	**8**
C_1	131.2	130.3	133.9	140.1	139.5	142.5
C_2	131.2	130.0	129.1	140.1	132.7	132.1
C_3	129.1	130.3	129.1	132.1	139.5	132.1
C_4	131.8	132.7	133.9	134.5	135.1	142.5
C_5	131.8	128.2	129.1	134.5	131.5	132.1
C_6	129.1	132.7	129.1	132.1	135.1	132.1

a) In DMSO-d_6-H_2O (4 : 1). b) In D_2O with an excess of sodium hydroxide.

the last column in Table 2).

Although an effort to record the spectrum of sodium benzoate in $CDCl_3$ was in vain, the benzoate anion in organic solvents was also generated by adding excess triethylamine. As may be seen in Table 2, the chemical shifts in $CDCl_3$ or DMSO-d_6 are independent of the solvent nature, but are different from those of the benzoate anion obtained in the D_2O solution. The downfield shifts of δ_{CO} and δ_{ipso} relative to those of benzoic acid in DMSO-d_6 were 2.9 ppm and 4.9 ppm respectively, smaller than those observed for the benzoate anion in D_2O (*vide ante*). That is, the chemical shifts of the benzoate anion in organic solvents are between these values of the free acid form, **1**, and of the completely ionized form, **3**. This may suggest that the negative charge on the carboxyl group is neutralized to some extent in a tight ion pair form, **4** or **5**.



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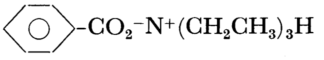

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Benzenedicarboxylic Acids. The ^{13}C NMR spectra of phthalic acid (**6**), isophthalic acid (**7**), and terephthalic acid (**8**) were obtained in a mixed solvent (with the same ratio as above) and in D_2O with an excess of sodium hydroxide. The results are given in Table 3.

The assignment of the peaks was aided by the additive rule for disubstituted benzene derivatives. The usefulness of the calculation for several compounds had also been tested previously in this laboratory.[4-5] Used for the additive calculation[6] were the chemical shifts of benzoic acid in the mixed solvent (Table 1) and of the benzoate anion in D_2O saturated with sodium hydroxide (Table 2). In the calculation, the increments of the shifts can not be estimated by using the benzene standard for its chemical shifts in a D_2O solution are not available. Therefore, the δ^C of meta carbon was set for the standard both in the mixed solvent and in basic D_2O (Table 4).

The agreement between the observed and the calculated chemical shifts of phthalic acid and its anion was not perfect (the largest discrepancy was 0.8 ppm). Similar disagreements are common for ortho-substituted benzenes,[7] where usually two bulky groups interact with one another. On the other hand, a fairly good agreement was established for isophthalic acid and terephthalic acid in two different solvents.

Analytical Applications. Terephthalic acid is in high demand as a material of polyester fibers and plastics. Numberless studies on synthesizing or manufacturing the material have been reported. One of the most successful findings is Henkel reaction[8] by which terephthalic acid is produced from benzoic, phthalic, and isophthalic acids.

The pathways of the Henkel reaction are given below, although the acid forms represent the corresponding alkali salts in actual reactions where carbon dioxide and catalysts such as cadmium iodide are also present.

The most routine process of analysis may be the acidification of the reaction mixture, followed by the extraction of the acids, esterification and finally gas-chromatographic separation. However, NMR spectroscopy would be more convenient for the analysis if rigorous accuracy were not crucial, as it is not for usual organic reactions. Unfortunately, the more accessible ^1H NMR method does not seem appropriate for the present case because spectral overlaps are inevitable.

The proton signal of carboxyl groups of terephthalic acid (δ^H=10.5—11.7) is too broad and weak to be used for the present analysis. One exception is the case when a reaction mixture composed of benzoic acid and terephthalic acid is made up in a DMSO solution. This happens in some related studies of benzenepolycarboxylic acids. When the method is applied to the crude reaction mixture of the Henkel process, acidification and extraction (and perhaps replacing the solvent with DMSO) are necessary because it contains exclusively water soluble alkali salts of the carboxylic acids.

Contrary to the ^{1}H NMR method, ^{13}C Fourier-transform NMR spectra with ^{1}H noise-decoupling give narrow, single peaks whose resonance frequencies are printed out from an attached computer memory.

Surveying Tables 1—3, it seems that one can distinguish the peaks of terephthalic aicd from the others. In fact, the spectra of mixtures of terephthalic acid with either benzoic acid (Fig. 2a) or phthalic acid and isophthalic acid (Fig. 2b) in basic D_2O demonstrate applicable analyses of the Henkel process (Fig. 1)

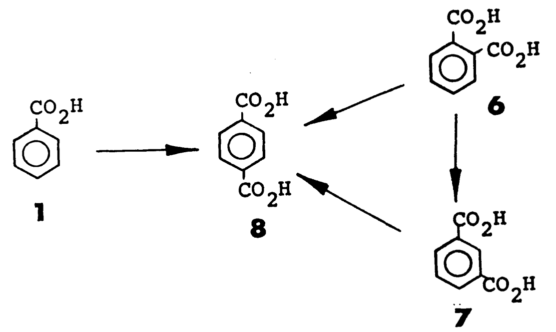

Fig. 1. Reaction paths of Henkel process.

When all these carboxylic acids are mixed, the only ambiguous distinction is the peak difference between benzoic acid and isophthalic acid. However, the mixed solvent instead of basic D_2O may be used for such a purpose.

Problems in Quantitative Determination. The application of ^{13}C NMR spectroscopy to quantitative analysis has recently been reported frequently.[9] Unlike the ^{1}H NMR, the ^{13}C peak intensity is affected by any nuclear Overhauser effects (NOE). Therefore, a simple integration of the peak intensity does not give quantitative amounts of carbon atoms. However, the amount of NOE on a particular carbon is usually independent of the sample concentrations, because the dipole-dipole (of proton) interaction dominates the ^{13}C relaxation. To confirm this accepted idea, benzoic acid was chosen to test the possibility of quantitative analysis.

A certain amount of benzoic acid was dissolved in basic D_2O with propionic acid (0.58 M). At lower concentrations, the peaks of carboxyl and ipso carbons were hidden in the noise levels. The relative peak intensities of the other ring carbons against methylene carbon of propionic acid (internal standard) were on fairly good straight lines in the range of 0.33—2.67M of benzoic acid (dotted lines in Fig. 3). These calibration lines, which had been expected to be straight are sufficient proof for the quantitative determination of other carboxylic acids, including therephthalic acid.

In connection with the NOE problem in the present analysis, pure oxygen, a paramagnetic substance, was saturated in the sample solutions. No improve-

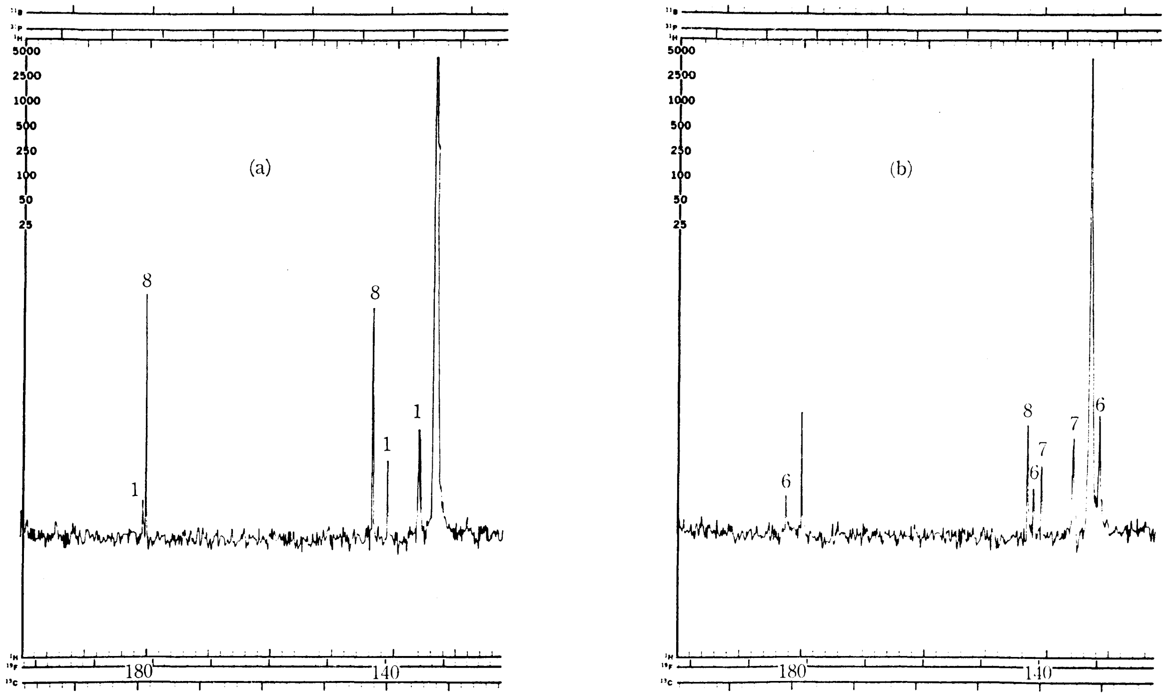

Fig. 2. ^{13}C NMR spectra of mixture samples.
(a) A mixture of terephthalic acid (**8**) of 200 mg and benzoic acid (**1**) of 100 mg in D_2O (3.3 ml) with sodium hydroxide of 300 mg.
(b) A mixture of **8** of 200 mg, phthalic acid (**6**) of 100 mg and isophthalic acid (**7**) of 100 mg in D_2O (4.3 ml) with sodium hydroxide 300 mg.

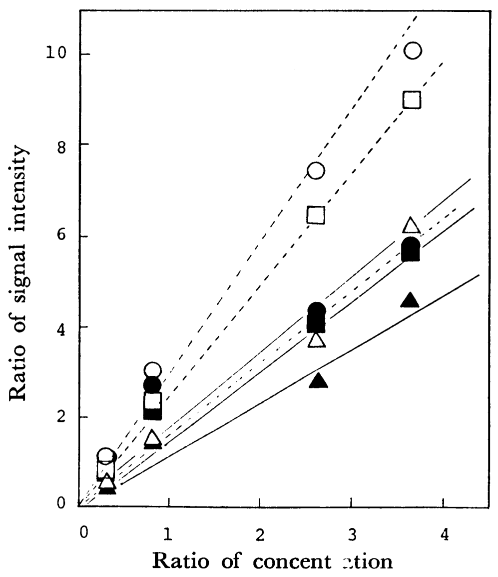

Fig. 3. Signal intensity ratios *versus* concentration ratios of sodium benzoate to methylene carbon atom of sodium propionate (0.58 M) either in aqueous solutions (open symbols with dotted lines) or in the solutions saturated with oxygen (blackened symbols with solid lines). Symbols are corresponding to ortho (circle), meta (square), and para (triangle) carbons of the benzoate.

ment for the determination was found, in spite of extra pretreatment before measurements.

Experimental

NMR Measurements. All the ^{13}C NMR spectra were recorded on a Varian XL-100-15 NMR spectrometer operating at 25.16 MHz in the pulsed Fourier transform mode with ^{1}H noise-decoupling with the 2 kHz band width at 8 mW. The pulse width of 60 μs (*ca.* 45° flip angle), with a pulse delay of 3 s, was applied. Spectral widths of 5000 Hz were swept with 4096 data points using a Varian DATA 620i computer with 8 K memory produced spectra with accuracies of better than 0.1 ppm. Normally 1000 transients were accummulated. Unless specified, a compound of *ca.* 500 mg and sodium hydroxide, when necessary, was dissolved in a solvent (3—5 ml) in a 12 ϕmm sample tube at a spinning rate of 10—16 rps at 26°. Tetramethylsilane (TMS) or sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS, δ_c 0.015) was the internal standard. Carbonyl carbon of methyl acetate (82% benzene-d_6 solution) showed a peak at 171.4 ppm, which was the exact mean value of those obtained on 65 different C-13 NMR machines throughout the country.[10]

Chemicals. All the aromatic carboxylic acids and sodium benzoate were of a guaranteed grade, while the triethylamine and sodium hydroxide were of a reagent grade. Dimethyl sulfoxide (DMSO) of a reagent grade was distilled from calcium hydride and stored over molecular sieves of Type 4 A. The deuterated solvents (D_2O, $CDCl_3$, and DMSO-d_6) for NMR spectroscopy were purchased from Merck Japan, Ltd. TMS and DSS were also of a NMR spectroscopic grade. Except for DMSO, none of them, including oxygen gas, was purified before use. A mixture of DMSO-d_6 and H_2O in a volume ratio of 4 to 1 was used in the present study (mixed solvent).

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References

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