行政院國家科學委員會補助專題研究計畫成果報告

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※ 自由基合成方法的開發與其在天然植物鹼合成上的運用 ※
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計畫類別：■個別型計畫 □整合型計畫
計畫編號：NSC89－2113－M－002－054－
執行期間：89 年 08 月 01 日至 90 年 07 月 31 日

計畫主持人：蔡蘊明
共同主持人：

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執行單位：國立台灣大學化學系

中 華 民 國九十年十月二十三日

行政院國家科學委員會專題研究計畫成果報告
自由基合成方法的開發與其在天然植物鹼合成上的運用

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一、中文摘要

本計畫利用矽基酮的自由基環化反應來製備矽化烯醇。主要使用的策略是利用β-消去反應，一種做法是將自由基的離去基置於一開始的自由基之上，另一種做法是降離去基置於羰基的α-位。這兩種做法所得之矽化烯醇具有百分之百的位置選擇性。

關鍵詞：矽基酮、自由基環化、矽化烯醇

Abstract

Acylsilanes with terminal α-stannyl bromide or xanthate functionalities are prepared. α-Stannyl radicals generated from these acylsilanes undergo intramolecular cyclizations to give cyclic silyl enol ethers regiospecifically. The radical processes involve radical cyclization, Brook rearrangement, and β-fragmentation in sequence. Tributylstannyl group serves as the radical leaving group. The newly formed σ-bond and π-bond are located between the same two carbon atoms. This approach is limited to the formation of five-membered ring. In another route, ω-bromo-α-phenylsulfonylacylsilanes are synthesized. The radical cyclizations of these α-sulfonylacylsilanes also give cyclic silyl enol ethers. The phenylsulfonyl moiety is the radical leaving group in this system. Furthermore, the newly formed σ-bond and π-bond are located at adjacent positions sharing a single carbon atom. The latter approach is effective for both five- and six-membered ring formation.

Keywords: Acylsilanes, Radical cyclization, Silyl enol ethers

二、緣由與目的*

Intramolecular cyclizations of radicals with carbonyl groups are known to be reversible processes.[1] To drive these reactions toward the cyclization side, there are two general strategies. One is to trap the cyclized alkoxy radical intermolecularly using excess tributyltin hydride,[2] silanes[3] or organophosphorous compounds.[4] The use of large excess of triethylborane also improves the cyclization efficiency.[5] This may be attributed to the trapping of the cyclized alkoxy radical by triethylborane.[5b] The other route relies on the presence of some intramolecular processes such that the cyclized alkoxy radicals are diverted to give other products in an irreversible way. The most notorious application in this direction is the ring expansion of 2-oxocyclopentylmethyl radical and systems alike pioneered by research groups of Beckwith and Dowd.[6,7] Radical cyclizations of acylgermanes give rise to cyclic ketones through β-scission of β-germyl alkoxy radicals.[8] Thio- and selenoesters also undergo similar reactions.[9] The complementary acylsilane cyclizations[10] give cyclic alcohols in the form of silyl ethers through irreversible radical-Brook rearrangements[10–12] of β-silyl alkoxy radical intermediates. In the case of tributyltin hydride-mediated pinacol coupling developed by Hays and Fu,[13] the cyclized γ-tributylstannyloxy alkoxy radical was trapped *via* an intramolecular homolytic substitution at tin. A 1,3-stannyl shift from carbon to oxygen is the driving force for the intramolecular cyclizations of α-stannyl radicals with formyl group.[14]

Among the intramolecular radical cyclization reactions of carbonyl compounds, the acylsilane[15] cyclization system is unique, in which a new carbon radical is generated after the radical-Brook rearrangement of β-silyl alkoxy radical. By introducing additional structural features, one may utilize the newly

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* 本報告已經被 JOC 接受。

generated carbon radical in useful ways. One possibility involves a pre-existing radical leaving group X at the β-position of the carbon radical. A β-scission will occur to generate a silyl enol ether in a regiospecific fashion. In principle, there are two possible approaches. Route-a starts from the generation of radical with the radical leaving group attached at the carbon carrying the initial radical. In this direction, we found that the tributylstannyl group served well as the desired radical leaving group.[16] An alternative approach (route-b) is to put the radical leaving group at the α-position of the carbonyl group. We found that this route can be realized by the use of phenylsulfonyl group.[17] In this project, we accomplished our full investigation of the use of these two approaches in the regiospecific formation of silyl enol ethers.[18]

三、結果與討論

In this study, we have successfully developed two routes in the synthesis of regiospecific cyclic silyl enol ethers employing intramolecular radical cyclizations of acylsilanes. Both approaches involve β-fragmentation of the cyclized α-silyloxy radical intermediates. The cyclizations of acylsilanes carrying terminal α-tributylstannyl bromide or xanthate functionalities adopt the tributylstannyl group as the radical leaving group for the β-fragmentation. This approach works only for five-membered ring formation. The other approach uses α-phenylsulfonylacylsilanes as the substrates. The α-phenylsulfonyl group serves as the radical leaving group. Although the latter approach works well for both five- and six-membered ring formations, the concomitant formation of phenylsulfinic acid causes some trouble. This side product can be removed by the use of excess (15 equiv) sodium bicarbonate powder. Interestingly, the α-sulfonylacylsilane approach is analogous to the ionic chemistry of acylsilanes in the synthesis of regio- and stereochemically defined silyl enol ethers developed by Reich *et. al.*[19]

Due to the difference in the direction of bond formation, the two radical approaches are complementary regarding the regiochemistry of cyclic silyl enol ether formation. Within the same route, tuning the position of the substituents on the acylsilane backbone will also lead to the formation of the desired regioisomer.

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參加 ACS Pacifichem 2000 報告

蔡蘊明

台灣大學化學系

中華民國八十九年十二月二十四日

我於十二月十四日的晚間搭乘華航班機前往本次的 ACS 會議地點夏威夷，到達時為當地的十四日中午，即刻趕赴會場報到，等拿到參加會議的名牌及資料，已是午間兩點多了，這是一個極大型的會議，總共參與者多達六千餘人，光是有機化學的部份，在同一時間就有高達十個場次同時進行演講，期中許多都是很值得參語的，但是由於我是被邀請在環化加成與成環策略小組給演講，因此在十四號與十五號兩天都待在該小組的演講廳，十六日上午及下午的演講因為環化加成與成環策略小組的演講已告一段落，因此有機會挑選我有興趣的題目去聽講，以下就這幾日所參與過的演講略述一二。

我第一個聽到的演講是 K. Tanino 的 [3+2] 與 [5+2] 環化加成反應的研究，由於他系出 Kuwajima 教授門下，在幾年前 Kuwajima 教授來台時就曾經提到過此一型態的化學。接著是 P. Wender 的金屬催化的環化加成反應，這與上一回他來台時所提到的化學類似，這個演講吸引了相當多的聽眾。星期五一大早在這個小組的演講是由 K. Tatsuta 的 [4+2] 環化加成以合成天然物的演講開始，接著是 D. L. Boger 利用 hetero-Diels-Alder 反應來架構含氮雜環的研究，其後為 M. Hirama 有關 ansamacrolide endiyne 之合成研究，然後是 M. Tius 有關 allenes 的合環反應，在他之後是 M. G. Banwell 的演講，那是有關 lamellarin 類天然物的合成，上午的最後一場是 H. Kogen 有關 globomycine 的合成。下午的部份在短暫的一個小時休息之後開始，首先是 M. Sasaki 有關 polyether 天然物的合成研究，接著是由 R. L. Danheiser 有關 vinylketenes，conjugated enyne 等化合物的合環反應，我的演講則跟在其後，是有關自由基與矽基酮的環化反應，我的演講結束後略事休息然後由 L. Overman 演講有關建立四級碳的合成方法，接著是韓國的 E. Lee 有關自由基環化反應合成雜環的方法，最後的壓軸則是陸天堯教授的雜環合成研究，至此該小組的演講系列已經結束。星期六的早上挑選了 K. C. Nicolaou 的演講開始，那是有關 DMP 與 IBX 的氧化反應，接著聽了 A. Fallis 有關 imine 的自由基環化反應以及 P. A. Evans 有關利用自由基環化運用在 batzellidine A 的合成，接著聽了 A. B. Smith 的 phorboxazole A 與 B 的合成和 G. Molander 有關不對稱合成的研究，午餐後聽了 P. Wipf 有關 Zr 得有機金屬化學在合成上的運用，接著聽了 T. V. RajanBabu 有關 Ni 得有機金屬化學。值此結束了星期六的演講，星期日上午打包回府，搭乘中午的華航班機歸國，回到台北已是十八號華燈初上之時了。

總括本次會議的參與收穫良多，可惜會程的安排造成許多場次的演講衝堂，很想參加卻做不到，這是最為遺憾的地方了。

參加 ACS Pacifichem 2000 論文

Radical cyclizations of acylsilanes in organic synthesis

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Radical additions to carbonyl compounds are potentially useful reactions. However, it is well known that this type of cyclizations is reversible in favor of the reverse reactions. On the contrary, radical cyclizations of acylsilanes of acylsilanes resulted in the formation of β-silyl alkoxy radicals. A radical-Brook rearrangement occurs immediately to give silyloxy group substituted carbon radicals. These new carbon radicals can be trapped intramolecularly by double or triple bonds to construct bicyclic skeleton. Several tandem radical cyclizations will be discussed. In the case of using triple bond as intramolecular radical terminator, an interesting hydrogen atom transfer occurs between the methyl group on silicon and the vinyl radical intermediate. This is followed by a third intramolecular cyclization to give a tricyclic compound. Structural factors affecting the formation of the tricyclic product will be discussed.