A Concise Synthesis of 5 *R-cis*-Hagen's-Gland Lactones by Chiron Approach

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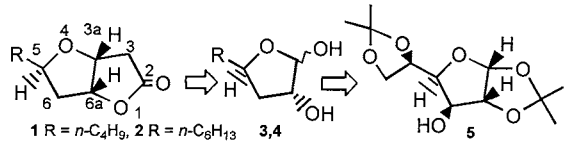
An enantiospecific and potentially general synthesis of bicyclic lactones **1** and **2** is described by chiron approach starting from 'diacetone-D-glucose'.

Hagen's gland secretions of parasitic wasps in the family Braconidae have been implicated in defense against predators and were discussed in connection with mating or courtship behavior.[1,2] Williams and coworkers[3] have shown by chemical analysis that glands of braconid wasps *Diachasmimorpha longicaudata* contain two bicyclic lactones tentatively identified as (3aα,5β,6aα)-5-butyltetrahydrofuro[3,2-*b*]fura-2(3*H*)-one **1** and a corresponding 5-hexyl derivative **2**[3] based on ^{1}H-NMR considerations. Absolute stereochemistry was established by Kitching et al[4] based on the synthesis of diastereomeric mixture of **1** and **2** by carbonylation-lactonization protocol.

In this report we describe a considerably simpler, enantiospecific synthesis of bicyclic lactones **1** and **2** by a potentially general pathway. For the assemblage of the tetrahydro furofuranone unit, retrosynthetic analysis dictated by chiron approach, diacetone-D-glucose **5** was transformed by known sequence of reactions to 3-deoxy diol **6**[5] and further to



(*cis* refers to the orientation of R relative to the ring-junction hydrogens)

the aldehyde ($NaIO_4$, CH_2Cl_2, aq. $NaHCO_3$) that on immediate reaction with alkylidenephosphoranes (*n*-$C_3H_7PPh_3Br$ and *n*-$C_5H_{11}PPh_3Br$, *n*-BuLi, THF, -78 °C, 3-4 h) severally gave **7** and **8** respectively in 87% yield. Hydrogenation of **7** and **8** (C_2H_5OH, Raney-Ni, 40 psi, H_2, 4 h) gave **9** and **10** respectively that on subsequent hydrolysis (aq. HOAc, cat. H_2SO_4, 45 °C, 5 h) gave the lactals **3** and **4** respectively in good overall yields. **3** and **4** on Wittig olefination (Ph_3P=$CHCO_2Et$, MeOH, 10 °C, 8 h) gave the required *cis*-bicyclic lactones **1** $[\alpha]_D$ +51.1° (*c* 1.0, $CHCl_3$) and **2** $[\alpha]_D$ + 49.7° (*c* 1.0, $CHCl_3$) in low yields (51-53%) along with *trans* olefins **13** and **14** (26-29%). Yields of **1** and **2** were improved to 70-75% (**13** and **14** in 11%) when a similar reaction of **3** and **4** was carried out with $(CF_3CH_2O)_2P(O)CHCO_2Et$. Formation of intermediates **11,12** and lactones **15,16** was not observed. ^{1}H and ^{13}C-NMR data of **1** and **2** are consistent with those reported in literature[3,6] and are virtually identical, they differ only in the integration of broad multiplet between δ 0.8-1.8.

In conclusion, enantiospecific synthesis of **1** and **2** has been achieved by chiron approach starting from 'diacetone-D-glucose', their potential role as biological control agents will be examined in due course. Application of this method for the construction of several other natural products containing such bicyclic lactones is in progress.

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References and Notes

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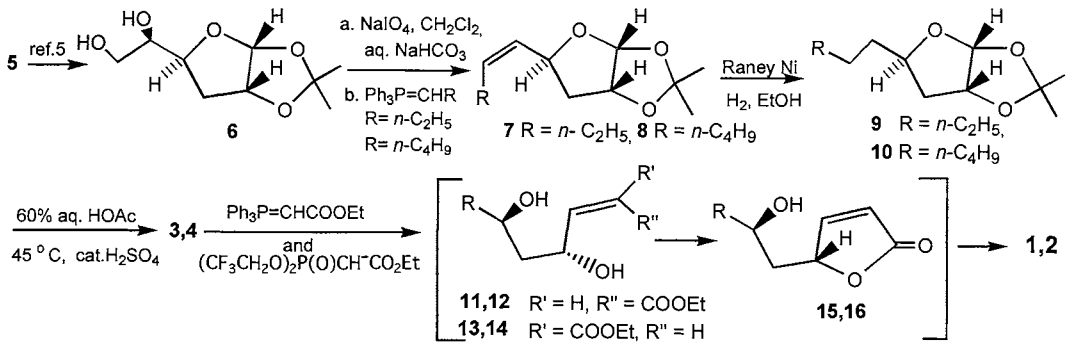
6 Spectral Data of **1**.^{1}H NMR (200 MHz, $CDCl_3$) δ= 0.8-1.8 (10H, m, H-6α and C_4H_9), 2.38 (1H, dd, *J*= 14.8 and 4.2 Hz, H-6β), 2.64 (1H, dd, *J*= 19.1 and 0.7 Hz, H-3β), 2.75 (1H, dd, *J*= 19.1 and 6.4 Hz, H-3α), 4.07 (1H, dddd, *J*= 10.0, 7.2, 5.2, and 4.2 Hz, H-5), 4.80 (1H, ddd, *J*= 6.4, 4.5, and 0.7 Hz, H-3a), and 5.11 (1H, dd, *J*= 4.9 and 4.5 Hz, H-6a); ^{13}C NMR (50 MHz, $CDCl_3$) δ= 13.8, 12.5, 28.0, 34.2, 36.5, 38.6, 77.2, 78.1, 84.8, and 175.9 (C=O). All the new compounds gave satisfactory elemental analysis.



Scheme 1.

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