

## LABORATORY OF ORGANIC UNIT REACTIONS

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The Laboratory was succeeded by Prof. S. Oka in 1973 after the former Head Prof. S. Kunichika's retirement. Studies on reactivities of unsaturated hydrocarbons carried out under the supervision of Dr. Kunichika not only succeeded in exploitation of a new synthetic method for methylmethacrylate from propylene but also brought many fundamental achievements concerning to various organic reactions, especially to those catalyzed by transition metals. Then the research interest has been directed to organotransition metal chemistry from both preparative and mechanistic viewpoints. The research field also has been spread over organic sulfur chemistry and bioorganic chemistry since Associate Prof. Dr. A. Ohno joined the group in 1974.

Some of main progresses in the last decade will be summarized.

### I. Studies on Reactivities of Unsaturated Hydrocarbons and Their Derivatives

#### 1. Synthesis of Methylacetylene by Pyrolysis of Propylene

The following results were added to those obtained before 1966. Addition of a small amount of iodine not only accelerated pyrolysis of propylene remarkably but also was effective for syntheses of methylacetylene and allene. Zero conversion method was used to identify the main primary and secondary products. A free radical chain mechanism has been proposed for the main reactions.

#### 2. Carboxylation with Nickel Catalysts

Carboxylation of methylacetylene which has lower reactivity than that of acetylene was investigated. Methyl methacrylate was obtained in satisfactorily high yields with nickel carbonyl catalyst under appropriate reaction conditions. Allene and propylene were also carboxylated successfully to methyl methacrylate and methyl isobutyrate, respectively.

### II. Studies on Reactions Catalyzed by Transition Metals

#### 1. Reactions of Allene with Palladium

In the course of the study on transition-metal-catalyzed reactions, it was realized that a study on elementary reactions in organometallic chemistry is necessary for a better understanding of metal-catalyzed reactions and also for a design of suitable catalysts. Allene is particularly suitable for this purpose because it gives stable  $\eta^3$ -allyl complexes by the reaction with transition metals. Using palladium as the metal component, some chemistry of insertion reaction was examined. Reaction of allene with palladium (II) salts gives  $\eta^3$ -allyl complexes and/or 2-allyl- $\eta^3$ -allyl com-

plexes depending on the reaction conditions. This observation was shown to be explained by the concept of insertion promoted by a  $\pi$ -acid. Another driving force for the insertion, the release of strain in a substrate complex, was demonstrated for the reaction of allene with 2,2'-bi-( $\eta^3$ -allyl)-dipalladium complexes. A new binuclear palladium complex of allene trimer ligand was isolated, which could be regarded as a model compound for polymerization of allene.

## 2. Cyanation of Aryl Halides Catalyzed by Palladium

The displacement reaction of various non-activated aryl halides with cyanide ion was investigated in the presence of palladium salts. Various aryl iodides and bromides were converted into the corresponding aryl cyanides almost quantitatively. Detailed examination on the catalyst, co-catalyst, solvent, and reaction condition showed that the reduced palladium species may be the active catalyst. The reaction is more useful for the syntheses of aryl cyanides than the conventional Rosenmund-von Braun reaction.

## 3. Palladium-Catalyzed Decomposition of Azides to Nitriles

Palladium metal has been found to catalyze the decomposition of benzyl azide to give benzonitrile, benzylamine, and N-benzylidenebenzylamine. The presence of a suitable hydrogen acceptor such as diphenylacetylene improved the yield of benzonitrile at the sacrifice of benzylamine, whereas the yield of N-benzylidenebenzylamine remained constant. The reaction was shown to be applicable to the preparation of some other nitriles including aliphatic ones. The present procedure provides a method to obtain various nitriles without elongating the skeletal carbon chain of the starting halides.

# III. Studies on Abnormal Substitution of Aromatic Compounds

## Halogenation of Aromatic Hydrocarbons by Metal Halides

Aluminium chloride and some other metal chlorides have been found to act as chlorinating agents for anthracene, in the presence of catalytic amount of nitrogen dioxide under an atmosphere of oxygen, giving mono- or di-chloroanthracene in satisfactorily high yields. This is the first example in which aromatic ring was oxidatively chlorinated with halides of metals that cannot change the valency. It was clarified that nitrogen dioxide is essential to the reaction and oxygen serves to reproduce nitrogen dioxide from the corresponding reduced species. The scope and the mechanism of this new reaction are under investigation.

# IV. Studies on Biomimetic Reactions

## 1. Reaction of NAD(P)H Model Compounds

In order to elucidate the mechanism of biological reductions with NAD(P)H-dependent dehydrogenases and to extend the reaction into organic syntheses, biomimetic reductions with NAD(P)H model compounds have been studied. A mechanism in which one-electron transfer is followed by successive transfers of a proton

and an electron from NAD(P)H or its models to a substrate was proposed and, based on the proposed mechanism, biomimetic respiratory chain coupled with an oxidative phosphorylation of ADP was constructed. Biomimetic asymmetric reductions were also achieved by using chiral model compounds. Some metal ions were found to catalyze the reduction as well as asymmetric induction and the role of these metal ions, or mimetic enzymes, are now being investigated.

## 2. Model Reactions of Biotin

It was found that intramolecular C→N and N→C migrations of acyl or alkoxy-carbonyl groups take place quite easily in some derivatives of 2-methylthio benzimidazole under mild conditions. The mechanism was studied and the result was discussed in relation to the mechanism of biological biotin-dependent carboxylation. Namely, was suggested the possibility of N-carboxylated biotin to be a biologically active species.

## V. Studies on the Chemistry of Thiocarbonyl Compounds

Reactions of thiocarbonyl compounds, mainly of thioketones, were investigated. It was found that a charge-transfer complex is involved as an intermediate of the reaction of thioketone with a nucleophile. Physico-chemical properties of thiocarbonyl group was also studied in relation to those of carbonyl groups. Thioketones were also subjected to photochemical reactions.

### Publications

(\* indicates an article published in Japanese)

1. S. Kunichika, Y. Sakakibara, and T. Okamoto: Reactions of Allenes. I. The Synthesis of Unsaturated Monocarboxylic Esters by Carboxylation Reaction of Allenes. Reaction Conditions and Products, *Bull. Chem. Soc. Japan*, **40**, 885 (1967).
2. S. Kunichika, S. Oka, H. Hayami: Synthesis of 5,5'-Oxydivaleric Acid from 1,1,1,5-Tetrachloropentane, *Bull. Inst. Chem. Res., Kyoto Univ.*, **45**, 418 (1967).
3. S. Kunichika, Y. Sakakibara, and T. Nakamura: The Synthesis of Methacrylic Esters by the Carboxylation Reaction of Methylacetylene. II. Catalytic Synthesis of Methyl Methacrylate Using Nickel Carbonyl as the Catalyst, *Bull. Chem. Soc. Japan*, **41**, 390 (1968).
4. S. Kunichika, Y. Sakakibara, and M. Taniuchi: The Synthesis of Methylacetylene by the Pyrolysis of Propylene. (V). The Pyrolysis of Allyl Halides, *Bull. Inst. Chem. Res., Kyoto Univ.*, **47**, 437 (1969).
5. S. Kunichika, Y. Sakakibara, and T. Okamoto: Polymerization of Allene with Nickel (II) Phosphine Complexes, *J. Chem. Soc., Japan, Ind. Chem. Sect.*, **72**, 1814 (1969).\*
6. E. LeGoff and S. Oka: Electrocyclic Additions to Pentacyclo [4.4.0.0<sup>2,5</sup>.0<sup>3,8</sup>.0<sup>4,7</sup>]deca-9-ene, *J. Amer. Chem. Soc.*, **91**, 5665 (1969).
7. T. Okamoto, K. Takagi, Y. Sakakibara, and S. Kunichika: Reactions of Allenes III. Reactivities of Allenes in Comparison with Acetylenes and Olefins, *Bull. Inst. Chem. Res., Kyoto Univ.*, **48**, 96 (1970).
8. S. Kunichika, S. Oka, and T. Sugiyama: Reaction of 1,2-Dichloroethane with Toluene, *ibid.*, **48**, 276 (1970).
9. T. Okamoto: Reaction of Allenes. IV. New Palladium Complexes Having a Bridged Allene Trimer Ligand, *Bull. Chem. Soc., Japan*, **44**, 1353 (1970).
10. S. Kunichika, Y. Sakakibara, and M. Taniuchi: The Synthesis of Methylacetylene by the Pyrolysis of Propylene. VI. The Pyrolysis of Allyl Iodide, *Bull. Chem. Soc. Japan*, **44**, 1388 (1971).
11. T. Okamoto: Ready Insertion of Allene into Di- $\mu$ -acetato-2,2'-bi- $\pi$ -allyldipalladium, *J. Chem. Soc., (D)*, 1126 (1970).

12. S. Kunichika, S. Oka, T. Sugiyama, C. Inoue, and M. Ichii: Friedel-Crafts Rearrangements of 1,2-Ditolylethanes, *Nihon Kagaku Zasshi (J. Chem. Soc., Japan, Pure Chem. Sec.)*, **92**, 539 (1971).\*
13. S. Kunichika, T. Okamoto, and K. Yoshikawa: Diels-Alder Reaction of Allene and Isoprene, *Bull. Inst. Chem. Res., Kyoto Univ.*, **49**, 109 (1971).
14. M. Ichii: Friedel-Crafts Alkylation I. Kinetics of the  $AlCl_3 \cdot CH_3NO_2$ -catalyzed Phenethylation of Benzene and Toluene in Nitromethane, *ibid.*, **49**, 114 (1971).
15. S. Kunichika, Y. Sakakibara, T. Okamoto, and K. Takagi: The Carboxylation Reaction Using Nickel Catalysts. VI. The Catalytic Reaction of Propene with Dihalobis-(triphenyl-phosphine) nickel, *ibid.*, **49**, 122 (1971).
16. T. Okamoto: Reactions of Allenes. V. The Reaction of Allene with Palladium Salts, *ibid.*, **49**, 409 (1971).
17. S. Kunichika, S. Oka, T. Sugiyama, and M. Ichii: Friedel-Crafts Rearrangements of 1,2-Diarylethanes, *ibid.*, **49**, 418 (1971).
18. S. Kunichika, Y. Sakakibara, T. Okamoto, and K. Takagi: The Carboxylation Reaction Using Nickel Catalysts. V. The Catalytic Reaction of Propene with Nickel Carbonyl and Nickel Carbonyl-Triphenylphosphine, *Bull. Chem. Soc. Japan*, **44**, 3405 (1971).
19. S. Kunichika, S. Oka, T. Sugiyama, and M. Ichii: Friedel-Crafts Rearrangements of 1-Phenyl-2-tolyethanes, *Nihon Kagaku Zasshi (J. Chem. Soc., Japan, Pure Chem. Sec.)*, **92**, 801 (1971).\*
20. S. Kunichika, S. Oka, T. Sugiyama, K. Nakamura, and K. Fukui: Studies on the Reaction of Malonic Ester with Formaldehyde, *ibid.*, **1**, 596 (1972).\*
21. M. Taniuchi: The Synthesis of Methylacetylene by the Pyrolysis of Propylene. (VII). The Catalysis of Iodine, *Bull. Inst. Chem. Res., Kyoto Univ.*, **50**, 383 (1972).
22. S. Kunichika, Y. Sakakibara, M. Taniuchi, and R. Okuda: The Synthesis of Methylacetylene by the Pyrolysis of Propylene. (VIII). The Pyrolysis of Allyl Bromide, *ibid.*, **50**, 393 (1972).
23. M. Taniuchi: The Synthesis of Methylacetylene by the Pyrolysis of Propylene. (IX). The Mechanism of the Iodine-Catalyzed Pyrolysis of Propylene, *ibid.*, **50**, 660 (1972).
24. M. Ichii: Friedel-Crafts Alkylation. II. The  $AlCl_3 \cdot CH_3NO_2$ -catalyzed Phenethylation of Benzene and Toluene with 2-Arylethyl Chlorides in a Nitromethane Solution, *Bull. Chem. Soc. Japan*, **45**, 2810 (1972).
25. M. Ichii, T. Sugiyama, and S. Oka: Friedel-Crafts Alkylation. III. The Reaction of Benzene with 2-Phenylethyl-1,1- $d_2$  and 2-(p-Chlorophenyl)-ethyl-1,1- $d_2$  Chlorides, *Bull. Inst. Chem. Res., Kyoto Univ.*, **50**, 404 (1972).
26. H. Suzuki, K. Kawamura, and T. Sugiyama: Chlorination of Some Bridge-Substituted Acenaphthenes and Related Compounds, *ibid.*, **51**, 186 (1973).
27. H. Suzuki and T. Sugiyama: The Jacobsen Reaction of Iodopseudocumenes and Related Compounds. Orientation in the Iodination of Halopseudocumenes, *Bull. Chem. Soc. Japan*, **46**, 586 (1973).
28. K. Takagi, T. Okamoto, Y. Sakakibara, and S. Oka: Palladium (II) Catalyzed Synthesis of Aryl Cyanides from Aryl Halides, *Chemistry Lett.*, **471** (471) (1973).
29. H. Suzuki, M. Terakawa, and T. Sugiyama: Addition Products Obtained from the Chlorination of 1,2-Dichloronaphthalene, *Bull. Inst. Chem. Res., Kyoto Univ.*, **51**, 373 (1973).
30. H. Suzuki, T. Iwao, and T. Sugiyama: A Convenient Laboratory Method for the Preparation of Thiophenecarbonitriles, *ibid.*, **52**, 561 (1974).
31. H. Hayashi, and S. Oka: Synthesis of Hydroxybenzyl Compounds, *ibid.*, **52**, 514 (1974).
32. K. Maruyama, M. Taniuchi, and S. Oka: Radical Addition Reactions to the Carbonyl Group. I. The Reaction of Aliphatic Aldehydes with Di-t-butyl Peroxide, *Bull. Chem. Soc. Japan*, **47**, 712 (1974).
33. K. Nakamura, A. Ohno, and S. Oka: An Improved Synthesis of Arylphenylamines, *Synthesis*, **882**, (1974).
34. Y. Ohnishi, M. Kagami, and A. Ohno: Reduction by a Model of NAD(P)H. Reduction of  $\alpha$ -Diketones and  $\alpha$ -Keto-alcohols by 1-Benzyl-1,4-dihydronicotinamide, *Tetrahedron Lett.*, **2437** (1975).
35. A. Ohno, T. Kimura, S. Oka, Y. Ohnishi, and M. Kagami: Reduction by a Model of NAD(P)H. Biomimetic Respiratory Chain Coupled with Oxidative Phosphorylation, *Tetrahedron Lett.*, **2371** (1975).
36. Y. Ohnishi, M. Kagami, and A. Ohno: Reduction by a Model of NAD(P)H. Photo-Activation of

- NADH and Its Model Compounds toward the Reduction of Olefins, *Chemistry Lett.*, 125 (1975).
37. A. Ohno, K. Nakamura, Y. Nakazima, and S. Oka Di-tert-Butyl Thioketone, *Bull. Chem. Soc., Japan*, **48**, 2403 (1975).
  38. K. Takagi, T. Okamoto, Y. Sakakibara, A. Ohno, S. Oka, and N. Hayama: Palladium (0) Catalyzed Syntheses of Ketones from Acyl Halides and Organomercury (II) Compounds, *Chemistry Lett.*, 951 (1975).
  39. A. Ohno, K. Nakamura, M. Uohama, and S. Oka: Reactions of Di-t-Butyl Thioketone, *ibid.*, 983 (1975).
  40. K. Takagi, T. Okamoto, Y. Sakakibara, A. Ohno, S. Oka, and N. Hayama: Nucleophilic Displacement Catalyzed by Transition Metal. I. General Consideration of the Cyanation of Aryl Halides Catalyzed by Palladium (II), *Bull. Chem. Soc. Japan*, **48**, 3298 (1975).
  41. A. Ohno, K. Nakamura, M. Uohama, S. Oka, T. Yamabe, and S. Nagata: Charge-transfer Intermediate in the Reaction of Thioketone with Nucleophiles, *ibid.*, **48**, 3718 (1975).
  42. Y. Ohnishi, M. Kagami, and A. Ohno: Reduction by a Model of NAD(P)H. Effect of Metal Ion and Stereochemistry on the Reduction of  $\alpha$ -Keto Esters by 1,4-Dihydronicotinamide Derivatives, *J. Amer. Chem. Soc.*, **97**, 4766 (1975).
  43. Y. Ohnishi, T. Numakunai, and A. Ohno: Reduction by a Model of NAD(H). Contribution of Metal Ion to Asymmetric Reduction of Trifluoroacetophenone, *Tetrahedron Lett.*, 3813 (1975).
  44. H. Hayashi, A. Ohno, and S. Oka: Palladium-catalyzed Decomposition of Azide. Formation of Benzonitrile from Benzyl Azide. *Bull. Inst. Chem. Res., Kyoto Univ.*, **53**, 489 (1975).
  45. T. Sugiyama, K. Tanioka, A. Ohno, and S. Oka: NO<sub>2</sub> Catalyzed Chlorination of Anthracene by Metal Halides, *Chemistry Lett.*, 3307 (1976).
  46. H. Hayashi, A. Ohno, and S. Oka: Palladium-Catalyzed Decomposition of Azides. I. Formation of Nitriles, *Bull. Chem. Soc. Japan*, **49**, 506 (1976).
  47. Y. Ohnishi, M. Kagami, T. Numakunai, and A. Ohno: Reduction by a Model NAD(H)H. VIII. Effects of Metal Ion on the Course and Stereochemistry of the Biomimetic Reduction of Olefin, *Chemistry Lett.*, 915 (1976).
  48. Y. Ohnishi and A. Ohno: Reduction by a Model of NAD(P)H. IX. ESR Study on the Biomimetic Reduction of Benzils with 1,-Benzyl-1,4-dihydronicotinamide, *ibid.*, 697 (1976).
  49. Y. Ohnishi, T. Numakunai, T. Kimura, and A. Ohno: Reduction by a Model of NAD(P)H. X. Asymmetric Reductions of Carbonyl Compounds in the Presence of Magnesium Perchlorate, *ibid.*, 2699 (1976).
  50. H. Suzuki, H. Yoneda, T. Hanafusa, and T. Sugiyama: Nitration of 9-Ethyl-10-methylantracene, 9-Ethylantracene, and 9-Methylantracene, *Bull. Inst. Chem. Res., Kyoto Univ.*, **54**, 176 (1976).

#### Reviews

1. T. Okamoto: Recent Progress in the Chemistry of Allenes, *Bull. Inst. Chem. Res., Kyoto Univ.*, **50**, 450 (1972).
2. A. Ohno, Y. Ohnishi: Reactions of NADH models, *Kagaku no Ryoiki, Zokan*, No. 110, 57 (1976).\*