A Thermodynamic Study by Infrared Spectroscopy of the Association of 2-Quinolone, Some Carboxylic Acids, and the Corresponding 2-Quinolone–Acid Mixed Dimers[1]

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Self-association of 2-quinolone in carbon tetrachloride was studied by infrared spectroscopy, using the absorption bands in the amide NH and carbonyl stretching regions. 2-Quinolone forms a cyclic dimer from which the enthalpy ($\Delta H°$, kcal/mol), free energy ($\Delta G°_{22}$, kcal/mol), and entropy ($\Delta S°$, eu) of association are −8.69, −6.11, and −8.76, respectively. Dimer formation is *via* a carbonyl–hydrogen bond, although evidence exists for the formation of a small amount of dimer *via* a π–hydrogen bond. 2-Quinolone was also found to form cyclic mixed dimers with carboxylic acids. Mixed dimers of 2-quinolone with benzoic, cyclohexanecarboxylic, and 4-cyclohexylbutanoic acids gave $\Delta H°$ values of −12.2, −10.3, and −10.4; $\Delta G°_{22}$ values of −6.36, −5.94, and −5.78; and $\Delta S°$ values of −19.9, −14.8, and −15.6, respectively. Thermodynamic data on the acid dimers and spectral data on the different systems studied are also reported. The 2-quinolone–carboxylic acid interaction is of importance because of the simultaneous occurrence of quinolones and carboxylic acids in many biologically derived materials.

Introduction

Several studies[2-7] have been made in which quinolones have been characterized by their infrared spectra; however, intermolecular interactions of these compounds have not generally been recognized. The lack of information in this area probably results from the extremely low solubility of most quinolones in suitable infrared solvents, although some efforts[6] have been made to find more suitable solvents. Consequently, most infrared studies of quinolones have relied heavily on the use of suspensions of solid quinolones, either as mulls or in KBr disks, thus hindering the detection or study of molecular interactions by infrared spectroscopy. *N*-Unsubstituted 2-quinolones are lactams which are capable of forming cyclic dimers through hydrogen bonding analagous to dimers formed by carboxylic acids. Dimer equilibrium studies of the closely related pyridones have been reported.[8-10]

Quinolones are important in the study of quinoline alkaloids and have been identified in the high-boiling fractions of petroleum crude oils.[11,12] The recent discovery in our laboratory of a strong interaction between quinolones and carboxylic acids in petroleum distillation residues, and the likely existence of this interaction in other biologically derived systems, prompted the present study of this interaction. Because of the molecular complexity of petroleum residues and the difficulties attendant in the isolation of the individual compounds from their natural environment for quantitative studies, we decided to conduct a model study of the interaction of 2-quinolone with several carboxylic acids to obtain thermodynamic data. To obtain these data on the 2-quinolone–carboxylic acid interaction, however, it was first necessary to obtain similar data on the self-association of 2-quinolone and the acids individually. Results on the self-association of both pure compound types and on the association of the mixed systems are reported.

Experimental Section

Materials. Carbon tetrachloride was Baker and Adamson[13] CP grade (water content < 0.001 *M*) and was found by infrared spectroscopy in 10-cm cells to

(1) The work upon which this report is based was done under a cooperative agreement between the Bureau of Mines, U. S. Department of the Interior, and the University of Wyoming.

(2) J. A. Gibson, W. Kynaston, and A. S. Lindsay, *J. Chem. Soc.*, 4340 (1955).

(3) D. J. Cook, R. S. Yunghans, T. R. Moore, and B. E. Hoogenboom, *J. Org. Chem.*, **22**, 211 (1957).

(4) M. F. Grunden and N. J. McCorkindale, *J. Chem. Soc.*, 2177 (1957).

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be free of interfering impurities. 2-Quinolone, Eastman White Label, was found to be of greater than 96% purity by potentiometric titration with perchloric acid. Recrystallization from ethanol produced no detectable changes in the infrared spectra. Infrared spectra also showed the absence of the possible contaminants, 4-quinolone or 2,4-quinolinediol. Benzoic acid was Baker and Adamson primary standard. Cyclohexanecarboxylic and 4-cyclohexylbutanoic acid, from Eastman, gave neutralization equivalents of 131.7 and 180.5, indicating 97.4 and 94.3% purity, respectively. Reagent purities were taken into account in calculating concentrations. The negligible effect of trace water in the spectral solvent on the infrared spectra was verified by the addition of 0.002 M water to a stock quinolone solution with no measurable change in the free or bonded NH and carbonyl bands.

Methods. Stock solutions (0.00197, 0.00984, 0.00912, and 0.00886 M at 24° for 2-quinolone, benzoic acid, cyclohexanecarboxylic acid, and 4-cyclohexylbutanoic acid, respectively) were prepared by weighing into a flask exactly the required amount of sample which was then dissolved in carbon tetrachloride. 2-Quinolone–acid mixtures having the same component normalities as the single component solutions were similarly prepared. A series of concentrations were prepared for study from each of the stock solutions by 5- and 10-fold dilutions with an additional $^5/_8$-fold dilution for 2-quinolone. Infrared spectra were obtained on the solutions at 8, 22, 35.7, 48.5, and 65°, each temperature controlled to within ±0.3°. Multiple infrared traces (3–6) of each analytical band were run and averaged to improve the precision of the absorbance measurements. All solutions were prepared and diluted at 24°. Solution concentrations were corrected for volume changes by eq 1 and 2.

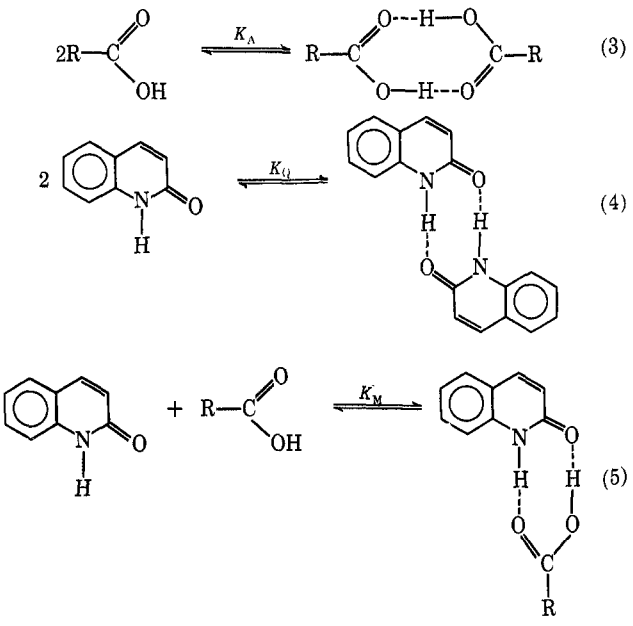
$$V_t = V_0(1 + 1.18384 \times 10^{-3}t + 0.89881 \times 10^{-6}t^2 + 1.35135 \times 10^{-8}t^3) \quad (1)$$

$$X_t = \frac{V_t}{V_{24}} \quad (2)$$

In these equations, t is the temperature in °C, V_t is the volume at temperature t, V_0 is the volume at 0°, and X_t is the volume correction factor for carbon tetrachloride. Solvent-compensated spectra with 4× base line expansion were recorded on a Perkin-Elmer Model 521 spectrophotometer after samples in KBr cells had attained temperature equilibrium in a Model VTC-140 Barnes variable temperature chamber. The frequency of the spectrophotometer was calibrated with standard polystyrene film. Cells of 1.06 and 5.07 cm were used while recording the OH, NH stretching regions; 0.100 and 1.06-cm cells were used for the carbonyl stretching region. Spectral slit openings were 125 μ for the OH and NH regions and 120 μ for the carbonyl region. Overlapping peaks in the spectra were resolved into their component peaks using a duPont Model 310 curve resolver.

Calculations and Results

Carboxylic acids are known to form cyclic dimers by hydrogen bonding. This study shows that 2-quinolone similarly forms a cyclic dimer, and further, forms a mixed, cyclic dimer with carboxylic acids. Therefore, the equilibria of interest are



where K_A, K_Q, and K_M are the equilibrium constants for the dimerization of the carboxylic acid, 2-quinolone, and mixed dimer, respectively. The equilibrium constants K_A and K_Q are given by the equation

$$K_A \text{ or } K_Q = \frac{C_B}{2C_F^2} \quad (6)$$

where C_B and C_F are the concentrations of the bonded (dimer) and monomer (free) species, respectively, each referred to one formula weight of quinolone or acid. The total acid or 2-quinolone concentration (C) is given by

$$C = C_B + C_F \quad (7)$$

The free NH and OH stretching bands were used to calculate the concentrations of 2-quinolone and carboxylic acid monomers. Dimer concentrations were calculated using the bonded carbonyl stretching bands. Molar absorptivities for the bands representing the free and bonded species (ϵ_F and ϵ_B), which are necessary to determine C_F and C_B, were obtained by the method of Allen and coworkers.[14] In this method ϵ_F and ϵ_B are estimated by a graphical solution of eq 7 in which

(13) Mention of specific brand names or models of equipment is made for information purposes only and does not imply endorsement by the Bureau of Mines.

(14) G. Allen, J. G. Watkinson, and K. H. Webb, *Spectrochim. Acta*, 22, 807 (1966).

Table I: Spectral Data on 2-Quinolone, Some Carboxylic Acids, and Their Mixed Dimers

	Stretching frequency,[a] ν, cm^{-1} 22.0°	$\Delta\nu$, cm^{-1} 22.0°	Molar absorptivity,[b] ϵ, l./cm per mole functional group 8.0°	22.0°	35.7°	48.5°	65.0°	Estimated precision[c]
2-Quinolone								
Free NH	3408		266	266	266	266	266	±13
Free C=O	1680		[d]	[d]	[d]	[d]	[d]	
Bonded C=O	1664	16	2420	2330	2240	2160	2040	±31
Benzoic acid								
Free OH	3543		239	227	217	210	204	±5
Free C=O	1743		1070		935		980	
Bonded C=O	1696	47	1005	945	910	890	880	±15
Cyclohexanecarboxylic acid								
Free OH	3535		178	172	167	164	160	±5
Free C=O	1752		653	600	560	530	503	±20
Bonded C=O	1706	46	977	957	938	922	901	±15
4-Cyclohexylbutanoic acid								
Free OH	3538		213	185	174	171	169	±5
Free C=O	1757		525		450		470	
Bonded C=O	1711	46	916	911	907	902	896	±20
2-Quinolone–benzoic acid								
Mixed dimer								
2-Quinolone C=O	1648	32						
Acid C=O	1674	69						
2-Quinolone–cyclohexanecarboxylic acid								
Mixed dimer								
2-Quinolone C=O	1651	29						
Acid C=O	1689	63						
2-Quinolone–4-cyclohexylbutanoic acid								
Mixed dimer								
2-Quinolone C=O	1651	29						
Acid C=O	1691	66						

[a] Limit of error ±2 cm^{-1} except ±3 cm^{-1} on mixed dimers. [b] Values reported obtained from best fit of ϵ *vs.* t plot. [c] Standard deviation of average from ϵ *vs.* t plot. [d] Reliable figure not available because of band overlap, estimated at about 1600.

C_F and C_B have been replaced by their equivalent expressions derived from the Beer–Lambert law, $A = \epsilon Cl$, where A is the absorbance of the infrared band and l is the cell length. Frequencies and molar absorptivities of the analytical bands are included in Table I.

Because of band overlap in the carbonyl region of the spectra of a mixture of 2-quinolone and carboxylic acid, molar absorptivities of the bonded carbonyl bands in the mixed dimers could not be determined accurately. Therefore, mixed dimer concentration, C_M, was determined by difference, using the acid absorption band according to the equation

$$C_M = C - (C_F + C_B) \tag{8}$$

where C, C_F, and C_B refer to the initial, monomer, and dimer concentration of acid (each referred to one formula weight of acid). The value C_F was determined using the absorbance of the free OH followed by calculation of C_B from eq 6. The equilibrium constant for the mixed dimer was then calculated by the equation

$$K_M = \frac{C_M}{C_F\text{ (acid)} \times C_F\text{ (2-quinolone)}} \tag{9}$$

in which the concentration of free quinolone was determined using the absorbance of the free NH band.

The enthalpies of association ($\Delta H°$) were calculated from the log K *vs.* $1/T$ plot which has a slope of $-\Delta H°/2.303R$. These plots were found to be linear in all cases. From the values of $\Delta H°$ and log K which were obtained, values of $\Delta G°$ and $\Delta S°$ were calculated at the various temperatures.

The spectral data for 2-quinolone, the carboxylic acids, and the mixed dimers are shown in Table I. In Table II the thermodynamic data are summarized. Within experimental error, $\Delta S°$ was found to be independent of temperature over the temperature range studied. Equilibrium constants reported are least-square values taken from the log K *vs.* $1/T$ plot with

Table II: Thermodynamic Functions for the Association of 2-Quinolone, Some Carboxylic Acids, and Their Mixed Dimers

	K,[a] l./mol							
	8.0°	22.0°	35.7°	48.5°	65.0°	$-\Delta H°$,[b] kcal/mol	$-\Delta S°$,[c] eu	$-\Delta G°$, kcal/mol at 22°
2-Quinolone	69,500 (400)	33,400 (200)	17,220 (80)	9,790 (50)	5100 (40)	8.69 ± 0.03	8.76	6.11
Benzoic acid	18,600 (250)	7,015 (105)	2,925 (45)	1,390 (20)	581 (9)	11.5 ± 0.1	21.4	5.19
Cyclohexanecarboxylic acid	9,725 (215)	3,840 (80)	1,665 (35)	815 (17)	355 (7)	11.1 ± 0.2	20.9	4.84
4-Cyclohexylbutanoic acid	9,140 (350)	3,450 (130)	1,455 (55)	685 (26)	292 (12)	11.4 ± 0.2	22.6	4.78
2-Quinolone–benzoic acid mixed dimer	144,000 (18,000)	51,300 (6300)	20,300 (2500)	9,160 (1140)	3640 (450)	12.2 ± 0.8	19.9	6.36
2-Quinolone–cyclohexane-carboxylic acid mixed dimer	60,600 (4800)	25,150 (2500)	11,500 (900)	5,880 (470)	2700 (220)	10.3 ± 0.5	14.8	5.94
2-Quinolone–4-cyclohexyl-butanoic acid mixed dimer	46,100 (2500)	19,200 (1030)	8,750 (500)	4,470 (250)	2040 (120)	10.4 ± 0.4	15.6	5.78

[a] Reported values from least-squares plot of log K *vs.* $1/T$. Standard deviation in parentheses. [b] Estimate of precision, ± one standard deviation. [c] Constant over temperature range.

precision of the data indicated by the standard deviation of the average shown in parentheses. Where more than one concentration was studied (see Methods section), no systematic variation of K with concentration was observed, and the K's reported are averaged values. The precision of the $\Delta H°$ values shown in Table II was calculated from the indicated precision of the K values. Accuracy of the $\Delta H°$ values is believed to be within 5% for the carboxylic acids and 10% for 2-quinolone and the mixed dimers.

Discussion

Before equilibrium data could be obtained it was necessary to determine molar absorptivities of the analytical infrared bands identified with the free and bonded species. Although the acids presented no special problems, the large equilibrium constants for the 2-quinolone system required the use of long path-length cells and very dilute solutions to obtain significant amounts of the free species. Precision of the calculated molar absorptivities for the free NH band was therefore somewhat limited by small absorbance bands in the more dilute solutions. The small intensity of this band is probably the reason this band is not reported by workers in the field. Within the limits of experimental measurements, no temperature dependence was found for the molar absorptivity of the free NH in 2-quinolone. This is consistent with the temperature independence of the free NH found by Chen and Swenson[15] for the closely related saturated lactams. The molar absorptivity of 266 l./mol cm (Table I) determined for the free 2-quinolone NH was considerably larger than the value of 109 l./mol cm reported[15] for six-membered ring saturated lactams.

A problem which made determination of the absorptivities of the 2-quinolone carbonyl bands difficult was the severe band overlap caused by the small $\Delta\nu$ (16 cm^{-1}, Table I) between the free and bonded bands. The band overlap was further complicated by nonuniform band envelopes. The free carbonyl peak in 2-quinolone, and probably most quinolones, has gone unrecognized by workers in the field who have apparently been consistently reporting the frequency of the bonded carbonyl. For example, McCorkindale,[6] although noting a small shoulder on the high-frequency side of the carbonyl band of some quinolones, includes this shoulder in calculating integrated intensities of the carbonyl band. Thus his integrated intensities include, but do not differentiate between, bonded and free species. To verify that McCorkindale reported the bonded carbonyl frequencies, we examined 2-quinolone in chloroform (the solvent used by McCorkindale) and found the bonded carbonyl frequency to be 1659 cm^{-1}, identical with the carbonyl frequency reported by McCorkindale.[6] We found the free carbonyl

(15) C. Y. S. Chen and C. A. Swenson, *J. Phys. Chem.*, **73**, 1363 (1969).

frequency in chloroform to be 1673 cm^{-1}. In this case the frequencies of bonded and free species are separated by only 14 cm^{-1}. Apparently, earlier workers have not worked with sufficiently dilute solutions and have not had sufficient band resolution to recognize the free carbonyl band.

In our work, a graphical curve resolver was used to resolve the complex carbonyl band of 2-quinolone and obtain absorptivities of the overlapping bonded and free species. Band absorptivities for the bonded band which gave consistent results in subsequent calculations were obtained by adjusting the width and height of the individual free and bonded bands so that their sum gave the best fit of both the curve maxima and the valley between the bonded and free bands, while ignoring minor fine structure on the extreme outside limits of the bands. Because of the large equilibrium constant for dimer formation, the free carbonyl band was usually small with respect to the bonded carbonyl band. As a result, the absorptivities determined for the free carbonyl were not precise. The free NH band was therefore used in the calculations to represent the amount of free 2-quinolone present. There was no significant overlap of the bonded carbonyl peak maximum by the free carbonyl band generated on the curve resolver. Therefore, errors in intensity measurements of the bonded carbonyl band were not introduced by resolving overlapping nonlinear absorption bands on the linear-responding curve resolver.

The small shift of the carbonyl band of 2-quinolone on dimer formation has already been noted. As shown in Table I it is only about $1/3$ as large as the $\Delta\nu$ for carboxylic acids. The $\Delta\nu$ for both carboxylic acids and 2-quinolone in the mixed dimer is considerably larger. For example, the $\Delta\nu$ for the 2-quinolone carbonyl increases from 16 cm^{-1} in the 2-quinolone dimer to 32 cm^{-1} in the mixed dimer with the aromatic acid, benzoic acid; the $\Delta\nu$ of the benzoic acid carbonyl increases from 47 cm^{-1} in the acid dimer to 69 cm^{-1} in the mixed dimer with 2-quinolone. Similar, but slightly smaller, increases are noted for the mixed dimers with the saturated acids cyclohexanecarboxylic acid and 4-cyclohexylbutanoic acid. The smaller $\Delta\nu$'s for the mixed dimers with saturated acids are probably a result of their slightly weaker hydrogen bond ($\Delta H°$, Table II).

Because of the differences in $\Delta\nu$'s between dimers and mixed dimers it was possible to observe all six carbonyl bands in the mixed system. The spectrum of the carbonyl region for the mixed system of 2-quinolone and 4-cyclohexylbutanoic acid is shown in Figure 1. The broad envelope approximates the infrared spectrum and is a summation of individual peaks under the envelope. The individual peaks were obtained using the curve resolver and represent the various carbonyl species present. As seen in Figure 1, band overlap is large. In initial attempts to calculate the enthalpies of the mixed dimers, we used the method of Baker and

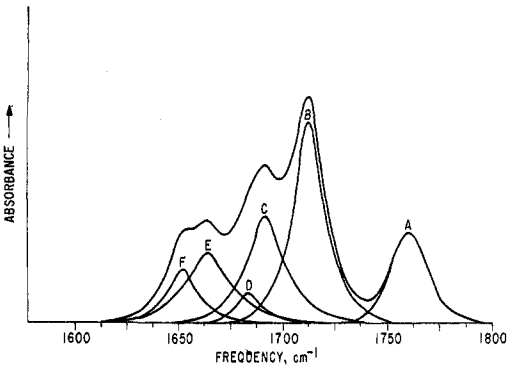


Figure 1. Resolution obtained on a curve resolver of carbonyl stretching region of a mixture of 2-quinolone (0.00186 M) and 4-cyclohexylbutanoic acid (0.0084 M) at 65° in CCl_4. Curve A, free acid C=O; B, acid dimer C=O; C, acid C=O, mixed dimer; D, free 2-quinolone C=O; E, 2-quinolone dimer C=O; F, 2-quinolone, mixed dimer.

Yeaman[16] in which enthalpies are calculated using absorption ratios after making some simplifying assumptions. This method circumvents the need to determine concentrations of the species present; however, it was not possible to resolve the intensity of the individual bands with sufficient precision to obtain good enthalpy values. In spite of the large variance in the enthalpies calculated by this method, results obtained did confirm that correct assignments had been made to the bands and that the correct equilibrium species had been assumed. That the major associated species are cyclic dimers and not linear or larger complexes is evidenced by the linearity of the log K *vs.* $1/T$ plots used to calculate enthalpies.

Although measurements of intensities of the resolved bands for the mixed dimer carbonyls lacked precision, the frequency assignments obtained at different temperatures, concentrations, and concentration ratios of acid to 2-quinolone were found to be consistent and reproducible. Thus, frequencies reported in Table I for the mixed dimer carbonyl bands are believed to be accurate to within ± 3 cm^{-1}.

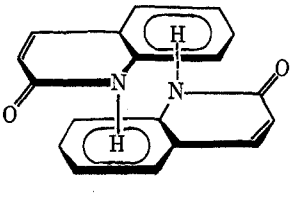
Because of the difficulty in obtaining accurate absorbance values of the mixed dimer in the complex spectra, thermodynamic properties of the mixed system were obtained by first calculating the monomer and dimer concentrations of the acid, using only the free OH band for the acid which can be accurately measured. The concentration of the mixed acid–quinolone dimer could then be calculated by difference. The amount of free quinolone was determined from its free NH band. Using this procedure it was unnecessary to resolve the complex carbonyl region to calculate the equilibrium data on the mixed dimers.

Upon examination of the spectra of 2-quinolone at different temperatures, a lack of correspondence was

(16) A. W. Baker and M. D. Yeaman, *Spectrochim. Acta*, 22, 1773 (1966).

noted between the intensities of the free carbonyl and the free NH bands. This was particularly evident at low temperatures (−14°) where considerable free carbonyl band remained after the free NH band had nearly vanished. Quantitatively these results are shown in Figure 2 in which the apparent molar absorptivities of the two bands are plotted against each other as a function of temperature at two different concentrations. (The apparent molar absorptivity assumes the stoichiometric concentration in calculating absorptivity.) On the basis of the dimer shown in eq 4, this plot should pass through the origin. The possibility that the excess carbonyl at the lower temperatures could result from a carbonyl-containing impurity in the 2-quinolone sample was virtually eliminated by consideration of the following observations: (1) recrystallization of the 2-quinolone from methanol produced no changes in the infrared spectra of the sample; (2) the possible contaminants of 4-quinolone and 2,4-quinolinediol did not have carbonyl adsorption bands characteristic of those found in the 2-quinolone sample; and (3) reaction of the 2-quinolone with hexamethyldisilazane, which reacts with the enol tautomer of the carbonyl group of 2-quinolone to form a silyl ether,[17] completely removed the carbonyl infrared absorption from the sample. Only carbonyl compounds which readily form enol tautomers can undergo this reaction.

The formation of a small amount of cyclic dimer *via* a π–hydrogen bond, as illustrated below, is proposed as an explanation for the excess carbonyl. In this dimer the



amide hydrogen is associated with the π electrons on the aromatic ring of the adjacent molecule, rather than the carbonyl group, leaving the carbonyl unassociated. The formation of some of this dimer would cause the free NH to decrease at a faster rate than the free C=O, in agreement with Figure 2. Similar associations are well known in phenolic systems[18-20] where the hydrogen of the phenolic OH forms a π–hydrogen bond with aromatics. An analogous association has been proposed for the dimerization of pyrrole through association of the NH proton of one molecule with the π electron ring system of the second.[21-23] Further indication of the presence of a π complex in 2-quinolone solutions was obtained from examination of the uv spectra of several solutions of 2-quinolone at different concentrations. When absorbance ratios of two different concentrations were plotted as a function of wavelength, an absorption band in the 2900-Å region was found to be concentration dependent, showing increased absorptivity with decreasing concentration, which is characteristic of

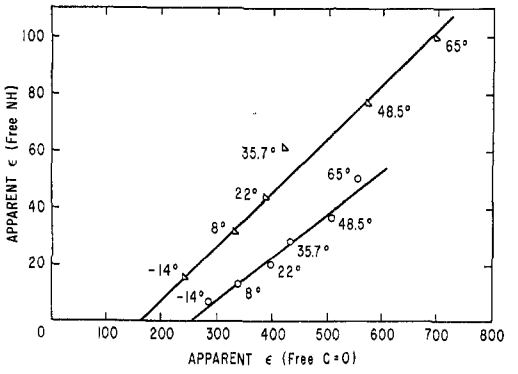


Figure 2. Relationship between apparent molar absorptivities of free NH and free C=O of 2-quinolone in CCl_4 as a function of temperature: O, 0.00197 *M* at 22°; Δ, 0.000394 *M* at 22°.

molecular association. This probably arises from perturbations of the electronic transitions of the π electrons. An additional attempt to confirm the presence of the NH–π bond in 2-quinolone by looking at the out-of-plane infrared bending vibrations of the aromatic hydrogens was not successful, probably because of the low absorptivities of these bands and the low concentrations used. Also, any effect seen by infrared would be only a second-order effect on the aromatic hydrogens.

If 2-quinolone dimers of both the π– and carbonyl–hydrogen bond types are present, the question arises as to what effect this would have on the thermodynamic data (Table II) which were calculated on the assumption that only the carbonyl–hydrogen bond was present. It is estimated, by comparing the apparent molar absorptivity (Figure 2) of the free carbonyl band with the calculated molar absorptivity of this band at infinite dilution (Table II), that a maximum of 10–15% of the dimer present at the lowest temperature and highest concentration studied is of the π complex type. This may cause the calculated molar absorptivity for the bonded carbonyl to be as much as 10–15% lower than the true value. However, because this calculated molar absorptivity is used in calculating the thermodynamic properties, these calculated properties (Table II) should quite accurately reflect the actual equilibria which include both dimer species. Because the π–hydrogen bond would contribute to the enthalpy, but is probably a much weaker bond[24] than the carbonyl–hydrogen bond, the actual enthalpy for the dimerization involving only the carbonyl–hydrogen bond may be

(17) J. C. Petersen, *et al.*, submitted for publication in *Anal. Chem.*
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(19) E. Osawa, T. Kato, and Z. Yoshida, *J. Org. Chem.*, **32**, 2803 (1967).
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(22) M. Gomel and H. Lumbroso, *Bull. Soc. Chim. Fr.*, 2200 (1962).
(23) H. Lumbroso, *J. Chim. Phys. Physiochim. Biol.*, **51**, 132 (1954).
(24) J. V. Hatton and W. G. Schneider, *Can. J. Chem.*, **40**, 1285 (1962).

5–10% higher than the value reported for 2-quinolone in Table II. The negligible effect of the π complexes on the enthalpy calculation is evidenced by the fact that the same enthalpy of association was obtained from calculations at four different concentrations.

Of primary interest in this study were the thermodynamic functions of 2-quinolone and its mixed dimer with carboxylic acids (Table II). The data for 2-quinolone were found to be quite different from the data for the saturated lactams studied by Chen and Swenson.[15] For example, ΔH° (kcal/mol), ΔS° (eu), and ΔG°_{22} (kcal/mol) for 2-quinolone were found to be -8.69, -8.76, and -6.11, compared with -5.90, -11, and -2.74 for the six-membered ring saturated lactam. As indicated by the ΔH° values, the hydrogen bond strength of 2-quinolone is about 1.5 as great as that of the saturated lactam. The marked tendency for 2-quinolone to associate is indicated by the large equilibrium constants for dimerization. At 22° the equilibrium constant is over two orders of magnitude greater for 2-quinolone than for the saturated lactam (33400 l./mol compared to 108 l./mol calculated from data of Chen and Swenson[15]). As might be expected, the thermodynamic functions of 2-quinolone were found to be quite similar to those of the closely related 2-pyridone. The ΔH°, ΔS°, and ΔG°_{25} for 2-pyridone are reported[10] to be -8.8, -12.0, and -5.25, respectively.

Thermodynamic properties of the benzoic acid dimer were found to be essentially the same as those reported by Allen and coworkers,[14] thus offering a check on the techniques used in this study.

The mixed dimers of 2-quinolone and carboxylic acids were found to associate through relatively strong hydrogen bonds (10.3–12.2 kcal/mol) of nearly the same strength as for the dimers of the carboxylic acids (11.1–11.5 kcal/mol) and greater than for the 2-quinolone dimer. Equilibrium constants for the mixed dimers were found to be larger than for the corresponding carboxylic acid dimers. The mixed dimer of the aromatic acid, benzoic acid, shows the greatest amount of association. These data show that the formation of the mixed dimer is important in mixtures of 2-quinolone and carboxylic acids. As an example, when a 1:1 M ratio of 2-quinolone and cyclohexanecarboxylic acid is mixed in carbon tetrachloride at 22°, each at an initial concentration of only 0.00337 M, 43% of all the acid and quinolone is present as the mixed dimer. Only 5% of the 2-quinolone and 14% of the carboxylic acid exist in the free or unassociated state under these conditions, the balance being accounted for by the dimers of the individual compounds.

Enthalpies reported for the mixed dimer are the sum of two hydrogen bonds which are not equivalent. The individual contributions of the NH–carbonyl and the OH–carbonyl bonds are not known. Entropy changes for the mixed dimer were intermediate between those for the acids and 2-quinolones.

In summary, the mixed dimers formed from carboxylic acids and 2-quinolone are strongly associated, hydrogen-bonded complexes and must be considered important in systems which contain these compound types.

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