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Molecular Recognition at the Interface. Synthesis and Monolayer Property of Long-Chain Derivatives of Kemp's Acid

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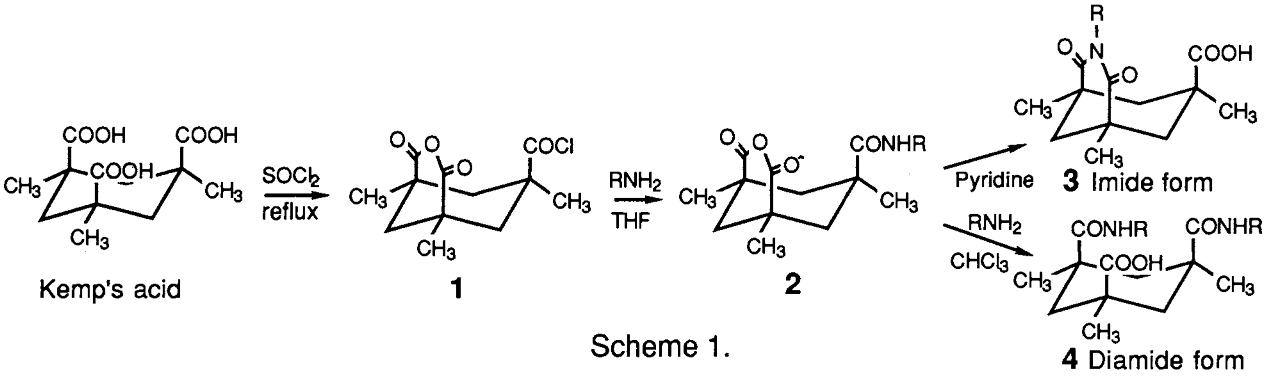
Monolayer formation of octadecyl derivatives of a cyclohexanetricarboxylic acid (Kemp's acid) was examined. A symmetrically substituted double-chain derivative gave a stable monolayer in which carboxylic acids formed cyclic dimers at the air-water interface.

Molecular recognition at the air-water interface has been studied in terms of enantiomeric selection1-3) and of host-guest interactions (crown ethers4-6) and cyclodextrins7)). Specific ion binding at the interface was further examined by using other ionophoric monolayers that possess the non-cyclic crown ether unit8) or the calixarene unit.9)

Specific pairing of hydrogen bonding is useful for precise recognition of organic molecules, as amply demonstrated by proteins and nucleic acids. There is an explosive growth in the synthesis of host molecules that are capable of molecular recognition through specific hydrogen bonding.10-12) We are interested in examining these phenomena at the air-water interface. A long-chain derivative of the cyclic resorcinol tetramer formed stable monolayers and selectively bound sugars in the subphase.13) The selectivity observed at the interface was different from that observed by Aoyama *et al.*11) in the bulk phase.

In the present investigation, we synthesized long-chain derivatives of Kemp's acid and studied their monolayer behavior. Rebek and coworkers conducted an extensive investigation on molecular recognition and catalysis by monomeric and dimeric derivatives of Kemp's acid.10)



Scheme 1.

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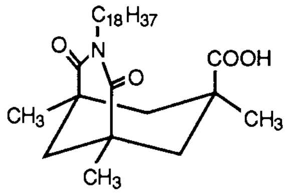
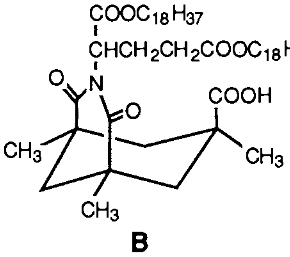
Long-chain derivatives of Kemp's acid were synthesized according to Scheme 1. Kemp's acid[14] (*cis,cis*-1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid) mp 230-234 °C, was treated with refluxing thionyl chloride to obtain **1**, mp 268-270 °C,[14] which was then allowed to react with long-chain amines to form anhydride-amides **2**. Treatment of **2** with pyridine at room temperature produced imides **3**. Reaction of **2** with equimolar amines gave diamides **4**. The final products, **A**-**D** were identified by IR and ^{1}H-NMR spectroscopies and by elemental analysis.[15]



A



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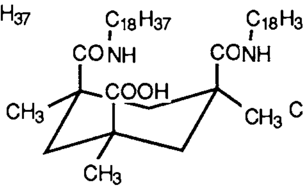

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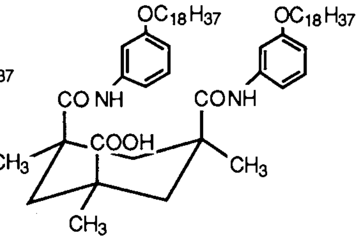

D

These compounds were spread on water from chloroform solutions (1-2 mM) and their monolayer characteristics were examined by a computer-controlled film balance (San-esu Keisoku, model FSD-50). As shown in Fig.1, compounds **A** and **B** form expanded monolayers with collapse pressures of 22 mN·m^{-1} and 31 mN·m^{-1}, respectively. The space-filling molecular models of these compounds suggest that regular molecular packing in which the carboxylic acid unit is in full contact with the aqueous phase and the alkyl chain is placed far from the interface, is not feasible. The relative bulkiness of the cyclohexane head and the single alkyl chain is not balanced in **A**. The head unit can not be positioned stably at the interface if the alkyl chain packing is optimized in **B**.

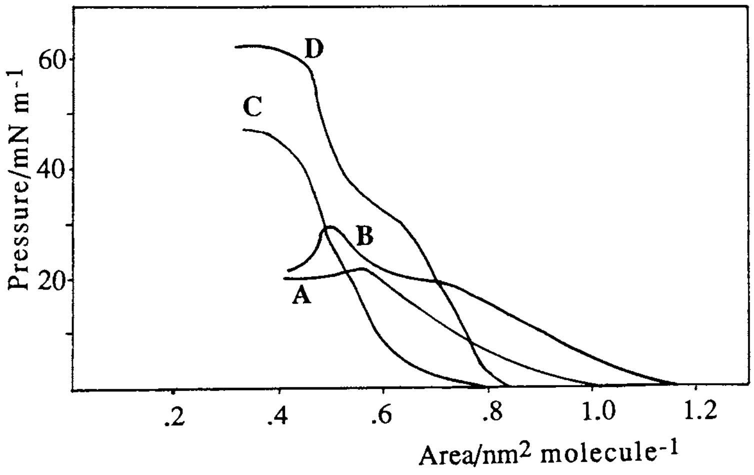

Fig.1. Pressure-area isotherms of monolayers of **A**-**D** at 20 ± 0.2 °C on pure water. Compounds **A** and **D** (imide form) give expanded monolayers, while **C** and **D** (diamide form) give condensed monolayers.

In contrast, diamides **C** and **D** formed more stable monolayers with collapse pressures of 45 mN·m^{-1} and 60 mN·m^{-1}, respectively. The alkyl chain packing appears to be much improved in these monolayers. The m-phenylene unit in the side chain of **D** is especially effective in this respect. The collapse behavior did not change if the compression-expansion cycle was repeated at surface pressures below 50 mN·m^{-1}, although some hystereses were noticed during the expansion step. The molecular cross sections estimated from the steepest portion of the π-A curves are 0.60 nm^2 for the latter monolayers. The cyclohexane head unit will assume 0.50 nm^2 if it is placed normal to the water surface. Therefore, the observed cross sections are suggestive of tilted molecular axes in the monolayer so as to assume better exposure of the carboxylic acid to the interface.

The improved stability of monolayers of **C** and **D** relative to those of **A** and **B** can be inferred from X-ray diffraction data (Rigaku Denki, RAD-R-32, Cu-Kα) of their cast films$^{16)}$ obtained by the reflection method. These compounds were dissolved in acetone (1-2 mM), spread on glass plates, and kept for 24 h at room temperature.

The long spacings observed for **A** and **B** are not longer than the extended molecular length (CPK model) and indicate the formation of either a highly tilted alignment or an interdigitated structure. The latter structure seems to be more probable because the head group is bulky. Compounds **C** and **D** gave long spacings of 5.4 nm and 5.5 nm, respectively. These figures are longer than the respective molecular lengths (3.2 nm and 3.6 nm), but shorter than two times of these lengths, and suggest formation of the tilted bilayer arrangements (57.4° and 50.1°). Therefore, the half bilayer structure (i.e., monolayer) must be stably formed from compounds **C** and **D** unlike compounds **A** and **B** that form the interdigitated structure rather than the (half) bilayer structure.

Specific pairs of the carboxylic acid unit in Kemp's acid have been shown to be effective for molecular recognition. It is thus expected that long-chain derivatives of Kemp's acid, when aligned at the air-water interface, would produce such specific pairs. The FT-IR technique (Nicolet, Model 710) was used for this purpose. The most stable monolayer **D** was deposited at 30 $\mathrm{mN \cdot m^{-1}}$ on a Ag-coated (100 nm) glass plate. A partial spectrum obtained by the RAS (reflection absorption spectroscopy) method is shown in Fig.2. The $\nu_{C=O}$ band at 1703 $\mathrm{cm^{-1}}$ indicates that the carboxylic acids in the LB film form the cyclic dimer rather than the side way dimer that should absorbs at a higher wavelength.$^{17)}$ The monomeric form is of course not probable for this band. Figure 3 display a schematic monolayer arrangement for

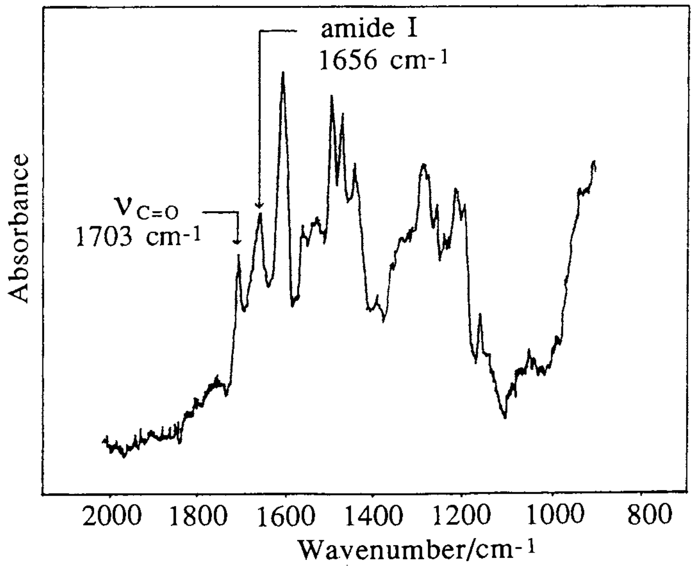

Fig.2. IR-RAS spectrum of a LB film of **D**, (1 layer, up stroke) deposited on a Ag-coated glass plate.

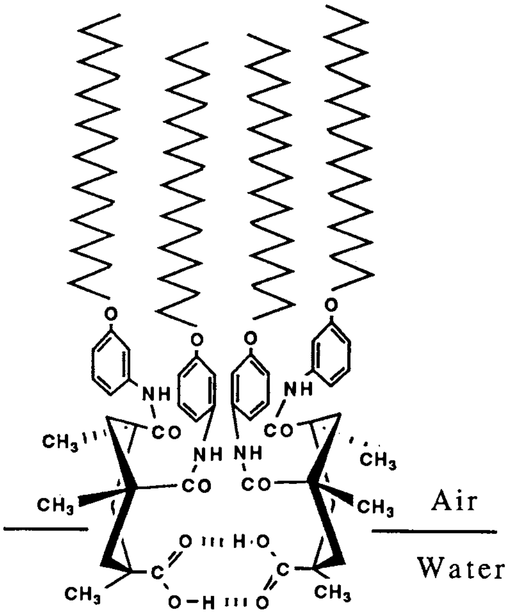

Fig.3. Schematic illustration of monolayer **D**.

D. A pair of the molecules face each other in order to form a cyclic carboxylic acid dimer.

In conclusion, we demonstrated that stable monolayers are prepared from long-chain derivatives of Kemp's acid. The carboxylic acid unit in the monolayer appears to be disposed specifically at the interface. This site would be employed for specific recognition via hydrogen bonding.

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15) Compound **A**: colorless crystals, mp 121-124 °C; Anal. Found: C, 73.20; H, 10.91; N, 2.87%. Calcd for $C_{30}H_{53}NO_4$: C, 73.28; H, 10.86; N, 2.85%. Compound **B**: colorless powder, mp 33-36 °C; Anal. Found: C, 72.49; H, 10.95; N, 1.59%. Calcd for $C_{53}H_{95}NO_8$: C, 72.81; H, 10.95; N, 1.60%. Compound **C**: colorless powder, mp 79-85 °C; Anal. Found: C, 76.15; H, 9.98; N, 3.47%. Calcd for $C_{51}H_{80}N_2O_5$: C, 76.46; H, 10.06; N, 3.50%. Compound **D**: colorless powder, mp 107-110 °C; Anal. Found: C, 76.04; H, 10.71; N, 2.95%. Calcd for $C_{60}H_{100}N_2O_6$: C, 76.22; H, 10.66; N, 2.96%.
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