

# 行政院國家科學委員會專題研究計劃成果報告

## 電子效應與主客化學(IV)

Electronic Effects and Host-Guest Chemistry (IV).

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主持人：鍾文聖 國立交通大學應化系 wschung@cc.nctu.edu.tw

### 一、中文摘要

本計畫研究的主題為電子效應與主客化學。我們將對位有不同取代基的 Nitrile Oxides (**5-Y**, 其取代基有氟、氯、溴、氰、硝基、甲基及甲氧基等)和已合成出的5-氟、或5-氯金剛硫酮(**2-F**)、金剛烯(**3-F**)及金剛亞胺(**4-X**)來探討電子效應及Cieplak's model的適用性。

這些5-取代金剛系列化合物與 phenyl nitrile oxide 的1,3-偶極環化加成反應生成兩種幾何異構產物，屬於一種 inverse electron demanding 的反應，與一般的Diels-Alder反應成對比。在1,3-偶極環化加成反應中是利用硫酮、金剛烯或金剛亞胺的HOMO與偶極的LUMO作用為主，而在 Diels-Alder反應中則是利用硫酮或金剛烯的LUMO與Diene的HOMO作用為主。我們發現此類1,3-偶極環化加成反應，仍然能利用過渡態 Hyperconjugation 理論來解釋，此部份成果已發表於 *J. Org. Chem.* **1999**, *64*, 1099-1107。

5-取代金剛亞胺與 phenyl nitrile oxide 行1,3-偶極環化加成反應時，產物的比例完全不受溫度或取代基的改變而影響。但是對於金剛硫酮及金剛烯與 phenyl nitrile oxide 行1,3-偶極環化加成反應時，產物的比例會受溫度或取代基的改變而影響，因此可以經線性 Hammett Plots 獲得反應常數 $\Delta\rho$ 的值，分別是+0.12 (**2-F**)及0.0 (**3-F**)。這樣小的

反應常數及先前研究所獲得的資訊，可以推測反應過渡態應是經由一步式的協和反應，且不具有電荷分佈差異。由溫度對產物 *E/Z* 比例的影響吾人首次獲得順式與反式過渡態的活化參數。Nitrile oxides 之所以有利於由順式面來攻擊，依據實驗及AM1計算結果，可以用過渡態超共軛理論來解釋。和儲三陽教授及蘇明德博士合作，利用Density Functional Theory及CCSD(T)的理論方法計算，對上述問題詳加探討，亦獲得很重要的成果，此部份成果已發表另一篇 *J. Org. Chem.* **1999**, *64*, 6710-6716。

在主客化學上，和文化大學林立錦教授實驗室合作，我們也有重要進展，成功的以六步驟合成法合成下原有四種不同醚機基取代的Calix[4]arenes，已發表一篇文章於 *J. Org. Chem.* **1999**, *64*, 2673-2679。

關鍵詞：1,3-偶極環化加成反應、Hammett Plots、Cieplak's model、溫度效應、Calix[4]arene、chiral host。

### Abstract

The 1,3-dipolar cycloaddition reactions of *p*-substituted benzonitrile oxides (**5-Y**) with 5-fluoroadamantan-2-thione (**2-F**) and 2-methyleneadamantane (**3-F**) as well as with variously 5-substituted-*N*-benzyladamantyl-2-imines (**4-X**) were examined. They produce two geometrically isomeric

$\Delta^2$ -1,4,2-oxathiazolines (7-F,Y),  $\Delta^2$ -isoxazolines (8-F,Y) and  $\Delta^2$ -1,2,4-oxadiazolines (11-X,Y), respectively. The face selectivity in the latter reaction was found to be ~1:1 regardless of the variations in 5-substituent and the temperature. For the former two reactions, the *p*-substituent was varied from electron-withdrawing (Y = F, Cl, Br, CN or NO<sub>2</sub>) to -releasing (Y = Me, or OMe). The face selectivity was measured in all cases. The differences  $\Delta\rho$  for the reactions of 2- and 3-F with 5-H were obtained from linear Hammett plots; they are +0.12 and 0.0; respectively. These low values and information from previous studies imply a concerted-one-step mechanism with very little charge distribution differences in the transition states. These effects on temperature on the *Z/E* product ratios provide us, for the first time, with activation parameter differences between the syn- and anti transition states; their values are discussed. The product bias resulting from the favored attack of nitrile oxide on the *su* face is discussed in terms of transition state hyperconjugation based on the experimental results and AM1 calculations. This work has been published in *J. Org. Chem.* **1999**, *64*, 1099-1107. Due to the interesting results further theoretical calculation was carried out in collaboration with Professor Chu, San-Yan and Dr. Su, Ming-Der, applying a Density Functional Theory and CCSD(T) methods. From this work, another paper was published in *J. Org. Chem.* **1999**, *64*, 6710-6716.

In collaboration with Professor Lin, L.-G. of Chinese Culture University we have also made important contribution in the host-guest chemistry area. For example, we have successfully made a series of Calix[4]arenes with four different lower rim substituents. Based on our results, one paper has been published in *J. Org.*

*Chem***1999**, *64*, 2673-2679.

Key words: 1,3-dipolar addition、Hammett Plots, Cieplak's model, temperature effects, Calix[4]arene, Chiral host。

## 二、緣由與目的

本研究是主持人持續進行的一個領域，而電子效應的探討在國內外也仍是個非常熱門的主題，因為其進行機制仍有許多不清楚之處待釐清。

## 三、結果與討論

經由本研究我們首次獲得面向反應的過渡態能量差異與電荷分布差異，使得吾人對電子效應的機制更加清楚了解，特別是在沒有立體障礙差異的金剛酮系列，相對於靜電場效應來說過渡態超共軛理論扮演非常重要角色。詳附件一之著作。

## 四、計劃成果自評

本計劃成果豐碩共發表論文四篇，分別是：(1) *J. Org. Chem.* **1999**, *64*, 1099-1107 (2) *J. Org. Chem.* **1999**, *64*, 2673-2679 (3) *J. Org. Chem.* **1999**, *64*, 6710-6716，及一篇 *Chem. Review* **1999**, *99*, 1387-1413。

## 2. Purposes and Objectives

The study of electronic effects in various sterically unbiased trigonal carbon centers continues to attract considerable theoretical and experimental attention. Among the many models, transition-state hyperconjugation and electrostatic field interaction are the two most popular explanations for the face selectivity results to be found in the literature. 5-Substituted adamantan-2-ones and their derivatives have proven to be useful probes in research aimed at understanding the electronic factors in face

selection. These studies of a variety of reactions indicate that the reagent prefers to attack the face antiperiplanar to the more electron-rich vicinal bonds, and the results can be reconciled with Cieplak's transition-state hyperconjugation model. °

### 3. Results and Discussion

The effects of *p*-substitution of benzonitrile oxides (5-Y) on the face selectivity of 1,3-dipolar cycloaddition reactions with 2-F and 3-F have been studied. The reaction constant differences  $\Delta\rho$  for these reactions are obtained from linear Hammett plots, which give a small positive value (+0.12) for thiones (2-F) and a zero slope for methyleneadamantanes (3-F). These small  $\Delta\rho$  values imply that the 1,3-dipolar cycloaddition is consistent with a concerted-one-step mechanism with a slightly different charge imbalance in the transition states.

Effects of temperature variation on the *Z/E* product ratios of the 1,3-dipolar cycloaddition reaction of 2-Cl and 3-Cl with parent nitrile oxide 5-H provide us, for the first time, with activation enthalpy and entropy differences between the two transition states of the *syn*- and *anti* attacks. The *syn*-attacks of the dipoles (5-X) on thiones 2-X and methyleneadamantane 3-X have a smaller activation enthalpy ( $\Delta H^\ddagger$ ) and a more negative activation entropy ( $\Delta S^\ddagger$ ) than the *anti*-attacks.

AM1 calculations of the HOMO-LUMO energies of 1-5 reveal that all the 1,3-dipolar reactions described here are LUMO (dipole)-HOMO (dipolarophile) controlled reactions; the rates decrease in the order  $k(\text{imine}) > k(\text{C=S}) > k(\text{C=CH}_2) \gg k(\text{C=O})$ .

### 4. Self-Evaluation

Most of our work are fulfilled as originally proposed, and the results have been sum up to two J. Org. Chem. Publications.

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