

## Synthesis and Structural Determination of (2R,4S,5S)-(+)-Threo-5-(2,2-dichloroacetamido)-4-(4-nitrophenyl)-2-aryl-1,3-dioxanes

Jun LIU, Xian Ming HU\*, Han Sheng XU

Department of Chemistry, Wuhan University, Wuhan 430072

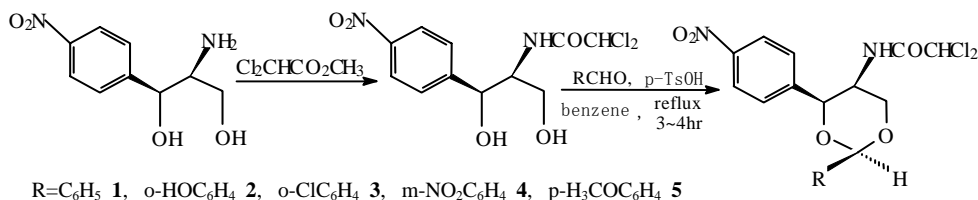
### Abstract:

(2R,4S,5S)-(+)-threo-5-(2,2-dichloroacetamido)-4-(4-nitrophenyl)-2-aryl-1,3-dioxanes were synthesized with high diastereoselectivity and good yields. The structures of acetals were determined and the configurations were confirmed by 2D-NMR (NOESY).

**Keywords:** Acetals, diastereoselective synthesis, chloramphenicol; 2D-NMR.

Acetals can be synthesized in a number of ways. The main problem in the acetal formation in acidic medium is to shift the equilibrium to the right by removal of the water formed during the reaction<sup>1</sup>. We synthesized (2R,4S,5S)-(+)-threo-5-(2,2-dichloroacetamido)-4-(4-nitrophenyl)-2-aryl-1,3-dioxanes by acetalation of (1S,2S)-(+)-2-(dichloroacetamido)-1-(4-nitrophenyl)-1,3-propanediol and aryl aldehydes with high diastereoselectivity and good yields (60~85%)<sup>2-4</sup>. (Scheme 1) Results of separation and analysis have shown that except for product (2R,4S,5S), the residue contains starting materials and some polymeric products (5~10%), no (2S,4S,5S) epimers were obtained.

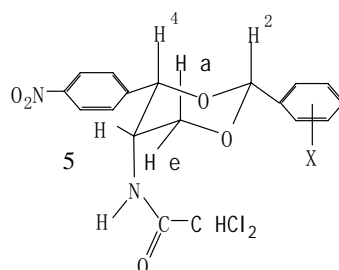
**Scheme 1.**



For the case of 5-(2,2-dichloroacetamido)-4-(4-nitrophenyl)-2-(3-nitrophenyl)-1,3-dioxane **4**, the structure has been confirmed by NOESY. The anticipated cross-peaks between H-2 and H-4 (Figure 1) are readily identified. As to other probable conformational relationships

between H-2 and H-4: (a) eq H-2- ax H-4, (b) ax H-2- eq H-4, (c) eq H-2- eq H-4, none of these cross-peaks are seen in the spectrum. Although the absence of certain cross-peaks does not necessarily prove that no interaction exists, it is likely that they would have been present if the mentioned conformational relationship (a) to (c) were realistic. CPK spacefilling models show that these three conformations (a) to (c) are highly unlikely, as a consequence of large unavoidable steric hindrance by axial substituents. According to the conformational analysis of compound **4**, we consider that the absolute configuration of these acetals is (2R,4S,5S).

**Figure 1.** Predicted conformation for **1-5**



Because the  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectra of all synthesized acetals resemble each other closely, we assume all these compounds with the same configuration.

### Acknowledgments

This work was supported by the fundation of national education committee for the scholars back from abroad, the science and technology fundation of Wuhan city, Red Heart K (Group) Co. Ltd.; We are grateful to Prof. Chui Yuxing (Beijing Medical University, NMR Lab) for technical assistance.

### References and notes

1. F. A. J. Meskens, *Synthesis*, **1981**, 501.
2. K. Jan; N. Jindrich *et al. Czech CS* 225, 278.
3. P. Ramaiah, A. S. Rao, *Organic Preparations and Procedures Int.* **1987**, 19 (2,3), 173.
4. J. C. Meslard; F. Subira; J. P. Vairon *et al. Bull. Soc. Chim. Fr.* **1985**, 1, 84.
5. J. C. Noulis; G. V. Binst; R. M. Martin, *Tetrahedron Lett.* **1967**, 4065.
6. Compd. **1**. m. p. 102. 7-103°C,  $[\alpha]_{\text{D}}^{21} +28$ . 6; compd. **2**. m. p. 101-102. 5°C,  $[\alpha]_{\text{D}}^{21} +38$ . 0; compd. **3**. m. p. 79. 5-79. 9°C,  $[\alpha]_{\text{D}}^{21} +31$ . 0; compd. **4**. m. p. 178-179°C,  $[\alpha]_{\text{D}}^{21} +21$ . 2; compd. **5**. m. p. 181-181. 5°C,  $[\alpha]_{\text{D}}^{21} +25$ . 7; The data of IR, NMR( $^1\text{H}$ ,  $^{13}\text{C}$ ) and MS of the compounds have been deposited in the editorial office of CCL.

Received 2 August 1998