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FTIR Spectral Study of Hydrogen Bonding in ω-Alkanedicarboxylic Acids in Dilute CCl_4 Solution

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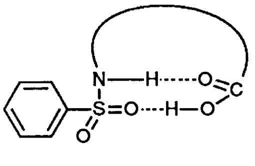
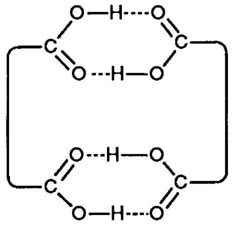
FTIR spectra of the title compounds, $HO_2C(CH_2)_nCO_2H$ (n = 4–14) **2**–**12**, were measured in dilute CCl_4 solution. For compounds **2**–**7**, double cyclic intermolecular hydrogen bonds (II) similar to those observed for glutaric acid **1** were found between the carboxy groups, while **8**–**12** had cyclic intramolecular hydrogen bonds (IVb). A zigzag correlation was found between the percentage (h) of the double cyclic intermolecular hydrogen-bonded molecules and the n value. The h values of odd-membered compounds were larger than those of even-membered ones and the latter values increased with increasing n value. The h value for **7** (n = 9), which forms a 28-membered ring, was 82%. The percentages of the cyclic intramolecular hydrogen-bonded molecules showed the high value of 97% for **12** (n = 14). Conformational analyses on compounds **1**–**12** were carried out using the AM1 method. The hydrogen bondings observed in solution are discussed on the basis of the results.

The thromboxane A_2 receptor antagonist S-145[1] and its chain-analogues [$PhSO_2NH(CH_2)_nCO_2H$ (n = 6–8, 10 and 11)] form intramolecular hydrogen bonds I involving a ring of many members which forms between the carboxy and sulphonamido groups, and there is a positive linear relationship between the percentage of the hydrogen-bonded molecules and the n value.[2–4] However, no information is available on the intramolecular hydrogen bonds in ω-alkanedicarboxylic acids [$HO_2C(CH_2)_nCO_2H$]. It has been also reported[5] that double cyclic intermolecular hydrogen bonds II involving a 16-membered ring in glutaric acid (n = 3) **1** are formed between the carboxy groups, but intramolecular hydrogen bonds are not. Therefore, we were interested in ω-alkanedicarboxylic acids (n = 4–14) **2**–**12**, which can form intermolecular hydrogen bonds II and III and intramolecular hydrogen bonds IVa and IVb.


I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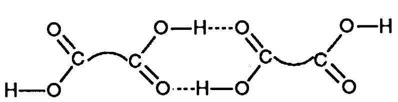
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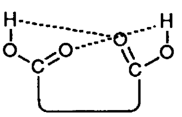
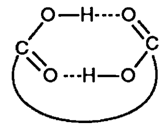

IVa


IVb

HOOC(CH$_2$)$_n$COOH

1 $n = 3$
2 $n = 4$
3 $n = 5$
4 $n = 6$
5 $n = 7$
6 $n = 8$
7 $n = 9$
8 $n = 10$
9 $n = 11$
10 $n = 12$
11 $n = 13$
12 $n = 14$

In order to study these hydrogen bonds, we carried out measurements of FTIR spectra on these compounds in dilute CCl_4 solution. The concentration dependence of the FTIR spectra of **3**, **5** and **7**–**12** was also measured. Full optimization curve analysis was applied to all spectra because of a separation of overlapping absorption bands. The correlation between the number (n) of methylene groups and the percentage (h) of the double cyclic intermolecular hydrogen-bonded molecules of type II was examined for ω-alkanedicarboxylic acids. To help determine the hydrogen bond structures of **2**–**12**, their geometries were optimized by the AM1 method.[6]

Experimental

Compounds **2**–**12** were obtained from commercial sources. They were purified by recrystallization. The elemental analyses were within ±0.3% of the theoretical values. FTIR spectra were recorded on a Nicolet 20SXB FTIR spectrometer at 27 °C. The solvent CCl_4 was dried over 4 Å molecular sieves and purified by distillation. The compounds were dissolved in CCl_4 at concentrations (c) below 3.1×10^{-5} mol dm^{-3} (cell length = 5.0 cm). All operations on the solutions were performed under nitrogen in a dry box. The curve-fitting calculations for peak separation of the observed spectra were carried out using the Nicolet FOCAS program. The AM1 calculation[6] was carried out on a VAX 6320 computer using MOPAC (Ver. 5.0) in the SYBYL molecular modelling system.

For compounds **2**, **4**, **6** and **8**, the FTIR spectra were measured for a saturated CCl_4 solution because of low solubilities. Since no ω-alkanedicarboxylic acid which is freely soluble in CCl_4 is available, the true molar absorption coefficients for the free and dimer $\nu_{C=O}$ bands of its carboxy groups were not obtained, where $\nu_{C=O}$ indicates the C=O stretching vibration. Hence the c values for **2**, **4**, **6** and **8** were estimated by the following approximation. In CCl_4 solution, we had previously found the value of the integrated intensity ($A/10^{-8}$ cm^2 s^{-1} molecule^{-1}) of the free $\nu_{C=O}$ band at 1759 cm^{-1} and the A value per $\nu_{C=O}$ band of the dimer at 1711 cm^{-1} for lauric acid [$CH_3(CH_2)_{10}CO_2H$] to be 133 and 170, respectively.[2] If compounds **2**–**12**, which have two carboxy groups, coexist in the free and hydrogen-bonded forms at equilibrium in CCl_4 solution, the total A values of their $\nu_{C=O}$ bands are presumed to be between 266 and 340. The total A value of the $\nu_{C=O}$ bands observed for **1**, **3**, **5**, **7** and **9**–**12** were in the range 292–314.

Table 1 FTIR spectral data[a] of compounds **1**–**12** in CCl_4 solution (5 cm cell)

Compound	n[b]	S[c]	Assignment[d]	ν/cm^{-1}	ε/dm^3 mol^{-1} cm^{-1}	$\Delta\nu_{\frac{1}{2}}$/ cm^{-1}	A/10^{-8} cm^2 s^{-1} molecule^{-1}	N[e] (%)	σ[f] (%)	$h(\rho)$[g] (%)	c[h]/10^{-5} mol dm^{-3}	σ_t[i] (%)
1[5]	3	16	F	1759.5	270.1	18.4	65.8	26.9	2.0	71.1	2.8459	18.6
			H	1722.8	900.0	15.1	179.5					
			H	1708.4	243.9	16.7	50.9					
2[j]	4	18	F	1760.0	686	20.5	177	68	3	29	(0.7073)	5
			H	1721.8	252	9.3	38					
			H	1713.7	262	18.0	65					
3	5	20	F	1759.1	122.1	16.5	24.7	12.2	0.2	87.6	2.8969	18.9
			H	1712.8	1375.1	14.2	283.0					
4	6	22	F	1758.7	488	19.7	123	49	3	48	(1.3706)	10
			H	1712.1	764	16.5	167					
5	7	24	F	1758.7	161.9	18.1	35.7	16.1	0.6	83.3	3.0070	19.4
			H	1710.8	1315.9	14.7	268.3					
6	8	26	F	1758.3	363	19.3	90	36	2	62	(1.7386)	13
			H	1711.2	956	15.4	200					
7	9	28	F	1758.4	171.2	16.6	35.7	17.0	0.7	82.3	2.9221	19.0
			H	1710.4	1327.2	13.7	264.2					
8	10	(15)	F	1758.4	152	19.0	35	15	0	(85)	(2.3115)	16
			H′	1712.4	1133	16.6	265					
9	11	(16)	F	1756.6	92.4	20.9	23.5	9.2	0.0	(90.8)	2.6030	17.5
			H′	1711.6	1147.8	17.0	268.7					
10	12	(17)	F	1759.0	38.1	18.0	8.4	3.8	0.0	(96.2)	2.6242	17.6
			H′	1710.8	1337.7	15.4	289.9					
11	13	(18)	F	1757.7	37.5	15.3	7.1	3.7	0.0	(96.3)	2.9884	19.3
			H′	1709.4	1478.3	14.3	296.3					
12	14	(19)	F	1759.0	26.8	18.0	6.0	2.7	0.0	(97.3)	2.9887	19.3
			H′	1709.7	1635.6	13.1	307.1					

[a] ν, ε, $\Delta\nu_{\frac{1}{2}}$ and A are the band frequency, the molar absorption coefficient, the band width at half-intensity and the integrated intensity, respectively. [b] Number of methylene groups. [c] Size of a ring formed by the double cyclic intermolecular hydrogen bonds II, where the value in parentheses is the size of a ring formed by the cyclic intramolecular hydrogen bond IVb. [d] F, H and H′ show free $\nu_{C=O}$ and intermolecular and intramolecular hydrogen-bonded $\nu_{C=O}$ bands, respectively, where $\nu_{C=O}$ is the C=O stretching vibration. [e] Percentage (N) of non-hydrogen-bonded molecules, $N = [\varepsilon/(2 \times 501.9)]100$, where 501.9 is the true ε value of free $\nu_{C=O}$ band of lauric acid[2] and its value was doubled because compounds **1**–**12** have two carboxy groups. [f] Assuming that the free molecules of 2 N% in **1**–**12** exist in equilibrium with dimers of the type III as well as in lauric acid, where the N value was doubled because compounds **1**–**12** have two carboxy groups, the percentage (σ) of their dimers were estimated using the equations,[3-5] $c_f = 2Nc/100$, $\log c_f = 0.245\sigma_0^{\frac{1}{2}} - 5.492$ and $\sigma = \sigma_0\ N/100$, where c_f is the concentration of free molecules, c is the total concentration, and σ_0 is the percentage of the dimers at c_f. Because the σ values estimated for all compounds are less than 3%, the existence of dimers of type III in **1**–**12** can be neglected in the curve analysis for the CCl_4 solutions examined. [g] Percentage (h) of the double cyclic intermolecular hydrogen-bonded molecules, $h = 100 - (N + \sigma)$, where the value in parentheses is the percentage (ρ) of the cyclic intramolecular hydrogen-bonded molecules, $\rho = 100 - (N + \sigma)$. [h] Concentration, where the value in parentheses was estimated because the compound could not be completely dissolved in CCl_4 (see text). [i] Percentage (σ_t) of dimers estimated based on the following assumptions: intermolecular II and intramolecular hydrogen bonds IV in **1**–**12** are not formed and an equilibrium in these compounds exists only between the free molecules and dimers of type III. Regression analysis was done between the c and σ values using the spectral parameters of lauric acid that we reported.[2] The analysis gave the equation, $\log c = 0.287\sigma^{\frac{1}{2}} - 5.484$ ($m = 7$, $r = 0.99$), where m is the number of data points and r is the correlation coefficient. The σ_t value of **1**–**12** was approximately estimated using the equation, $\log 2c = 0.287\sigma_t^{\frac{1}{2}} - 5.484$, where the c value was doubled because these compounds have two carboxy groups. [j] The exact parameters were not obtained because of very low solubilities.

Therefore, we assumed that the total A value of **2** is 280, that of **4** and **6** is 290 and that of **8** is 300 because the total A value probably increases with increasing h value. The c values of these compounds were estimated from these A values. Although these estimated c values change slightly with each FTIR spectrum measurement, the variation of the h values was within ±2%. In addition, it was assumed that the value of molar absorption coefficients and the A values of the $\nu_{C=O}$ bands in **2**–**12** are equal to those of lauric acid because the pKa_1 and pKa_2 values of $HO_2C(CH_2)_nCO_2H$ are almost the same if n is greater than two.[7]

Results and Discussion

Double Cyclic Intermolecular Hydrogen Bonding in **1**–**7** *and Cyclic Intramolecular Hydrogen Bonding in* **8**–**12**.—The spectral parameters of the $\nu_{C=O}$ bands for the carboxy groups in **1**–**12** and their assignments are listed in Table 1, together with the percentages (N) of non-hydrogen-bonded molecules, (σ) of dimers of type III, (h) of double cyclic intermolecular hydrogen-bonded molecules and (ρ) of cyclic intramolecular hydrogen-bonded molecules. The percentage (σ_t) of the dimers, which was estimated based on the assumption that an equilibrium exists only between the free molecules and the dimers of type III, was also listed in Table 1. The FTIR spectra of **2** and **3** and the results of the peak separations for their spectra are shown in Fig. 1. In general, the stronger the hydrogen bond, the greater the lower wavenumber shift of the hydrogen-bonded ν_{OH} and $\nu_{C=O}$ bands.

For compounds **1**–**12**, the intensity of the free $\nu_{C=O}$ bands at *ca.* 1759 cm^{-1} for the carboxy groups decreased and a new band appeared at lower wavenumbers. Correspondingly, the intensity of the free ν_{OH} band at *ca.* 3533 cm^{-1} decreased and a new broad band appeared at *ca.* 3000 cm^{-1}. The percentage (h or ρ) of hydrogen-bonded molecules, $100 - (N + \sigma)$, in **1**–**12** is much larger than the σ_t value estimated for these compounds, and their σ values are very small. These results suggest that compounds **2**–**12** form double cyclic hydrogen bonds II similar to those found for **1**,[5] indicative of a large association constant, or various intramolecular hydrogen bonds as shown previously.[5]

The free $\nu_{C=O}$ band in **1**–**12** was not observed at

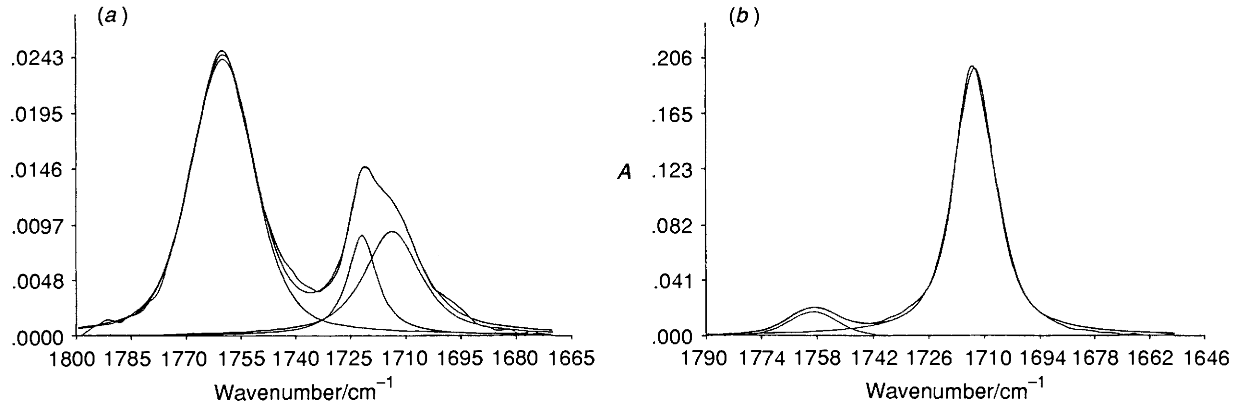


Fig. 1 FTIR spectra of **2** and **3** in CCl_4 solution and the results of peak separation of their spectra. Spectra were obtained using a 5.0 cm cell; **2** 0.7073 × 10^{-5} mol dm^{-3} (*a*) and **3** 2.8969 × 10^{-5} mol dm^{-3} (*b*).

Table 2 Energy difference (ΔE)[a] between U-shaped and linear conformers and non-bonded distances (R) of U-shaped conformer for compounds **1**–**12** by AM1 calculation

Compound	ΔE/kcal mol^{-1}	Distance[b]/Å		Distance[c]/Å	
		$R_{O\cdots O}$	$R_{O\cdots H}$	$R_{O\cdots O}$	$R_{O\cdots H}$
1	1.73	3.768	3.979	3.950	4.181
	(−0.76	3.166	3.229	3.561	3.868)[d]
2	0.83	4.249	4.458	4.602	4.821
3	2.60	2.767	2.301	2.999	2.576
4	1.47	2.826	2.201	2.841	2.205
5	−0.55	2.824	2.186	2.831	2.181
6	−0.33	2.866	2.134	2.846	2.137
7	−1.18	2.950	2.147	2.826	2.152
8	−1.13	3.014	2.131	2.976	2.123
9	−0.32	2.991	2.122	2.974	2.138
10	−1.53	3.023	2.101	3.062	2.127
11	−0.21	3.035	2.102	2.931	2.117
12	−0.80	3.051	2.086	2.986	2.123

[a] Difference of the heat of formation between the conformers. [b] Back non-bonded distance between oxygen and oxygen or hydrogen atoms (see Fig. 2). [c] Front non-bonded distance between oxygen and oxygen or hydrogen atoms (see Fig. 2). [d] Ref. 5; *ab initio* MO method at 3-21G (*) level (GAUSSIAN 86), where ΔE is the total energy difference.

wavenumbers higher than 1760 cm^{-1}, indicative of a *trans*-carboxy group, in which the torsion angle H–O–C=O (τ) is *ca.* 180°.[8] The carboxy group, in which the τ value had changed from 0 to 90°, was found to have become extremely unstable according to the *ab initio* MO calculations.[5,9] If compounds **2**–**12** do not form the double cyclic intermolecular II and cyclic intramolecular hydrogen bonds IVa or IVb, the $100 - (N + \sigma)$ values are less than 50%. However, these values of all compounds were estimated to be more than 60%, when the values of **2**, **4** and **6** at 3 × 10^{-5} mol dm^{-3} were estimated as mentioned below. These results suggest that if these compounds form hydrogen bonds, they should form bonds of type II, IVa or IVb. For compounds **3**–**12**, one sharp hydrogen-bonded $\nu_{C=O}$ band was observed in the narrow range of 1713–1709 cm^{-1}. These values are similar to the 1711 cm^{-1} band of the lauric acid dimer.[2] Furthermore, the hydrogen bonding interaction ability of π-electrons on the C=O bond as in IVa is much weaker than that of n-electrons as in IVb.[10] These results suggest that compounds **3**–**12** do not form hydrogen bonds of type IVa, but those of type IVb or II.

For compounds **1**–**12**, a linear conformer and several U-shaped conformers were energetically optimized by the AM1 method. The energy differences (ΔE) between the U-shaped and the linear conformers are listed in Table 2 together with the non-bonded distances ($R_{O\cdots O}$ and $R_{O\cdots H}$) of the U-shaped conformer. Stereoviews of the U-shaped conformer optimized for **1**–**12** are shown in Fig. 2. The U-shaped conformers of **5**–**12** are more stable than the linear one, but unstable in **1**–**4**. However, the latter compounds have U-shaped conformations with local minimum energy. The U-shaped conformer of **1** with the *h* value of 71% has been found to be more stable than the linear one by *ab initio* calculations.[5] As shown in Fig. 2, all of the carboxy groups exist in planar conformation (τ *ca.* 0°) as predicted by the *ab initio* calculations[5,9] and the larger the *n* value, the flatter the two carboxy groups are in relation to each other.

For compound **2**, the $R_{O\cdots H}$ values optimized by the AM1 calculation are much larger than the sum (2.6 Å) of the van der Waals radii of these atoms. This suggests that compound **2** does not form cyclic intramolecular hydrogen bonds IVb, but does form double cyclic intermolecular hydrogen bonds II similar to those observed for **1**.[5] In addition, compound **2** gave two intermolecular hydrogen-bonded $\nu_{C=O}$ bands as shown in Fig. 1, suggesting that an equilibrium exists between two conformers of the 18-membered ring. Although the $R_{O\cdots H}$ values of **3**–**12** are smaller than 2.6 Å, it is presumed that in compounds with a small *n* value, cyclic intramolecular hydrogen bonds IVb cannot form because their two carboxy groups do not lie in the same plane due to the conformational restriction, but the double cyclic intermolecular hydrogen bonds II can form. On the other hand, it is also presumed that in compounds with a large *n* value, the cyclic intramolecular hydrogen bonds IVb can form because the two carboxy groups nearly lie in the same plane. When the *n* value is more than nine, these groups nearly lie on the same plane, as shown in Fig. 2.

To examine these assumptions, the concentration dependence of the FTIR spectra of **3**, **5** and **7**–**12** was measured. A significant decrease in the $100 - (N + \sigma)$ value was observed for **3**, **5** and **7** at concentrations below 3 × 10^{-6} mol dm^{-3}, when compared with the result for that at 3 × 10^{-5} mol dm^{-3}, but not for **8**–**12**. These results indicate that compounds **3**, **5** and **7** form a very large ring due to double cyclic intermolecular hydrogen bonds II similar to those found for **1** and **2**, while compounds **8**–**12** form cyclic intramolecular hydrogen bonds IVb. From these findings, it is deduced that the hydrogen bonds in **4** and **6** are of the same type as those of the former compounds. Thus, the hydrogen-bonded structures of **2**–**12** in dilute CCl_4 solution were revealed, and the result was found to be consistent with those from the AM1 calculations. These phenomena markedly differ from those observed for $PhSO_2NH(CH_2)_nCO_2H$.[4]

Correlations between h *and* n *Values*.—Fig. 3 shows plots of the N, σ, h and ρ values against the n and S values, where S is the size of the ring formed by the double cyclic intermolecular or cyclic intramolecular hydrogen bonds. The h values of **2**, **4**

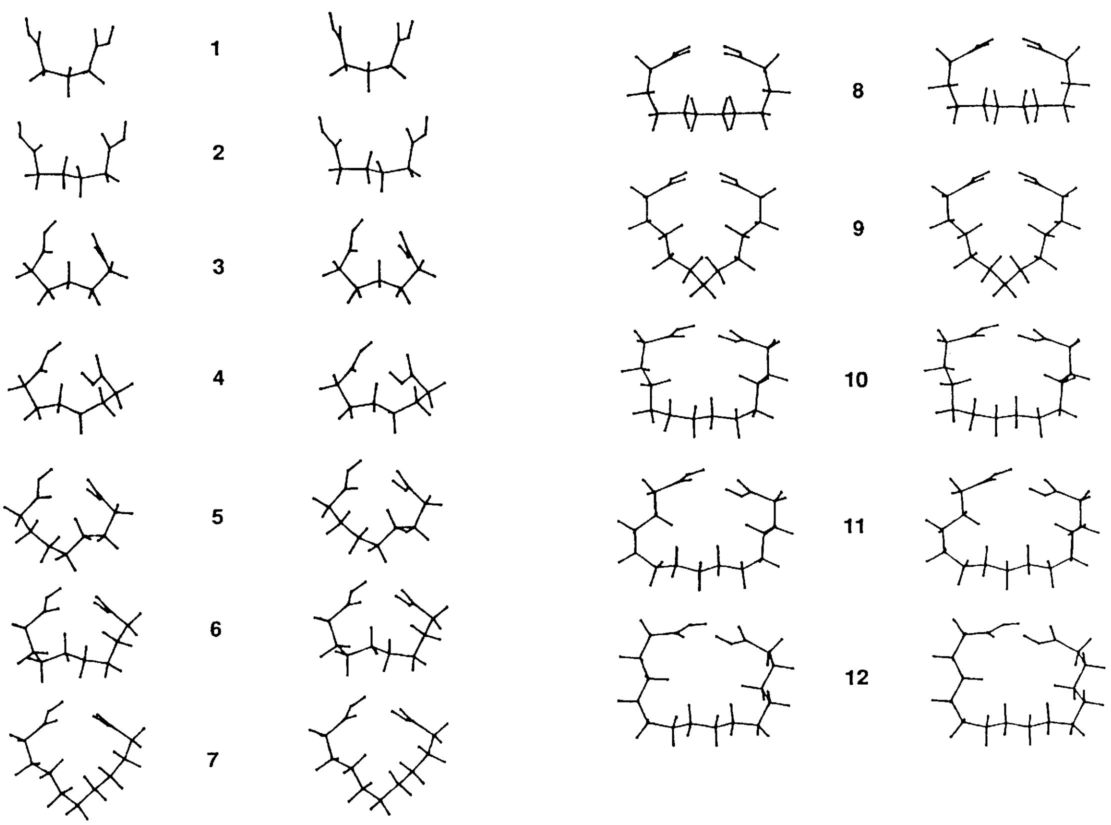


Fig. 2 Stereoviews of the conformations for **1**–**12** optimized by AM1 calculations. These may not be the most stable U-shaped conformers because a complete systematic search was not carried out over all the conformational space. Numbers indicate compounds.

and **6** are estimated to be small due to low solubilities. Assuming that the relationships between the *c* and *h* values in these compounds are similar to those between the *c* and *h* values in glutaric acids,[5] the *h* values of **2**, **4** and **6** at 3 × 10^{-5} mol dm^{-3} were estimated from these relationships to be 61% for **2**, 65% for **4** and 72% for **6**. These values are plotted against the *n* and *S* values in Fig. 3.

In even-membered compounds, the *h* values increased with increasing *n* or *S* value. The ρ values also increased with increasing *n* or *S* value. The correlation between the *h* and *n* values was found to be a zigzag line, and the *h* values of the odd-membered compounds were larger than those of the even-membered ones.* This indicates that the formation of 16-, 20-, 24- and 28-membered rings due to the double cyclic intermolecular hydrogen bonds II in the odd-membered compounds occurs more easily than that of 18-, 22-and 26-membered rings in the even-membered ones. It has been reported[11] that in dimeric cyclophanes (n = 4–9), the calculated strain energies, which are mainly attributed to the methylene chains, of the odd-membered compounds are smaller than those of the even-membered ones. This suggests that the *h* values in ω-alkanedicarboxylic acids are primarily governed by these strain energies.

In conclusion, we have found that compounds **2**–**7** form double cyclic intermolecular hydrogen-bonded dimers involving 18- to 28-membered rings, respectively, while compounds **8**–**12** form the cyclic intramolecular hydrogen-bonded monomer involving 15- to 19-membered rings, respectively. This information should be very important for understanding the hydrogen bonding of dicarboxylic acids, and studying their molecular interactions.

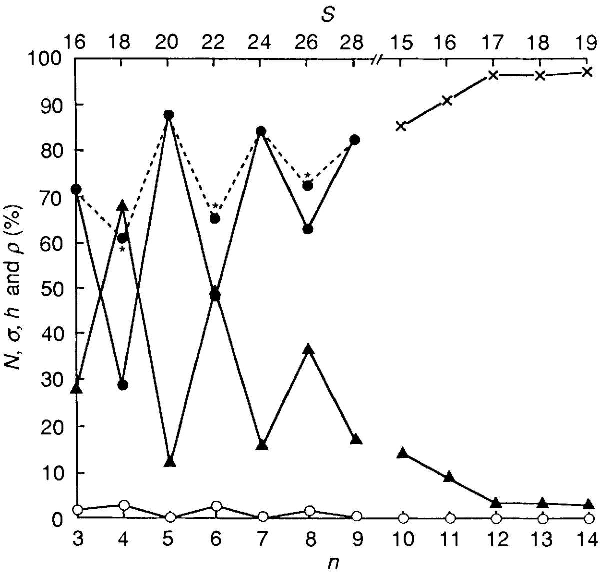


Fig. 3 Variations of *N* (▲), σ (○), *h* (●) and ρ (×) with chain length for HO$_2$C(CH$_2$)$_n$CO$_2$H in CCl$_4$ solution at concentrations below 3.1 × 10^{-5} mol dm^{-3}. * Estimated *h* value at 3 × 10^{-5} mol dm^{-3} (see text).

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* The zigzag correlation between the melting point (m.p.) and the *n* value in ω-alkanedicarboxylic acids is well known. Thus the correlation between the *h* and m.p. values was examined. In spite of the fact that these values widely differ in their physical properties, two correlations were found between these values: the *h* value of the odd-membered compounds roughly increases with an increasing m.p. value while, in the case of the even-membered compounds, the *h* value decreases.

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