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MOLECULAR DESIGN OF NOVEL CARBO- AND HETEROPOLYCYCLES

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Abstract

Recent results on molecular design of novel carbo- and heteropolycycles based on unique ring structures such as adamantane, [60]fullerene, and squaric acid are reviewed. Designs of reactive intermediates and synthetic blocks for this purpose are also studied based on selected hetero-atom compounds.

Keywords: adamantane, strain, imine, heteromodified admantane, [60]fullerene, iminophosphorane, organofluorine compound, squaric acid, fine chemicals

Contents

1. Introduction

In modern chemical industry, research and developement of new materials with special properties and functions, and of intelligence materials are highly demanded for technological innovations. For developement of these materials, it is essential to provide so-called speciality chemicals like fine chemicals and intermediates, as well as performance products.[1] From this point of view, we have been studying molecular design and synthesis of novel carbo- and hetero-polycycles as one of practical methods for development of new speciality chemicals. Firstly we have focused on synthesis of functionalized derivatives starting from three-dimensional carbopolycycles with unique structures such as adamantane and [60]fullerene. Adamantane and other diamondoid hydrocarbons are constructed by sp^3 carbon corresponding diamond lattice carbon, and [60]fullerene and other higher fullerenes are constructed by strained sp^2 carbon on a curved surface different from unstrained sp^2 carbon of planer graphite (Fig 1).[2] Secondly we have concentrated our efforts to synthesize hetero-atom compounds such as F, Si, P, and S from their high potential as unique reagents and unique synthetic blocks. Thirdly we have employed highly strained small ring compounds like squaric acid as the starting building block from our interest in the strain-reactivity relationship[3,4] and in their high potential as new speciality chemicals. This memoir summarizes our very recent endeavors in these emerging and exciting areas.

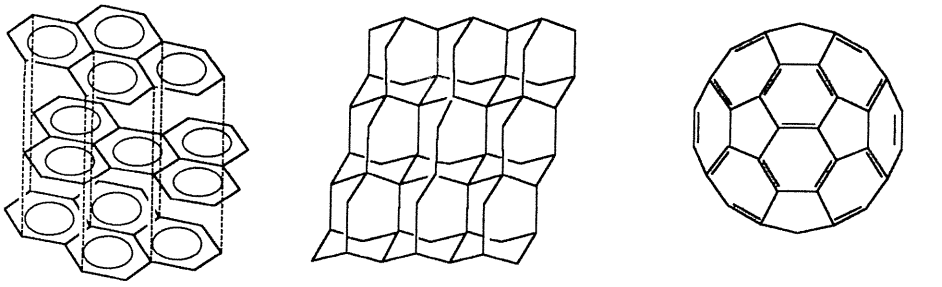


Fig. 1. Allotropic forms of carbon.

2. Molecular Design of Polycycles based on Adamantane Derivatives

2. 1. Adamantane and Related Compounds

Three dimensional polycyclic compounds constructed in principle by spirocyclic **2a**, fusocyclic (fusedcyclic) **2b**, and pontecyclic (bridgedcyclic) **2c** rings (Fig. 2),[5] and their

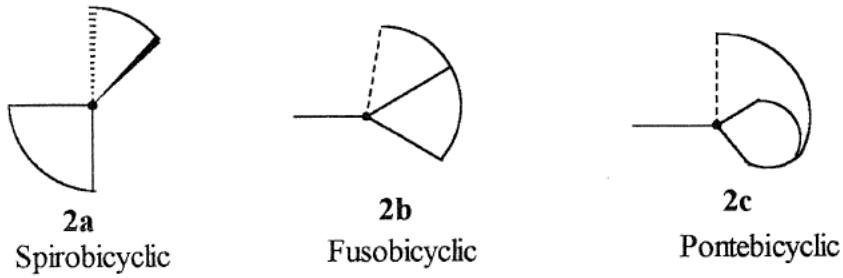


Fig. 2. Classification of bi(poly)cycles by a central carbon.

combination have drawn considerable attention in recent years from their unique physical, chemical, and biological properties. Heteroanalogues of these polycycles have characteristic unique rigid stereochemistry as well as fixed conformations of heteroatoms, and are of particular interest as novel typed heterocycles. Although a wide variety of structurally, functionally, and biologically interesting classes of compounds like cryptands, some alkaloids, cyclonucleosides may fall under this category in a broad sense, we focused on heteromodified adamantane and related derivatives, in particular aza-modified type compounds, as one of so-called heterocage compounds in a more narrow sense. Studies on such heteromodified adamantanes seems to be not extensive compared to the carbocyclic systems.[6] This might be due to the lack of efficient synthetic routes to these heteroanalogues.

For adamantane **3a** and related stabilomers, the efficient synthetic route have been developed by the acid-catalyzed rearrangemnt,[7] i.e., adamantane rearrangement, found by

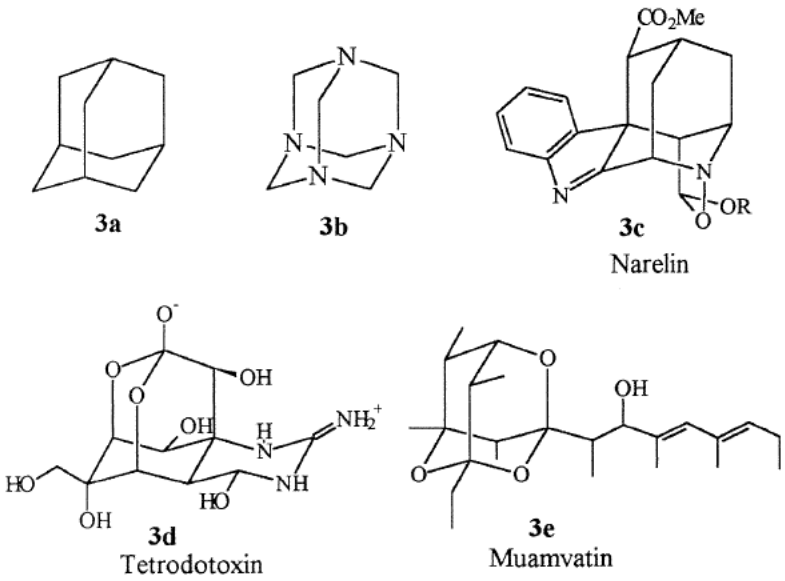


Fig. 3. Adamantane and heteroadamantane derivatives.

Schleyer[8], and now adamantane, and some related derivatives can be available commercially even in industrial scale.[9] Such efficient synthetic routes for heteroanalogues have been the subject of intense interest for organic chemists with the exception of long known hexamethylenetetramine (methenamine, urotoropine)[10] **3b**. There are also known a few but biologically very interesting natural products that possess heteroadamantane skeletons. For examples, an indole alkaloid narelin[11] **3c** from *alstonia scholaris* has 2-azaadamantane ring, tetrodotoxin[12] **3d** from puffer fish involves dioxaadamantane ring, and muamvatin[13] **3e** isolated from the Fijian mollusc *S. normalis* has a novel trioxaadamantane skeleton respectively (Fig. 3). From above point of view, we have developed already[14,15] i) regio- and stereoselective functionalization methods of adamantane and related cage hydrocarbons via cationic intermediates,[16] ring-fragmentation/Pi-route cyclization route,[17,18] and synthetic routes to modified adamantane skeletons such as bishomoadamantanes[19,20] and methanoadamantanes[21] by ring enlargements and ring contractions etc, ii) synthetic routes to heteromodified adamantanes including spiroheterocycles via transannular reactions[22,23] and various cycloaddition reactions,[24] and iii) synthetic methods for bridgehead- and bridge-imines.[25,26] In this memoir only some selected recent results developed in our group will be discussed.

2. 2. *New Aspects of Bridgehead Functionalization via Radical Intermediates*

Until recently most of the methods for functionalization of bridgehead compounds like adamantane rely on polar S_N1 type substitution reactions under electrophilic conditions, and less attention has been paid to the radical-mediated substitution reaction. In 1988 we have demonstrated a useful way of preparing bridgehead and bridge-substituited adamantane derivatives by using radical chain process (Fig. 4).[27] The adamantyl radical having a higher SOMO is nucleophilic favoring an electrophilic unsaturated bond. Thus, the reaction of 1-bromoadamantane **4a** and 2.0 equiv of acrylonitrile in the presence of 1.2 equiv of Bu_3SnH and 5 mol % of AIBN in toluene under reflux for 2 h yielded the desired 1-cyanoethyladamantane **4d** in 80% yield. This method can be extended successfully to synthesize bis-**7**, tris-**11**, and tetra-bridgehead substituted derivatives **12** as well as bridge-substituted derivatives **10** (Fig. 5). It should be noted here that bis-substitution via cationic process using $TiCl_4$ as the catalyst was not successful. Futhermore, above method have been successfully applied to functionalization of dodecahedrane recently by Paquette et al., revealing general applicability

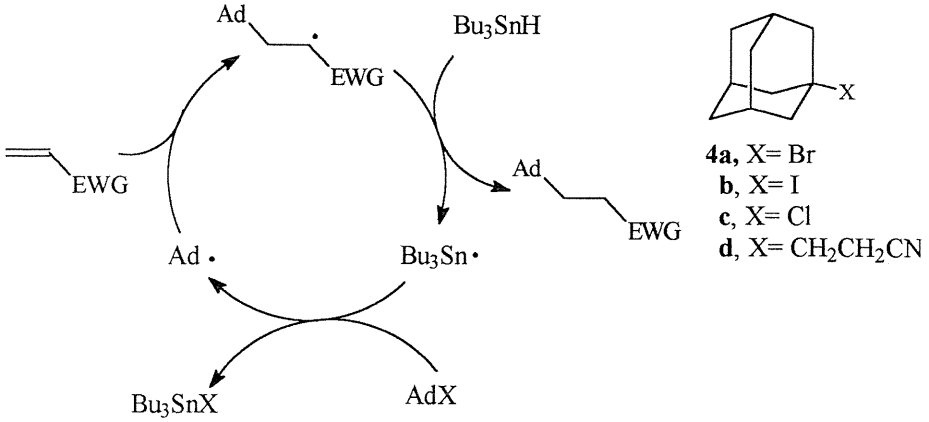


Fig. 4. Radical chain reaction of **4** with an alkene.

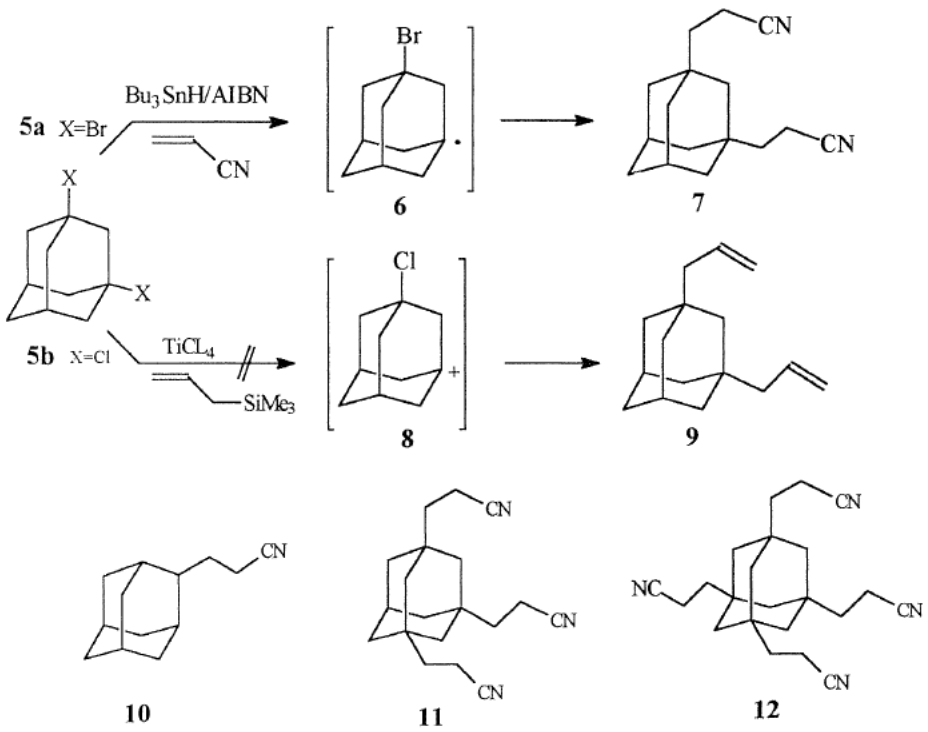


Fig. 5. Multifunctionalization with acrylonitrile.

Table 1. Cross-coupling reactions of *ter*-alkyl halides with Grignard reagents in dichloromethane.

$$RX + R'MgX' \rightarrow R\text{-}R' + MgXX'$$

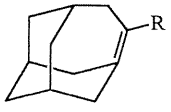
entry	RX	R′MgX, R′ =	time[a] (h)	product[b]	yield (%)
1	**4a**	Bu	5	1-AdBu	56
2	**4a**	Et	5	1-AdEt	61
3	**4a**	Ph	8	1-AdPh	57
4	**4a**	3-MeC_6H_4	8	1-AdC_6H_4Me(3)	57
5	**4a**	3-Indolyl	4	1-AdIndolyl(1)	22
6	**4b**	Bu	5	1-AdBu	56
7	**4b**	Me	5	1-AdMe	58
8	**4c**	Bu	5	1-AdBu	60
9	**4c**	CH_2CH_2Ph	5	1-AdCH_2CH_2Ph	65
10	**4c**	CH_2Ph	8	1-AdCH_2Ph	50
11	**4c**	$CH_2CH{=}CH_2$	5	1-Ad$CH_2CH{=}CH_2$	57
12	*ter*-BuCl	CH_2CH_2Ph	3	*ter*-BuCH_2CH_2Ph	54

[a] At room temperature for entries 5, 12, and at reflux temperature for all others.
[b] Usually adamantane was formed in 15–25% yield.

of this method if the appropriate precursor is available.[28] We have also developed a convenient cross-coupling reaction of *tert*-alkyl halide including 1-adamantyl halides **4a-c** with Grignard reagents by using dichloromethane as a non-Lewis basic medium.[29] By this method a variety of bridgehead substituted derivatives were obtainable in reasonable yields (Table 1). The reaction using 5-hexenylmagnesium bromide as a radical probe afforded uncyclized/cyclized coupling products in a 6/4 ratio, suggesting the significant participation of the single-electron-transfer process in these reactions. Thus, this cross-coupling reaction provides a novel synthetically useful method for construction of a quarternary carbon by direct combination using readily available Grignard reagents.

2. 3. *Conjugatively Stabilized Bridgehead Olefins as Novel Synthetic Blocks*

Bridgehead olefins have attracted continuous attention since Bredt first reported the prohibition of a double bond at a bridgehead. Various studies have been performed to understand the nature of such bonds, and the experimental and theoretical results have been reviewed several times.[30] The current understanding of the relative stability of bridgehead olefins can be expressed by the rules suggested by Wiseman who evaluated the system as a trans-cycloalkene[31] and Schleyer who considered olefin strain energy.[32] Homoadamant-3-ene (**15**) (Fig. 6) is a bridged cycloheptene with an olefin strain energy of 20 kcal/mol, suggesting that it can be observed only at very low temperature.[32] The introduction of a substituent to such bridgehead olefins is believed to alter their stability and reactivity. In fact, 4-(1-adamantyl)homoadamant-3-ene (**16**) was shown to be amazingly stable due to steric protection by Jones et al.[33] However, the possible conjugative stabilization effect of a substituent on this straind olefin is not demonstrated yet. And hence, we have examined the generation of phenyl- and methoxycarbonyl-substituted homoadamant-3-enes (**13**) and (**14**), which are, in fact, confirmed as considerably stable due to mainly a conjugative effect and could be useful synthetic blocks in molecualr desgin of polycyclic systems as summarized in Fig. 7 and 8).[34] The ring expansion of adamantylcarbene (-carbenoid) generated from decomposition of the diazo precursors **17** and **25** was much more efficient via catalysis with $Rh_2(OAc)_4$ in dichloromethane than by photolysis or thermolysis. 4-Phenyl- and -methoxycarbonyl-substituted bridgehad olefins **13** and **14** were considerably stable even 0°C-room temperature; more than half of **13** and **14** survived in solution at room temperature after 12 h and 1 h, respectively, while parent homoadamant-3-ene **15** was recorded to be unstable even at −20°C.[35] Bridgehead olefins **13** and **14** reacted with various reagents to give fragmentation, addition and rearrangement products (Fig. 7 and 8). Both olefins were reactive with atmospheric oxygen yielding bicyclo[3.3.1]nonanones **19** and **27** in good yields via O_2-addition and subsequent bond cleavage. However, each reactivity toward electrophiles and nucleophiles were quite contrasting. On acid treatment **13** isomerized to 4-olefin **18**, while **14** gave adducts **26** in high yields. Nucleophilic addition of ethanol and aniline did not occur toward **13**, and only thiophenol afforded an adduct **20** in very low yield presumably via a radical pathway. The reactions of DMAD (dimethyl acetylenedicarboxylate), and methyl α-cyanoacrylate gave unusual [2+2+2]cycloadduct **21**, and a formal [4+2]cycloadduct **22** after



13, R= Ph
14, R= COOMe
15, R= H
16, R= 1-Ad

Fig. 6. Homoadamant-3-enes.

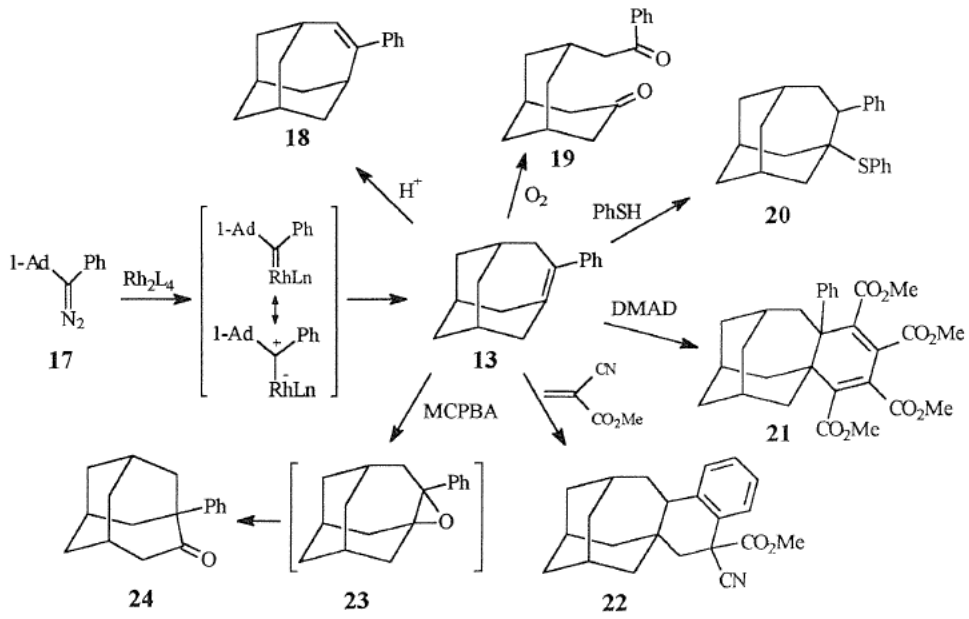


Fig. 7. Reactions of 4-phenylhomoadamant-3-ene.

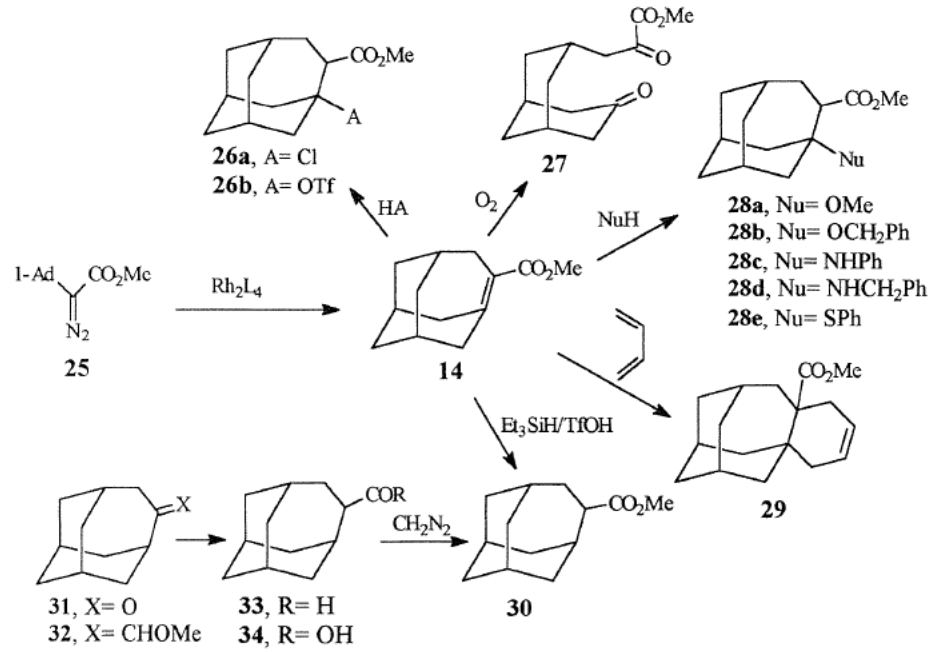


Fig. 8. Reactions of 4-methoxycarbonylhomoadamant-3-ene.

oxidative rearomatization, respectively. Epoxidation with MCPBA (*m*-chloroperbenzoic acid) gave rise to 3-phenylhomoadamant-4-one **24** as a result of homoadamantyl-homoadamantyl rearrangement of the oxirane-fused homoadamantane **23** (Fig. 7). In contrast, nucleophilic addition toward **14** with alcohols, amines and thiophenol occurred very smoothly affording the corresponding adducts **28a-e** in 42–80% yields. The cycloaddition with 1,3-butadiene gave [4+2]cycloadduct **29**. The reduction was achieved with triethylsilane in the presence of trifluoromethanesulfonic acid to give methyl homoadamantane-4-carboxylate **30**, whose skeletal integrity was supported by an alternative synthesis from homoadamantan-4-one **31** via **32**, **33**, and **34** (Fig. 8).

In summary, bridgehead olefins substituted with phenyl and methoxycarbonyl groups were formed in a homoadamantane system using the 1,2-carbon shift of the carbene (carbenoid) intermediate. Among the methods used to decompose the diazo precursors, catalysis with $Rh_2(OAc)_4$ was the most effective for producing the desired bridgehead olefin. The 1,2-shift of the Rh-carbene complex was significantly affected by its polarized structure. These bridgehad olefins were considerably stable than unsubstituted one by strain relief of the double bond as a result of conjugation with the 4-substituent and to some extent by steric protection. These olefins have been demonstrated to be useful synthons for 3,4-disubstituted homoadamantane derivatives.

2. 4. Synthesis of Heteromodified Adamantanes and Related Hetero-Cage Compounds

As stated in the begining of this section, we have been pursuing practical synthetic routes to heteromodified adamantanes and related hetrero-cage compounds as novel heteropolycycles. Some of typical examples are summarized in Figures 9 and 10 (for azahomoadamantane related compounds, see next section 2. 1. 4). The transannular carbene C-H insertion reaction was applied successfully at the early stage of this project as exemplified by facile synthesis of **35**[22] and **36**.[36] The dihalocarbene addition/ring opening/transannular cyclization provided one-pot procedure for synthesis of 5-oxaprotoadamantane **37**.[23] Heterocyclization via nucleophilic transannular reaction was useful for synthesis of thiahomoadamantane **38**,[37] novel hetero-bird cage **39**,[38] and tricyclonucleoside derivative **40**.[39,40] Intramolecular Friedel-Craft acylation reaction of a thiabicycloalkenyl system provided a facile route to 7-thiaprotoadamantane **41**.[41] Intramolecular radical cyclization of bicycloalkenylacylthio radical afforded 3-thia-2-homoprotoadamantan-2-one derivative **42** in a high yield.[42] Intramolecular cycloadditions have been a powerful tool in synthesis of polycycles including natural products. We have developed intramolecular cycloaddition routes to heterotetracycles mainly from functionalized bicycloalkenyl system which are readily available by intermolecular Diels-Alder reaction of cyclic dienes and also by fragmentation reaction of adamantanone and its derivatives as described previously. For example, photochemical [2+2]cycloaddition (intramolecular Paterno-Büchi reaction) of 3-endo-acylbicyclo[3.3.1]non-6-ene gave regiospecifically 2,4-oxabridged protoadamantane **43**.[43] The intramolecular 1,3-dipolar cycloaddition of C-bicycloalkenylnitrones[24] provided an efficient route to epoxyimino-adamantane **44** and -noradamantane **45**, and N-bicycloalkenylnitrones[44,45] gave **46**, **47**, **48** and **49**. This methodology was successfully extended to regiospecific synthesis of diazabridged **50** and **51** via azomethine imines,[46] and **52** and **53** via azide derivative respectively.[47] These heteromodified adamantanes and heterocage compounds were useful for synthesis of regio- and stereospecifically functionalized polycyclic systems.

Intermolecular cycloadditions have been utilized extensively for synthesis of adamantane-spiro-heterocycles (Fig. 10). For example, [4 + 2]cycloaddition reactions of adamantanethione with dienes,[48] α,β-unsaturated carbonyl compounds,[49] and *o*-quinodimethanes[50] provided a facile route to adamantane-2-spiro-thiaheterocycles **54**, **55**, and **56** respectively.

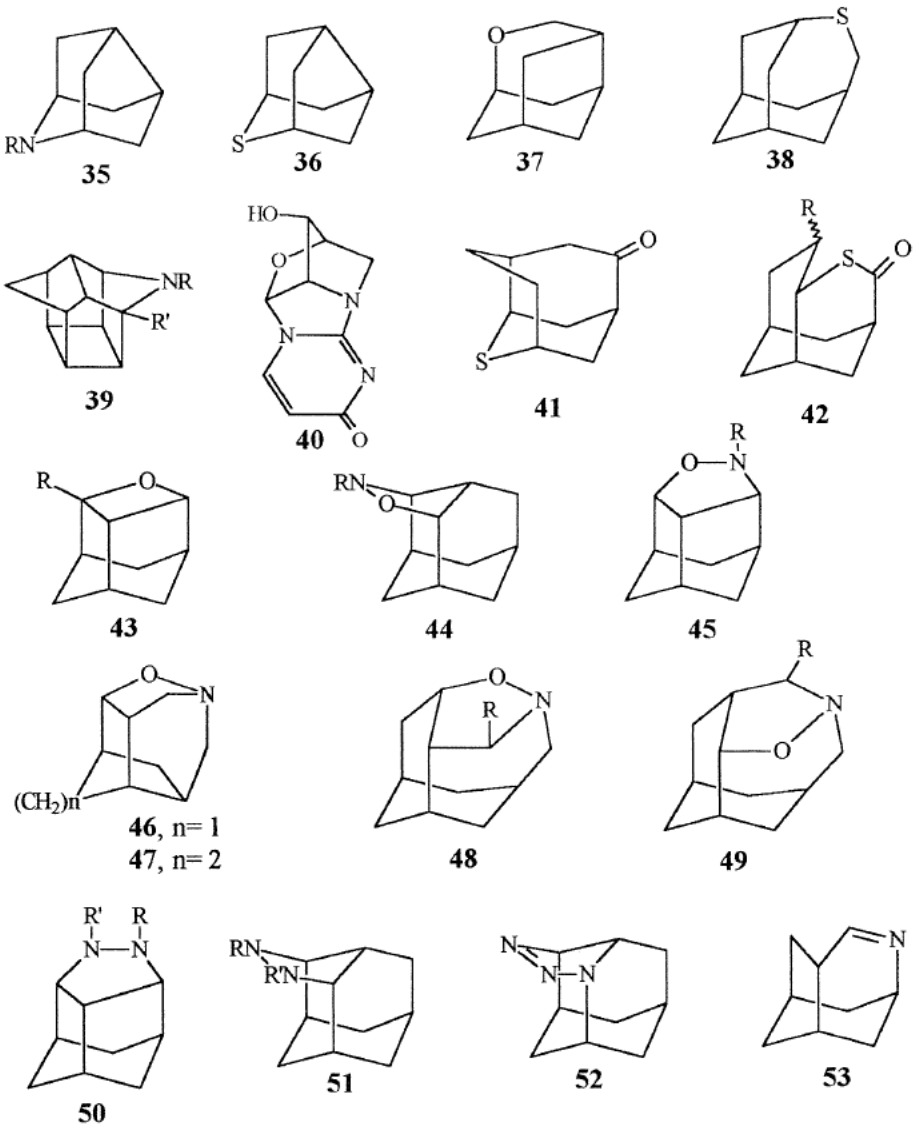


Fig. 9. Some examples of novel heterobridged polycycles.

Similarly 1,3-dipolar cycloadditions of adamantanethione with nitrile oxide, nitrilimines, and diazoalkanes afforded **57**, **58**, **59**, and **62**.[51] Various ionic- and cycloadditions toward adamantylidenemethane derivatives provided also convenient routes to adamantane-2-spiro compounds such as **61** and **62**.[52-54] On the other hand, novel adamantan-2-spiro-imidazolidinone derivatives **60** were obtained by ring-contraction of homoadamantane-4,5-dione with guanidines.[55] Some of these compounds were found to be biologically active (see section 6).

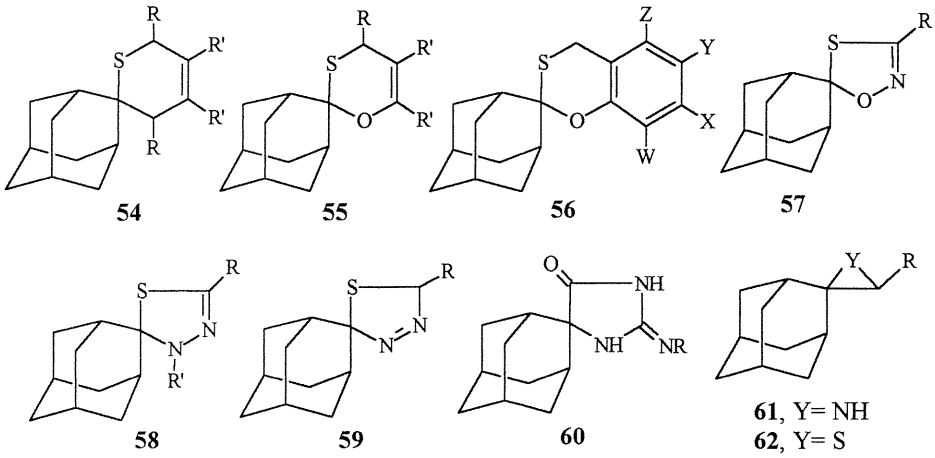


Fig. 10. Some examples of adamantane-2-spiroheterocycles.

2. 5. *4-Azahomoadamant-4-enes as Novel Synthetic Intermediates*

We have developed synthetic methods for bridgehead imines **63—71** (Fig. 11) based on azide functionalization of carbopolycyclic systems.[25,26] The chemistry of bridgehead imines as one of heteroanalogues of bridgehead olefins has drawn attention only for last 20 years contrary to carbocyclic bridgehead olefins that have been a topic of organic chemistry for over seventy years (cf. section 2.3.).[30-33] The photochemical ring expansion of appropriate bridgehead azides provided one of the most general methods for generation of highly strained bridgehead imines. We have also developed intramolecular aza-Wittig route to considerably strained 4-azahomoadamant-3-ene **65** and 4-azahomobrend-3(4)-enes.[56] The advantage of this method is a regiospecific generation of the imine under nonphotochemical conditions, while the photolytic route suffers from nonregioselective formations of the imines as well as a limitation of applicable reagents to photostable ones. Thus, 4-azahomoadamantano[3,4]fused heterocycles could be obtainable from bridgehead imine **65** generated by both photolytic and aza-Wittig routes (Fig. 12). These novel fused heterocycles are difficult to prepare by other routes.

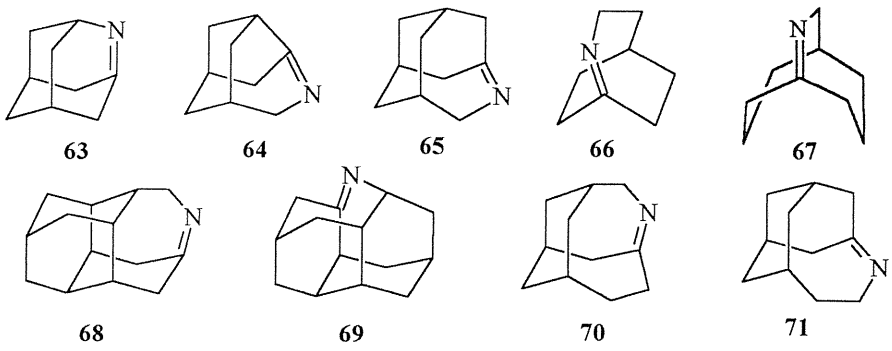


Fig. 11. Representative bridgehead imines generated.

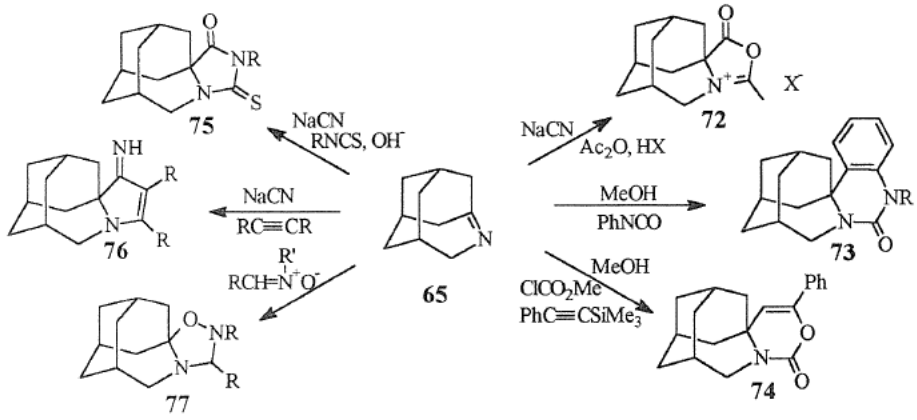


Fig. 12. Reactions of bridgehead imine **65**.

On the other hand, 4-azahomoadamant-4-enes **78** and **79** readily available from 2-azidoadamantanes and/or 2-adamantanols are stable imine,[57,58] and can be regarded as potentially useful synthetic blocks for 4-azahomoadamantano[4,5]fused type heterocycles.[25,26,59] As summarized in Fig. 13, they were reactive enough in various cycloadditions and ionic reactions due to an imine nitrogen, affording **81**—**84**. Novel pyrrole derivatives **85** were obtainable from several routes. The imines were converted to 2-azaadamantane derivatives **88** via photochemical ring-contraction of oxaziridine **87** which was readily obtainable by MCPBA oxidation. Photochemical cyclization of enamides **89** under oxidative and nonoxidative

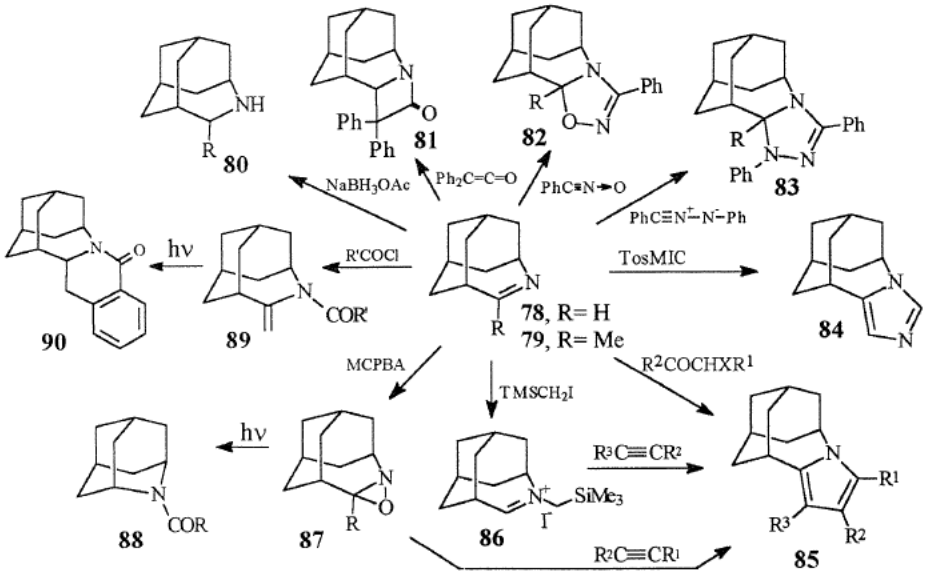


Fig. 13. Reactions of bridge imines **78**, **79**.

conditions provided a facile route to pyridone and isoquinolinone derivatives **90**.[60,61] Thus, a variety of 4-azahomoadamantano[4,5]fused heterocycles could be synthesized from **78** and **79**. For further study on developement of the unique synthetic block, we synthesized **91** and **92** as novel homoadamantane-incorporated nitrones and examined their reactions as summarized in Fig. 14.[62-67] These nitrones were prepared by oxidation of the corresponding amines in high yields as hygroscopic solids.[62,63] The reaction with alkynes proceeded even at below room temperature to afford thermally unstable isoxazoline **93** regiospecifically in high yields. These isoxazolines when R = Me rearranged thermally to pyrrole derivatives **94** in high yields. However, the reaction with phenylacetylene gave unstable cycloadducts **95** with different regiochemistry, which was rearranged thermally to pyrrole **94** also when R = Me, and was cleaved to vinylogous amide **96** for R = H (Fig. 14).[63] We found the reaction of **92** with methyl propiolate in aqueous solution gave directly a regioisomeric pyrrole **94** ($R^1 = H$, $R^2 = CO_2Me$) which is different from the pyrrole **94** ($R^1 = CO_2Me$, $R^2 = H$) derived thermally from **93**. From these facts, the thermal rearrangement of **93** to **94** was rationalized to proceed via the acylaziridine route, while the direct formation of **94** in aqueous solvent, via the [3.3]sigmatropic rearrangement/cyclodehydration route, respectively.

During study of nitrones **91** and **92**, we found also that an unactivated C ≡ N triple bond such as acetonitrile and benzonitrile is reactive enough to behave as a hetero-dipolarophile as long as the reacting nitrones can resist decomposition under the required thermal conditions. With activated nitriles such as cyanoformate, the cycloadduct is formed with ease. These results demonstrate the feasibility of nitrone cycloaddition method for direct and convenient synthesis of 2,3-dihydro-1,2,4-oxadiazole ring system which is difficult to prepare by other routes.[64-66] The reaction with alkenes afforded regio- and stereoisomeric mixture, but the reaction with allenes gave methyleneisoxazolidines **100** and **101**, which are isomerized

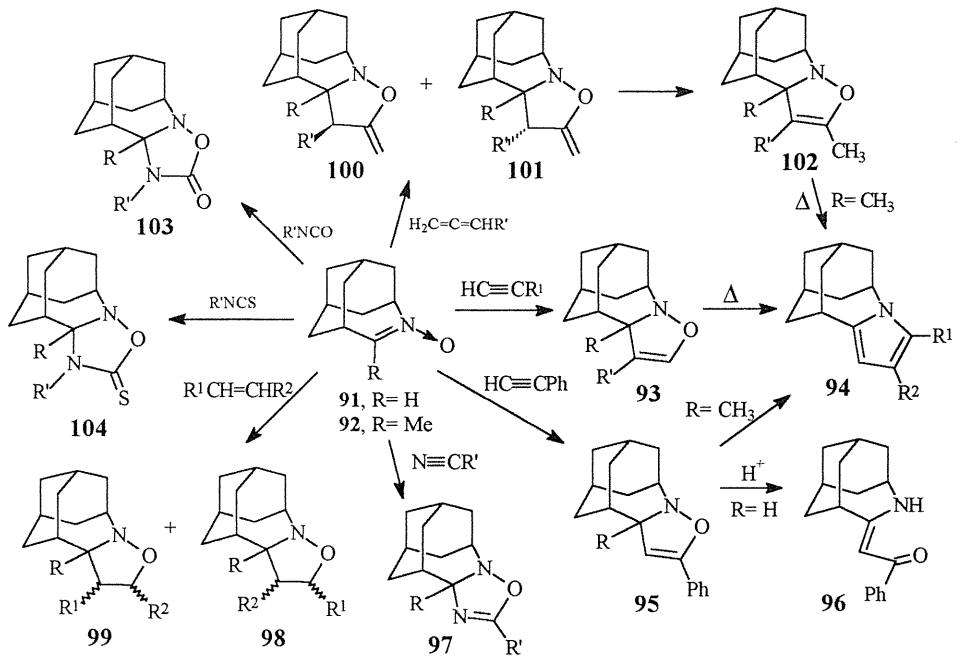


Fig. 14. Reactions of 4-azahomoadamant-4-ene N-oxides **91**, **92**.

to isoxazoline **102**.[68] The reactions with isocyanates and isothiocyanates afforded 1,2,4-oxadiazolidin-5-ones and -thiones **103** and **104** respectively in high yields.[67]

In summary, 4-azahomoadamant-4-enes **78** and **79** readily derivable from commercially available 2-adamantanols are shown to be useful bilding blocks for synthesis of novel polycyclo-type nitrogen heterocycles which are of interest as new fine chemicals.

3. Molecular Design of [60]Fullerene Derivatives

3. 1. Functionalization of Fullerenes

Organic functionalization of fullerenes developed quite rapidly after discovery of a method for bulk production of the fullerenes by Krätschmer and Huffman in 1990.[69-72] A variety of organic derivatives of C_{60} and to a minor extent of C_{70} have been synthesized and many of them exhibit promising potential as new materials[73] as well as having pharmaceutical applications.[74] These novel spherical molecules constructed with strained sp^2 carbon are found to be very reactive and behave like electron-deficient polyolefins.[70-72] Most of the chemical transformations that have been examined with C_{60} are addition reactions to the external fullerene framework. These addition reactions involve cycloadditions, nucleophilic additions, radical additions, transition metal complex formations, hydrogenations, halogenations, epoxidations and others. The major driving force for all addition reactions to the fullerene cage is the reduction of strain, since about the 80% of the heat of formation of C_{60} is due to strain energy.[70,71] The addition of the addends to one double bond of the fullerene framework already release about 10 kcal/mol of strain energy. Many of these addition reactions show a remarkable regioselectivity. For monoadditions which convert just one double bond into a single bond in the fullerene framework, only one or two isomers, depending on the type of addition, are formed. These are the 1,2- or 1,4-isomers and in the case of methano- and hetero-analogues the ring closed 6-6 ring bridged or opened 5-6 ring bridged isomers etc. For higher adducts new addends seem to be prone to prefer defined positions to addends already bound to the fullerene core as exemplified by the formation of octahedral addition pattern.[75] Thus fullerene chemistry is currently one of the most rapidly expanding and attractive areas. However, number-controlled and regio-selective synthetic methods for fullerene derivatives are yet challenging problems in current organic chemistry.

At the begining of our research, we have developed a convenient and economical extraction/purification procedure of C_{60} from carbon raw soot by "Soot on Column" method using Norit I/Celite system.[76] Then, we have examined the reactivity of C_{60}/C_{70} toward radicals generated from azo compounds having cyano or ester function.[77] Interestingly, their reactivities toward C_{60} were found to be higher than those toward C_{70}. The thermal reaction of C_{60} with 1.0 equiv. of azobisisobutyronitrile afforded 1:1 addition products such as $C_{60}(CMe_2CN)_2$, however, the reaction site could not be determined because of contamination of isomers. As the next reactivity study of C_{60}, we focused our attention to thermal cycloaddition reactions, in particular [2+4]cycloaddition reactions. We found C_{60} is reactive enough as 2-π component even toward EWG (electron-withdrawing group)-substituted 1,3-dienes such as ester, cyano, sulfonyl, and nitro-substitued dienes as well as other substituted 1,3-dienes such as trimethylsilyloxydienes. These reactions provide an efficient route to functionalized fullerene derivatives.[78] In this memoir, we describe our recent efforts on synthetic design of heterocycle-containing fullerene derivatives.

3. 2. *Synthesis of Heterocycle-Containing [60]Fullerene Derivatives*

Fullerene derivatives functionalized with heterocycles, or trivial fulleroheterocycles among these derivatives are of particular interest because: (a) even a simple combination of fullerenes with structurally diverse heterocycles provides a multitude of derivatives, (b) heterocycles are themselves intriguing and important functional groups, (c) functional conversions can be carried out with relative ease by heterocyclic modification and heterocyclic ring-opening, and (d) bond-formation between fullerene-carbons and various heteroatoms provides a new aspect of functionalization.

In this paper, fullerene derivatives covalently linked with heterocycles through fullerene carbon-heterocycle ring carbon bonds (type I in Fig. 3-1), and fullerene derivatives fused with heterocycles through fullerene carbon-heterocycle heteroatom bonds (type II) will be described focusing attention on their synthetic methods. For both types, multiple substitutions (type III) are possible, and heteofullerenes containing heteroatoms instead of core carbons are also conceivable, however, these types are challenging targets for the future or constitute theoretical problems at the present stage.[79]

Following pioneering work by Wudl et al., a variety of [m+2] cycloadditions have been successfully carried out ranging from m = 1 to m = 4 with C_{60} being the 2-π component (acting as ene or enophile).[80] The cumulative results revealed that C_{60} is reactive enough to give the corresponding adducts but their synthetic use is restricted by the ease of cycloreversion to the starting materials. Some types of cycloadducts are remarkably stable.[81] This is an important requirement for possible applications and further derivatization. The stable adducts can be formed by irreversible addition of highly reactive species such as carbene and nitrene. If the cycloaddition is reversible, besides kinetic control, thermodynamic control becomes important. On the other hand, the unstable cycloadducts can be converted to more stable products by dinitrogen extrusion from the cycloadducts of diazo compounds or azides. The stability of the cycloadducts was enhanced simply by chemical conversion of the formed double bond to a single bond as demonstrated by hydrolysis of 2-siloxy-1,3-diene adducts.[78-79] Alternatively stabilization of the Diels-Alder adducts is achieved by incorporating the formed double bond into an aromatic ring as in the case of isobenzofuran.[83] With this aim, *o*-quinodimethanes introduced by Müllen et al[84] have been efficiently utilized as dienes to afford tetrahydronaphtho-fused C_{60} derivatives bearing interesting functionalities on the benzene ring.[85]

We have employed heterocyclic quinodimethanes as the diene unit to construct fullerenes linked with heterocycles. Thus, type I thiophene derivative of C_{60} **3-1** was readily obtained by the reaction of C_{60} with 2,3-dimethylene-2,3-dihydrothiophene[86] generated *in situ* by 1,4-elimination from the corresponding dibromide (Fig. 3-2).[87] A furan-linked derivative **3-2** was similarly obtained with 2,3-dimethylene-2,3-dihydrofuran[88] prepared from the corresponding ester by FVP (Fig. 3-3).[89] As a point of interest, compound **3-2** was very sensitive to light in an oxygen atmosphere presumably due to photosensitized oxidation.[90]

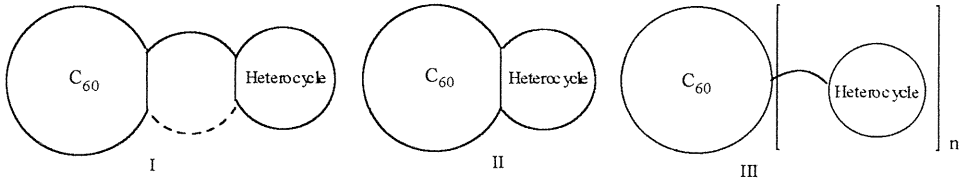
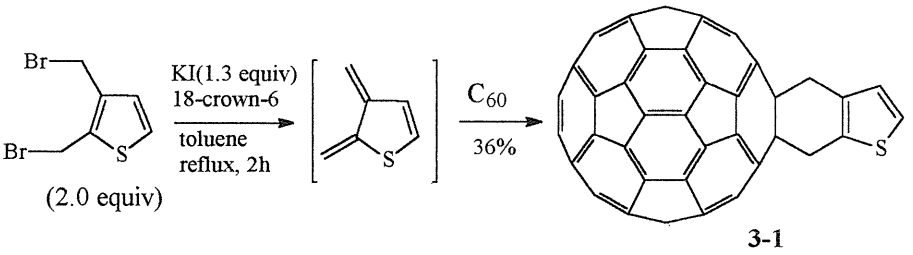
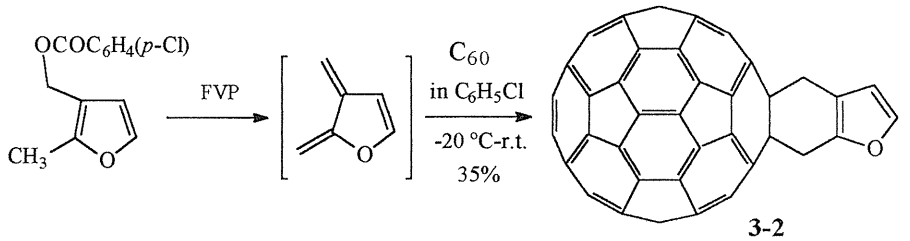


Fig. 3-1. Linking types of fullerene with heterocycles.



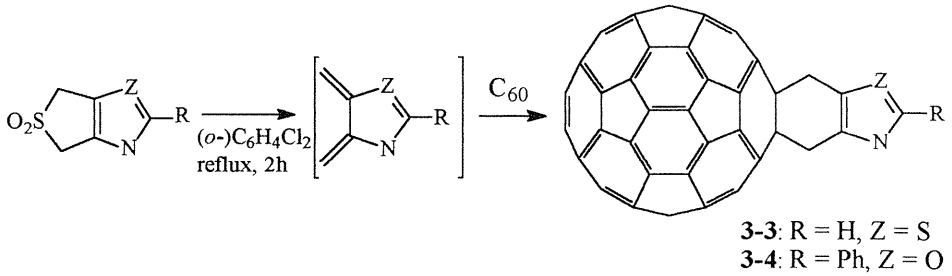
3-1

Fig. 3-2.



3-2

Fig. 3-3.



3-3: R = H, Z = S
3-4: R = Ph, Z = O

Fig. 3-4.

Fullerene derivatives **3-3** and **3-4** linked with thiazole ring and 2-phenyloxazole ring respectively were obtained in 51 and 39% yields respectively by the reaction of C_{60} with 4,5-dimethylene-4,5-dihydrothiazole and -2-phenyl-4,5-dihydrooxazole generated in situ from the corresponding sulfones (Fig. 3-4).[91] However, *N*-phenyl-2-oxazolidinone derivative **3-5** was not obtained by the reaction of C_{60} with N-phenyl-4,5-dimethylene-2-oxazolidinone[92] (Fig. 3-5), indicating limits to this approach. Indole and quinoxaline derivatives **3-6** and **3-7** were obtainable similarly in 48 anhd 27% yields respectively.

As the first example of the hetero Diels-Alder reaction, we have demonstrated that the reaction of C_{60} with *o*-quinone methide generated *in situ* from *o*-hydroxybenzylalcohol proceeds cleanly to yield a chroman-fused C_{60} derivative **3-8** (Fig. 3-6).[93] Thus, hetero atom-bonded ring fusion with C_{60} (Type II) is readily realized by the hetero Diels-Alder route. We

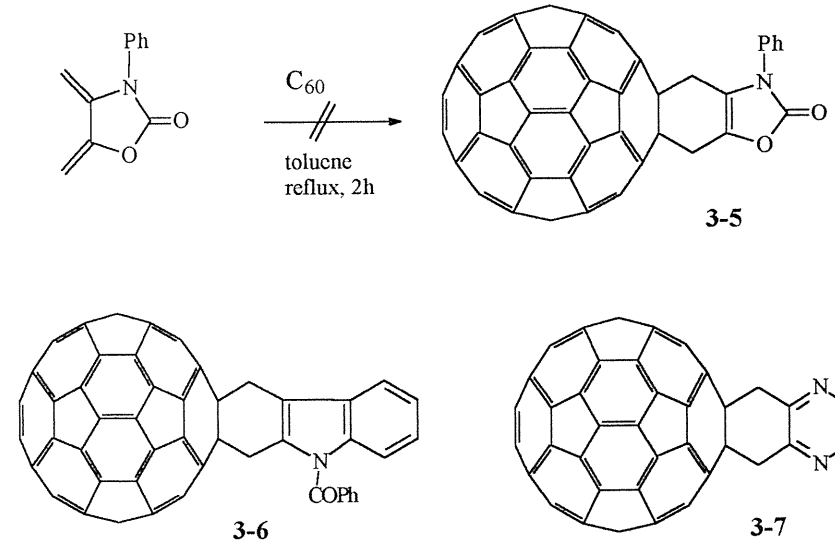


Fig. 3-5.

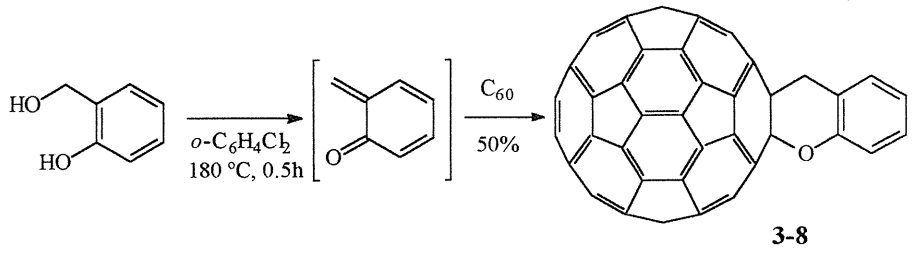


Fig. 3-6.

have extended to a thia analog and obtained a thiochroman-fused derivative **3-10** using *o*-thioquinone methide generated thermally from benzothiet[94] **3-9** (Fig. 3-7).[95] In the ^{1}H NMR spectrum, thiochroman **3-10** revealed the thiochroman ring methylene as doublet signals at δ 4.48 and 5.07, which coalesced at 80°C to indicate the equivalency of the methylene proton, and hence, compatibility with the assigned 6,6-fusion product. The corresponding $\Delta G^{\ddagger}$ is calculated as 16.2 kcal/mol. Sulfides are known to be oxidized to sulfoxides with singlet oxygen, and also the efficient generation of singlet oxygen by photosensitization with C_{60} is well known.[90] Therefore, the self-sensitized photooxygenation of **3-10** was attempted by bubbling oxygen into a toluene solution of **3-10** under irradiation. However, none of oxidation products were produced. The results can be rationalized in terms of steric inhibition of the second step based on a proposed bimolecular mechanism.[96] On the other hand, MCPBA oxidation afforded the corresponding sulfoxide **3-11** in 89% yield, which was further oxidized to the sulfone **3-12** under the same conditions (Fig. 3-7). As shown in Fig. 3-8,[97] dihydrothiopyran-fused fullerenes **13a-b** were obtained by the hetero Diels-Alder reaction of

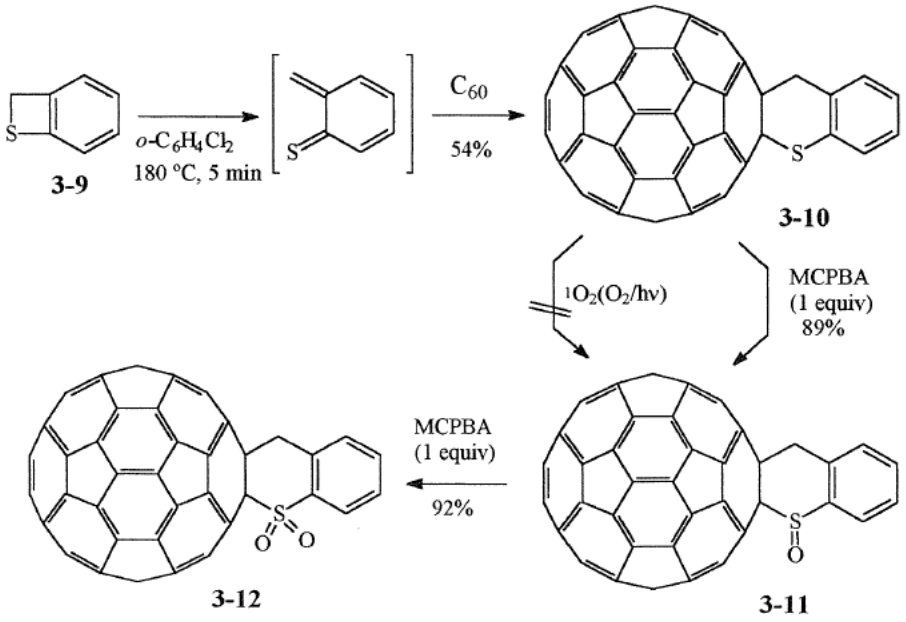


Fig. 3-7.

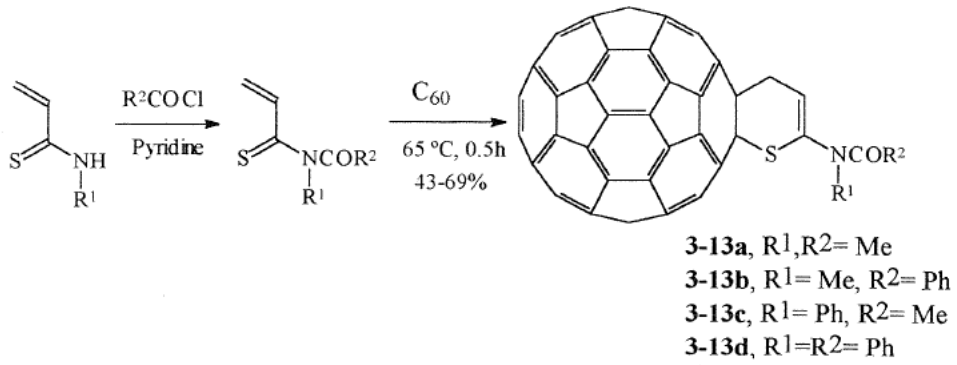


Fig. 3-8.

α,β-unsaturated thiocarbonyl compounds which are prepared *in situ* from thioacrylamides and acyl chloride.[98]

The hetero Diels-Alder reaction of C_{60} with 1,3-bis(silyloxy)-2-azadiene opened a facile route to pyridone-fused fullerenes (Fig. 3-9).[99] The cycloaddition of C_{60} with 1,3-bis(*t*-butyldimethylsilyloxy)-2-azadiene[100] took place cleanly at room temperature to afford *t*-butyldimethylsilyloxy pyridone **3-14** in a good yield after acid treatment at room temperature. Further treatment of **3-14** with acidic EtOH/$CHCl_3$ under reflux gave quantitatively the corresponding ethoxy derivative **3-15**. The ethoxy group was removed by Et_3SiH reduction

to give the pyridone-fused C_{60} **3-16** in high yield (Fig. 3-9). This compound may be a good precursor for a synthesis of novel δ-amino acid derivatives on the fullerene surface. The reaction with 1-thia-3-aza-1,3-diene[101] **3-17** gave exclusively azadiene adduct **3-18** (Fig. 3-10).

Heterocyclic five-membered ring fusion to C_{60} was achieved chiefly by 1,3-dipolar cycloadditions including diazoalkanes,[102] azides,[103,104] nitrile oxides,[105] nitrilimines,[106] azomethine ylides,[107,108] sulfinimides,[109] and cyclic dipoles.[110] Among many synthetically useful 1,3-dipoles, nitrones have not been reported to add fullerenes. In facts, we attempted to react C_{60} with several selected nitrones such as 2,2-dimethyl-3,4-dihydro-2*H*-pyrrole *N*-oxide and *N*-benzylidene-phenylamine *N*-oxide, however, stable adducts were not formed. On the other hand, trimethylsilyl nitronate, i.e.,*N*-trimethylsilyloxynitrone[111] generated *in situ*, reacted cleanly with C_{60} at room temperature to afford a 1:1 cycloadduct **3-19** which was isolated as [6,6]-fulleroisoxazoline **3-20** after acid treatment (Fig. 3-11). The nitrile oxide also gave fulleroisoxazolines[112] but this nitronate route provides an attractive complement and its further application is currently being investigation in our laboratory.

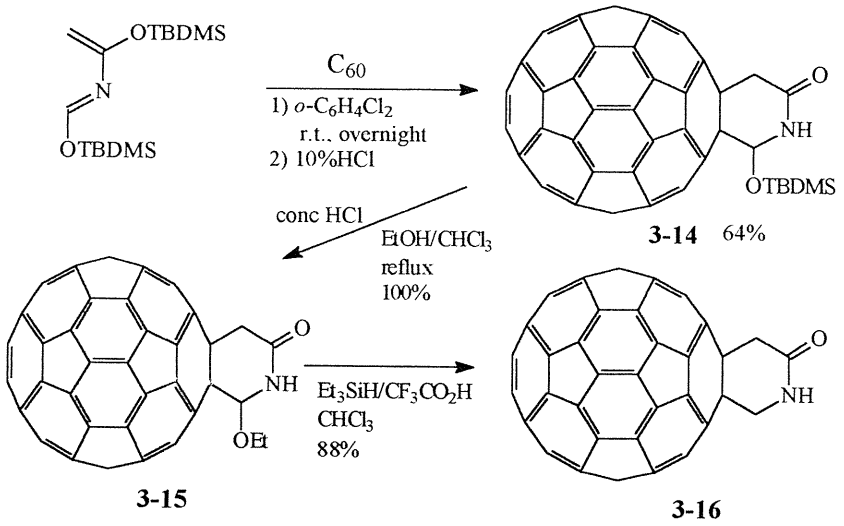


Fig. 3-9.

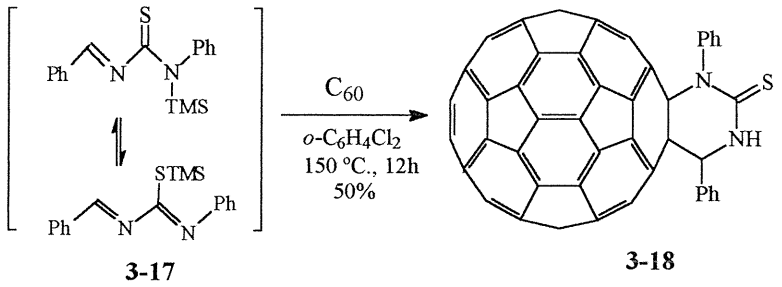
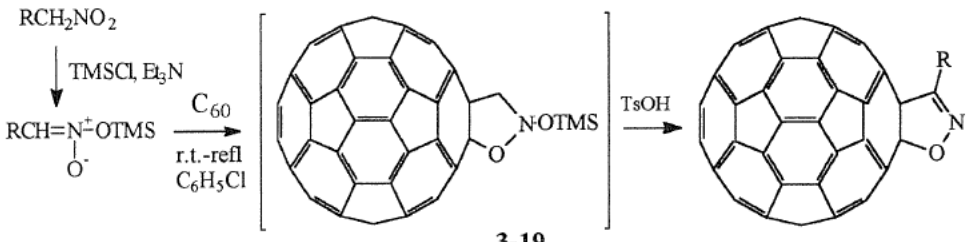
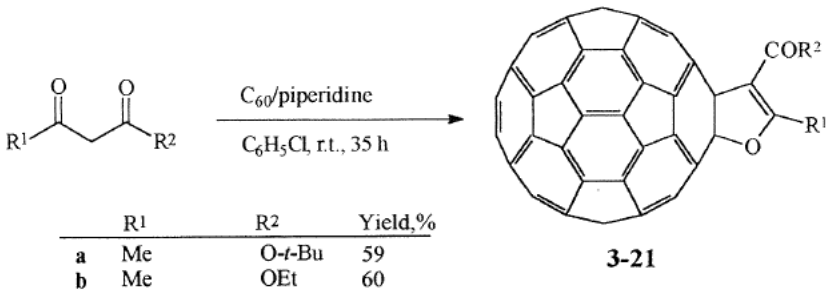


Fig. 3-10.



	R	Reaction Condn.	Yield,%
a	H	rt, 15 min	43
b	Me	rt, 3h	38
c	C_6H_5	refl, 5h	12
d	$CH_2CH_2CO_2Et$	rt, 3h	42
e	CH_2CH_2CN	rt, 3h	31
f	$CH_2CH_2CO_2H$	rt, 5h	23
g	$CH_2CH_2COCH_3$	rt, 4h	22

Fig. 3-11.



	R1	R2	Yield,%
a	Me	O-*t*-Bu	59
b	Me	OEt	60
c	-$C_6H_4(o)$-		39
d	CH_2CO_2Me	OMe	27
e	Me	Me	48
f	-$(CH_2)_3$-		49

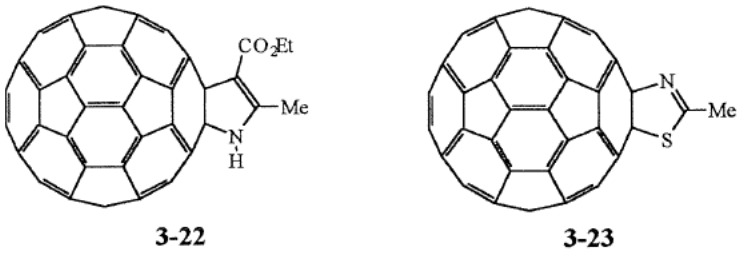


Fig. 3-12.

In addition to above well established 1,3-dipolar cycloaddition methods for synthesis of heterocycle-fused fullerenes, we have found novel formal [3+2] cycloadditions of β-dicarbonyl compounds to C_{60}; their ambiphilic nature is understood by the reaction with C_{60} in the presence of a base at both ends of the methylene carbon and carbonyl oxygen to give a dihydrofuran-fused C_{60} derivative after simultaneous oxidation (Fig. 3-12).[113] Cycloadditions of this type are known to occur with normal olefins if a metallic oxidant can initiate the reaction.[114] In contrast, the reaction with C_{60} proceeded without the aid of a metallic oxidizing reagent. Thus, the reaction was carried out simply by treating C_{60} with 1.5 equiv. of *t*-butyl acetoacetate as a typical example and 3 equiv. of piperidine in chlorobenzene at ambient temperature under a nitrogen atmosphere. After 1.5 days, standard work-up and chromatography afforded the dihydrofuran-fused fullerene **3-21a** in 59% yield together with C_{60} (40% recovery). As a base piperidine is superior to triethylamine which gave none of the expected product. Use of a catalytic amount of the base resulted in a high decreased yield. Use of ambient reaction temperature gave better results than reactions carried out at *ca.* 60°C. Although the mechanistic aspect of this novel cyclization is not clear at present, the reaction provides a unique formal oxidative [2+3] cycloaddition route, being useful for C_{60} heterocycle-fusion. As regards another examples of general binucleophilic systems HX=Y=ZH (X, Y, Z=C, N, O, S), we have examined the reactions of β-aminoacrylate ester and thioamide, which afforded [6,6]-4,5-dihydropyrrolino- and 4,5-dihydorothiazolino-fused fullerenes **3-22** and **3-23** in 10 and 52% yield respectively. These preliminary results suggest this novel oxidative cyclization is broadly applicable to the functionalization of fullerenes.

4. Molecular and Reagent Designs based on Hetero-Atom Compounds

4. 1. Synthesis of Nitrogen Heterocycles via Aza-Wittig Reaction

Phosphazo compounds contaning a nitrogen-phosphorus double bond (phospha-λ^5-azenes) **4-1** are called iminophosphoranes and were first prepared by the reaction of tertiary phosphines with organic azides (so-called Staudinger reaction) by Staudinger and Meyer more than seventy years ago. In 1950, Kirsanov prepared these phosphazo compounds by reaction of phosphorus pentachloride with amines (Kirsanov reaction). To date, various types of iminophosphoranes have been prepared and the related chemistry involving mechanistic and structural studies, synthesis and reactions of their derivatives and their synthetic applications have been developed. Their reaction with aldehyde or ketones affords the corresponding imines (the Wittig imination or aza-Wittig reaction) (Fig. 4-1.). However, in contrast to the Wittig olefination with phosphoranes (the Wittig reaction), synthetic application of the aza-Wittig reaction, in particular to heterocyclic synthesis, have been neglected until the successful intramolecular version (Fig. 4-2.) for bridgehead imine synthesis by us[56] drew the attention of synthetic chemists (see section 2. 4.). During the last 12 years, extensive studies have been reported on heterocyclic synthesis by utilizing aza-Wittig reaction. This review will focus on our very recent application of the aza-Wittig reaction, with emphasis on new synthesis of important nitrogen heterocycles.[115,116]

Iminophosphoranes as aza-ylides react both at the nitrogen (strongly nucleophilic) and the phosphorus (available vacant 3d-orbital) atoms. Therefore, derivatives of an iminophosphorane can be prepared with relative ease, in particular by using N-trimethylsilyl and/or P-alkoxyiminophosphoranes. However, one of the most fascinating reactions for heterocyclic synthesis is the imination of carbonyl compounds (Fig. 4-1.). The intramolecular version has drawn considerable attention because of its high potential in heterocyclic synthesis (Fig. 4-2.).[115,116]

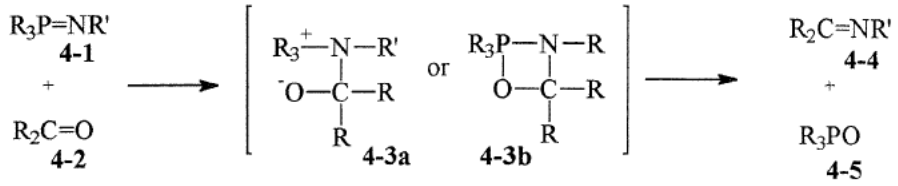


Fig. 4-1.

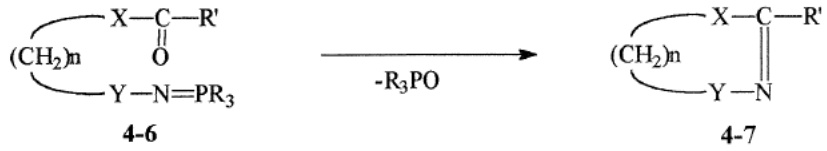


Fig. 4-2.

The cumulative experimental results reveals the following reactivity rules in the intramolecular aza-Wittig reaction:

(a) Chain length (product ring-size and ring strain factors): generally 5, 6, or 7-membered cyclic imines can be obtainable but 3- and 4-membered rings cannot because of excessive strain of the corresponding intermediate oxazaphosphetanes **4-3**.

(b) The reactivity of carbonyl group: in general, only aldehydes and ketones are sufficiently reactive but ester, amide, and imide carbonyls are also reactive depending on the chain length.

(c) Substituent groups on N and P: for Y = alkyl and aryl groups, the Wittig-imination occurs but for the case of Y = acyl, the corresponding nitriles are produced except for one example.[56] The substituent R on P has a considerable effect on the reactivity but the higher reactivity of tributylphosphine, for example, does not always results in better yields for heterocyclic synthesis because of side-reactions.

We have continued to develop new synthetic methods of important nitrogen heterocycles via intramolecular as well as intermolecular aza-Wittig reactions based on the above reactivity rules. Here we summarize briefly some of recent examples synthesized by aza-Wittig methodology as the key-step in Fig. 4-3. Lactams could be converted to a bridged imidazolone **4-8** via acylation and α-azidation followed by intramolecular aza-Wittig reaction.[117] A convenient short-step synthesis of rutecarpine **4-9** and tryptanthrin **4-10** as quinazoline alkaloids containing indole skeleton has been developed via intramolecular aza-Wittig reaction.[118] The former is an alkaloid of *Evodia rutaecarpa* and known as one of the constituents in the Chinese drugs 'Wou-Chou-Yu' and 'Shih-Hu', and the latter is antimycotic and known as the active principle of a traditional remedy in Okinawa against dermatophytic infections. Quinazolinone annelation of γ-lactam provided an efficient route to deoxyvasicinone **4-11**.[117] Bisquinazolinone annelation of bislactam via azidobenzoylation followed by intramolecular aza-Wittig reaction gave **4-12**, which gave 16-membered tetraazamacrocycle **4-13** via reductive ring-expansion.[119] Both optical isomers of quinazoline alkaloid vasicinone **4-14a** and **4-14b** were obtained by asymmetric oxidation of deoxyvasicinone **4-11**, while (*S*)-isomer was alternatively prepared by aza-Wittig method using 3(*S*)-hydroxy-γ-lactam as a chiral synthon.[120] An anticancer drug, batracyclin **4-15** was prepared by the aza-Wittig method as a mild new synthetic route.[121] 2,3-Disubstituted pteridinone derivatives **4-16** have been synthesized by

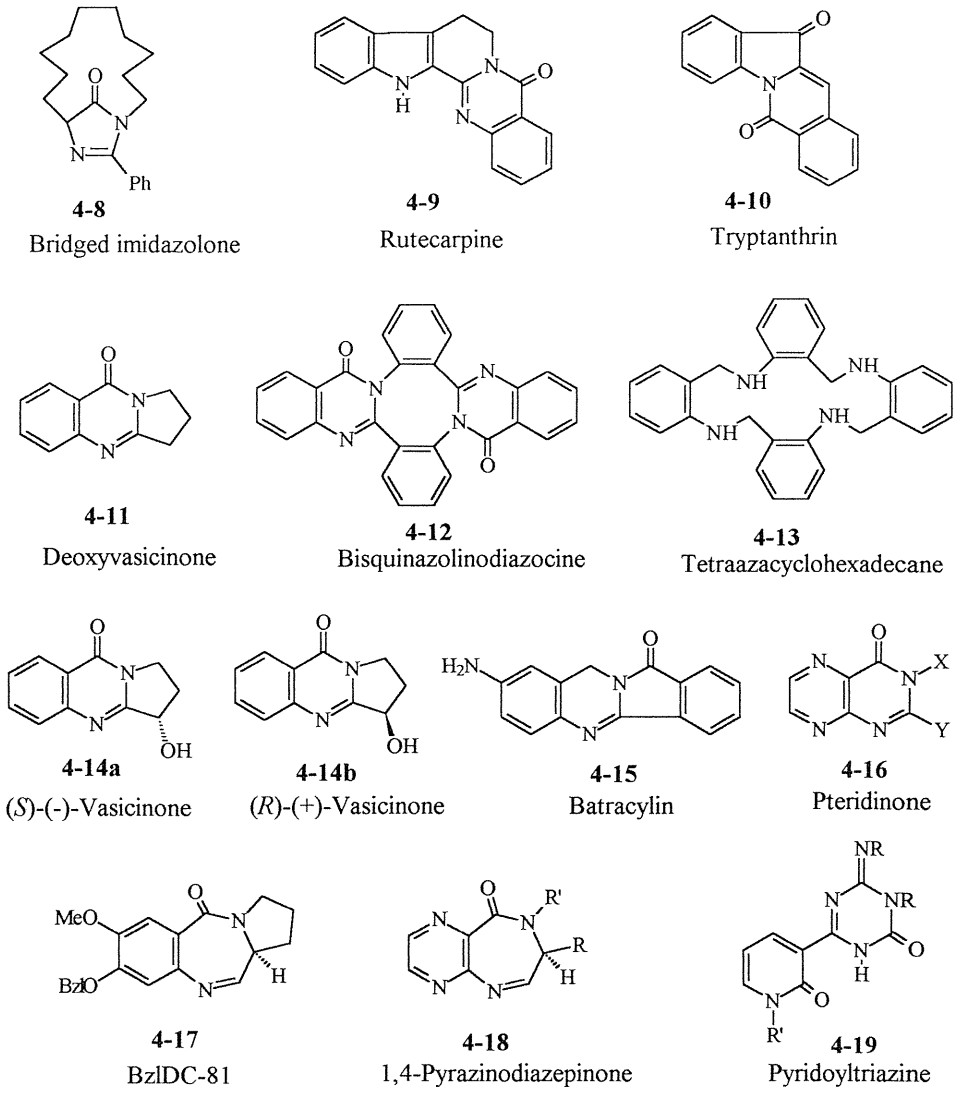


Fig. 4-3. Some examples of heterocycles and natural products prepared by aza-Wittig methodology.

intermolecular aza-Wittig reaction/heterocyclization sequence in one-pot procedure.[122] A new and efficient synthesis of an antitumer antibiotic BzlDC-81, **4-17** has been developed by intramolecular aza-Wittig route,[123] and also the same method has been extended to synthesis of a new type of diazepinones **4-18**.[125] The carbodiimide derived from 2-aminonicotinate via aza-Wittig reaction with arylisocyanate and primary amines underwent a novel ring-transformation presumably via [4+2]cycloaddition followed by ring-cleavage and recyclization to afford pyridoyltriazine derivative which structure was confirmed by X-ray crystallographic analysis.[125] These fruitful results may demonstrate that the aza-Wittig methodology provides a potent tool for synthesis of nitrogen heterocycles and heterocyclic natural products

such as alkaloids.

4. 2. Synthesis of New Synthetic Blocks for Organofluorine Compounds

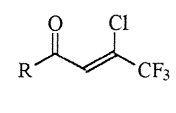
In view of rapidly growing role of organofluorine compounds particularly in material, pharmceutical and agrochemical science, organic synthesis of organofluorine compounds is becoming more important.[126] The success of the synthesis depends heavily on the availability of versatile fluorine-containing building blocks because introduction of fluorine and polyfluoroalkyl groups to organic molecules at the late stage of the synthesis still encounters technical and economical problems.[127] Therefore, we have been continuing to develop fluorine-containing building blocks from readily available starting materials and their application to molecular designs. In this memoir we discuss briefly our recent endeaver in this area.

Representative examples of prepared organofluorine compounds are listed in Fig. 4-4. We have developed a convenient method for preparation of β-chloro-β-(trifluoromethyl) α, β-unsaturated carbonyl compounds **4-20** using $RuCl_2(PPh_3)_3$ catalyst from trimethylsilyl enol ethers and CF_3CCl_3.[128] This compound was useful 1,3-dipolarophile as demonstrated by synthesis of β-(trifluoromethyl)pyrroles **4-24** via cycloaddition of Münchnones.[129] A novel difluoroallyl carbonyl compounds **4-21** were obtaioned by Ru(II)- or Cu(I)-induced radical reaction of $CF_2ClCCl_2\cdot$ from CF_2ClCCl_3 to silyl enol ethers, followed by reductive dechlorination of the adducts.[130]

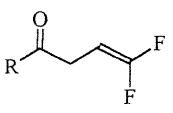
Various alkyl radicals generated by the photoreaction of a series of Barton ester reacted with 1,1-dichloro-2,2-difluoroethene to give radical adducts as the major product. These adducts were converted to the corresponding α,α-difluoroalkanecarboxylic acid and the methyl ester **4-22** by solvolysis with $AgNO_3/H_2O$-THF and $AgNO_3$/MeOH.[131] The compounds **4-22** are versatile starting materials for the synthesis of the difluoromethylene ketones and difluoroalkaneamides as difluromethylene analogs of peptides. By the same method, difluoro-γ-amino butyric acid **4-25** and difluoro-γ-lactam **4-26** were also synthesized.[131] The method was also successfully applied to synthesis of difluorocyclohexenone derivatives **4-29**, **4-30**, and **4-31** as novel fluorine-contaning synthetic blocks.[132]

As a useful synthetic block for trifluoromethylated compounds, 1,1,1-trifluoro-3-phenylsulfonylpropene **4-23a** has been prepared from methyl phenyl sulfone and nonexpensive ethyl trifluoroacetate.[133] 1,3-Dipolar cycloaddition of **4-23a** with nitrones yielded regio- and stereoselectively isooxazolidines **4-27** which were converted into trifluoromethylated *syn*-3-amino alcohols **4-28** by desulfonylation, followed by reductive cleavage of the N-O bond.[133] 5-Trifluoroacetylated 4-homoadamantanone **4-32** was readily obtainable by the reaction of 4-homoadamantanone and ethyl trifluoroacetate in the presence of sodium hydride.[134] This compound has been shown to be a convenient synthetic block for synthesis of homoadamantano[4,5]fused 5-, 6- and 7-membered heterocycles having trifluoromethyl group, **4-33** and **4-34**.[134,135]

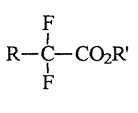
We have developed also synthetic routes to indolizidines, quinolizidines, and pyrrolizidines having trifluoromethyl group at the fusion-position using radical cyclization and acyliminium cyclization.[136] The Staudinger/aza-Wittig reaction of 6,6,6-trifluoro-5-oxohexanoyl azide with PPh_3 gave cyclic enamide **4-35**. After haloaralkylation, haloalkylation, or halobenzoylation of **4-35**, the haloalkyl derivatives were treated with Bu_3SnH with AIBN to give indolizidine and quinazolizidine derivatives **4-36**, **4-37**, **4-38**, **4-39**, and **4-40**. Cyclic tautomers, hydroxylactams, of 5,5,5-trifluoro-4-oxopentanoyl amides with N-aralkyl group gave pyrrolidine and quinolizidine derivatives **4-41** and **4-42** on treatment with trifluoromethanesulfonic acid.



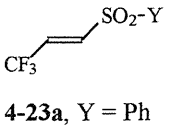
4-20



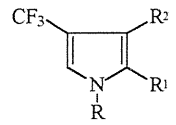
4-21



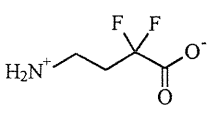
4-22



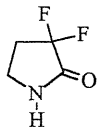
4-23a, Y = Ph
4-23b, Y = chiral auxiliary



4-24



4-25



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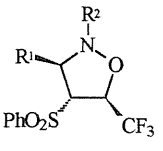
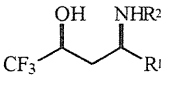


4-27



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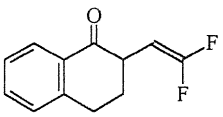
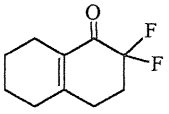
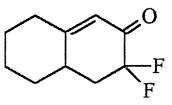


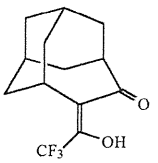
4-29



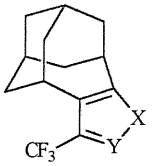
4-30



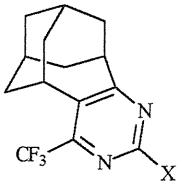
4-31



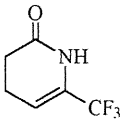
4-32



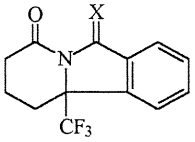
4-33a, X-Y = N-O
4-33b, X-Y = O- N
4-33c, X-Y = RN-N



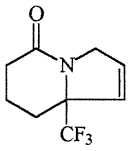
4-34



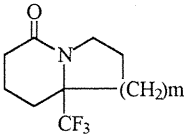
4-35



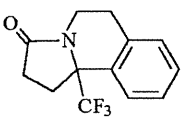
4-36, X= O
4-37, X= CH_2



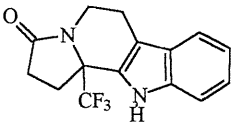
4-38



4-39, m = 1
4-40, m = 2



4-41



4-42

Fig. 4-4. Examples of fluorine-containing synthetic blocks prepared.

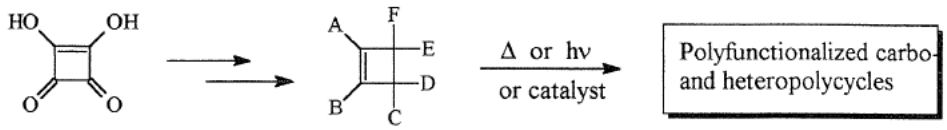
5. Small Ring Compounds as Versatile Synthetic Blocks

5. 1. *Introduction*

The unusual bonding of small ring compounds and the strain release associated with cleavage of cyclopropanes and cyclobutanes offer the possibility of recognizing that structural unit when it is a part of a larger molecule. These structural fragments may be considered as pseudofunctional group which may be chemoselectively manipulated. The structural and reactivity concepts have evolved into the developement of reagents that incorporate a cyclopropyl ring or a cyclobutyl ring into substrate to permit the developement of chain extension and annulations etc. From these viewpoints, chemistry of small ring compounds have drawn persistent attention for long time, and have been continued to be attractive work space for organic chemists.[137-140] One of the authors started synthetic and reactivity studies on aziridine and azirine as hetero-small ring compounds in 1962.[141] We also have started studies on chrysanthemic acid as a vinylcyclopropane system involved as the acid component of pyrethrin I in 1966, and have developed useful applications as a a^6 synthon, for example, to synthesis of modified isoprenoids.[142] In this memoir, we summarize briefly only our very recent efforts on developing squaric acid as versatile synthetic block for polyfunctionalized carbo- and heteropolycycles.[143]

5. 2. *Squaric Acid as New Synthetic Block for Polyfunctionalized Carbo- and Heteropolycycles*

Cyclobutenediones and cyclobutenones derived from squaric acid **5-1**, a commercially available four-membered oxocarbon, have recently utilized as C_4-synthon for highly substituted cyclic compounds (Fig. 5-1).[144] While squaric acid itself as one of nonbenzenoid 2π aromatic compounds has been studied theoretically and applied as a key component of advanced materials such as functional dyes, it also provides a wide variety of cyclobutenediones and cyclobutenones having multiple substitution patterns by virtue of its useful functionality.[145] Thus derived cyclobutenones may be convertible to target molecules by their regio- and stereoselective rearrangement. Current method of addition to squaric acid family relies on nucleophilic addition of organometallic reagents as summarized in Fig. 5-2. On the contrary, electrophilic reactions seem to be neglected except for Friedel-Crafts type arylation, and hence, we have examined electrophilic reaction of squaric acid family **5-2**, **5-3** with unsaturated organosilanes **5-4**. We found that squaric acid chlorides and diester reacted with a variety of unsaturated organosilanes in the presence of Lewis acid catalyst such as $TiCl_4$ to give addition and/or substitution products after dechlorosilylation either via 1,2- or1,4-mode of addition (Fig. 5-3).[146,147] The 1,2- vs. 1,4-addition selectivity can be controlled primarily by the presence of one substitutent on both **5-2** or **5-3** and **5-4**. 1,2-Addition occurs with chlorides, and 1,4-addition with diester. 1,4-Addition prevails over 1,2-addition if **5-4** is substituted doubly at the reactive site γ to a Si group. This addition mode is controlled also by



5-1 Squaric acid

Fig. 5-1.

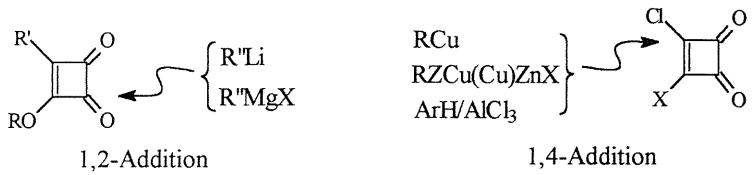


Fig. 5-2. Addition modes toward squaric acid family.

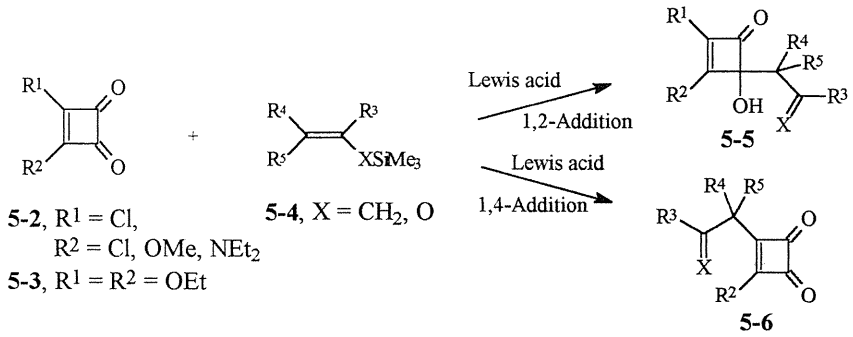


Fig. 5-3. Electrophilic additions of unsaturated organosilanes.

reaction temperature and the catalyst. Thus, readily obtained 4-allyl-2-chloro-4-hydroxycyclobutenones, after acetylation to **5-7** were subjected to thermolysis in an aromatic solvent under reflux. The rearrangement underwent cleanly via α,β-unsaturated chloroketene intermediate **5-8** to give bicyclo[3.2.0]heptenones **5-9** in good yields (Fig. 5-4).[148,149] On the other hand, the 4-acylmethyl-4-hydroxycyclobutenones **5-10** rearranged stereoselectively to γ-acylmethylenetetronates **5-13** with (*Z*)-geometry via **5-11** and **5-12** (Fig. 5-4).[148,149] As

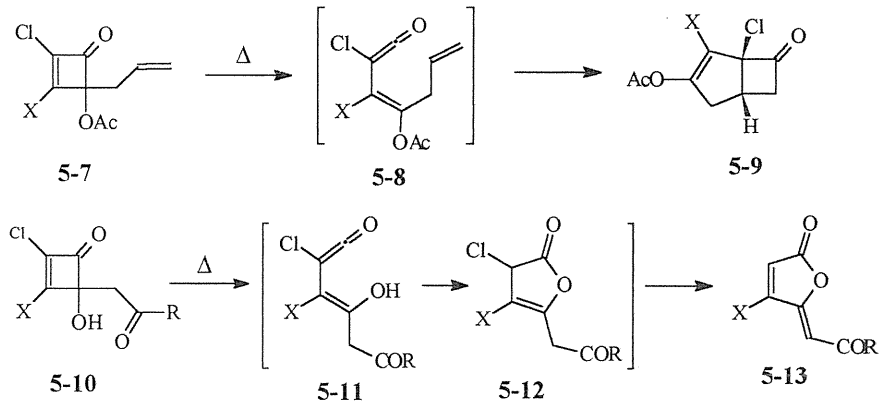
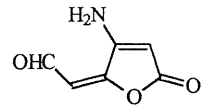
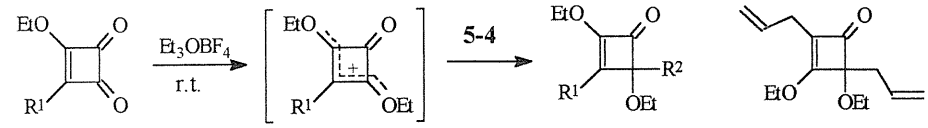


Fig. 5-4. Thermal rearrangements of chlorocyclobutenones.



5-14 (*E*)-Basidalin



5-3, R1 = OEt
5-15, R1 = alkyl, alkenyl, aryl, H

5-16

5-17, R2 = CN
5-18, R2 = CH_2COR

5-19

Fig. 5-5. Functionalization via ethoxycarbenium ion species.

for C_3-substituent on the cyclobutene ring, replacing of a methoxy group with an amino group reversed the stereochemistry of the product. This novel efficient route to tetronates was successfully applied to the total synthesis of (*E*)-basidalin **5-14**, isolated from *Leucoagaricus naucina*, and known to exhibit antibacterial and antitumor activities.[149,150]

A new type of addition reaction of organosilanes **5-4** to the diester **5-3** via unique ethoxycarbeniumu ion species **5-16** has been developed by the use of Meerwein's salt to furnish ethyl cyanation (**5-17**), acylmethylation (**5-18**), and ethyl allylation (**5-19**) (Fig. 5-5).[151,152] This method could be applicable to regioselective synthesis of 4-allyl-4-ethoxycyclobutenones **5-23** with alkyl, alkenyl, aryl, and alkynyl substituents at 2-position using Lewis acid catalysis from both 2,4- and 4,4-diethoxycyclobutenones **5-20** and **5-21** (Fig. 5-6). These products were cleanly transformed to the corresponding highly substituted bicyclo[3.3.0]heptenones **5-25** without appreciable side reactions (Fig. 5-6).[153,154] This methodology was successfully extended to synthesis of tricyclic ring systems **5-26** and **5-27**. Furthermore, the compound **5-26** was converted to an angular triquinane skeleton **5-28**, often found in bioactive triquinane sesquiterpenes via a regioselective ring-enlargement of the cyclobutanone moiety, demonstrating the synthetic utlity of above new functionalization of squaric acid derivatives/ring transformation sequences.[153,154] The Lewis acid promoted functionalization of **5-21** with phenyl(trimethylsilyl)acetylene afforded 4-alkynyl derivative **5-29** (R = Ph) as a normal substitution product (Fig. 5-7). However, the reaction with bis(trimethylsilyl)acetylene yielded 2-methylene-4-cyclopentene-1,3-dione derivative **5-30** (R = $SiMe_3$). Butyl(trimethylsilyl)acetylene gave both products. This unprecedent rearrangement resulted from novel 1,2-silyl migration followed by ring expansion of thus formed vinyl cation **5-32**. The ring expansion was nonstereospecific producing both *E*- and *Z*-isomers of 2-(1-silylalkylidene) cyclopentenediones. As for the mechanism, a ring-opening/5-exo trig. ring-closure pathway is suggested based on PM3 semiempirical calculation results.[143] To the best of our knowlege, the present 1,2-silyl migration is the first example in the alkynylsilane chemistry and for the ring-expansion reaction (Fig. 5-7). 2-Iodoalkylidenecyclopentene-1,3-dione derivatives **5-34** were also obtained by iodination of **5-29** presumably via ionic rearrangement of hypoiodite intermediate **5-35** (Fig. 5-8).[155]

We found novel oxidative rearrangement of 4-hydroxycyclobutenones **5-36** with lead tetraacetate affording 5-acetoxy-2(*5H*)-furanones (**5-41**) and 5-ylidene-2(*5H*)-furanones

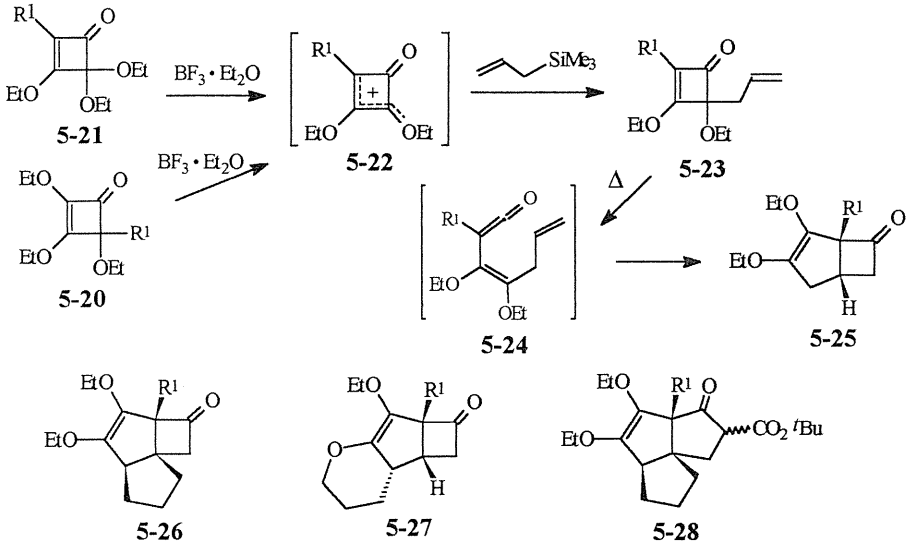


Fig. 5-6. Synthesis of 4-allyl-4-ethoxycyclobutenones and bicyclo[3.2.0]heptenones.

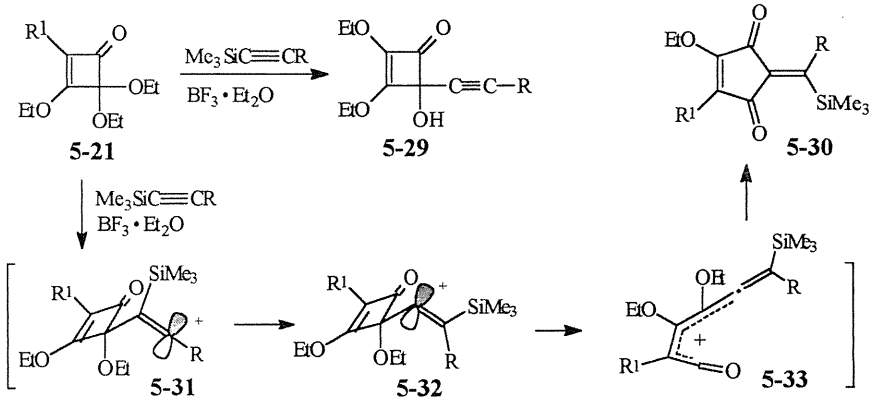


Fig. 5-7. 4-Alkynyl-4-hydroxycyclobutenones and 1,2-silyl migratory ring expansion.

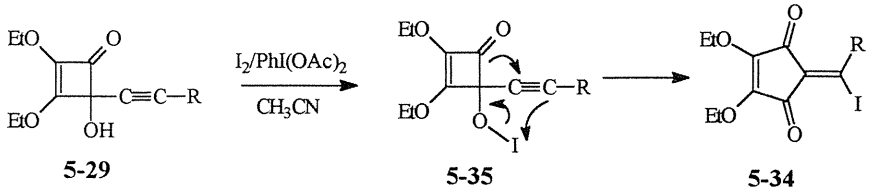


Fig. 5-8. Ring expansion of 4-alkynyl-4-hydroxycyclobutenones via hypoiodite.

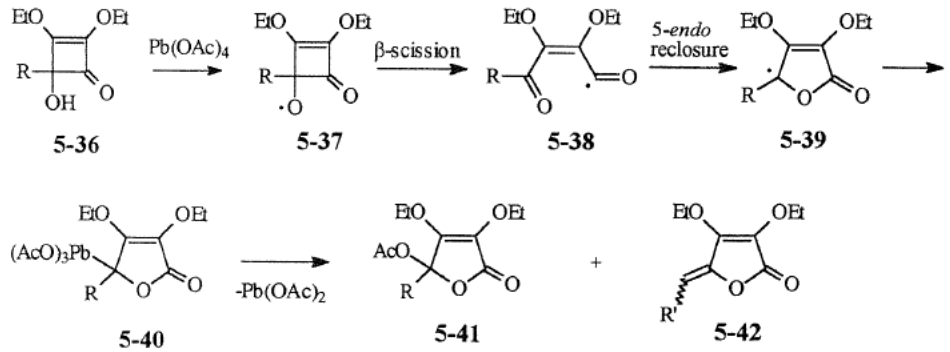


Fig. 5-9. Oxidative rearrangement of 4-hydroxycyclobutenones.

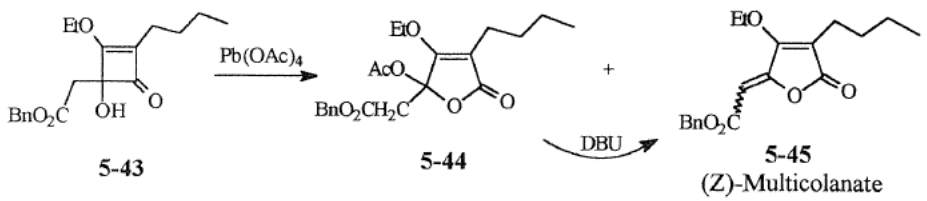


Fig. 5-10. Application to Synthesis of (*Z*)-Multicolanate.

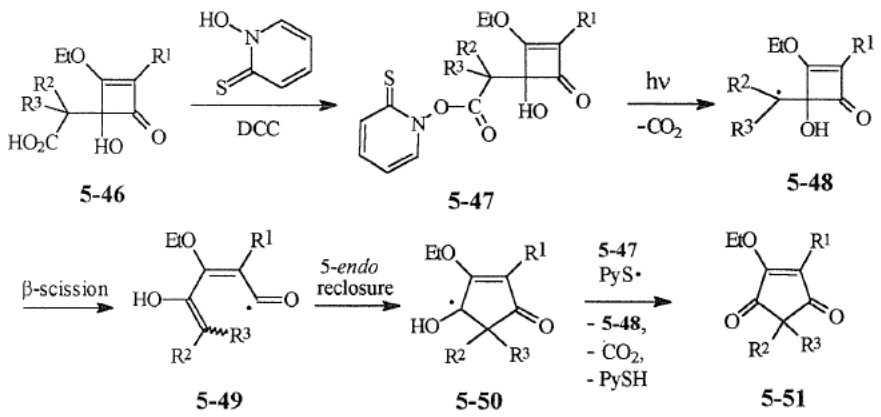


Fig. 5-11. Carbon-centered radical triggered rearrangement of hydroxycyclobutenone.

(**5-42**) (Fig. 5-9).[156,157] This new ring enlargement proceeds via oxy-radical triggered ring-opening (*β*-scission) and subsquent 5-*endo* reclosure. This novel rearrangement was extended to saturated 4-membered *α*-ketol and the versatility of above funanone synthetic method was demonstrated in the stereoselective synthesis of natural product, (*Z*)-multicolanate **5-45**[158] from **5-43** derived from diethyl squarate (**5-3**) (Fig. 5-10). A carbon-centered radical **5-48**

generated by photolysis of a mixed anhydride **5-47** (Barton's ester) of thiohydroxamic acid and 4-oxo-2-cyclobutenylacetic acid **5-46** was demonstrated to behave similarly, and afforded 4-cyclopentene-1,3-dione **5-51** rather than furanone as a rearranged product via similar β-scission to **5-49** followed by 5-*endo* recyclization to **5-50** and addition and elimination reactions (Fig. 5-11).[156,157] These novel radical-mediated rearrangements of cyclobutenones was explained most reasonably by a pentadienoyl radical to cyclopentenone radical cyclization or its oxa version as the significant key process based on semiemprical PM3 calculations. In addition, the radical-triggered ring opening of cyclobutenes and subsquent 5-*endo* ring closure is suggested to become a new general ring-expansion methodology.

6. Concluding Remarks

Building block methodologies provide viable solution for the assembly of highly functionalized molecules that would require lengthy steps using other methods. On the other hand, introduction of functional groups to starting material or available material is indispensable for developement of useful building blocks. From these viewponts, we have discussed on our efforts to design and synthesize novel carbo- and heteropolycycles focusing adamantane and related heterocyclic compounds in section 2, organic functionalization of [60]fullerene in section 3, iminophosphoranes and organofluorine compounds as selected hetero-atom compounds in section 4, and finally squaric acid derivatives as one of the small ring compound series in section 5. Our efforts have led to fruitful results making a great potential for use of our methods in general synthesis as well as for use of the derived compounds as novel fine chemical materials in various fields, particularly, in medicinal, pharmaceutical and agrochemical fields, because some interesting biological properties such as anti-mutagenic, NGF-activation, anticancer, antibacterial, antifungal, antiparkinsonian, and MAO-inhibitory etc were found among some of tested compounds. Details are not discussed here since these studies are still in progress in corporation with other institutes and it is beyond the scope of this memoir.

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References

1) Polastro, E. (1991). in "*Speciallity Chemicals*" (ed. B. Pearson), pp.1–13, Elsevier Applied Science, London.
2) Dresselhous, M. S.; Dresselhous, G.; Eklund, P. C. (1996). in "*Science of Fullerenes and Carbon Nanotubes*" Chapter 2, Academic Press, San Diego.
3) For example, see (1989). "*Strain and Its Implications in Organic Chemistry*" (ed. A. de Meijere, S. Blechert), Kluwer Academic Publisher, Dordrecht.
4) Greenberg, A.; Liebman, J. F. (1978). "*Strained Organic Molecules*" Academic Press, New York.
5) Gund, P.; Gund, T. M. (1981). *J. Am. Chem. Soc.* **103**, 4458–4465
6) Fort, Jr., R. C. (1976). in "*Adamantane, The Chemistry of Diamond Molecules*" Chapter 6, Marcel Dekker, New York.
7) Ganter, C. (1992). in "*Carbocyclic Cage Compounds*" (ed. E. Osawa, O. Yonemitsu), Chapter 10, VCH Publishers, New York.
8) Schleyer, P. v. R. (1957). *J. Am. Chem. Soc.* **79**, 3292.
9) Tominaga, K.; Hag, M. (1985). *Chemical Economy and Engineering Review*, **17**, 23–30.
10) Restani, P.; Galli, C. L. (1991). *Crit. Rev. Toxicol.*, **21**, 315–328.
11) Morita, Y.; Hesse, H.; Schmidt, H.; Banerji, A.; Chatterjee, A. (1977). *Helv. Chim. Acta* **60**, 1419–1435.
12) The Merck Index, (1996). 12th ed., 9382, and references cited therein.
13) Roll, D. M.; Biskupiak, J. E.; Mayne, C. L.; Ireland, C. M. (1986). *J. Am. Chem. Soc.* **108**, 6680–6682.
14) Eguchi, S.; Ohno, M. (1987). *Dyestuffs and Chemicals* **32**, 330–339.
15) Eguchi, S. (1986). *Nagoya University Chemical Instrument Center News* **5**, 1–2.
16) For example, see Sasaki, T.; Eguchi, S.; Katada, T.; Hiroaki, O. (1977). *J. Org. Chem.* **42**, 3741–3743.
17) Sasaki, T.; Eguchi, S.; Toru, T. (l969). *J. Am. Chem. Soc.*, **91**, 3390–3391.
18) Sasaki, T.; Eguchi, S.; Hiroaki, O. (1976). *J. Org. Chem.* **41**, 1803–1807.
19) Sasaki, T.; Eguchi, S.; Toru, T.; Itoh, K. (1972). *J. Am. Chem. Soc.* **95**, 1357–1360.
20) Sasaki, T.; Eguchi, S.; Hattori, S. (1978). *Tetrahedron* **34**, 67–71.
21) Sasaki, T.; Eguchi, S.; Hirako, Y. (1977). *J. Org. Chem.* **42**, 2981–2985.
22) Sasaki, T.; Eguchi, S.; Kiriyama, T. (1969). *J. Am. Chem. Soc.* **91**, 212–213.
23) Sasaki, T.; Eguchi, S.; Kiriyama, T. (1973). *J. Org. Chem.* **38**, 2230–2234.
24) Sasaki, T.; Eguchi, S.; Suzuki, T. (1982). *J. Org. Chem.* **47**, 5250–5255.
25) Eguchi, S.; Okano, T.; Takeuchi, T. (1987). *Heterocycles* **26**, 3265–3284.
26) Eguchi, S.; Takeuchi, H. (1986)). *J. Synth. Org. Chem., Jpn.* **44**, 726–735.
27) Ohno, M.; Ishizaki, K.; Eguchi, S. (1988). *J. Org. Chem.* **53**, 1285–1288.
28) Paquette, L. A.; Lagerwall, D. R.; Korth, H.-G. (1992). *J. Org. Chem.* **57**, 5413–5419.
29) Ohno, M.; Shimizu, K.; Ishizaki, K.; Sasaki, T.; Eguchi, S. (1988). *J. Org. Chem.* **53**, 729–733.
30) For example, see Shea, K. J. in ref. 3, pp.133–141.
31) Wiseman, J. R.; Pletcher, W. A. (1970). *J. Am. Chem. Soc.* **92**, 956–962.
32) Maier, W. F.; Schleyer, P. R. (1981). *J. Am. Chem. Soc.* **103**, 1891–1901.
33) Sellers, S. F.; Klebach, T. C.; Hollowood, F.; Jones, M., Jr. (1982). *J. Am. Chem. Soc.* **104**, 5492–5493.
34) Ohno, M.; Itoh, M.; Umeda, M.; Furuta, R.; Kondo, K.; Eguchi, S. (1996). *J. Am. Chem. Soc.* **118**, 7075–7082.
35) Martella, D. J.; Jones, M., Jr.; Schleyer, P. R.; Maier, W. F. (1979). *J. Am. Chem. Soc.* **101**, 7634–7637.
36) Sasaki, T.; Eguchi, S.; Hioki, T. (1978). *J. Org. Chem.* **43**, 3808–3810.
37) Sasaki, T.; Eguchi, S.; Ban, H. (1983). *J. Org. Chem.* **48**, 4073–4076.
38) Sasaki, T.; Eguchi, S.; Kiriyama, T. 1971, *Tetrahedron Lett.* 2651–2654.

39) Minamoto, K.; Azuma, K.; Tanaka, T.; Iwasaki, H.; Eguchi, S. (1988). *J. Chem. Soc. Perkin Trans. 1* 2955–2961.
40) Minamoto, K.; Azuma, K.; Hoshino, Y.; Eguchi, S. (1989). *Chem. Lett.* 825–828.
41) Sasaki, T.; Eguchi, S.; Yamada, S.; Hioki, T. (1982). *J. Chem. Soc. Perkin Trans. 1* 1953–1958.
42) Toru, T.; Kanefus, T.; Maekawa, E.; Ueno, Y.; Kondo, K.; Eguchi, S. (1988). *Bull. Chem. Soc. Jpn.* **61**, 2675–2677.
43) Sasaki, T.; Eguchi, S.; Suzuki, T. (1980). *J. Org. Chem.* **45**, 3824–3827.
44) Eguchi, S.; Furukawa, Y.; Suzuki, T.; Kondo, K.; Sasaki, T. (1985). *J. Org. Chem.* **50**, 1895–1899.
45) Sasaki, T.; Eguchi, S.; Suzuki, T. (1981). *Heterocycles* **15**, 251–254.
46) Eguchi, S.; Furukawa, Y.; Suzuki, T.; Sasaki, T. (1988). *J. Chem. Soc., Perkin Trans. 1* 719–723.
47) Eguchi, S.; Suzuki, T.; Toi, N.; Sasaki, T. (1990). *Heterocycles* **30**, 237–240.
48) Katada, T.; Eguchi, S.; Sasaki, T. (1986). *J. Org. Chem.* **51**, 314–320.
49) Katada, T.; Eguchi, S.; Esaki, T.; Sasaki, T. (1984). *J. Chem. Soc., Perkin Trans. 1* 1869–1874.
50) Katada, T.; Eguchi, S.; Esaki, T.; Sasaki, T. (1984). *J. Chem. Soc., Perkin Trans. 1* 2649–2653.
51) Katada, T.; Eguchi, S.; Sasaki, T. (1984). *J. Chem. Soc., Perkin Trans. 1* 2641–2647.
52) Sasaki, T.; Eguchi, S.; Esaki, T.; Suzuki, T. (1979). *Tetrahedron* **35**, 1073–1078.
53) Sasaki, T.; Eguchi, S.; Hirako, Y. (1976). *Tetrahedron Lett.* 541–544.
54) Sasaki, T.; Eguchi, S.; Hirako, Y. (1976). *Tetrahedron* **32**, 437–440.
55) Sasaki, T.; Eguchi, S.; Hattori, S. (1975). *Synthesis* 718–719.
56) Sasaki, T.; Eguchi, S.; Okano, T. (1983). *J. Am. Chem. Soc.* **105**, 5912–5913.
57) Sasaki, T.; Eguchi, S.; Toi, N. (1977). *Heterocycles* **7**, 315–320.
58) Sasaki, T.; Eguchi, S.; Toi, N. (1978). *J. Org. Chem.* **43**, 3810–3813.
59) Eguchi, S. (1993). *Japanese Scientific Monthly* **46**, 945.
60) Eguchi, S.; Asai, K.; Takeuchi, H.; Sasaki, T. (1987). *J. Chem. Soc., Perkin Trans. 1* 1171–1175.
61) Eguchi, S.; Ogura, I.; Terada, Y. (1995). *Heterocyclic Commun.* **1**, 365–373.
62) Yu, Y.; Ohno, M.; Eguchi, S. (1991). *Tetrahedron Lett.* **32**, 4965–4968.
63) Yu, Y.; Ohno, M.; Eguchi, S. (1993). *Tetrahedron* **49**, 823–832.
64) Yu, Y.; Ohno, M.; Eguchi, S. (1994). *J. Chem. Soc., Chem. Commun.* 331–332.
65) Yu, Y.; Ohno, M.; Eguchi, S. (1994). *J. Chem. Soc., Perkin Trans. 1* 4965–4968.
66) Yu, Y.; Ohno, M.; Eguchi, S. (1995). *Synthesis* 498–500.
67) Yu, Y.; Ohno, M.; Eguchi, S. (1991). *Heterocyclic Commun.* **1**, 365–373.
68) Yu, Y. (1966). PhD Thesis, Nagoya University.
69) Eguchi, S., Ohno, M., (1993). *Kikan Fura-ren*, **1**(3), 99–113.
70) Hirsch, A. (1994). "*The Chemistry of Fullerenes*", Georg Thieme Verlag, Stuttgart.
71) (1994). in "*Fullerenes*", (ed. K. M. Kadish, R. S. Ruoff), The Electrochemical Society Inc., Pennington, Chapt. IX. (Organic Functionalization).
72) (1995). "The Chemistry of Fullernes", (ed. R. Taylor), World Scientific, Singapore.
73) Williams, R. M.; Zwier, J. M.; Verhoeven, J. W. (1995). *J. Am. Chem. Soc.* **117**, 4093–4099, and references cited therein.
74) Scrivens, W. A.; Tour, J. M.; Creek, K. M.; Pirisi, L. (1994). *J. Am. Chem. Soc.* **116**, 4517–4518, and references cited therein.
75) Lamparth, I.; Herzog, A.; Hirsch, A. (1996). *Tetrahedron* **52**, 5065–5075.
76) Eguchi, S.; Ohno, M. (1994). *Tannsokurasuta-nyu-su* **2**(1), 42.
77) Ohno, M.; Shibata, S.; Eguchi, S. (1995). *Fullerene Sci. Tech.* **3**(1), 29–35.
78) Ohno, M.; Azuma, T.; Kojima, S.; Shirakawa, Y.; Eguchi, S. (1996). *Tetrahedron* **52**, 4983–4994.
79) Lamparth, I.; Nuber, B.; Schick, G.; Skiebe, A.; Grösser, T.; Hirsch, A. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 2257–2259.
80) Sliwa, W. (1993). *Fullerene Sci. Tech.* **3**, 243–281. (a recent review on cycloadditions)

81) For example, see Gügel, A.; Kraus, A.; Spikermann, J.; Belik, P.; Müllen, K. (1994). *Angew. Chem., Int. Ed. Engl.* **33**, 559–560.
82) An, Y.-Z.; Anderson, J. L.; Rubin, Y. (1993). *J. Org. Chem.* **58**, 4799–4798.
83) Prato, M.; Suzuki, T.; Foroudian, H.; Khemani, Q. Li. K.; Wudl, F.; Leonetti, J.; Little, R. D.; White, T.; Rickborn, B.; Yamago, S.; Nakamura, E. (1993). *J. Am. Chem. Soc.* **115**, 1594–1595.
84) Belik, P.; Kraus, A.; Gügel, A.; Spickermann, J.; Walter, M.; Beer, F.; Müllen, K. (1994). in Ref 3, pp.701–712.
85) Belik, P.; Gügel, A.; Kraus, A.; Walter, M.; Beer, F.; Müllen, K. (1995). *J. Org. Chem.* **60**, 3307–3310.
86) Chadwick, D. K.; Plant, A. (1987). *Tetrahedron Lett.* **28**, 6085–6088.
87) Ohno, M.; Koide, N.; Eguchi, S. (1995). *Heterocyclic Commun.* **1**, 125–128.
88) Trahanovsky, W. S.; Hunang, Y.-C.; Leung, M.-K., J. Org. Chem., **1994**, *59*, 2594–2598.
89) Ohno, M.; Koide, N.; Eguchi, S. (1995). *69th Annual Meeting of Chem. Soc. Jpn.* Abstract Papers, II, p.1346, Kyoto, 1995.
90) For photooxygenation with O_2/C_{60}, see Tokuyama, H.; Nakamura, E. (1994). *J. Org. Chem.* **59**, 1135–1138 and references cited therein.
91) Chou, T.-s.; Chen, H.-C.; Tsai, C.-Y. (1992). *Tetrahedron Lett.* **33**, 4201–4204.
92) Hernandes, R.; Sanchez, J. M.; Gomez, A.; Trujillo, G.; Aboytes, R.; Zepeda, G.; Bates, R. W.; Tamariz, J. (1993). *Heterocycles* **36**, 1951–1956.
93) Ohno, M.; Azuma, T.; Eguchi, S. (1993). *Chem. Lett.* 1832–1833.
94) Kanakarajan, K.; Meier, H. (1983). *J. Org. Chem.* **48**, 881–883.
95) Ohno, M.; Kojima, S.; Eguchi, S. (1995). *Tetrahedron Lett.* **36**, 6899–6872.
96) Past, D. J.; Cottard, F.; Jumelle, L. (1994). *J. Am. Chem. Soc.* **116**, 8978–8984.
97) Ohno, M.; Kojima, S.; Eguchi, S. (1995). *J. Chem. Soc., Chem. Commun.* 565–566.
98) Barnish, I. T.; Fishwick, C. W. G.; Hill, D. R.; Szantay, Jr., C. (1989). *Tetrahedron Lett.* **30**, 4449–4452.
99) M. Ohno, Kojima, S.; Yashiro, A.; Eguchi, S., 9th Fullerene Symposium, Abstract Paper, p.65, 1995, Yokohama.
100) Sainte, F.; S.-Poncin, B.; H.-frisque, A-M.; Ghosez, L. (19982). *J. Am. Chem. Soc.* **104**, 1428–1430.
101) Barluenga, J.; Thomas, M.; Ballesterous, A.; Lopez, A. (1995). *Synthesis* 985–988.
102) Smith III, A. B.; Strongin, R. M.; Brard, L.; Furst, G. T.; Romanov, W. J.; Owens, K. G.; King, R. C. (1993). *J. Am. Chem. Soc.* **115**, 5829–5830.
103) Prato, M.; Li, Q.; Wudl, F.; Lucchini, V. (1993). *J. Am. Chem. Soc.* **115**, 1148–1150.
104) Grosser, T.; Prato, M.; Lucchini, V.; Hirsch, A.; Wudl, F. (1995). *Angew. Chem., Int. Ed. Engl.* **34**, 1343–1345.
105) Meier, M. S.; Poplawska, M., (1993). *J. Org. Chem.* **58**, 4524–4525.
106) Matsubara, Y.; Tada, H.; Nagase, S.; Yoshida, Z. (1995). *J. Org. Chem.* **60**, 5372–5373.
107) Maggini, M.; Scorrano, G.; Prato, M. (1993). *J. Am. Chem. Soc.*, **115**, 9798–9799.
108) Shu, L.-H.; Wang, G.-W.; Wu, S.-H.; Wu, H.-M.; Lao, X.-F. (1995). *Tetrahedron Lett.* **36**, 3871–3874.
109) Brizzolara, D.; Ahlemann, J. T.; Roesky, H. W.; Keller, K. (1993). *Bull. Soc. Chim. Fr. 130,* 745–747.
110) Duczek, W.; Niclas, H.-J. (1995). *Tetrahedron Lett.* **36**, 2457–2460.
111) Torssell, K. (1978). *Acta, Chem. Scand.* **B32**, 118–124.
112) Meier, M. S.; Poplawska, M. (1996). *Tetrahedron* **52**, 5043–5052.
113) Baciocchi, E.; Ruzziconi, R. (1991). *J. Org. Chem.* **56**, 4772–4778.
114) Ohno, M.; Yashiro, A.; Eguchi, S. (1996). *J. Chem. Soc., Chem. Commun.*, 291–292.
115) Eguchi, S.; Matsushita, Y.; Yamashita, K. (1992). *Org. Prep. Proced. Int.* **24**. 209–243.
116) Eguchi, S.; Okano, T. (1993). *J. Synth. Soc., Jpn.* **51**, 203–211.
117) Takeuchi, H.; Hagiwara, S.; Eguchi, S. (1989). *Tetrahedron* **45**, 6375–6386.
118) Eguchi, S.; Takeuchi, H.; Matsushita, Y. (1992). *Heterocycles* **33**, 153–156.

119) Eguchi, S.; Matsushita, Y.; Takeuchi, H. (1992). *J. Org. Chem.* **57**, 6975–6979.
120) Eguchi, S.; Suzuki, T.; Okawa, T.; Matshihita, Y.; Yashima, E.; Okamoto, Y. (1996). *J. Org. Chem.* **61**, (in press).
121) Eguchi, S.; Goto, S. (1995). *Heterocyclic Commun.* **1**, 51–54.
122) Okawa, T.; Eguchi, S.; Kakehi, A. (1996). *J. Chem. Soc., Perkin Trans. 1* 247–254.
123) Eguchi, S.; Yamashita, K.; Matsushita, Y.; Kakehi, A. (1995). *J. Org. Chem.* **60**, 4006–4012.
124) Okawa, T.; Eguchi, S. (1996). *Tetrahedron Lett.* **37**, 81–84.
125) Okawa, T.; Osakada, N.; Eguchi, S.; Kakehi, A. (1996). Submitted for publication.
126) Welch, J. T. (1991). in "*Selective Fluorination in Organic and Bioorganic Chemistry*" ACS Symposium Series 456, Washington, D. C.
127) For example, see Takeuchi, Y. (1988). *J. Synth. Org. Chem., Jpn.* **46**, 145–159.
128) Okano, T.; Uekawa, T.; Sawaki, H.; Eguchi, S. (1990). *Synlett* 403–404.
129) Okano, T.; Uekawa, T.; Morishima, N.; Eguchi, S. (1991). *J. Org. Chem.* **56**, 5259–5262.
130) Okano, T,; Shimizu, T.; Sumida, K.; Eguchi, S. (1993). *J. Org. Chem.* **58**, 5163–5166.
131) Okano, T.; Takakura, N.; Nakano, Y.; Okajima, A.; Eguchi, S. (1995). *Tetrahedron* **51**, 1903–1920.
132) Ishihara, H. (1995). Master Thesis, Nagoya University.
133) Tsuge, H.; Okano, T.; Eguchi, S. (1995). *J. Chem. Soc., Perkin Trans. 1* 2761–2766.
134) Umada, A.; Okano, T.; Eguchi, S. (1994). *Synthesis* 1457–1462.
135) Eguchi, S.; Umada, A.; Okano, T. (1996). *Heterocycles* 42, 333–339.
136) Okano, T.; Sakaida, T.; Eguhci, S. (1996). *J. Org. Chem.* submitted for publication.
137) (1986). "*Topics in Current Chemistry*", (ed. A de Meijere), **133**, Springer-Verlag, Berlin.
138) (1987). "*Topics in Current Chemistry*", (ed. A de Meijere), **135**, Springer-Verlag, Berlin.
139) (1988). "*Topics in Current Chemistry*", (ed. A de Meijere), **144**, Springer-Verlag, Berlin.
140) (1990). "*Topics in Current Chemistry*", (ed. A de Meijere), **155**, Springer-Verlag, Berlin.
141) Eguchi, S.; Ishii, Y. (1963). *Bull. Chem. Soc.* Jpn. **36**, 1434–1437.
142) Ohno, M.; Matsuoka, S.; Eguchi, S. (1986). *J. Org. Chem.* **51**, 4553–4558, and its preceding papers.
143) Yamamoto, Y. (1996). PhD Thesis, Nagoya University.
144) Moore, H. W.; Yerxa, B. R. (1992). *Chemtracts: Org. Chem.* **5**, 273–313.
145) West, R. (1980). "*Oxocarbons*", Academic Press, New York.
146) Ohno, M.; Yamamoto, Y.; Eguchi, S. (1991). *J. Chem. Soc., Perkin Trans. 1* 2272–2273.
147) Ohno, M.; Yamamoto, Y.; Shirasaki, Y.; Eguchi, S. (1993). *J. Chem. Soc., Perkin Trans. 1* 263–269.
148) Ohno, M.; Yamamoto, Y.; Eguchi, S. (1993). *Tetrahedron Lett.* **34**, 4807–4810.
149) Yamamoto, Y.; Ohno, M.; Eguchi, S. (1994). *Tetrahedron* **50**, 7783–7798.
150) Iinuma, H.; Nakamura, H.; Iitaka, Y.; Obayashi, A. (1983). *J. Antibiot.* **36**, 448–450.
151) Yamamoto, Y.; Nunokawa, K.; Ohno, M.; Eguchi, S. (1993). *Synlett* 781–783.
152) Yamamoto, Y.; Nunokawa, K.; Okamoto, K.; Ohno, M.; Eguchi, S. (1995). *Synthesis* 571–576.
153) Yamamoto, Y.; Ohno, M.; Eguchi, S. (1995). *Chem. Lett.* 525–526.
154) Yamamoto, Y.; Ohno, M.; Eguchi, S. (1996). *Bull. Chem. Soc. Jpn.* **69**, 1353–1362.
155) Yamamoto, Y.; Ohno, M.; Eguchi, S. (1995). *Tetrahedron Lett.* **36**, 5539–5542.
156) Yamamoto, Y.; Ohno, M.; Eguchi, S. (1994). *J. Org. Chem.* **59**, 4707–4709.
157) Yamamoto, Y.; Ohno, M.; Eguchi, S. (1995). *J. Am. Chem. Soc.* **117**, 9653–9661.
158) Begley, M. J.; Gedge, D. R.; Pattenden, G. (1978). *J. Chem. Soc., Chem. Commun.*, 60–61.