## Reaction of Troponoids and Organometallic Compounds. III<sup>1,2)</sup>. Synthesis and Reaction of 2,7- and 2,3-Diphenyltropone<sup>3)</sup>

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(Received April 21, 1958)

In the reaction of 2-phenyltropone and phenylmagnesium bromide, two compounds with the composition  $C_{19}H_{14}O$ , m.p. 87°C and 130°C, were obtained<sup>4)</sup>. From their analytical values and ultraviolet and infrared spectra, one of these was assumed to be 2,7-diphenyltropone but there still remained a doubt about this structure for the following reasons. The first is the fact that this reaction would be substitution of a ring hydrogen with phenyl, which would be very unlikely to The second is that 2,7-diphenyloccur. tropone is an unknown compound and it would probably have properties fairly different from tropones due to a hindered carbonyl group.

The present paper deals with the synthesis of 2,7-diphenyltropone by an unequivocal process, establishing the structure of the foregoing products from the Grignard reaction, and at the same time, examinations are made on the properties of tropones substituted in the 2and 7-positions<sup>5)</sup>.

2, 7-Diphenyltropone was synthesized by reaction of 3-phenyltropolone and the phenyllithium. Doering and Hisky<sup>6)</sup> had already obtained 2-phenyltropone by the reaction of tropolone and phenyllithium. Later Haworth and Tinker<sup>7</sup> proved that although an abnormal substitution occurred in the Grignard reaction of 4methyltropolone methyl ethers, the reaction of the copper complex of 4-methyltropolone and phenyllithium resulted in the normal substitution, affording 6-methyl-2-phenyltropone. Since the reaction of tropolones and phenyllithium results firstly in the formation of the lithium salt of tropolones, it may be assumed that it would result in the normal substitution, as in the case of the copper complex, to form 2-phenyltropones.

Actually, the reaction of 3-phenyltropolone and phenyllithium afforded two kinds of compound, one of m. p.  $132^{\circ}C$  (I) and the other of m. p.  $147^{\circ}C$  (II).

These were assumed to be the corresponding diphenyltropones from their analytical values and the infrared absorption

Part I: T. Nozoe, T. Mukai, J. Minegishi and T. Fujisawa, Science Repts. Tohoku Univ., 1, 37, 388 (1953).
Part II: K. Kikuchi, J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zassi), 77, 1439 (1956).

<sup>3)</sup> This paper was read before the Local Meeting of Tohoku District of the Chem. Soc. Japan held in Hirosaki on September 27, 1956.

<sup>4)</sup> T. Nozoe, T. Mukai and others, unpublished work. 5) A number of 2,7-dibenzyltropones were synthesized, of which the chemical behavior has not been much described. N. J. Leonard, L. A. Miller and J. W. Berry, J. Am. Chem. Soc., 79, 1482 (1957).

<sup>6)</sup> W. von E. Doering and C. F. Hisky, ibid., 74, 5688 (1952).

<sup>7)</sup> R. D. Haworth and P. B. Tinker, J. Chem. Soc. 1955, 911.

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spectra<sup>8)</sup> shown in Fig. 1. As will be shown later, II was identified as 2, 3-diphenyltropone by its conversion into 2, 3-diphenylbenzoic acid. I was identified with one of the products, of m. p. 130°C, from the foregoing reaction of 2-phenyltropone and phenylmagnesium bromide as expected. From the course of these two reactions, it may be concluded that I is 2, 7-diphenyltropone. It follows, therefore, that the reaction of tropolone and phenyllithium results in the normal substitution.



Fig. 1. I. R. absorption spectra of 2,7and 2, 3-diphenyltropone diphenyl-(I) (II) in KBr.

The reaction of tropolone methyl ether and methylmagnesium iodide does not give 2-methyltropone<sup>9)</sup>, but, since 2-alkyltropones are obtained by the reaction of tropolone and methyllithium<sup>10)</sup> or n-butyllithium<sup>6)</sup>, it may be assumed that a lithium compound convenient for the formation of tropones is formed as an intermediate. This may be illustrated as shown below with the reaction of 3-phenyltropolone and phenyllithium as an example. This reaction is rather interesting when compared with the fact that a ketone and not a carbinol is formed in the reaction of free carboxylic acid and an organolithium compound<sup>11)</sup>.

The ultraviolet spectra of 2, 3- (II) and



Both I and II have weak basicity and do not form picrates. Passage of hydrogen chloride gas through the benzene solution of I or II only precipitates a part of the hydrochloride.

Since the two reactive sites, 2- and 7positions, in I are blocked, the reactivity of 2,7-diphenyltropone is of interest. I is extremely stable to alkalis and amines, and it remains unchanged on heating with dilute alkali or p-toluidine in ethanol solution<sup>1,13</sup>). Heating with hydroxylamine or hydrazine fails to effect amination of the ring<sup>1,13</sup>). I does not react with ketonic reagents such as 2, 4-dinitrophenylhydrazine<sup>1,13</sup>). These facts indicate that the substitution of 2- and 7-positions of the tropone ring with a bulky group like phenyl results in an extremely great increase in stability and the above reactions characteristic to tropones in general are not observed.

In contrast to the stability of I, 2, 3-diphenyltropone (II) is labile to alkali and on heating with dilute alkali in ethanolic solution, it forms an acid substance as colorless crystals, m. p. 178°C. The ultraviolet spectrum of this substance is shown in Fig. 2, which indicates that it does not contain the tropone ring<sup>12</sup>). Since alkaline rearrangement of 2-phenyltropone results in the formation of diphenyl-2-carboxylic



8) I. R. spectra are measured using Perkin-Elmer Model 21 double beam spectrophotometer by Mr. Yusaku Ikegami of the Chemical Research Institute Non-aqueous Solutions, to whom the author is deeply indebted.



Fig. 2. U. V. absorption spectra of 2, 7diphenyl-(I), 2, 3-diphenyltropone (II) and a compound melted at 178°C in methanol.

<sup>9)</sup> T. Nozoe, T. Mukai and J. Minegishi, Proc. Japan Acad., 27, 419 (1951).

T. Mukai, to be published.
H. F. Bluhm, H. V. Donn and H. D. Zook, J. Am. Chem. Soc., 77, 4406 (1955).

M. Tsuboi, This Bulletin, 25, 369 (1952).

T. Nozoe, T. Mukai and K. Takase, Science Repts. 13)

Tohoku Univ., I, 39, 164 (1956).

acid<sup>1)</sup>, the rearrangement product of II was assumed to be 2, 3-diphenylbenzoic acid but mixed fusion with 2, 3-diphenylbenzoic acid resulted in depression of the melting point. The reaction must have been quite specific and examination is still in progress as to the structure of this rearrangement product.

II easily forms a 2, 4-dinitrophenylhydrazone and gives 2-amino-6,7-diphenyltropone (III) by reaction with hydrazine<sup>1,13)</sup>. Alkali hydrolysis of III affords 3, 4-diphenyltropolone (IV) which shows the coloration with ferric chloride characteristic of tropolone. The ultraviolet spectrum of IV, shown in Fig. 3, exhibits the



Fig. 3. U. V. absorption spectra of 2amino-6, 7-diphenyltropone (III), 3, 4diphenyltropolone (IV), methyl ether of IV (V) and 2, 3-diphenylbenzoic acid (VI) in methanol.

maximum absorptions at 323 and  $374 \text{ m}\mu$ , which is a tropolone type<sup>14</sup>), but it seems to be different from that of 3-phenyltropolone<sup>1)</sup> since there is a maximum at  $285 \text{m}\mu$ . IV forms a methyl ether (probably  $V^{15}$ ) on the application of diazomethane and reaction of the methyl ether with sodium methoxide in absolute methanol, followed by hydrolysis gives compound VI of m. p. 162°C. 2, 3-Diphenylbenzoic acid had already been synthesized by K. Alder et al.<sup>16</sup>, who reported the compound to melt at 161°C, so that VI must be identical with it. From the series of reactions of II to VI, the structure of II was established as 2, 3-diphenyltropone. Fig. 3 gives the ultraviolet spectra of V and VI.

Next, bromination of these two diphenyltropones was carried out. Application of



an excess of bromine to I in acetic acid first afforded a dibromide VII which, on treatment with sodium acetate, formed a monobromo compound VIII. Ultraviolet absorption spectra of VII and VIII are shown in Fig. 4. From the result of



Fig. 4. U. V. absorption spectra of brominated compounds of I (VII and VIII), of II (IX and X) and 2,7-diphenylsuberone (XI) in methanol.

dehydrobromination of VII and the fact that the ultraviolet spectrum of VII is shifted to a shorter wave-length region, it is assumed that VII is a bromine addition product. On the other hand, the absorption curve of VIII is similar to that of I, shifted slightly to a longer wavelength region, which indicates that VIII may be considered to be a bromine substituted compound. Experiments to determine the position of the bromine were not carried out but it has been pointed out that bromine addition does not take place at the double bond with the phenyl group in the bromination of 2-phenyltropone<sup>17</sup>). It follows, therefore, that VII would be the compound with bromine addition in  $C_4$ — $C_5$  positions and VIII is most probably 4-bromo-2, 7-diphenyltropone. In the ultraviolet spectrum of VII there is a certain amount of absorption in a region near  $300 \text{ m}\mu$ , so that an unsaturated ketonic structure like VII seems to be most appropriate.

Bromination of II in acetic acid also results in the formation of a tetrabromide IX whose treatment with sodium acetate to effect dehydrobromination affords a dibromo compound X. Since there are two phenyl substituents in  $C_2$  and  $C_3$  position of II, it follows that bromine addition

<sup>14)</sup> T. Nozoe, Fortshr. Chem. Org. Naturst., 13, 232 (1956).

<sup>15)</sup> There are two isomers of methyl ether of 3-phenyltropolone, of which the ether corresponding to V was more easily isolated than another isomer. (cf. Ref. 1). 16) K. Alder, J. Haydn, K. Heimbach and K. Neufang, Ann., 586, 110 (1954).

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must take place in  $C_4-C_5$  and  $C_6-C_7$  double bond<sup>17)</sup>. Ultraviolet spectra of IX and X, indicated in Fig. 4, show that the absorption of IX is low in intensity and there is a good probability that it is an addition product, while the absorption of X is shifted to a longer wave-length region than that of II and it is probably safe to conclude that X is a bromine substituted compound.





Hydrogenation of I with palladiumcharcoal as a catalyst resulted in facile absorption of hydrogen and 2, 7-diphenylsuberone (XI) was formed. The ultraviolet spectrum of XI in Fig. 4 shows the absorption of two phenyl at groups  $259m\mu^{18}$ , while its infrared spectrum in Fig. 5 shows absorptions for C=O at 1706 for C=C of phenyl at 1603 and for CH<sub>2</sub> at 2935 and



diphenylsuberone (XI) in KBr.

2860 cm<sup>-1</sup>, which support the structure of XI. In connection with the examination of unsaturated characters, both I and II were heated with maleic anhydride in xylene but no addition products were obtained.

## Experimental<sup>19</sup>)

**Reaction of 3-Phenyltropolone and Phenyllithium.** — To a solution of phenyllithium, obtained from 0.42 g. (0.06 g. at.) of lithium, 4.7 g. (0.03 mole) of bromobenzene, and 18 cc. of ether, a solution of 1.00 g. (0.005 mole) of 3-phenyltropolone in 18 cc. of ether and 18 cc. of benzene was added dropwise in a nitrogen stream, when a slight generation of heat was observed. The mixture was stirred for 2 hours at room temperature and dilute sulfuric acid was then added under ice-cooling to effect decomposition. The organic solvent layer was separated, washed with water, and dried over anhydrous sodium sulfate. Evaporation of the solvent left 1.2 g. of dark reddish brown oil which was dissolved in benzene, saturated with hydrogen chloride gas, and the oily hydrochloride that separated out was collected by decantation. This was decomposed with water, extracted with carbon tetrachloride, and the solution was passed through an alumina column. Evaporation of the solvent from the initial carbon tetrachloride eluate afforded 180 mg. of colorless crystals I, m. p. 130~132°C. Recrystallization from ethanol gave colorless microplates, m. p. 133°C.

Anal. Found: C, 87.97; H, 5.65. Calcd. for  $C_{19}H_{14}O$ : C, 88.34; H, 5.46%.  $\lambda_{\max}^{MeOH}m\mu$  (log  $\varepsilon$ ): 226(4.37), 279(4.06), 340(4.01).

The alumina column was then eluted with benzene and evaporation of benzene from the effluent left 130 mg. of colorless crystals II, m. p. 146°C. Recrystallization from ethanol afforded colorless plates, m. p. 147°C.

Anal. Found: C, 88.40; H, 5.47. Calcd. for  $C_{19}H_{14}O$ : C, 88.34; H, 5.46%.  $\lambda_{\max}^{MeOH}m\mu$  (log  $\varepsilon$ ): 227(4.39), 292(4.03).

The benzene solution obtained after removal of the oily hydrochloride was washed with water and then passed through an alumina column. Initial effluent afforded 60 mg. of I, m. p. 132°C, and the latter eluate afforded further 110 mg. of II, m. p. 146°C. By mixed fusion, I was identified with the compound, m. p. 130°C, obtained from the reaction of 2-phenyltropone and phenylmagnesium bromide<sup>4</sup>).

Addition of ethanolic solution of picric acid to the ethanolic solution of I or II failed to afford any crystalline picrate.

2, 4-Dinitrophenylhydrazone of II was obtained as dark red crystals, m. p. 208°C (decomp.).

Anal. Found: N, 12.24. Calcd. for  $C_{25}H_{18}O_4N_4$ : N, 12.87%.  $\lambda_{\max}^{MeOH} m\mu \ (\log \epsilon)$ : 400(4.36).

On the other hand, application of 2, 4-dinitrophenylhydrazine to I in ethanol, in the presence of a trace of hydrochloric acid, with heating resulted in the recovery of I.

Behavior of the Diphenyltropones (I and II) to Alkali. — To a mixed solution of 1 cc. of ethanol and 1 cc. of 2N potassium hydroxide, 20 mg. of II was added and the mixture was refluxed on a water bath for 1.5 hours, when the solution turned brown in color and a small amount of resinous solid separated out. Ethanol was then evaporated from the mixture, water was added, and solid matter was filtered off. The filtrate was acidified and extracted with chloroform, from which 10 mg. of a pale yellow oil was obtained.

<sup>17)</sup> T. Mukai, Science Repts. Tohoku Univ., I, 38, 280 (1954).

<sup>18)</sup> In the series of Ph-(CH<sub>2</sub>)<sub>n</sub>-Ph (n>1), the absorption band is situated near 260 mµ and is not so intense (e < 3000). cf. A. E. Gillam and E. S. Stern "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry" Edward Arnold Ltd., London (1955), p. 64. 19) m.p. are uncorrected. The microanalyses were carried out by Mr. Shinichi Ohyama and Miss Ayako Iwanaga, to whom the author's deep gratitude is hereby expressed.

Trituration of this oil with cyclohexane effected crystallization and colorless crystals which sintered at  $170^{\circ}$ C and melted at  $175 \sim 178^{\circ}$ C were obtained. This substance showed depression of the melting point on admixture with 2, 3-diphenylbenzoic acid (VI), m. p.  $162^{\circ}$ C, described later.

On the other hand, the same treatment of 20 mg. of I with ethanolic potassium hydroxide solution by refluxing for 4 hours afforded 20 mg. of crystals melting at  $124 \sim 126^{\circ}$ C, indicating the complete recovery of I.

Reaction of the Diphenyltropones (I and II) with Hydrazine or Hydroxylamine. -a) To a solution of 40 mg. of II dissolved in 0.2 cc of ethanol, 0.10 cc. of 80% hydrazine hydrate was added and the mixture was heated on a water bath for a few minutes, from which 30 mg. of 2-amino compound was obtained as yellow crystals of m. p. 253~258°C. Recrystallization from ethanol afforded gold colored scales III, m. p. 260°C.

Anal. Found: C, 83.36; H, 5.67; N, 5.92. Calcd. for  $C_{19}H_{15}ON$ : C, 83.49; H, 5.53; N, 5.13%.  $\lambda_{\text{max}}^{\text{MoOH}} \pi \mu (\log \varepsilon)$ : 242(4.35), 270(4.25), 346(4.00), 406(4.14).

I is recovered on reacting with hydrazine in the same manner. Application of hydrazine to a mixture of I and II results in amination of II alone and I remains inactive. This is a convenient method for the separation of I and II.

b) A mixture of 30 mg. of II, 30 mg. of hydroxylamine hydrochloride, 0.5 cc. of absolute ethanol, and 0.5 cc. of pyridine was refluxed on a water bath for 2 hours. The solvent was evaporated from the mixture and water was added, from which 25 mg. of yellow crystals, m.p.  $210 \sim 213^{\circ}$ C, separated out. Recrystallization from ethanol raised the melting point to  $212 \sim 213^{\circ}$ C.

Anal. Found: N, 4.80. Calcd. for  $C_{19}H_{15}ON$ : N, 5.13%.  $\lambda_{\max}^{MeOH}m\mu$  (log  $\varepsilon$ ): 237(4.30), 345(3.70), 403(3.72).

From the color of this substance and its ultraviolet spectrum, it is still doubtful that the substance is an oxime and probable occulusion of III may be considered.

I is completely recovered on similar reaction with hydroxylamine.

Formation of 3, 4-Diphenyltropolone (IV). —A solution of 120 mg. of III dissolved in a mixture of 6 cc. of ethanol and 2 cc. of 6N potassium hydroxide was refluxed for 12 hours on a water bath, ethanol was evaporated, and the residue was diluted with water. The solution was neutralized to weak acidity, extracted with benzene, and evaporation of benzene left 110 mg. of pale brown crystals, m. p.  $160\sim165^{\circ}$ C. Recrystallization from ethanol afforded 100 mg. of colorless crystals (IV), m. p.  $173^{\circ}$ C.

Anal. Found: C, 83.08; H, 5.41. Calcd. for  $C_{19}H_{14}O_2$ : C, 83.20; H, 5.15%.  $\lambda_{max}^{Me0H}m\mu$  (log  $\epsilon$ ): 235(4.39), 285(4.11), 323(3.87), 365(3.83), 374(3.85).

Formation of 3, 4-Diphenyltropolone Methyl Ether (V) and Aromatization Rearrangement of V.—To 2cc. of 2.8% ethereal solution of diazomethane, 70 mg. of IV was added and the mixture was allowed to stand in a cool place overnight. Evaporation of ether left 70 mg. of pale yellow needles, m. p.  $140 \sim 144^{\circ}$ C. Recrystallization from benzene-cyclohexane mixture gave V melting at  $147^{\circ}$ C.

Anal. Found: C, 83.31; H, 5.39. Calcd. for  $C_{20}H_{16}O$ : C, 83.31; H, 5.59%.  $\lambda_{\max}^{MeOH}m\mu$  (log  $\varepsilon$ ): 235(4.37), 287(4.09), 355(3.89).

A solution of 60 mg. of the methyl ether V dissolved in 3 cc. of absolute ethanol containing 10 mg. of sodium was refluxed for 30 hours, 5 cc. of water was added, and the mixture was heated again for 3 hours. Ethanol was evaporated, the residue diluted with water, and the solution extracted with ether to remove any neutral substance. The aqueous layer was neutralized until the acidity was weak, extracted with benzene, and benzene residue gave 20 mg. of colorless crystals. Recrystallization from benzene-cyclohexane mixture afforded colorless crystals, m. p.  $162^{\circ}$ C. Reported m. p. for 2, 3-diphenylbenzoic acid is  $161^{\circ}$ C<sup>16</sup>).

Bromination of 2, 7-Diphenyltropone (I).— A mixture of 200mg. of I and 300mg. (5mol. equiv.) of bromine in 7 cc. of acetic acid was warmed, sealed in a vessel, and allowed to stand for 6 days. Evaporation of acetic acid over potassium hydroxide in a vacuum desiccator left 100 mg. of pale yellow crystals, m. p.  $115^{\circ}$ C (decomp.). The filtrate obtained after removal of these crystals was evaporated and 150 mg. of orange solid obtained.

Its treatment with ethanol and benzene afforded 60mg. of pale yellow crystals, m.p. 123°C(decomp.).

Recrystallization of the former from ethanol and benzene gave 80 mg. of pale yellow needles VII, m. p.  $120^{\circ}C$  (decomp.), which were identified with the later-obtained crystals by mixed fusion.

Anal. Found: C, 54.58; H, 3.41. Calcd. for  $C_{19}H_{14}OBr_2$ : C, 54.78; H, 3.34%.  $\lambda_{max}^{MeOH}m\mu$  (log  $\varepsilon$ ): 227(4.28).

Dehydrobromination of the Bromine Adduct VII.—A mixture of 60 mg. of VII and 50 mg. of sodium acetate in 2 cc. of ethanol and 1 cc. of benzene was refluxed for 2 hours, the solvent was evaporated, and the residue was diluted with water. Extraction with benzene and evaporation of solvent afforded 50 mg. of orange yellow oil which solidified to crystals of m. p. 75~80°C. The carbon tetrachloride solution of this substance was passed through an alumina column and the crystals obtained therefrom were recrystallized from ethanol to pale yellow needles VIII, m. p. 92°C.

Anal. Found: C, 68.01; H, 3.91. Calcd. for  $C_{19}H_{13}OBr$ : C, 67.60; H, 3.89%.  $\lambda_{\max}^{MeOH}m\mu$  (log  $\varepsilon$ ): 229(4.20), 285(4.01), 347(3.94).

Bromination of 2, 3-Diphenyltropone (II). —To a solution of 50 mg. of II dissolved in 3 cc. of acetic acid, 130 mg. (4.5 mol. equiv.) of bromine was added and the mixture was allowed to stand for 3 days at room temperature. Acetic acid was evaporated over potassium hydroxide and 100 mg. of orange crystals, m. p. 123~130°C, was obtained. Recrystallization from benzene-cyclohexane mixture afforded pale yellow plates IX, m. p. 131°C (decomp.).

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Anal. Found: C, 40.35; H, 2.74. Calcd. for  $C_{19}H_{14}OBr_4$ : C, 39.41; H, 2.41%.  $\lambda_{max}^{MeOH}m\mu$  (log  $\varepsilon$ ): 305(3.43).

Dehydrobromination of Bromine Adduct IX.—To a solution of 60 mg. of IX dissolved in 2 cc. of ethanol, 30 mg. of sodium acetate was added and the mixture was refluxed on a water bath for 3 hours. Ethanol was evaporated from the mixture, the residue was dissolved in carbon tetrachloride, and the solution was passed through an alumina column. The column was eluted with benzene, and evaporation of the solvent from both eluates left 30 mg. of pale yellow crystals, m. p.  $135 \sim 160^{\circ}$ C, which recrystallized from ethanol to pale yellow needles X, m. p.  $167^{\circ}$ C.

Anal. Found: C, 55.19; H, 3.01. Calcd. for  $C_{19}H_{12}OBr_2$ : C, 54.81; H, 2.88%.  $\lambda_{max}^{MeOH}m\mu$  (log  $\varepsilon$ ): 258(4.33), 295(4.10).

**Catalytic Reduction of 2,7-Diphenyltropone (I).**—To a solution of 50 mg. of I dissolved in 10 cc. of methanol, 10 mg. of 5% palladiumcharcoal was added and the mixture was hydrogenated at ordinary temperature and pressure. The absorption of hydrogen ceased after 14.2 cc. (3 mol. equiv.) of hydrogen had been absorbed. The filtrate obtained after removal of the catalyst was evaporated and the colorless crystalline residue was recrystallized from methanol to 40 mg. of colorless needles XI, m. p. 143°C. Anal. Found: C, 86.72; H, 7.11. Calcd. for  $C_{19}H_{20}O$ : C, 86.32; H, 7.63%.  $\lambda_{\max}^{MeOH} m \mu \ (\log \epsilon)$ : 259(2.79).

Diels-Alder Reaction of the Diphenyltropones (I and II).—A solution of 50 mg. of I and 40 mg. of maleic anhydride dissolved in absolute xylene was refluxed for 4 hours and the residue obtained on evaporation of the solvent was recrystallized from ethanol to 40 mg. of pale yellow crystals, m. p. 132°C, identified with I by mixed fusion.

The same treatment of II with maleic anhydride also resulted in its recovery but the amount recovered was smaller. However, no addition product was obtained even in this case.

The author takes this opportunity to express his sincere gratitude to Professor Tetsuo Nozoe for his kind guidance throughout the course of this work, to Professor Shuichi Seto for much helpful advice and to Mr. Mutsuo Ishii for his cooperation in carrying out the experiments.

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