Selective Preferential Esterification of the Dicarboxylic Acids with Longer Carbon Chain by Diazomethane in the Presence of Dicarboxylic Acids with Shorter Carbon Chain by Adsorbing and Aligning the Acids on Alumina

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(Received November 6, 1987)

Selective monoesterification of a dicarboxylic acid with longer carbon chains by diazomethane in a mixture of dicarboxylic acids, [dodecanedioic acid (C_{12}) plus glutaric acid (C_5), adipic acid (C_6), pimelic acid (C_7), suberic acid (C_8), or sebacic acid (C_{10})] was achieved by adsorbing and aligning the acids on alumina. The larger the difference in the number of carbon atoms, the higher the selectivity. In the case of the combination of C_{12} and C_5 the highest selectivity was observed and the preferential 89% formation of the monomethyl ester of C_{12} was obtained in contrast to the 9% formation for the monomethyl ester of C_5. Selective reactions were also observed in the case of the combination of C_{10} and C_4, and that of C_{12} and *trans*-1,4-cyclohexanedicarboxylic acid.

The use of solid adsorbents such as alumina and silica gel as a reaction medium is becoming increasingly widespread in organic synthesis.[1–6] Usually it is the reagents that are supported. Reagent-doped adsorbents can be used to achieve some very mild and consequently selective organic transformations. Recent examples are given for the use of solid adsorbents as substrate support. Solid adsorbents are used deliberately as the reaction field for substrates to achieve highly selective reaction, in which the substrate molecules orient and/or are captured with suppression of translational movement on the surface of the solid adsorbents. This gives rise to the chance for highly selective reactions, for example ozonolysis of aliphatic ester,[7] terminal (ω) chlorination of octanoic acid,[8] enone photocycloaddition,[9] selective synthesis of crown ether,[10] *O*-methylation of alcohol[11] and monomethyl esterification of dicarboxylic acid.[12]

Fatty acids in general, when adsorbed on air-water interfaces, occupy an area of 0.205 nm^2 per molecule independent of chain length or molecular weight.[13] The molecules are aligned with their axis perpendicular to the interface in a close-packed, rigid array. We could develop a method for selective synthesis of the monomethyl esters of dicarboxylic acids with the aid of this phenomenon.[12] Aliphatic dicarboxylic acids were considered to be adsorbed as a monomolecular layer on alumina and to form a stable membranelike structure with the aid of van der Waals interactions between the methylene groups as in Fig. 1a.

If two kinds of dicarboxylic acids are adsorbed as in Fig. 1b, a facile reaction of the non-adsorbed carboxyl group of the longer chain dicarboxylic acid is easily recognized, while the shorter one would be expected to be hardly reactive. We reported briefly this new type of selective reaction proceeding on an aluminum surface on which the monomethyl esterification of dodecanedioic acid (C_{12}) proceeded preferentially in the presence of other shorter chain acids.[14] This paper presents details of this reaction and application of this adsorption-reaction procedure to other dicarboxylic acids.

Results and Discussion

Effect of Surface Coverage (θ) on Monomethyl Esterification of Suberic Acid (C_8). Figure 2 shows the formation of monomethyl ester of C_8 under the various θ values of C_8 on alumina. The value of θ is estimated as follows; θ=adsorption amount of C_8/

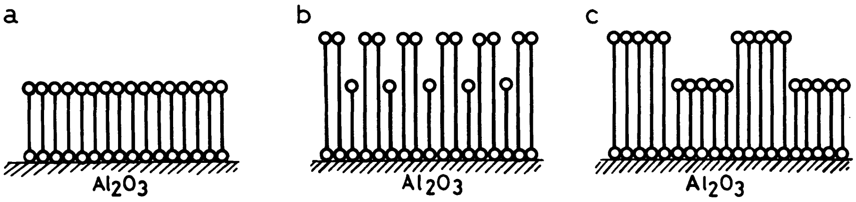

Fig. 1. Models for the aggregation of aliphatic dicarboxylic acids adsorbed on alumina, open circle represents carboxyl group and thick line represents aliphatic carbon chain: a) monomolecular layer of the acid; b) well-mixed aggregation of the mixture of two kinds of the acids; c) mosaic aggregation of the mixture of two kinds of the acids.

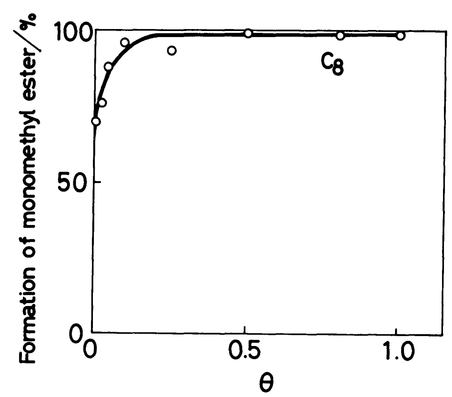

Fig. 2. Dependence of surface coverage (θ) on monomethyl ester formation for suberic acid (C_8): θ= adsorption amount of C_8/saturation amount (4.0×10^{-4}mol g-$Al_2O_3^{-1}$). The adsorption sample was suspended in cyclohexane. About 6 molar equivalents of diazomethane was added at room temperature.

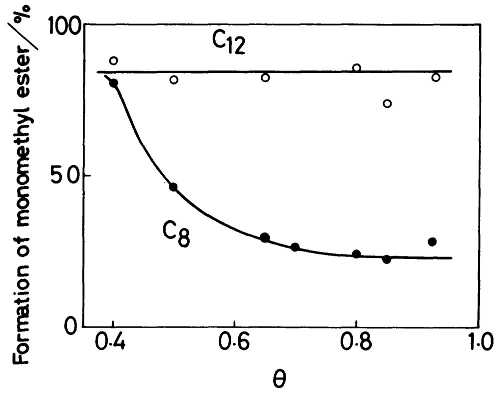

Fig. 3. Dependence of surface coverage (θ) on preferential monomethyl esterification of dodecanedioic acid (C_{12}) (○) in a mixture of C_{12} and suberic acid (C_8) (●): θ=adsorption amount (C_{12}+C_8)/saturation amount (4.0×10^{-4} mol g-$Al_2O_3^{-1}$). The adsorbed sample contained C_{12} and C_8 in a molar ratio of 2 to 1. Cyclohexane was used as a suspending agent. About 6 molar equivalents of diazomethane was added at room temperature.

saturation amount (4.0×10^{-4} mol g-$Al_2O_3^{-1}$).[12] The monomethyl ester was formed quantitatively in the range where the θ value exceeds 0.4 while the monomethyl ester was not formed quantitatively in the range where the value is less than 0.4. Quantitative formation of the monomethyl ester in the higher range of the θ value suggests that the adsorbed molecules would form the monomolecular layer in which one of the two carboxyl groups is chemisorbed on alumina with the rest of the carboxyl group in a position remote from the surface as shown in Fig. 1a.

Effect of θ on Selective Reaction. Selective monomethyl esterification of one of the dicarboxylic acids in a mixed system was attempted, and the effect of the surface coverage was examined by use of C_{12} and C_8 in a 2:1 molar ratio. As shown in Fig. 3, the difference in reactivities of C_{12} and C_8 developed with increase in θ value. The formation of the monomethyl ester of C_8 decreased with increase in the θ value, and the formation for the monomethyl ester of C_{12} and that of C_8 became constant where the θ value exceeded about 0.8. The value of 0.8 was an adequate value for a sufficiently selective reaction, in which preferential 89% formation for the monomethyl ester of C_{12} was obtained in contrast to the 28% formation for the monomethyl ester of C_8 besides 1% formation for the dimethyl ester of C_{12}, 10% intact C_{12} and 72% intact C_8.

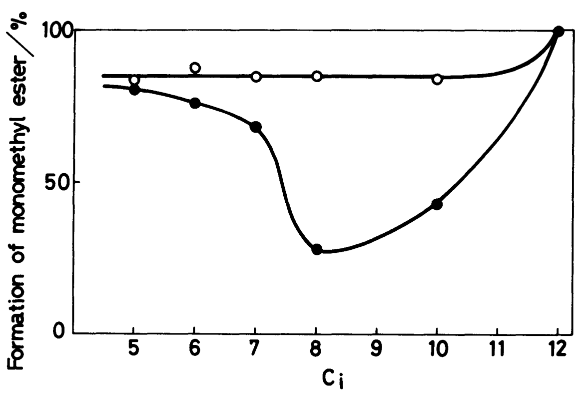

Fig. 4. Monomethyl ester formation for dodecanedioic acid (C_{12}) (○) and shorter chain acid (C_i) (●) adsorbed in the molar ratio of 2 to 1 where C_i means the aliphatic dicarboxylic acid having *i* carbons. The adsorbed sample consisted of a total of 0.32 mmol of the acids per gram of alumina (θ=0.8). About 6 molar equivalents of diazomethane was added at room temperature.

The same reactivity of the carboxyl groups of C_{12} and C_8 was confirmed in the following way. In a homogeneous reaction in a 1% DMF solution, the reactivities of C_{12} and C_8 were the same yielding the monomethyl esters in about 50% maximum yield at the same conversion.

Effect of Carbon Chain Length for the Selectivity at Low Ratio of C_{12}/Shorter Chain Dicarboxylic Acid (C_i). Various kinds of dicarboxylic acids were tested by combining with C_{12} for the selective monomethyl esterification of C_{12}. Figure 4 shows that the combination of C_{12} and C_8 was most effective for selective monomethyl esterification, 89% formation for the monomethyl ester of C_{12} and 28% formation for that of C_8, when the adsorption sample containing C_{12} and C_i in 2/1 molar ratio was used. From the alternative model as shown in Fig. 1b, the shorter chain dicarboxylic acids would be expected to be hardly reactive. But actually in the case of glutaric acid (C_5), adipic acid (C_6), and pimelic acid (C_7), the shorter the carbon chain of the dicarboxylic acids, the lower the selectivity became. Nonselective reaction occurred in the case of the combination of C_{12} and C_5.

Nonselective reaction was also observed even in a case of the combination of C_{12} and C_8 when the same quantity of C_{12} and C_8 was used, and equal amounts of their monomethly esters were obtained quantitatively. The determining factor for the selective reaction appears to be the state of aggregation of the components acids. Selective reaction occurs when the two kinds of acids are adsorbed as in Fig. 1b. Based on the measurement of the surface pressures of mixed monolayers of pentadecanoic acid with acetates of its near neighbors in chain length, Matuo et al. found the interaction between the two components in a mixed monolayer decreased with an increase in the difference in chain length between the two components.[15] The formation of the aggregate as shown in Fig. 1b seems to be acceptable in the case of the combination of C_{12} and C_{10}, but in the case of the combination of the C_{12} and the much shorter carbon chain acids the formation of the aggregate seems to be difficult. Probably each acid might aggregate independently. The low selectivities in the combination of C_{12} and the much shorter carbon chain acids are considered to be due to the formation of "island"[16] aggregates of each kind of acids as shown in Fig. 1c.

Selective Monomethyl Esters Formation of C_{12} and C_i in Various Molar Ratios of Acids. As mentioned above, the selectivity decreased when the same quantity of C_{12} and C_8 was used. The effect of the molar ratio of C_{12} to C_i was examined. Figure 5 shows the selective monomethyl esterification of C_{12} with the increase in the molar ratio. The amount of the monomethyl ester of C_{12} formed was held preferentially high and constant regardless of the ratios, while that of the shorter carbon chain acids drastically changed. In the case of the combination of C_{12} and C_5 the higher ratio ($\geqslant 6$, more than six) of C_{12}/C_5 led to a decrease of monomethyl ester of C_5 formed, though the formation of the monomethyl ester could not be suppressed at a lower ratio (less than 4). In the case of the combination of C_{12}/C_8 the formation of the monomethyl ester of C_8 was sufficiently suppressed even at the lower ratio. In a region higher than 6/1 the formation for the monomethyl esters of both of the shorter carbon chain acids sufficiently decreased, and their values became constant; 28% for C_8, 9% for C_5. Two kinds of acids in both of the combinations at the higher molar ratio might be adsorbed on alumina as in Fig. 1b, in which shorter carboxylic acid molecules are surrounded with the longer on alumina surface. It is considered that in the combination of C_{12} and C_5 the state of aggregation of the acid mixture changed from the aggregate as shown in Fig. 1c to that of Fig. 1b with increase in the ratio, and the selective reaction then occurred.

Effect of Chain Length of Acid on the Selective Formation of Monomethyl Eater of C_{12} at High Ratio of C_{12}/C_i. A molar ratio of 6/1 for C_{12} to shorter chains was a large enough ratio to ensure an adequate protection of the shorter chain acids. Accordingly we tried the selective monomethyl esterification using this ratio. The results shown in Fig. 6 illustrate the selective preferential monomethyl esterification of C_{12}. Figure 6 presents a great contrast from Fig. 4 in that differences in the chain length of the shorter chain acids affected their reactivities. On the other hand, most of C_{12} reacted in every case. The larger the difference in the number of carbon atoms, the higher the selectivity obtained. The combination of C_{12} and C_5 was most effective for selective monomethyl esterification. An 89% yield of the monomethyl ester of C_{12} was obtained in contrast to a 9% yield for the monomethyl ester of C_5.

This method was applied to the other combination of acids. The formation of each monomethyl ester under the same reaction conditions described in this paragraph was as follows; C_{10}/C_6=81%/21% and C_{12}/*trans*-cyclohexanedicarboxylic acid=88%/45%.

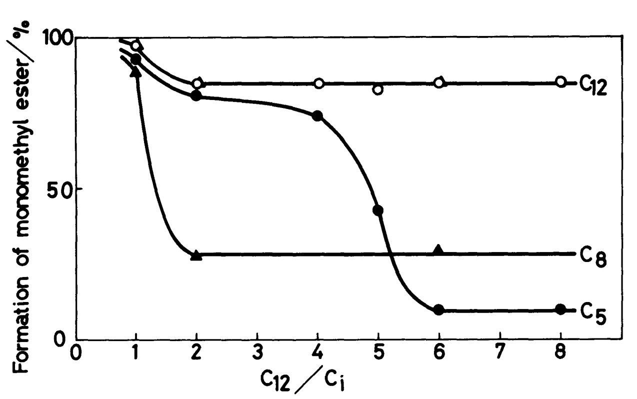

Fig. 5. Effect of the molar ratio of C_{12} to C_i on the formations of monomethyl esters: samples containing C_{12} (○) and C_5 (●); samples containing C_{12} (△) and C_8 (▲), respectively. The adsorbed sample consisted of a total of 0.32 mmol of the acids per gram of alumina (θ=0.8). About 6 molar equivalents of diazomethane was added at room temperature.

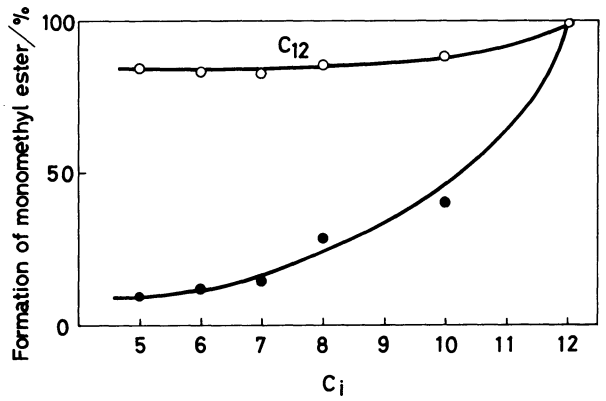

Fig. 6. Selective monomethyl ester formation for dodecanedioic acid (C_{12}) (○) and C_i (i=5—8,10) (●) adsorbed in the molar ratio 6:1 and a total of 0.32 mmol of the acids per gram of alumina (θ=0.8) where C_i is the aliphatic acid having i carbon atoms. About 6 molar equivalents of diazomethane was added at room temperature.

Interestingly, in the former case (the combination of C_{10} and C_6) 60% for the difference between the formation of each monomethyl ester was observed as in the case of C_{12}/C_8. These two values for the two systems are similar, and the difference in carbon number (the number 4) between two components acids is the same in both systems. This agreement demonstrates the adequate protection of shorter chain acids in which the differences in chain length of the shorter chain acids affects the reactivity of the shorter chain. No selective monomethyl esterification was observed in the case of the combination of C_{12}/terephthalic acid and C_{12}/isophthalic acid.

Experimental

Materials. Diazomethane was prepared from *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide[17] without ether and was carried in a stream of nitrogen through a dry tube containing potassium hydroxide pellets and then into the reaction vessel. Alumina {the reference catalyst of the Catalysis Society of Japan (JRC-ALO-5);γ-type, 60—200 mesh, modal pore diameter 5.5 nm, Na_2O content 0.02%, adsorption capacity of 4.0×10^{-4} mol g^{-1}[12] of aliphatic dicarboxylic acid} was dried at 110 °C for a day and stored in a desiccator. Other materials were commercially available and used without further purification.

Preparation of Adsorption Samples. One gram of alumina powder was added to a 10 mL of *N,N*-dimethylformamide (**DMF**) solution containing 0.32 mmol of total amounts of two different carboxylic acids, dodecanedioic acid (C_{12}) plus glutaric acid (C_5), adipic acid (C_6), pimelic acid (C_7), suberic acid (C_8), sebacic acid (C_{10}), *trans*-1,4-cyclohexanedicarboxylic acid, terephthalic acid, or isophthalic acid to produce 80% surface saturation. The mixture was allowed to stand for 8 h at 30 °C with occasional shaking. The DMF was then slowly removed under reduced pressure.

Reaction Procedure. About 6 molar equivalents of diazomethane was introduced in a stream of dry nitrogen into a vigorously agitated reaction vessel containing 500 mg of the adsorbed sample and about 5 g of cyclohexane at room temperature. After all the diazomethane had been consumed or passed through the reaction vessel (about 45 min), the alumina was transferred to a glass column and eluted with **DMF**. After the eluate had been concentrated under reduced pressure, the products were analyzed by GSC with a Chromosorb 101 column, and/or HPLC with a ODS column. No reaction other than esterification was observed. Any other information about experimental section was described in the previous work.[12]

References

1) A. McKillop and D. W. Young, *Synthesis,* **1979**, 401; **1979**, 481.

2) G. H. Posner, *Angew. Chem., Int. Ed. Engl.,* **17**, 487 (1978).

3) A. Cornelis and P. Laszlo, *Synthesis,* **1985**, 909.

4) M. Hojo, *Yuki Gousei Kagaku Kyoukai Shi,* **42**, 635 (1984).

5) T. Ando, J. Ichihara, and T. Hanafusa, *Kagaku Sousetsu,* **47**, 166 (1985).

6) T. Chihara and H. Ogawa, *Shokubai,* **28**, 519 (1986).

7) A. L. J. Beckwith, C. L. Bodkin, and T. Duong, *Aust. J. Chem.,* **30**, 2177 (1977); A. L. J. Beckwith and T. Duong, *J. Chem. Soc., Chem. Commun.,* **1978**, 413; **1979**, 690.
690.

8) N. C. Deno, R. Fishbein, and C. Pierson, *J. Am. Chem. Soc.,* **92**, 1451 (1970).

9) R. Farwaha, P. de Mayo, and Y. C. Toong, *J. Chem. Soc., Chem. Commun.,* **1983**, 739.

10) J. Yamawaki and T. Ando, *Chem. Lett.,* **1980**, 533.

11) H. Ogawa, T. Hagiwara, T. Chihara, S. Teratani, and K. Taya, *Bull. Chem. Soc. Jpn.,* **60**, 627 (1987).

12) H. Ogawa, T. Chihara, and K. Taya, *J. Am. Chem. Soc.,* **107**, 1365 (1985).

13) N. K. Adam, *Proc. R. Soc. London, Ser. A,* **101**, 452 (1922).

14) H. Ogawa, T. Chihara, S. Teratani, and K. Taya, *J. Chem. Soc., Chem. Commun.,* **1986**, 1337.

15) H. Matuo, K. Motomura, and R. Matuura, *Bull. Chem. Soc. Jpn.,* **54**, 2205 (1981).

16) J. T. Davies and E. K. Rideal, "Interfacial Phenomena," Academic Press, New York and London (1961), Chap. 5, p. 234.

17) Th. J. de Boer and H. J. Backer, *Org. Synth.* Coll. Vol. IV, 250 (1963).