Intramolecular Nucleophilic Addition to Photochemically Generated Ketenes as a Versatile Route to Lactones and Lactams; Synthesis of a Mosquito Pheromone, Goniothalamin, Argentilactone, and the *Streptomyces* L-Factor

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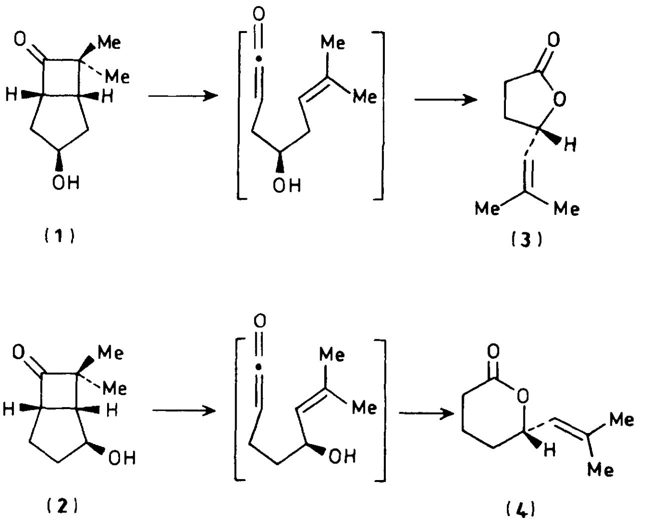
Photolysis of hydroxy-, dihydroxy- and amino-bicyclo[*n*.2.0]alkanones has been used as the key step in the synthesis of naturally occurring lactones including a mosquito pheromone, goniothalamin, argentilactone, and the *Streptomyces* L-factor, and of a γ-lactam.

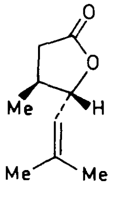
We have reported that photolysis of hydroxybicyclo-[3.2.0]heptanones (**1**) and (**2**) results in the formation of lactones (**3**) and (**4**), respectively, by intramolecular trapping of intermediate ketenes (Scheme 1).[1,2] These lactones were key intermediates in syntheses of (+)-eldanolide (**5**),[1—3] and the leukotriene B_4 intermediate (**6**).[1,4] We now report three significant extensions to our earlier work, which greatly increase the versatility of intramolecular trapping of photochemically generated ketenes as a route to lactones (and lactams) of defined stereochemistry. We illustrate this versatility by syntheses of four naturally occurring lactones and a lactam. The three extensions are: (i) selective trapping by diols, (ii) the use of 7-monosubstituted bicyclo[3.2.0]heptanones, and (iii) trapping by an amino group.

Selective trapping by a diol is exemplified by our synthesis of the oviposition attractant pheromone (**7**) of the mosquito, *Culex pipieris fatigans*[5] (for earlier syntheses see ref. 6), shown in Scheme 2. Although the yield of the photochemical step was only *ca.* 25%, the required δ-lactone (**8**) was the only isolable product.

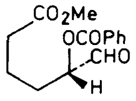
The use of a 7-monosubstituted bicyclo[3.2.0]heptanone is illustrated by our syntheses of goniothalamin (**9**)[7] and argentilactone (**10**)[8] from the common precursor (**11**), as shown in Scheme 3. The excellent yield of the photochemical step in this case is noteworthy.



Scheme 1



(5)



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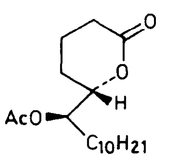
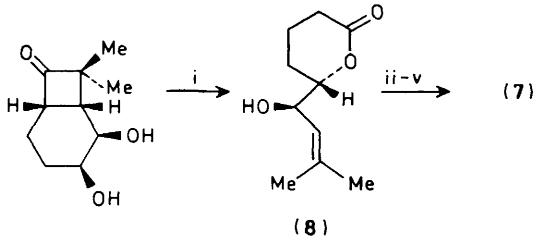
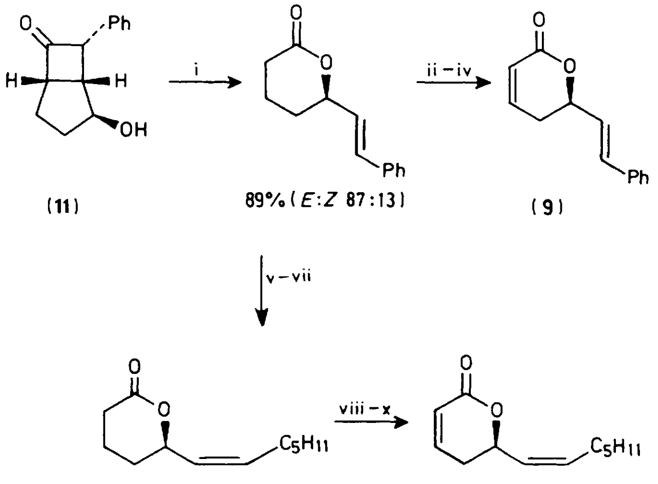


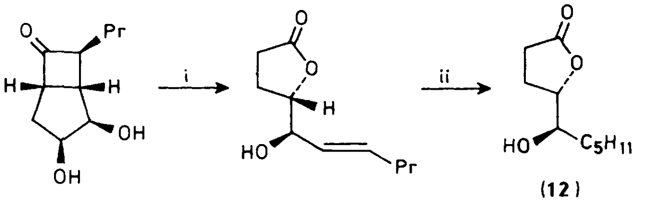
(7)



Scheme 2. *Reagents and conditions*: i, *hν*; ii, Ac_2O, 4-dimethylaminopyridine; iii, O_3, then Me_2S; iv, $Me(CH_2)_8PPh_3Br$, Bu^tOK; v, H_2, Pd/C.

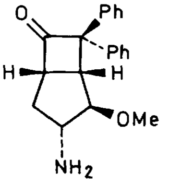


Scheme 3. *Reagents and conditions*: i, *hν*; ii, lithium di-isopropylamide; iii, PhSeBr; iv, H_2O_2; v, O_3. vi, Me_2S; vii, $C_5H_{11}CH_2PPh_3Br$, Bu^tOK; viii, $LiN(SiMe_3)_2$; ix, PhSeBr; x, H_2O_2.

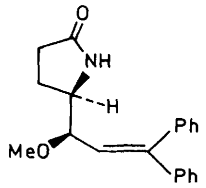


(12)

Scheme 4. *Reagents and conditions*: i, *hν*; ii, H_2, Pd/C.



(13)



(14)

Both selective trapping and a 7-monosubstituted bicycloheptanone are utilised in a very short synthesis of the *Streptomyces* L-factor (**12**),[9] shown in Scheme 4. It is remarkable that even a 7-*alkyl* group leads to cleavage of the C(6)—C(7) bond.

Finally, we report a preliminary result, which indicates that our methodology can be used to synthesise lactams. Photolysis of the amine (**13**) gave the lactam (**14**) in 45% yield.

All the syntheses reported in this Communication are of racemic materials. However, our earlier studies[1,2] have shown that when chiral starting materials are used the overall stereochemical control is excellent. The required chiral materials are in principle obtainable by microbiological resolution (*cf.* ref. 2) or by methods such as asymmetric dihydroxylation,[10] and work along these lines is continuing.

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