

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

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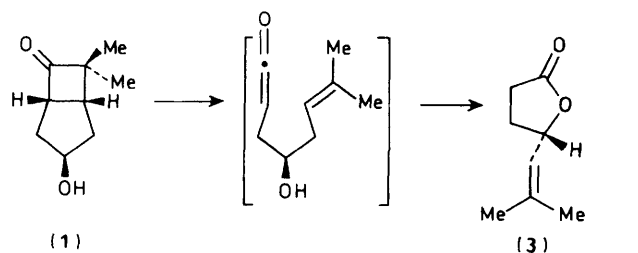
Photolysis of hydroxy-, dihydroxy- and amino-bicyclo[*n*.2.0]alkanones has been used as the key step in the synthesis of naturally occurring lactones including a mosquito pheromone, goniiothalamine, argentilactone, and the *Streptomyces* L-factor, and of a  $\gamma$ -lactam.

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).<sup>1,2</sup> These lactones were key intermediates in syntheses of (+)-eldanolide (**5**),<sup>1-3</sup> and the leukotriene B<sub>4</sub> intermediate (**6**).<sup>1,4</sup> We now report three significant extensions to our earlier work, which greatly

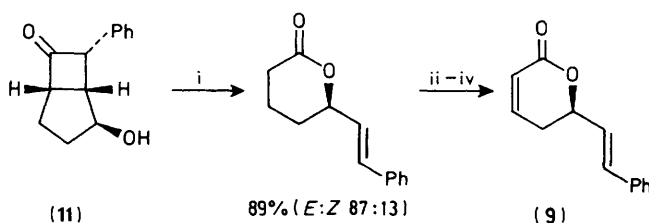
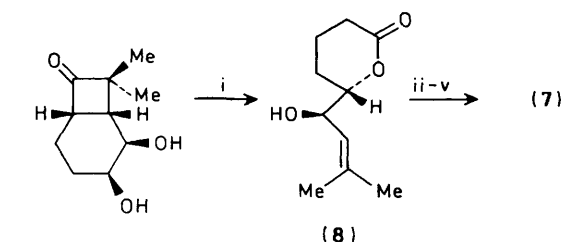
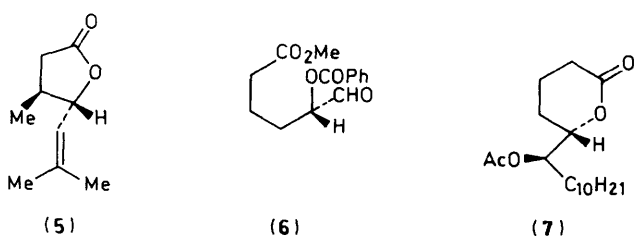
increase the versatility of intramolecular trapping of photochemically generated ketenes as a route to lactones (and lactams) of defined stereochemistry. We illustrate this versatility by syntheses of four naturally occurring lactones and a lactam. The three extensions are: (i) selective trapping by 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 pipiens fatigans*<sup>5</sup> (for earlier syntheses see ref. 6), shown in Scheme 2. Although the yield of the photochemical step was only ca. 25%, the required  $\delta$ -lactone (**8**) was the only isolable product.

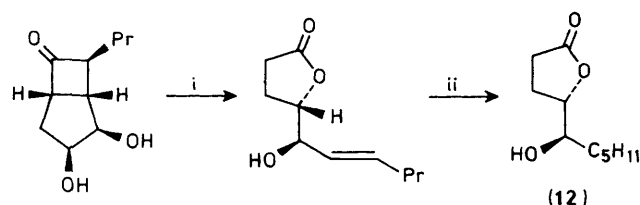
The use of a 7-monosubstituted bicyclo[3.2.0]heptanone is illustrated by our syntheses of goniiothalamine (**9**)<sup>7</sup> and argentilactone (**10**)<sup>8</sup> from the common precursor (**11**), as shown in Scheme 3. The excellent yield of the photochemical step in this case is noteworthy.



Scheme 1

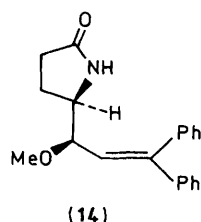
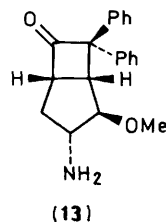


Scheme 3. Reagents and conditions: i, hv; ii, lithium di-isopropylamide; iii, PhSeBr; iv, H<sub>2</sub>O<sub>2</sub>; v, O<sub>3</sub>; vi, Me<sub>2</sub>S; vii, C<sub>5</sub>H<sub>11</sub>CH<sub>2</sub>PPh<sub>3</sub>Br, Bu<sup>t</sup>OK; viii, LiN(SiMe<sub>3</sub>)<sub>2</sub>; ix, PhSeBr; x, H<sub>2</sub>O<sub>2</sub>.



Scheme 4. Reagents and conditions: i, hv; ii, H<sub>2</sub>, Pd/C.

Scheme 2. Reagents and conditions: i, hv; ii, Ac<sub>2</sub>O, 4-dimethylaminopyridine; iii, O<sub>3</sub>, then Me<sub>2</sub>S; iv, Me(CH<sub>2</sub>)<sub>8</sub>PPh<sub>3</sub>Br, Bu<sup>t</sup>OK; v, H<sub>2</sub>, Pd/C.



Both selective trapping and a 7-monosubstituted bicycloheptanone are utilised in a very short synthesis of the *Streptomyces* L-factor (12),<sup>9</sup> 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<sup>1,2</sup> 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,<sup>10</sup> and work along these lines is continuing.

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