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Microwave-assisted Allylic Oxidation at C-13 Position of 14-Deoxysinenxan A

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Abstract: Microwave-assisted allylic oxidation at C-13 position of 14-deoxysinenxan A was described. This new method (150℃/10 min/5 bar on microwave synthesizer) led to a better yield of compound **1** and shorter reaction time.

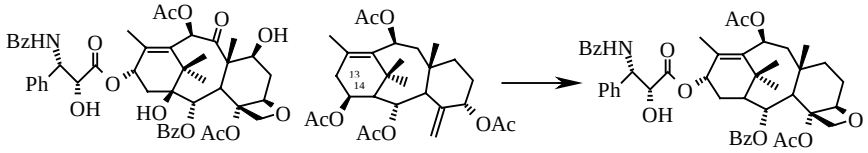
Keywords: Allylic oxidation, microwave, 14-deoxysinenxan A.

The important anticancer agent paclitaxel, so far, continues to show impressive clinical efficacy againts ovarian, breast and lung cancer. It is also the subject of intense interest in the chemical, biological and medical communities today [1].

Sinenxan A (SIA), which is readily available as a biosynthetic taxane, has the same taxane skeleton with that of paclitaxel. The development of a procedure using SIA as starting material for the preparation of bioactive paclitaxel analogues would be significant. An ongoing program in our laboratory is the synthesis of 1, 7, 9-trideoxy-paclitaxel *via* SIA.

Compound **1** is the key intermediate in our synthetic route. M. Zhang *et al.* have reported the oxidation of 14-deoxy-SIA at C-13 position by PCC to give compound **1** [2] (**Table 1,** entry 1). But the low yield and rigorous conditions obstructed the application of this method.

Microwave energy is a more efficient means of heating. Microwave-assisted reactions were carried out in a closed reactor in general. The higher temperature over the boiling point of the solvent and the higher pressure than the normal conditions in the system are obtained. So microwave-assisted organic synthesis can



paclitaxel sinenxan A(SIA) 1, 7, 9-trideoxypaclitaxel

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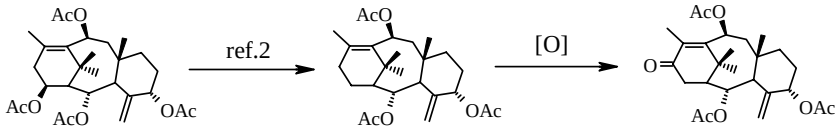
Scheme 1



SIA 14-deoxySIA 1

Table 1 Oxidation at C-13 position of 14-deoxy-SIA

Entry	Substrate	Reagents / Solvent	Conditions	Isolated yield (%)	
				Starting material	1
1[2]	14-deoxy-SIA	PCC/NaOAc/Celite/benzene	90℃, 4.5 hr	24	50
2	14-deoxy-SIA	PCC/NaOAc/benzene	90℃, 4.5 hr	15	38
3	14-deoxy-SIA	PCC/NaOAc/Celite/benzene	100℃,10 min,4 bar [a]	10	70
4	14-deoxy-SIA	PCC/NaOAc/benzene	100℃,10 min,4 bar [a]	10	72
5	14-deoxy-SIA	PCC/NaOAc/benzene	150℃, 5 min, 5 bar [a]	12	62
6	14-deoxy-SIA	PCC/NaOAc/benzene	150℃,10 min,5 bar [a]	0	73
7	14-deoxy-SIA	PCC/NaOAc/benzene	150℃,15 min,5 bar [a]	0	72

[a] Microwave synthesizer is Emrys ™ Optimizer by Personal Chemistry Co. Ltd. of Sweden. Reaction temperature was pre-set.

usually promote reactions and most of the reactions can be complete in short time. Side reactions for sensitive substrates could be avoided due to the short reaction course [3]. We applied microwave conditions to the allylic oxidation of 14-deoxy-SIA and found the reaction could be complete in 10 min (entry 6) [4]. Celite was applied in the traditional method as dispersant of PCC (entries 1, 2). In our method, celite was not necessary because of the uniformity of heating by microwave (entries 3, 4). Moreover, absence of celite reduced the adsorption of compound **1** in the operation after reaction. Low reaction temperature and shorter reaction time caused incomplete conversion of the starting material (entries 4, 5). In the other side, prolongation of reaction time also caused decline of yield along with increase of side products, which compound **1** would transform to 13, 14-dioxyl compound and some open-ring compounds (entry 7). The yield was fair compared with that of common reaction conditions (entry 1). The ^{1}H NMR and ^{13}C NMR spectra were identical with that of an authentic sample .[2]

In conclusion, an efficient microwave-assisted allylic oxidation at C-13 position of 14-deoxysinenxan A has been developed to prepare **1**. This new method retained the skeleton of taxane, shortened the reaction time and gave a better yield. The synthesis of 1, 7, 9-trideoxypaclitaxel *via* SIA is in progress.

Acknowledgments

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References and Notes

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3. M. Collins, *American Genomic/Proteomic Technology*, **2001**, *1*, 40; H. Koshima, *Kagaku Kogyo*, **2002**, *53*, 786.
4. Reaction procedure: 14-deoxy-SIA (40 mg, 0.089 mmol) in dry benzene (10 mL) was placed in special reactor for microwave synthesizer. PCC (578 mg, 2.69 mmol, 30 eq) and anhydrous NaOAc(220 mg, 2.69 mmol, 30 eq) was added to the reactor. The reactor was closed under N_2. Reaction temperature and time were pre-set. After reaction, the mixture was filtered and washed by EtOAc. The filtrate was concentrated and chromatographed to give compound **1** (30 mg, 73%).

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