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# Syntheses of Argentilactone 11 and Goniothalamin 15

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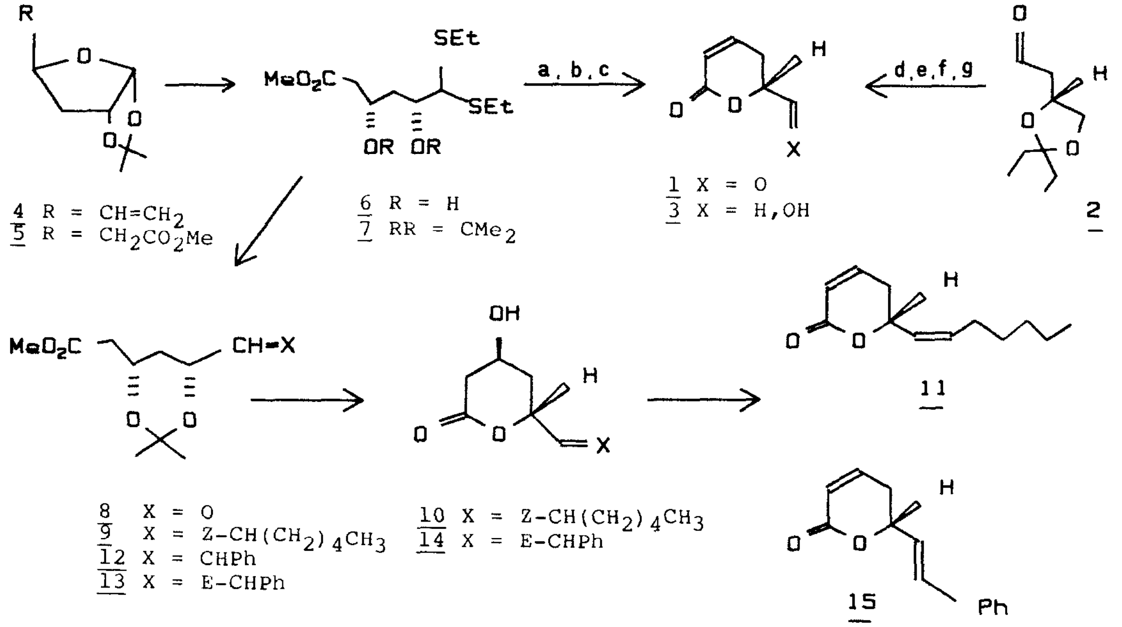
Abstract: Syntheses of (-)-(5R)-argentilactone 11 and (+)-(5R)-goniothalamin 15 are described starting from olefin 4.

The olefinic $\alpha,\beta$-unsaturated $\delta$-lactone subunit is a feature found in natural products such as argentilactone[1], goniothalamin[2], CI-920[3], PD 113 270[3] and anamarine[4]. All of these may, in principle, be synthesized from aldehyde 1 by a Wittig reaction. We were able to prepare this aldehyde in an impure form in very low yield only, (see scheme) and oxidation of alcohol 3, obtained from 2 as described, failed in our hands.

The problem was solved in the following way. Hydroboration[5] of olefin 4[6] (9-BBN/ THF/ reflux 5 hours/ 99% yield) followed by Jones oxidation and methylation gave ester 5 in 73% yield. Careful monitoring was required during formation of the thioacetal 6[7] ($ZnCl_2$/ EtSH, EtOAc/ $0^{\circ}$, 20 minutes/ 83% yield) since a significant amount of side product (with the same $R_F$ as the starting material) was formed if the reaction was left to proceed too long. Thioacetal 6 was transformed (acetone/ 2,2-dimethoxypropane/ pTSA/ 83%) to acetonide 7, which when deprotected (HgO/ $HgCl_2$/ acetone/ $H_2O$) gave crude aldehyde 8. This was used as such for the Wittig reaction (hexyltriphenylphosphonium bromide/ n-BuLi/ THF/ HMPA) to give olefin 9 (50% yield from acetonide 7) as its cis isomer only. Cyclization of olefin 9 (TFA/ THF/ $H_2O$ 1:2:1) to give lactone 10 (47% yield), followed by elimination of the hydroxyl group (2eq $MeSO_2Cl$/ 4eq $NEt_3$/ $CH_2Cl_2$/ $-50^{\circ}$ ) gave, after purification by flash chromatography, (-)-(5R)-argentilactone 11 in 90% yield[8]. In a similar fashion, reaction of crude aldehyde 8 with the anion of benzyltriphenylphosphonium chloride gave olefin 12 in 57% yield from acetonide 7 ( E:Z / 1:9 ). This was converted to a 7:3 mixture of its E and Z isomers respectively (PhSH/ AIBN/refluxing benzene/6 hours) according to the procedure of Schwarz et al[9]. Separation and recycling gave a 75% yield of olefin 13. Cyclization gave lactone 14 which could be transformed, as for argentilactone, into (+)-(5R)-goniothalamin 15[10] (54% yield from olefin 13).



a) pTSA/$CH_2Cl_2$/room temp, b) 2eq $MeSO_2Cl$/4eq $NEt_3$/$CH_2Cl_2$/-50°,
c) NCS/$AgNO_3$/$CH_3CN$,$H_2O$ (71%), d) $CBr_4$/$PPh_3$/Zn dust/$CH_2Cl_2$,
e) 2eq n-BuLi/ $ClCO_2Me$, f) $H_2$/Lindlar cat., g) 1% HCl in MeOH.

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## References and Notes

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8) The $^1$NMR data was in accordance with that reported by Priestap et al[1] HRMS, m/e calcd for $C_{12}H_{18}O_2$ 194.1306, found 194.1321 $[\alpha]_D$ -20.7° (c 5.5, EtOH); lit.[1] $[\alpha]_D$ -21.1° (c 2.25, EtOH).
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10) The $^1$NMR data was in accordance with that reported by Hulbucek et al[2] HRMS, m/e calcd for $C_{13}H_{12}O_2$ 200.0837, found 200.0889 $[\alpha]_D$ +128° (c 2.5, MeOH); lit.[2] $[\alpha]_D$ +135° (0.7% in MeOH).

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