A New Synthesis of Medium Ring and Macrocyclic Acetylenic Lactones from Oxabicycloalkenones *via* their Tosylhydrazones[1]

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Tosylhydrazones **4a–d** of vinylogous lactones **1a–d** on treatment with *N*-bromosuccinimide, under strictly controlled conditions, give the title acetylenic compounds **5a–d** in 65–90% yield.

Medium ring and macrocyclic lactones are important natural products and we have developed several methods for their synthesis,[2,3] including recently the ring expansion of some oxabicycloalkenones **1a–d** to α-chloroketones **3a–d**, *via* their chlorohydrins **2a–d**.[2b,d] Our studies to convert these chloroketones into the corresponding acetylenic and ethylenic compounds are continuing and we now report a novel two-step conversion of **1a–d** to the title acetylenic lactones by the fragmentation of their tosylhydrazones **4a–d** provoked by *N*-bromosuccinimide (NBS),[4] under suitable conditions (Scheme 1).

The vinylogous lactones **1a–d**, prepared by known methods,[2b,5,6] were converted into their tosylhydrazones under standard conditions by gentle refluxing (1–3 h) with tosylhydrazine (1.1 equiv.) in methanol, containing a drop of acetic acid or dilute hydrochloric acid (m.p.s, *t*/°C: **4a**, 175–176; **4b**, 165–167; **4c**, 160–162; **4d**, 169–171). The fragmentation was carried out as follows. To a stirred and cooled (−10 to −15 °C) solution of **4a–d** (5 mmol) in water–*tert*-butyl alcohol (1 : 9; 20 ml) and acetone (20 ml) [**4a** and **4d** also required tetrahydrofuran (20 ml)] was added *N*-bromosuccinimide (2 g, 11.23 mmol) in one portion. The mixture effervesced and turned orange–yellow. After stirring for 15 min, aqueous NaHSO$_3$ solution (2.7 mol l^{-1}; 50 ml) was added, followed by water (100 ml), and the mixture heated at 50–60 °C for 1 h. After cooling and extraction with hexane, the usual work-up gave a yellowish liquid in a quantitative yield. Purification by flash chromatography and/or short-path distillation furnished the pure lactones in 65% (**5a**) to 90% (**5b–d**) yield. Apart from the usual characterization by IR, Raman† (C≡C, ν/cm^{-1}: 2230–2235m and 2290–2294w), and ^{1}H and ^{13}C NMR spectroscopy, these products were hydrogenated to the known compounds: phoracantholide I **6a**,[2a–c] 15-hexadecanolide **6d**[7–9] and dihydrorecifeiolide **6c**.[9,10]

Acetylenic lactones have been prepared earlier either by the oxidative coupling of terminal diacetylenes[11] or by the

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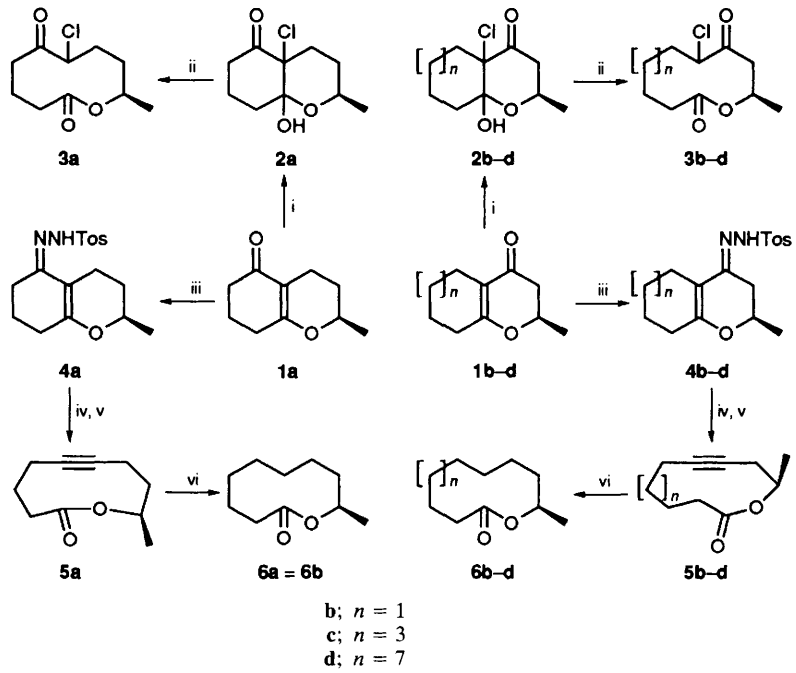
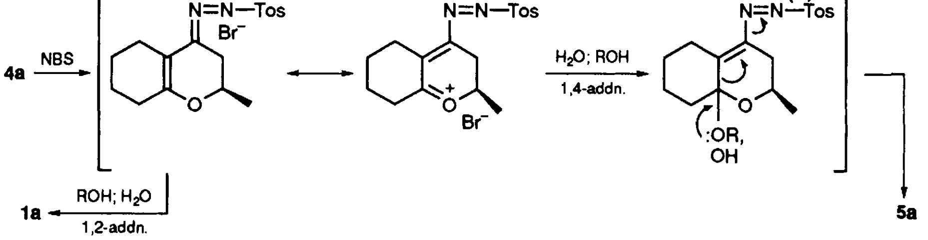
† These acetylenes are IR-inactive.



Scheme 1 *Reagents and conditions*: i, HOCl, EtOAc; ii, DABCO (1,4-diazabicylo[2.2.2]octane), $CHCl_3$, heat; iii, $TosNHNH_2$, MeOH, H^+, heat; iv, aq. Bu^tOH, acetone, NBS, −10 °C; v, aq. $NaHSO_3$, 55 °C; vi, Pd–C, H_2 (Tos = p-$MeC_6H_4SO_2$)



Scheme 2

cyclization of other suitable acyclic precursors.[12–14] A different approach[15] exploits the cobalt-complexed bending of the acetylenic bond to prepare some 11-membered alkynic lactones by an intramolecular procedure.[16] The present methodology is different and is applicable for the ring expansion of both heteroannular and homoannular vinylogous lactones **1a–d**. The closest analogy is the conversion of some bicyclic enones into cycloalkynones, involving the fragmentation of their tosylhydrazones.[4] In fact, based on the proposed mechanism of this fragmentation,[4] we thought that the presence of vinylic oxygen in our substrates **4a–d** would possibly favour the desired 1,4-addition of the nucleophile (ROH, H_2O) over the 1,2-addition, which simply hydrolyses the tosylhydrazone (Scheme 2). This expectation‡ has been realized and we are now investigating the scope of this new method.

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‡ Extra proof for the 1,4-addition of ROH will be provided in the full paper.