Aldol Condensations of Aldehydes over Disodium Phthalocyanine[1,2]

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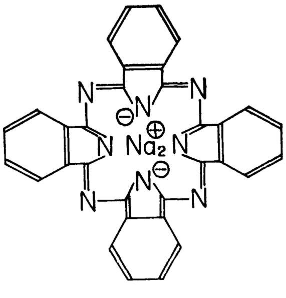
Disodium phthalocyanine (Pc–Na_2) acts as a base for the aldol condensations of aldehydes, although it shows no effect upon those of ketones. In the aldol condensation of isobutyl aldehyde by Pc–Na_2 in *n*-hexane, 2,6-diisopropyl-5,5-dimethyl-1,3-dioxane-4-ol (III) is produced through two processes with different rates; the reaction proceeds first by the slower rate, and then by a more rapid rate after a certain reaction period. The process is different from that of the catalysis by sodium ethoxide. During the reaction, Pc–Na_2 is converted to sodium-free phthalocyanine (Pc–H_2) *via* an intermediate. The formation of the intermediate results in the retardation of the aldol condensation with the product and phthalocyanine anions. Furthermore, the adsorption of water on Pc-Na_2 brings about the retardation of the reaction.

In acid-base catalyses of organic compounds, the formation of a complex between catalyst and substrate brings about a rate enhancement and a specificity toward the catalyzed reaction. These catalyzed reactions are found in processes in frozen solutions,[3] in inclusion compounds,[4] in micellar solutions,[5] and in polymeric compounds[6] which have been studied as models for enzymic catalysis. Now we will attempt to study the dimerization of two substrates over a plate-like organic molecule with a character of an acid or a base. The present investigation will deal with the heterogeneous base-catalysis of Pc–Na_2 on the aldol condensations of aldehydes and ketones. The Pc–Na_2 contains ion pairs as an active site in a planar-macrocyclic π-system, and might have an affinity for aldehydes and ketones. Our purpose in this paper is to investigate the specific action of Pc–Na_2 as a base for the aldol condensation, and to find the correlation between the reactivity and the features of the chemical structure of Pc–Na_2.



Pc–Na_2

Experimental

Materials. All of the aldehydes and ketones were purchased from commercial sources. These materials were distilled through a Vigreux column before use. The solvents were dried by the usual methods and were distilled twice before use. The Pc–Na_2 was prepared by heating sodium and *o*-phthalonitrile in *n*-amyl alcohol at 130—140°C according to the method reported by Barrett, Dent, and Linstead.[7] The purification was carried out by the following method: 10 g of Pc–Na_2 was dispersed in 20 ml of hot *n*-amyl alcohol, filtered off, washed several times with 20 ml of anhydrous ether, and dried over calcium chloride under the reduced pressure of 1 mmHg at 100°C for 3 hr, unless stated otherwise. The sodium content of the Pc–Na_2 used here was 7.99% (Calcd for Pc–Na_2: 8.24%). The IR spectrum of Pc–Na_2 had absorptions characteristic of the structure of the phthalocyanine dianion at 1640, 1040, and 790—770 cm^{-1}. On the other hand, the IR spectrum of Pc–H_2 agreed with that of α- and/or β-phthalocyanine, described in the literature.[8] The visible spectrum of Pc–Na_2 observed by means of a KBr plate showed broad absorptions at 620 (sh) and 720 mμ, while that of Pc–H_2 showed them at 650 and 740 (sh)mμ.

Procedures for Reactions. Similar procedures were used for all the reactions. In a typical experiment, a solution of 8.0 g of isobutyl aldehyde in 10 ml of *n*-hexane was placed in a 100-ml flask containing a Teflon stirring bar, and the flask was placed in a thermostat bath at 25±1°C. Immediately after nitrogen gas had passed into the system for 3 min, 0.1 g of Pc–Na_2 was added to the solution, the flask was capped with a stopper, and the solution was stirred vigorously by means of a magnetic stirrer. After a reaction period, 80 ml of *n*-hexane was added to the system to stop the reaction, the resulting solution was filtered off, and the precipitate was washed repeatedly with *n*-hexane. The combined *n*-hexane layer was then washed with a small amount of a 5—10 wt% hydrochloric acid solution and then water. *n*-Hexane and the volatile components were completely removed under reduced pressure. In the reaction time of 20 hr, 6.0 g of a residual oil was obtained; this oil was then submitted to an analysis of its product. On the other hand, the distillation of the oil (bp 90—91°C/2 mmHg) yielded 5.6 g (70%) of a mixture of 2,6-diisopropyl-5,5-dimethyl-1,3-dioxane-4-ol (III)[9] and the monoisobutyrate of 2,2,4-trimethyl-1,3-pentanediol (IV), which could be

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[2] Presented at 24th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1971.

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separated by glc.

Analyses of Products. All of the products were identified by a comparison of their IR and NMR-spectra, the results of elementary analyses of their 2,4-dinitrophenylhydrazone, their retention times in glc, and their molecular weights with those of authentic specimens prepared by the methods described in the literature.[10] The identification of IV was based on the observation that the molecular weight was 218 (calcd for monoester, 216), and the alkaline hydrolysis of the ester gave, quantitatively, 2,2,4-trimethyl-1,3-pentanediol and isobutyric acid. However, IV was regarded as a mixture of two monoisobutyrates with an isobutyroyl group at the 1- or 3-hydroxyl group. The red-brown polymeric material (Va) prepared from acetaldehyde was converted to the 2,4-dinitrophenylhydrazone. Anal. Found: C, 57.46; H, 5.90; N, 11.06%. The avarage molecular weight of Va was 320. The IR spectrum of Va exhibited bands at 3400, 2950-2800, 1710, 1680, 1440, 1370, and 1100 cm^{-1}. The UV spectrum of Va in ethanol had absorptions at 233, 285, 324, and 360 mμ.

The amounts of all the products except for III and IV were determined by means of distillation. The amounts of III and IV were determined by the following method: after completely removing the reaction solvent, 0.1 g of the residue, containing III and IV, was dissolved in 2 ml of methanol, and then into the solution there was added a solution of 0.4 g of 2,4-dinitrophenylhydrazine in 100 ml of a 2 N hydrochloric acid solution. The resulting solution was kept standing overnight. The precipitate was then filtered off, dried over calcium chloride, and weighed. From the weight of the precipitate, the amount of III was determined within an error of ±3%. Furthermore, it was confirmed by glc that the mixture consists of only III and IV. The amount of IV was determined by substracting the amount of III from 0.1 g of the mixture. The value thus obtained agreed with that determined by the glc analysis within an error of ±2—3%.

Analysis of the Sodium Cation. A weighed amount (0.1—0.2 g) of a sample in a crucible was burned cautiously with a small flame, and then it was heated strongly for 3—5 hr to change it completely to ash. The ash was dissolved in 20 ml of distilled water and was then titrated with 1/10 N hydrochloric acid, using methyl orange as the indicator. The sodium content could be measured within an error of ±2% by this method.

Results and Discussion

Action of Pc–Na$_2$ as a Base. When Pc–Na$_2$ was dispersed in acetonitrile or ethyl acetate, no product was obtained, but the Pc–Na$_2$ was recovered unchanged. However, a dispersion of Pc–Na$_2$ in aldehydes resulted in the corresponding condensation products, such as I, II, III, IV, and V. The yields of these products changed depending on the structure of the starting aldehydes, as Table 1 shows. In the aldol condensation of acetaldehyde, the red-brown polymeric material (Va) was obtained in a 70% yield. The values of m and n of Va were 3—4 and 2—3 respectively. The IR spectrum of Va was similar to that of the polymer produced by using $(CH_3)_3N$[11] and Na–Hg[12] as the catalyst. The aldol condensation of propionaldehyde or n-butyraldehyde by Pc–Na$_2$ gave the corresponding aldols (Ia or Ib) and α,β-unsaturated aldehydes (IIa or IIb). Isobutyl aldehyde was converted to 2,6-diisopropyl-5,5-dimethyl-1,3-dioxane-4-ol (III) and the monoisobutyrate of 2,2,4-trimethyl-1,3-pentanediol (IV) in 21 and 50% yields respectively through a secondary reaction of the intermediate aldol. The sodium-cation content of the recovered phthalocyanine in all cases was in the range of 4.60—5.90%, which changed with the reaction conditions. The IR spectrum of the recovered phthalocyanine had the characteristic absorpions due to the phthalocyanine anion at 1642, 1040, and 790—770 cm^{-1}, and that due to the sodium-free phthalocyanine at 1000 cm^{-1}.

$RCH_2CH(OH)CHRCHO$

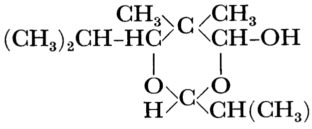
I　a: $R=CH_3$

　b: $R=CH_3CH_2$

$RCH_2CH{=}CRCHO$

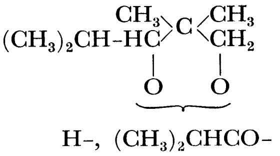
II　a: $R=CH_3$

　b: $R=CH_3CH_2$



$(CH_3)_2CH\text{-}HC\overset{CH_3}{\diagdown}C\overset{CH_3}{\diagup}CH\text{-}OH$, $O\text{-}C(H)(CH(CH_3)_2)\text{-}O$

III



$(CH_3)_2CH\text{-}HC\overset{CH_3}{\diagdown}C\overset{CH_3}{\diagup}CH_2$, $\underbrace{O\quad O}_{H\text{-},\ (CH_3)_2CHCO\text{-}}$

IV

$RCH_2(\text{-}CH{=}CR\text{-})_m(\text{-}CH(OH)CHR\text{-})_nCHO$

V　a: $R=H$

　b: $R=CH_3$

　c: $R=CH_3CH_2$

Table 1. Aldol condensations of aldehydes by Pc–Na$_2$ without solvent[a)]

RR′CHCHO R	R′	Product	Yields, %[b)]
H	H	Va	70[c)]
CH_3	H	Ia, IIa, Vb	13, 15, 22[c)]
CH_3CH_2	H	Ib, IIb, Vc	25, 23, 3[c)]
CH_3	CH_3	III, IV	21, 50

a) The amount of Pc–Na$_2$ dispersed: 3.3 mol% in aldehydes. The reaction was carried out under a nitrogen atmosphere at room temperature for 20 hr.

b) The yields of I, II, III, and IV were based on aldehydes.

c) This was calculated by weight of polymer/weight of aldehyde × 100.

Ketones, such as acetone, methyl ethyl ketone, and acetophenone, could not undergo self-condensation by Pc–Na$_2$, not even at 100°C, although the sodium ethoxide-catalyzed condensation of acetone gave the polymeric material and phorone in 10 and 11% yields respectively. However, Pc–Na$_2$ acted as a base for the mixed condensation of isobutyl aldehyde and either acetone or methyl ethyl ketone (the molar ratio of isobutyl aldehyde to ketone; 2.4 or 2) under the same conditions as have been described above as giving

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mainly the ketols (VIa and VIb) in 38 and 43% yields, and the α,β-unsaturated ketones (VIIa and VIIb) in 40 and 4% yields, respectively, based on the starting amounts of ketones. In addition to these products, a mixture of III and IV was obtained in a 39% yield in the case of acetone, based on the starting amount of isobutyl aldehyde. Thus, it was found that Pc–Na$_2$ acts as a base for aldehydes and ketones, and that the action is specific for the aldol condensations of aldehydes.

$RCOCH_2CH(OH)CH(CH_3)_2$ $RCOCH{=}CHCH(CH_3)_2$
VI a: $R{=}CH_3$ VII a: $R{=}CH_3$
b: $R{=}C_2H_5$ b: $R{=}C_2H_5$

Aldol Condensation of Isobutyl Aldehyde Catalyzed by Sodium Ethoxide. Sodium ethoxide was dispersed or dissolved in *n*-hexane, ethanol, and dimethyl sulfoxide, all containing isobutyl aldehyde. Sodium ethoxide, dispersed in *n*-hexane, changed from a solid to an emulsion state as the reaction proceeded, and III and IV were obtained as the products. In the case of the ethanol solvent, however, IV was converted further to 2,2,4-trimethyl-1,3-pentanediol and ethyl isobutyrate by the ester-exchange reaction. As Table 2 shows, it was observed in all cases that III is formed predominantly without an induction period. As the reaction time increased, however, the yield of III decreased and that of IV increased. The trends for the consecutive formation of IV were observed distinctly in the cases of the ethanol and dimethyl sulfoxide solvents. On the other hand, the heterogeneous catalysis in the *n*-hexane solvent tended to give a high yield of III, even in a prolonged reaction time. However, the increase in the amount of sodium ethoxide resulted in a rise in the yield of IV. IV would be produced by the intramolecular Cannizzaro reaction of the anion of III, derived from III with a base. Therefore, the effective concentration of the base must be of importance in the formation of IV.

The Condensation by Pc–Na$_2$. In *n*-hexane and acetonitrile solvents, III was first produced predominantly in the slow rate, as is shown in Fig. 1. After 6 hr, the rate of the formation of III increased rapidly. When the yield of III reached about 60%, it was observed that III began to be converted to IV, as Table 3 shows. The fractional yield of IV in a longer reaction time became higher than in the case of sodium ethoxide. In the ethanol solvent, III and IV were first produced without the slow step; IV was converted further to 2,2,4-trimethyl-1,3-pentanediol and ethyl isobutyrate as the reaction time increased. These facts indicate that the dianion of Pc–Na$_2$ is transferred to ethanol, thus leading to the homogeneous catalysis by the ethoxide anion. Furthermore, the adsorption of two moles of water per mole of Pc–Na$_2$ resulted in a retardation of the condensation of isobutyl aldehyde by Pc–Na$_2$; that is, the yield of III in *n*-hexane was 30—40% after the reaction time of 9 hr. However, the presence of water resulted in the formation of III predominantly.

TABLE 2. ALDOL CONDENSATION OF ISOBUTYL ALDEHYDE BY SODIUM ETHOXIDE[a]

Solvent	C_2H_5ONa, mol/l	Reaction time, hr	Yield of Product, % III	IV[b]
n-Hexane	3.0×10^{-1}	2	68	16
	3.0×10^{-1}	20	65	20
	1.8×10^{-3}	20	80	5
Ethanol	1.8×10^{-3}	2	19	1
	$9\ \ \times10^{-2}$	2	51	(27)
	1.8×10^{-1}	2	6	(78)
	1.0×10^{-1}	20	0	20(31)
Dimethyl sulfoxide	9.0×10^{-3}	2	13	0
	4.5×10^{-2}	2	51	34
	9.0×10^{-2}	2	8	82
	9.0×10^{-2}	20	7	84

a) The concentration of isobutyl aldehyde: 5.5 mol/l.
Reaction temperature: 25°C.
b) The brackets indicated the yield of diol.

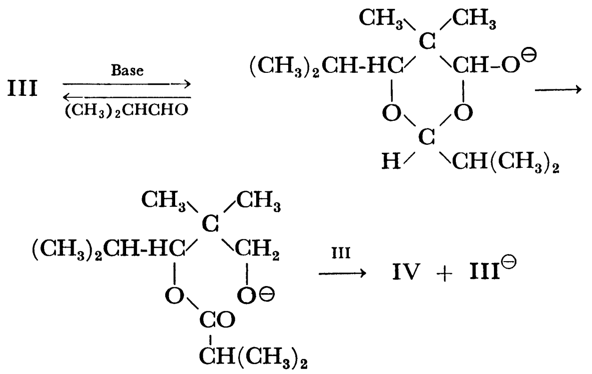

TABLE 3. Pc–Na$_2$ CATALYZED ALDOL CONDENSATION OF ISOBUTYL ALDEHYDE[a]

Solvent	Reaction time, hr	Yield of Product, % III	IV[b]
n-Hexane	6	11	2
n-Hexane	8	55	8
n-Hexane	15	34	41
Ethanol	20	0	22(55)

a) The concentration of isobutyl aldehyde: 5.5 mol/l.
The amount of Pc–Na$_2$ dispersed: 9.0×10^{-2} mol/l.
Reaction temperature: 25°C.
b) The brackets indicated the yield of diol.

Removal of the Sodium Cation from Pc–Na$_2$. After the aldol condensation of isobutyl aldehyde by the 100°C-dried Pc–Na$_2$ in *n*-hexane had been carried out for a reaction period under the conditions described above, the precipitate was collected by filtration and subsequently dried. The sodium content and the IR and visible spectra of the precipitate were measured. As is shown in Fig. 1, the curve of the change in the sodium content consisted of two steps. The flexion of the curve almost coincided with that of the formation curve of III. Furthermore, the formation of III was nearly parallel with the removal of the sodium cation during the period of the slow formation of III, the amount of III produced being 1.5—2 larger than that of the sodium cation removed.

On the other hand, the IR spectrum of the precipitate changed as the reaction proceeded. The ab-

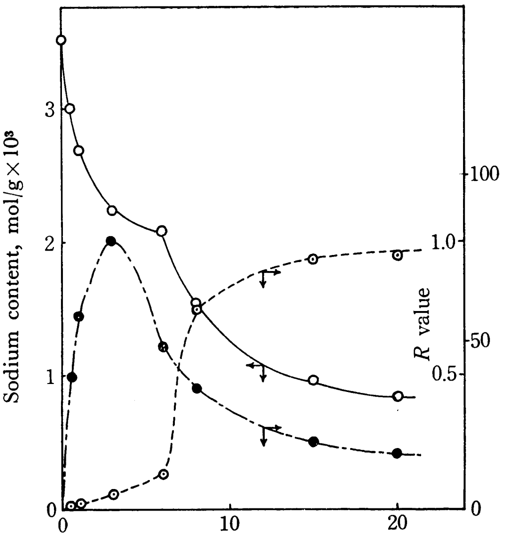

Fig. 1. The change of the sodium content (○) and the R value (●) of the recovered phthalocyanine, and the yield of the product (⊙) against the reaction time: the concentration of isobutyl aldehyde; 5.5 mol/l and the amount of Pc-Na$_2$ dispersed; 9×10^{-2} mol/l.

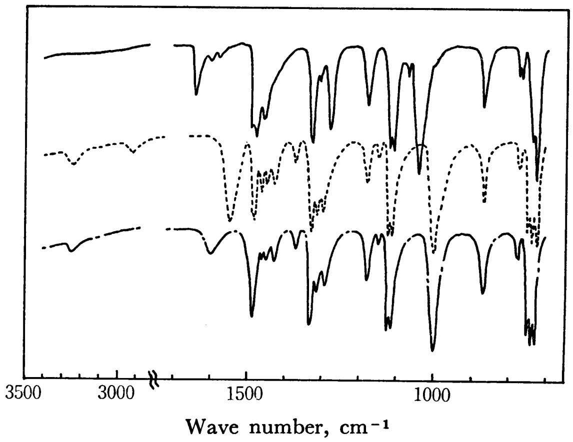

Fig. 2. The IR spectra of Pc-Na$_2$ (——), Pc-H$_2$ (———) and the intermediate (----).

sorption peaks of the phthalocyanine anion and dianion at 1640 and 1040 cm^{-1} decreased, while that of the sodium-free phthalocyanine at 1000 cm^{-1} increased. In addition, a new band appeared at 1550 cm^{-1} (Fig. 2). The new band increased rapidly as the reaction proceeded, and then decreased. In Fig. 1, the ratio (R) of the intensity of the new band to that of a band at 870 or 1120 cm^{-1}, the intensity of which did not differ from Pc-Na$_2$ to Pc-H$_2$, is plotted against an interval of the reaction time. The maximum of the intensity ratio was observed in the reaction time of 3 hr, which lay in the slow step. When the reaction was carried out in 1/10 less Pc-Na$_2$ than that shown in Fig. 1, the intensity ratio was observed to reach a maximum sharply with a higher value in a shorter reaction time; then it decreased at a slower rate. These facts indicate that a stable intermediate exists in the reaction process. The sodium content of the intermediate with the maximum value of R at 1550 cm^{-1} was 3.86%. This value means that the intermediate is a monosodium phthalocyanine derivative. Its visible absorption spectrum, as observed by means of a KBr plate, showed two absorptions, at 650 and 750 mμ, although that of Pc-H$_2$ had absorptions at 650 and 740 (sh) mμ, as is shown in Fig. 3. The new band at 1550 cm^{-1} did not change even when the intermediate was heated at 100°C under a reduced pressure of 1 mmHg for 2 hr, but it disappeared when it was dispersed in ethanol, and the resulting IR spectrum agreed with that of Pc-H$_2$. Thus, the intermediate was a monosodium derivative with IR and visible spectra which differed from those of Pc-Na$_2$, Pc-NaH, and Pc-H$_2$, and with the departing sodium cation with a slow rate. However, the structure of the intermediate is not yet clear. When the intermediate was converted to Pc-H$_2$, the reaction proceeded rapidly by means of a catalysis similar to that in the case of sodium ethoxide. However, the consecutive formation of IV occurred more easily in the presence of the phthalocyanine molecule than in the case of sodium ethoxide. This may be caused by the fact that the product anion is concentrated over the phthalocyanine molecule.

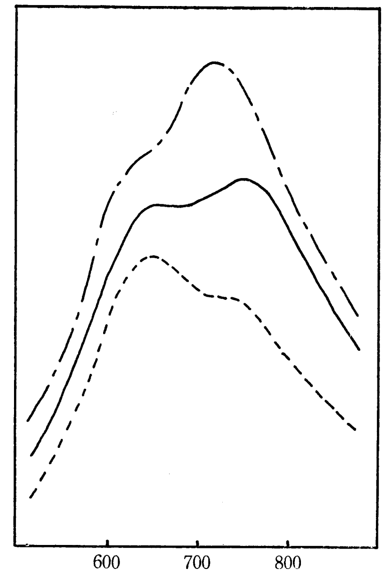

Fig. 3. The visible absorption spectra of Pc-Na$_2$ (———), Pc-H$_2$ (----) and the intermediate (——) by KBr plate.