

行政院國家科學委員會補助專題研究計畫 成果報告
 期中進度報告

利用倍半雙環[2.2.2]辛烯稠合醌與共軛雙烯的環化反應製成分子夾

Preparation of molecular clips through cycloaddition of
sesquibicyclo[2.2.2]octenyl-fused quinones with conjugated dienes.

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執行單位：東海大學 化學系

中 華 民 國 97 年 10 月 27 日

Abstract

1,4-benzoquinone can incorporate into bicyclo[2.2.2]octenes to form new dienophiles for construction of a variety of polycarbocycles containing face-to-face ethylene bridges.

Sesquibicyclo[2.2.2]octenes having exocyclic 1,3-butadienes undergo readily cycloaddition with naphthoquinone to form anthracene grafted spacer molecules. Transannular interactions of grafted chromophores with parallel ethylene bridges are observed by UV absorption and NMR analyses.

Keywords. bicyclo[2.2.2]octenes, laticyclic conjugation, anthraquinones.

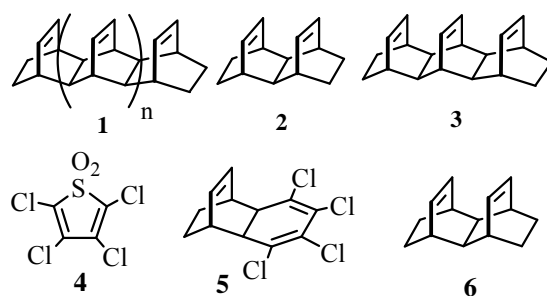
摘要

1,4-苯醌與雙環[2.2.2]辛烯併合可形成一種新的親雙烯化合物，進而建構一系列具有面對面乙烯架橋的多碳環。含有環外1,3-丁二烯的倍半雙環[2.2.2]辛烯很容易和萘醌進行環化加成反應，而最後形成蔥稠合的隔間分子。利用紫外線與核磁共振光譜分析可觀察雙環[2.2.2]辛烯分子架構中併合的發色團與平行乙烯架橋間的跨環交互作用。

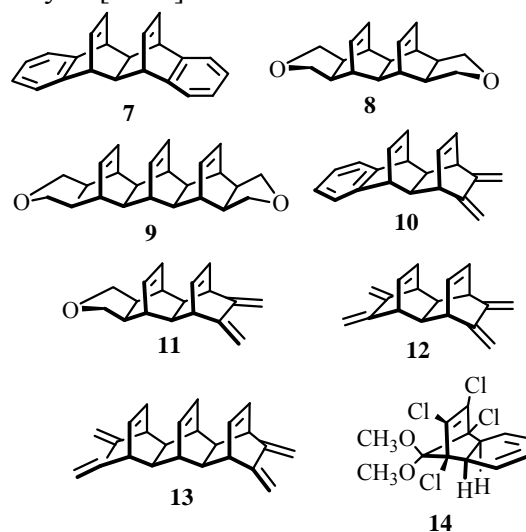
關鍵詞：雙環[2.2.2]辛烯、緯環式共軛、蔥醌。

Introduction

Rigid molecules with two double bonds facing each others in close proximity represent the simplest laticyclic conjugated systems.¹ X-ray structural analyses show that the distance between the facing double bonds in condensed bicyclo[2.2.2]octenes (**1**) is close to 3.04 Å.² Photoelectron excitation spectroscopic analyses and chemical properties of the all-syn oligocondensed bicyclo[2.2.2]octenes **1** with two to six ethylene bridges indicate the presence of laticyclic conjugation.² Molecular modeling shows that these systems have carbon framework of curved topology as polynorboranes³ and hetero-bridged [n]polynorbornanes.⁴ The trajectory surface of bridges is suitable for the study of laticyclic orbital interactions.⁵ Such compounds can also be utilized as the molecular spacer or intercalator in the



donor-bridge-acceptor systems for the studies of electron transfer or energy transfer.⁶ The syntheses of bicyclo[2.2.2]octenes **2-3** were performed from the Diels-Alder reaction of tetrachlorothiophene dioxide⁷ (**4**) with dihydrobarrelene followed by SO₂ extrusion. The resulting cycloadduct **5** underwent repeatedly cycloaddition with dihydrobarrelene to provide **3** with all-syn configuration after dechlorination with sodium. This concept was further applied to the cycloaddition of sesquibicyclo[2.2.2]octadiene **6** with tetrachloride **5** and extended to the synthesis of oligocondensed bicyclo[2.2.2]octenes with laticyclic conjugation six bridges in the bicyclo[2.2.2]octenes units.



Previously, we have described the synthesis of sesqui- and sesterbicyclo[2.2.2]octene derivatives **6-9**⁸ that are composed of bicyclo[2.2.2]octene units having all the bridged double bonds positioned on the same face in close proximity² and reported the results of transannular photocyclizations and brominations between the double bonds in these systems. Carbocyclic molecules grafted by the exocyclic *s-cis*-butadiene units can be used as ligands for the preparation of metal complexes⁹ and as building blocks for the

construction of bridged polycyclic systems via Diels-Alder cycloaddition with dienophiles.¹⁰ Along this line, we have also synthesized *syn*-sesquibicyclo[2.2.2]octenes that are attached with one or bilaterally two exocyclic *s-cis*-butadiene units, such as **10-13**¹¹⁻¹² and shown that they reacted well with dienophiles resulting in the formation of corresponding cycloadducts in good yields.¹³ Sesquibicyclo[2.2.2]octane grafted with dienophiles such as maleic anhydride¹³ or *p*-benzoquinone¹⁴ are shown to proceed highly π -facial diastereoselectivity in Diels-Alder reaction. Such structures of the products would provide a new insight in repetitive Diels-Alder cycloaddition for construction of U-shaped cavity molecules such as molecular tweezers and clips¹⁵ and macrocycles.¹⁶

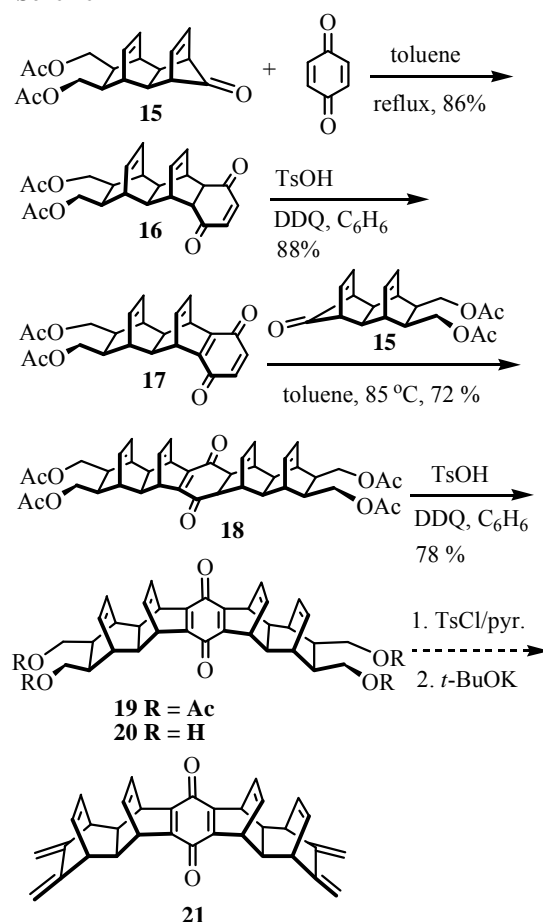
To extend these excellent results, we decided to investigate if such π -facial stereoselectivity could also take place in the reactions of sesquibicyclo[2.2.2]octenyl *p*-benzoquinones with conjugated exocyclic 1,3-butadien **12**. The stereochemical outcome from the Diels-Alder reactions of **6** with different quinone dienophiles will produce new types of molecular clips after transformation of cyclohexendione to a planar *p*-benzoquinone or benzene ring intercalator. In addition, we also report the synthesis of bisquinolino-fused sesquibicyclo[2.2.2]octane from Friedlander reaction and describe the detection of intramolecular π orbital interactions by UV absorption.

Results and Discussion

I. Preparation of 1,4-benzoquinone **21**.

The arc-shaped clip molecule **21**, containing a *p*-benzoquinone spacer unit and bilateral exocyclic 1,3-butadienes is suitable for studies of π -facially stereoselective [4 + 2] cycloaddition. The novel stereochemistry outcomes and their ribbon-type concave topology define a cavity in which a substrate molecule can be bounded by multiple non-covalent interactions.¹⁷ Cycloaddition of *p*-benzoquinone (*p*-BQ) with diacetate **15** which could be obtained from 1,8,9,10-tetrachloro-11,11-dimethoxy-*endo*-tricyclo[6.2.1.0^{2,7}]undeca-3,

Scheme 1



5,9-triene (**14**) during the synthesis of tetracyclic hexaene **12** gave cycloadduct **16** in good yield as shown in scheme 1.

Enolization of cyclohexene-1,4-dione of the resulting cycloadduct **16** followed by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation afforded sesquibicyclo[2.2.2]octene fused *p*-benzoquinone **17**. Cycloaddition of the 1,4-benzoquinone moiety of **17** with the cyclohexadiene moiety generated in situ through a thermal decomposition of diacetate **15** furnished tetraacetate **18** as the only product. The highly stereoselective cycloaddition was resulted from the syn-face of 1,4-benzoquinone moiety of **17** approached by Alder's rule toward the cyclohexadiene face from less hindered exo position. The structural identification was further confirmed after the next oxidation step. Treatment of the 1,4-Cyclohexendione ring intercalated between two sesquibicyclo[2.2.2]octenes of **18** with DDQ in toluenesulsonic acid benzene solution converted to the corresponding 1,4-benzoquinone. Stereochemical analysis

of face-to-face ethylene bridges was performed by NMR studies on the resulting **19** to establish the relative stereochemistry.

The structural assignment of **19** is consistent with spectroscopic data. Nine types of hydrogen absorptions in the ^1H NMR spectrum and the eleven lines in the ^{13}C NMR spectrum apparently confirmed the C_{2v} -symmetry of tetraacetate **19**. The absorption signals for the vinyl hydrogens on the ethylene-bridges appear at δ 5.89 and 5.80, indicating that they are on the mutually shielded double bonds. This anisotropic shielding effect is evidently demonstrated by the carbocyclic system composed of *syn*-fused bicyclo[2.2.2]octene units, in which double bonds are positioned face-to-face in close proximity with laticyclic topology. The lowest intensity of carbonyl carbon on 1,4-benzoquinone ring appearing at 180.5 ppm in ^{13}C NMR spectrum and signal absorption at 1643 cm^{-1} in IR spectrum are due to the effect enone conjugation. Basic hydrolysis of **19** gave tetraol **20** in good yield. With tetraol **20** in hand, progress toward the synthesis of **21** through tosylation and elimination steps continues and will be reported in due course.

II. The synthesis of ethylene bridged laticyclic polycarbocycles.

Tetracyclic hexaene **12** is readily available in eight steps from **13**.¹¹ Exocyclic bis-1,3-butadienes of this type are very attractive starting materials for the preparation of polycarbocycles by means of successive Diels-Alder cycloadditions. Preliminary results from the addition of 1,4-benzoquinone with tetracyclic hexaene **12** was not successful due to the low yields and complicated reactions. However, the similar reaction was carried out by using naphthoquinone which containing only one reactive double bond to give the stereoisomeric tetrahydroanthraquinones **22a** and **22b**. Diels-Alder adducts are not expected to occur easily due to the steric interaction in transition state as shown in Figure 1. Therefore, two products are possible from the Diels-Alder reactions of naphthoquinone with exocyclic dienes via

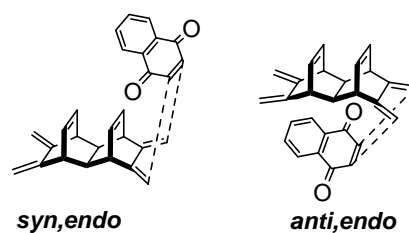


Figure 1. Sterically disfavored anti-Alder additions of naphthoquinone **1** on exocyclic butadiene **2**. The π -faces relative to the etheno-bridge in **2** are denoted by *syn* and *anti* and in naphthoquinone **1** by *exo* and *endo*.

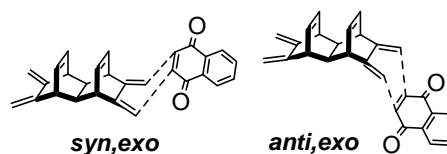
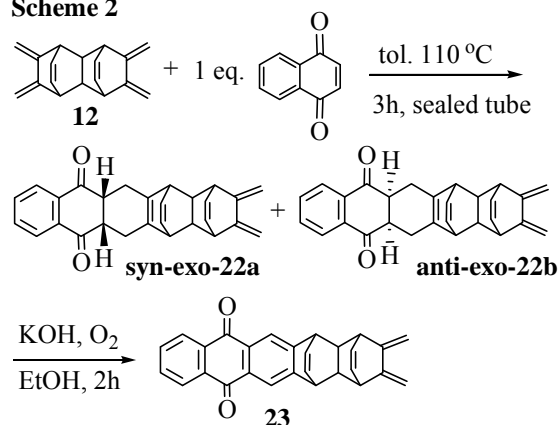
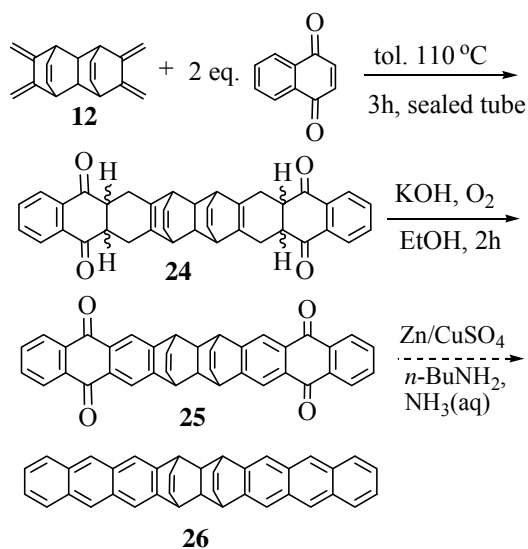


Figure 2. Sterically more favored transition states in the Diels-Alder reactions of naphthoquinone **1** with exocyclic butadiene **2** leading to two possible cycloadducts in accordance with the Alder rule.

Scheme 2



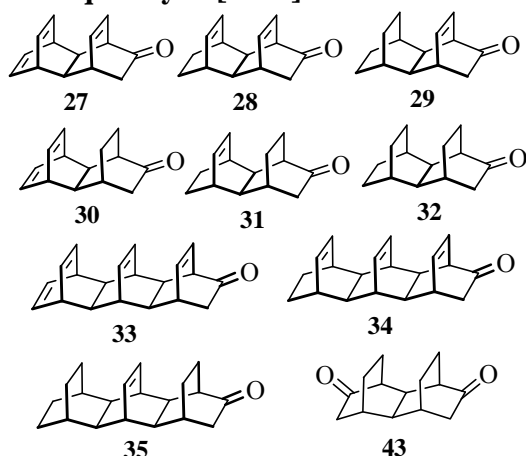
Scheme 3



modes of addition in accordance with the Alder rule as shown in Figure 2. Subsequent oxidation of the resulting isomers **22** by

stirring with KOH/EtOH solution under oxygen atmosphere afforded the corresponding anthraquinone **23**. Cycloaddition of tetracyclic hexaene **12** with 2 equivalent of naphthoquinone furnished bistetrahydroanthraquinones **24**, which was subsequently oxidized to the bisanthraquinone **25** by treatment with KOH in ethanol solution under oxygen atmosphere. The overall isolated yield of **25** was 58 %. The structure of **25** was characterized by NMR spectroscopy. The protons of bridged C=C double bonds appear at 6.24 ppm as a doublet of doublets ($J = 4.5, 3.0$ Hz) in the ^1H NMR spectrum and the carbonyl carbon of anthraquinone appear at 183.3 ppm in the ^{13}C NMR spectrum. Using zinc dust reduction in aqueous ammonia/*n*-butylamine solution with catalytic amount of anhydrous copper sulfate, we are working to produce new derivative of octacene **26**.

III. Synthesis and Friedländer reaction of sesquibicyclo[2.2.2]octenediones.

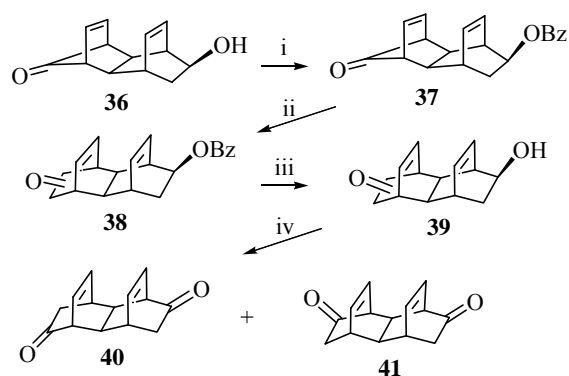


As we have long been interested in the syntheses and reactions of polycyclic hydrocarbons, we have previously prepared a series of tetracyclic and hexacyclic ketone derivatives **27** – **35**, and examine the transannular orbital interaction between olefin and keto chromophores on the basis of ^{13}C -NMR and UV spectroscopy.¹⁸ Although the chemical shift did not vary significantly, the ethylene bridge β -position to keto chromophore gave more shielding on the carbon atom of carbonyl group. This shielding effect was largest when three ethylene bridges are located in *syn* position, and resulted in 5.7 ppm difference in comparison of hexacyclic ketone **33** with **35**

as shown in Table 1. For the further extension of this work, we report the synthesis of sesquibicyclo[2.2.2]octenediones **40** and **41** and show out the intramolecular interaction between two keto groups through parallel interaction. We also find that quinoline-fused bicyclo[2.2.2]octenes can be successfully prepared from Friedländer reaction¹⁹ and be able to use them for investigation of photoreaction and charge transfer interaction.

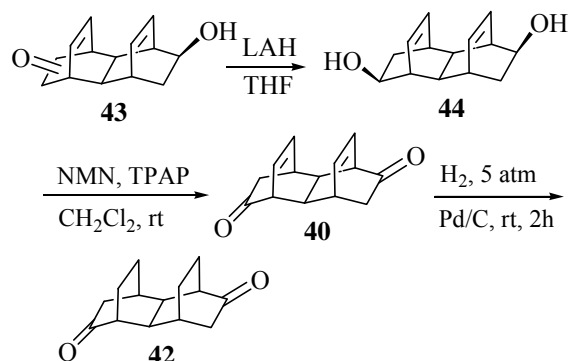
A mixture of sesquibicyclo[2.2.2]octenediones **40** and **41** was prepared from **36** through a series of protection of hydroxyl group followed by ring enlargement, deprotection, and oxidation steps. Several attempts to separate isomers **40** and **41** by chromatography and crystallization were unsuccessful. However, this resulting mixture underwent Friedländer condensation to form a pair of separatable isomers, quinolines **45**

Scheme 4



i. $\text{C}_6\text{H}_5\text{COCl}$, pyr., rt, 2 h; ii. $\text{H}_2\text{C}=\text{C}(\text{Cl})\text{COCl}$, $\text{BF}_3\text{-Et}_2\text{O}$. iii. NaOCH_3 , CH_3OH ; iv. PDC, CH_2Cl_2

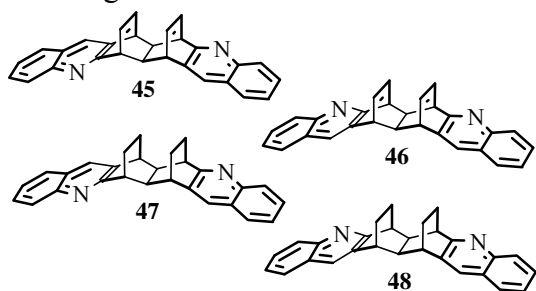
Scheme 5



and **46**. The two quinoline π system in **45** or **46** do not appear interact very strongly as indicated by the measurement of UV absorption spectra. The absorption maximum are shifted ca. 4 nm to longer wavelength in

45 or **46** as compared to hydrogenated **47** or **48**. This bathochromic shift is indicative of small delocalization through face-to-face ethylene bridges and accompany with a decrease of the $n-\pi^*$ excitation.

In our earlier report on sesquibicyclo[2.2.2]octene, we were able to isolate the pure sample of tetracyclic 4,9-diol **44** from the mixture of products in LAH reduction of **43**.^{8a} Oxidation of tetracyclic 4,9-diol **44** by tetrapropylammonium perruthenate (TPAP) was performed to yield tetracyclic 4,9-dione **40** in high yield. Compared with the ¹³C NMR spectrum of hydrogenated 4,9-dione **42**, carbonyl carbon of **40** absorbed at 209.9 ppm with 4.7 ppm upfield shift (Table 1). The shielding effects are clearly from interaction of carbonyl groups with parallel ethylene bridges. For 4,9-dione **42** as compared to **32** we find a upfield chemical shift of 2.3 ppm. This shielding effects



implies that two carbonyl groups interact through long distance of σ bonds.

Table 1. Chemical shifts of carbonyl carbons in the structures of syn-fused bicyclo[2.2.2]octenes.

compounds	27	28	29	30
chemical shifts (ppm)	211.9	211.8	212.6	216.4
compounds	31	32	33	34
chemical shifts (ppm)	217.3	216.8	211.5	211.5
compounds	35	40	41	42
chemical shifts (ppm)	217.2	209.8	209.5	214.5
compounds	43			
chemical shifts (ppm)	214.3			

In conclusion, we have demonstrated that 1,4-benzoquinone can incorporate into bicyclo[2.2.2]octenes to form new

dienophiles for construction of a variety of polycarbocycles containing face-to-face ethylene bridges.

Sesquibicyclo[2.2.2]octenes having exocyclic 1,3-butadienes undergo readily cycloaddition with naphthoquinone to form anthracene grafted spacer molecules. Transannular interactions of grafted chromophores with parallel ethylene bridges are observed by UV absorption and NMR analyses.

References:

- Goldstein, M. J.; Hoffmann, R. *J. Am. Chem. Soc.* **1971**, *93*, 6193
- (a) Grimme, W.; Gossel, J.; Lex, J. *Angew. Chem. Int. ed. Engl.* **1998**, *37*, 473. (b) Grimme, W.; Wortmann, J.; Frowein, D.; Lex, J.; Chen, G.; Gleiter, R. *J. Chem. Soc., Perkin Trans. 2*, **1998**, 1893. (c) Abbasoglu, R. *J. Mol. Model* **2006**, *12*, 991.
- Warrener, R. N. *Eur. J. Org. Chem.* **2000**, 3363-3380.
- Warrener, R. N.; Margetic, D.; Foley, P. J.; Butler, D. N.; Winling, A.; Beales, K. A.; Russell, R. A. *Tetrahedron*, **2001**, *57*, 571-582.
- (a) Bobbins, T.A.; Toan, V.V.; Givens, III., J.W.; Lightner, D.A.; *J. Am. Chem. Soc.*; **1992**, *114*, 10799-10810. (b) Jones, G. A.; Carpenter, B. K.; Paddon-Row, M. N. *J. Am. Chem. Soc.* **1998**, *120*, 5499-5508.
- (a) Lokan, N.; Paddon-Row, M. N.; Smith, T. A.; Rosa, M. L.; Ghiggino, K. P.; Speiser, S. *J. Am. Chem. Soc.* **1999**, *121*, 2917-2918. (b) Koeberg, M.; de Groot, M.; Verhoeven, J. W.; Lokan, N. R.; Shephard, M. J.; Paddon-Row, M. N. *J. Phys. Chem. A* **2001**, *105*, 3417-3424. 1. (c) Paddon-Row, M. N. *Aust. J. Chem.* **2003**, *56*, 729. (d) Chakrabarti, S.; Liu, M.; Waldeck, D. H.; Oliver, A. M.; Paddon-Row, M. N. *J. Am. Chem. Soc.* **2007**, *129*, 3247.
- Grimme, W.; *e-EROS Encyclopedia of Reagents for Organic Synthesis*, **2001**, John Wiley & Sons, Ltd..
- (a) Lin, C.-T.; Hwang, B.-P.; Chou, T.-C. *J. Chin. Chem. Soc.* **1993**, *40*, 159-167. (b) Lin, C.-T.; Wang, N.-J.; Yeh, Y.-L.; Chou, T.-C. *Tetrahedron*. **1995**, *51*, 2907-2928.

- (c) Lin, C.-T.; Wang, N.-J.; Tseng, H.-Z.; Chou, T.-C. *J. Org. Chem.* **1997**, *62*, 4857-4861. (d) Lin, C.-T.; Hsu, H.-C.; Chou, T.-C. *J. Org. Chem.* **1999**, *64*, 7260-7264.
9. Granozzi, G.; Lorenzoni, E.; Roulet, R.; Daudey, J.-P.; Ajo, D. *Organometallics* **1985**, *4*, 836-841.
10. (a) Jolliffe, K. A.; Langford, S. J.; Ranasinghe, M. G.; Shephard, M. J.; Paddon-Row, M. N.; *J. Org. Chem.*; **1999**, *64*(4); 1238-1246. (b) Klärner, F.-G.; Burkert, U.; Kamieth, M.; Boese, R.; Benet-Buchholz, J. *Chem. Eur. J.* **1999**, *5*, 1700-1707. (c) (d) Mondal, Rajib; Shah, Bipin K.; Neckers, Douglas C. *J. Am. Chem. Soc.*, **2006**, *128*(30), 9612-9613. (d) Mondal, R.; Adhikari, R. M.; Shah, B. K.; Neckers, D. C., *Org. Lett.*, 2007, **9** (13), 2505 -2508.
11. Lin, C.-T.; Chou, T.-C. *J. Org. Chem.* **1990**, *55*, 2252-2254.
12. Lin, C. T.; Chen, K.Z.; Chou, T. C. *Tetrahedron*, **2003**, *59*, 1493.
13. Lin, C.-T.; Hsu, H.-C.; Wang, M.-F., Chou, T.-C. *Tetrahedron*. **2000**, *56*, 5383-5390.
14. Wong, C. F.; Thesis of master degree, *Tunghai University*, **2000**.
15. (a) Klarner, F. -G.; Polkowska, J.; Panitzky, J.; Seelbach, U. P.; Burkert, U.; Kamieth, M.; Baumann, M.; Wigger, A. E.; Boese, R.; Blaser, D. *Eur. J. Org. Chem.* **2004**, 1405. (b) Klarner, F.-G.; Panitzky, J.; Blaser, D.; Boese, R. *Tetrahedron*, **2001**, *57*, 3673.
16. (a) Komatsu, K. *Eur. J. Org. Chem.* **1999**, 1495. (b) Foley, P. J.; Warrener, R. N. *Syn. Comm.* **2001**, *31*, 3011. (c) Scott, L. T. *Angew. Chem. Int. Ed.* **2003**, *42*, 4133.
17. Klarner, F.-G.; Panitzky, J.; Preda, D.; Scott, L. T. *J. Mol. Model.*, **2000**, *6*, 318.
18. Chen, K. J. *Thesis*, Tunghai University, **1996**. (b) Lee, Y. L. *Thesis*, Tunghai University, **1999**.
19. Muchowski, J. M.; Maddox, M. L. *Can. J. Chem.* **2004**, *82*, 461. and references cited herein.

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