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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經由雙環[2.2.1]庚烯酮的光化學重排反應合成環戊烷類天然物和前列腺素

Synthesis of Iridoid Monoterpenes and Prostaglandins *via* Photochemical Rearrangement of Bicyclo[2.2.1]hept-5-en-2-one

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執行期間： 89 年 08 月 01 日至 90 年 07 月 31 日

計畫主持人：戴火木

共同主持人：

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執行單位：嘉南藥理科技大學

中 華 民 國 九 十 年 十 月 二 十 日

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Synthesis of Iridoid Monoterpenes and Prostaglandins, *via* Photochemical Rearrangement of Bicyclo[2.2.1]hept-5-en-2-one

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計畫參與人員：劉文夫（研究助理）

一、中文摘要

同向-7-雙環[2.2.1]庚烯酮 **1** 經光化學重排反應，得到[5,4]駢環化合物 **2**，此化合物經選擇性的擴環成雙環[3.3.0]和 1-氧代雙環[3.3.0]辛烯酮，前述擴環後的雙環系統可分別合成環戊烷類天然物和前列腺素。

關鍵詞：環戊烷類天然物；依瑞多依得；前列腺素；光化學重排；3-氮雙環[4.3.0]壬烷類生物鹼。

Abstract

The synthesis of cyclopentanoid natural products, iridoid monoterpenes and prostaglandins, was achieved from a common intermediate **2**, which was obtained from **1** *via* photochemical rearrangement.

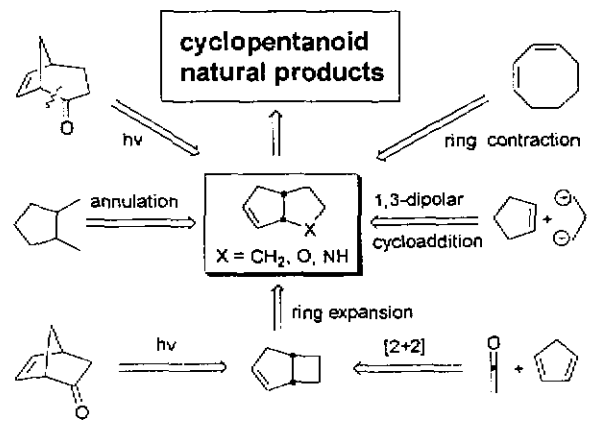
Keywords: Cyclopentanoid Natural Products; Iridoid Monoterpenes; Prostaglandins; Photochemical Rearrangement.

Introduction

Cyclopentanoid natural products have proliferated in the last four decades. Several of these families, such as iridoid monoterpenes,[1] diquinanes,[2] and triquinanes[3] have received the attention of synthetic chemists due to the complexicity of the structure and their biological activities. This has stimulated interest to prepare such substances and to meet the methodological challenges of constructing cyclopentanoid skeletons.[4]

A number of strategies have been developed in the building up of *cis*-bicyclo[3.3.0]octene skeleton (scheme I), which is one of the most important precursor in the synthesis of cyclopentanoid natural products.[5] Among the numerous methods of constructing *cis*-bicyclo[3.3.0]octene, ring expansion of *cis*-bicyclo[3.2.0]heptenones are not only an effective procedure to *cis*-bicyclo[3.3.0]octenes but also to 1-oxo- or 1-aza- bicyclo[3.3.0]octenes.[6] However, the [2+2] cycloaddition of cyclopentadiene and ketene approach to the construction of bicyclo[3.2.0]heptenone has been restricted by the functionalization of the cycloadducts.[7] Photochemical behavior of β, γ-unsaturated ketones has been well studied.[8] Nevertheless, only a few examples of photochemical rearrangement of bicyclo[2.2.1]heptenones have been reported, most of them concentrated in mechanistic studies. In this paper, we report photochemical rearrangement of bicyclo[2.2.1]hept-5-en-2-one **1** to *cis*-bicyclo[3.2.0] hept-2-en-7-one **2**, as the key step in the synthesis of iridoids and prostaglandins.

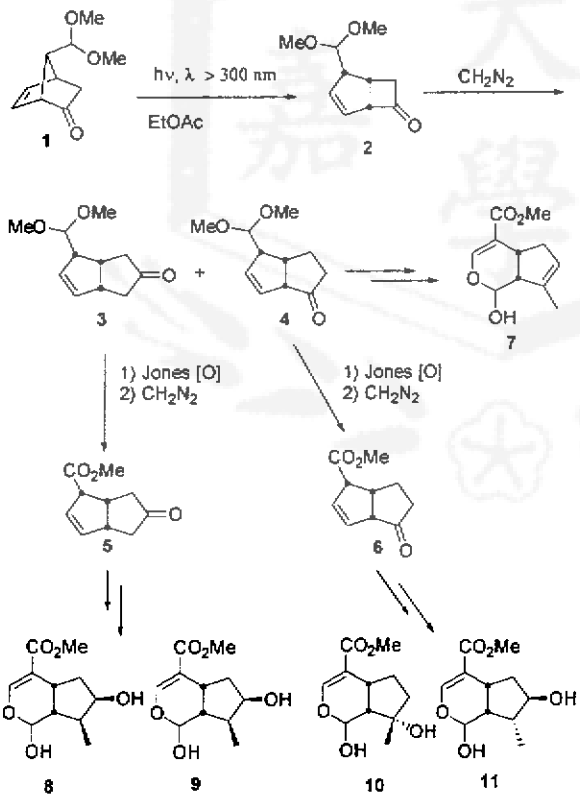
Scheme I



Results and discussion

The readily available bicyclo[2.2.1]heptenone **1** was chosen as the starting material.[9] Irradiation of **1** in cyclohexane in Rayonet reactor (λ > 300 nm) afforded the 1,3-acyl shift product bicyclo[3.2.0] heptenone **2** in 80% yield. Subsequent ring enlargement of **2** with diazomethane gave a mixture of cyclopentanone **3** and regioisomer **4** in 1.5:1 ratio. Both diquinanes **3** and **4** were useful in the synthesis of iridoids. The ^{1}H and ^{13}C NMR data of **4** were identical with those of an authentic sample previously produced in our laboratory.[10] Since compound **4** has been transformed into 10-deoxygeniposide (**7**), this work constitutes a formal total synthesis of 10-deoxygeniposide (**7**).[10]

Scheme II

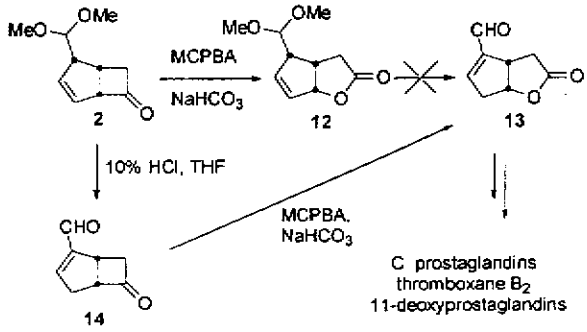


Treatment of **3** with Jones reagent followed by methylation of the resulting acid with diazomethane, acetal **3** was converted to ester **5**. The ^{1}H and ^{13}C NMR spectra of **5** were identical with those of an authentic sample previously produced in our laboratory.[11] Since compound **5** had been already transformed to loganin (**8**) and hydroxloganin (**9**), this work constitutes a formal total synthesis of loganin (**8**) and hydroxloganin (**9**).[11]

Treatment of **4** with Jones reagent followed by esterification the resulting acid with diazomethane furnished keto ester **6**. The ^{1}H and ^{13}C NMR spectra of **6** were identical with those of an authentic sample previously produced in our laboratory.[12] Since compound **6** had been already transformed to mussaenoside (**10**) and 8-epiloganin (**11**), this work constitutes a formal total synthesis of mussaenoside (**10**) and 8-epiloganin (**11**).[12]

The route to the synthesis of prostaglandins is shown in scheme III. Baeyer-Villiger oxidation of **2** with MCPBA in basic condition provided lactone **12** in 93% yield. Further treatment of the acetal **12** with varied aqueous acid solution resulted in complex mixture.[13] After great efforts, the synthesis of **13** was achieved as follows: Hydrolysis of **2** with hydrochloride in aqueous THF solution afforded aldehyde **14**, which was subsequently reacted with MCPBA to yield the Baeyer-Villiger oxidation product **13**. The structure of **13** was confirmed by comparison of the ^{1}H NMR spectra with an authentic sample provided by Renaud.[14] Since compound **13** has been previously converted to prostaglandins[15] and thromboxane B_2,[16] this procedure constitutes a new approach to the synthesis of racemic prostaglandins.

Scheme III



In summary, the successful synthesis of iridoids

and prostaglandins demonstrate the utility of the photochemical rearrangement of bicyclo[2.2.1]hept-5-en-2-one **1** as a key step in the synthesis of cyclopentanoid natural products. Efforts toward the synthesis of other natural products are currently underway in our laboratory.

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