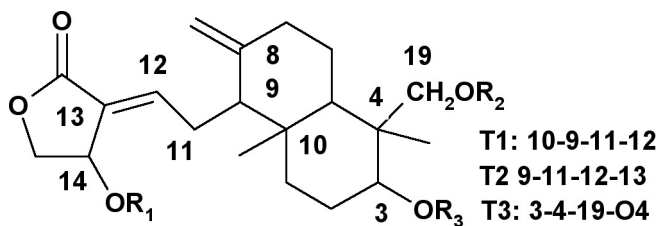


**Effect of Blocking Groups on the Conformation and Intermolecular Interactions of Andrographolide.** C.H. Schwalbe<sup>1</sup>, C.J. Bache<sup>1</sup>, D.L. Rathbone<sup>1</sup>, S.R. Sagineedu<sup>2</sup>, S.R. Jada<sup>2</sup>, J. Stanslas<sup>2</sup>, M.F.G. Stevens<sup>3</sup>, <sup>1</sup>School of Life & Health Sciences, Aston Univ., Birmingham B4 7ET, UK, <sup>2</sup>Dept. of Biomedical Sciences, Univ. Putra Malaysia, 43400 Serdang, Selangor, Malaysia, <sup>3</sup>The Pharmacy School, Univ. of Nottingham, University Park, Nottingham NG7 2RD, UK.

The natural product andrographolide (**A**) has interesting biological effects, including anti-cancer, hypotensive, and anti-inflammatory, which it is desirable to elicit separately.



With R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = H, **A** (CSD refcode ZZLUK03) forms hydrogen-bonded chains at both ends of the molecule. We have blocked one or more of these sites: previously with R<sub>1</sub> = acetyl in compound **I**, now with R<sub>2</sub>-R<sub>3</sub> = the cyclic isopropylidene (**II**) and R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = acetyl (**III**). In **I** and **II** the hydrogen-bonded chains persist where not blocked. With ranges for **A** – **III** of only 17° in torsion angle T1 and 10° in T2 the

central chain is little affected by changes on the periphery, although computer models suggest other possible low-energy conformations. Products of addition to **III** at C8 such as the HCl adduct WUKXOP show a more kinked chain with smaller magnitudes of T1 and T2. T3 ranges from gauche to trans, the smallest magnitude found within the ring of **II** and the largest to accommodate the acetyl groups in **III**.