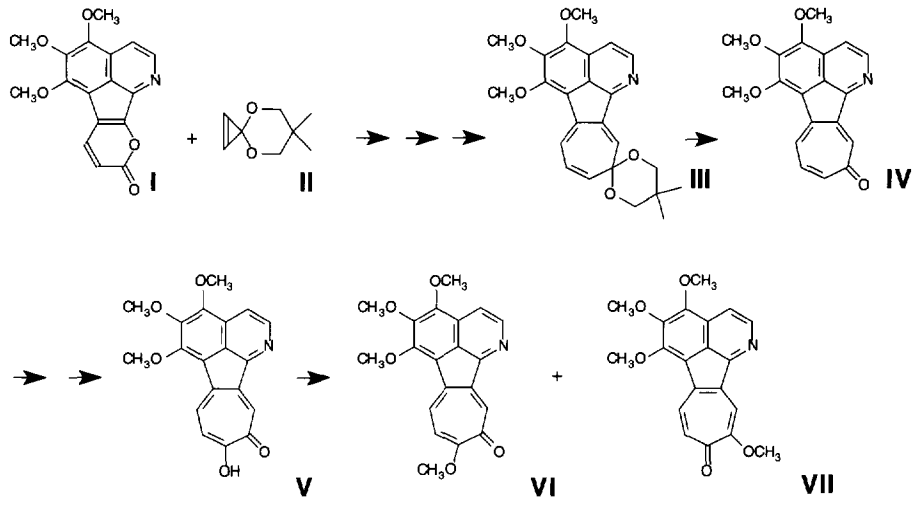
Total synthesis of tropoloisoquinolines

The total synthesis of the naturally occurring tropoloisoquinolines grandirubrine, imerubrine and isoimerubrine are reported by Boger, D.L. and Takahashi, K. [*J. Am. Chem. Soc.* (1995) 117, 12452–12459]. The synthetic approach utilized a [4+2] cycloaddition of the α-pyrone **I** with a cyclopropeneone ketal **II** followed by subsequent retro-Diels-Alder loss of carbon dioxide and norcaradiene rearrangement to the cycloheptatrienone **III**. Hydrolysis of the ketal yielded granditropone **IV**, which was converted into grandirubrine **V** by regioselective hydroxylation. *O*-methylation of grandirubrine yielded both imerubrine **VI** and isoimerubrine **VII** (Scheme 1).

Scheme 1

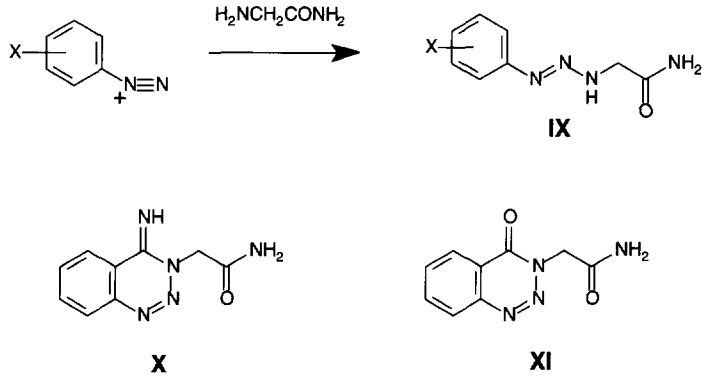


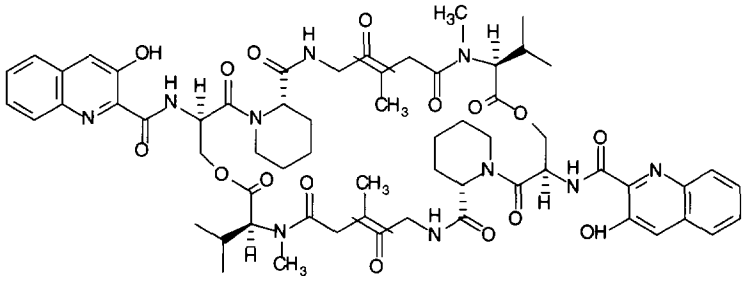
Total synthesis of (–)-sandramycin

Sandramycin **VIII** is a potent antitumour antibiotic which has previously been isolated from a *Norcardioides* sp. (ATCC 39419). Boger, D.L., Chen, J-H. and Saionz, K.W. [*J. Amer. Chem. Soc.* in press] describe the total synthesis and DNA-binding properties of this member of the growing class of natural cyclic decadepsipeptides including the luzopeptins and quinaldopeptins.

The synthetic strategy employed the late-stage introduction of of the heteroaromatic side-chains to allow the synthesis of analogues to modify the extent of intercalation of these side-chains, the coupling of symmetrical pentadepsipeptides, a 32-membered macrocyclization and a convergent route for the assembly of the pentadepsipeptide precursors. This allowed the potentially labile ester linkage to be introduced in the final stages. The major DNA binding was shown to be attributable to the cyclic decadepsipeptide, with the additional heteroaromatic chromaphores causing incremental increases in the binding consistent with the binding of the decadepsipeptide to the minor groove of DNA (with stabilization by bisintercalation of the heteroaromatic groups). DNase I footprinting studies demonstrated that sandramycin binds preferably to regions of DNA containing alternating A and T residues.

Scheme 2





VIII

1-Aryl-3-(caramoylmethyl)triazenes

1-Aryl-3-alkyltriazenes have been used as precursors for the synthesis of nitrogen heterocycles. Jollimore, J.V., Vaughan, K. and Hooper, D.L. [*J. Org. Chem.* (1996) 61, 210–214] describe the synthesis, spectroscopic analysis and cyclization to novel 1,2,3-benzotriazines of a series of amide analogues of the 1-aryl-3-alkyltriazenes, the 3-(caramoylmethyl)triazenes **IX**. The 3-(caramoylmethyl)triazenes were formed by the reaction of aryl diazonium salts with glycinamide (Scheme 2). The reaction was shown to work well with arenes containing electron-withdrawing groups in the ortho- or para-positions. The triazenes with cyano or reactive ester groups in the ortho-position were found to spontaneously cyclize to give 1,2,3-benzotriazene heterocycles **X** and **XI**.