Communications to the Editor

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A FORMAL SYNTHESIS OF (+)-DISPARLURE FROM AN OPTICALLY ACTIVE 2-FURYLCARBINOL

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(4S,5S)-5-Hydroxy-4-pentadecanolide (**7**), a key intermediate for the synthesis of (+)-disparlure (**8**), has been synthesized from (S)-1-(2'-furyl)undecanol (**3**) using highly syn-selective reduction of 2-alkoxyketone **5**.

KEYWORDS ——— (4S,5S)-5-hydroxy-4-pentadecanolide; (+)-disparlure; asymmetric synthesis; reduction; 2-furylcarbinol

Recently, Sato[1)] and we[2)] have independently developed an efficient preparation of an optically active 2-furylcarbinols **2** based on the Sharpless kinetic resolution methodology. We also reported[2)] an asymmetric synthesis of (5R,6S)-6-acetoxy-5-hexadecanolide (**6**), a mosquito oviposition attractant pheromone, from the optically active (S)-**3** (>98% ee) employing a stereoselective reduction of 2-hydroxyketone **5** as a key step (Chart 1). In connection with synthesis of polyoxygenated natural products from furan derivatives,[3)] we here describe a simple and efficient transformation of the optically active **3** into a highly versatile hydroxylactone **7**, which constitutes a formal synthesis of (+)-disparlure (**8**),[4)] the pheromone of the gypsy moth (Porthetria dispar).

To establish the stereoselective introduction of 1,2-syn and/or anti diol functionalities, we first examined the reduction of hex-2-enopyranoside derivatives **4**, having a diastereomixture (ca 1:1) at an anomeric position, under various conditions (Chart 2). Reduction of **4a** with metal hydrides, such as sodium borohydride and lithium aluminum hydride, gave predominantly **9** rather than **10** in a ratio of 2 - 1:1.[5)] A similar result was obtained in the hydrogenation of **4** employing platinum oxide in ethyl acetate to afford diols **11** and **12** in a ratio of 3:2. We then investigated the stereoselective reduction of the 2-alkoxyketone **5**,[6)] whose selectivity can be controlled to give either the syn or anti diol by the proper choice of reducing agent and alcohol protecting group. The results are shown in Table I. The anti selectivity obtained from the reaction of **5** with zinc borohydride[6b)] in ether (entry 4, 5 and 12) can be rationalized by assuming the Cram's chelation model. When the bulky t-butyldiphenylsilyl ether was employed (entry 7-10), the syn selectivity occurred with "ate" complexes such as Red-Al[6)] and L-Selectride[7)] to produce the Cram product **13**. Interestingly, reduction of **5** (R=H) with sodium borohydride in methanol (entry 1-3) showed the moderate syn selectivity, which might be explained by considering the dipolar model.

Both syn and anti diols **13** and **14** were easily separated as their corresponding acetonides **15** and **16**, which were further transformed into the hydroxy lactones **7** and **19**, respectively, as follows (Chart 3). Hydrolysis of the dithioacetal **15** employing red mercuric oxide and boron trifluoride etherate gave the aldehyde **17**, $[\alpha]_D^{23} = -25.51^\circ$ ($\underline{c}$=0.29, $CHCl_3$), in 87% yield, whose oxidation[8)] with sodium chlorite and 2-methyl-2-butene in $\underline{t}$-butyl alcohol afforded the carboxylic acid **18**, $[\alpha]_D^{26} = -25.9^\circ$ ($\underline{c}$=1.795, $CHCl_3$), in 99% yield. Deprotection of the acetonide **18** followed by lactonization in the usual manner gave the hydroxy lactone **7**, $[\alpha]_D^{25} = +25.76^\circ$ ($\underline{c}$=1.319, $CHCl_3$) [lit.[9)] $[\alpha]_D^{20} = +29.2^\circ$ ($\underline{c}$=1.2, $CHCl_3$) , whose spectroscopic data were identical with those reported.[9)] Similar treatment of **16** afforded the corresponding lactone **19**, $[\alpha]_D^{23} = -13.72^\circ$ ($\underline{c}$=0.976, $CHCl_3$).[10)] The ^{1}H-NMR data of **19** were identical with those reported.[9)] Finally, the enantiomeric excess of both hydroxy lactones **7** and **19** was determined on the basis of ^{1}H-NMR (270 MHz) analysis of the corresponding MTPA esters of **7**, **19**, and their racemic compounds, indicating the optical purities of **7** and **19** to be >98%. Since **7** was already converted into (+)-disparlure, this constitutes a formal synthesis of (+)-disparlure.

In conclusion, we have successfully applied ($\underline{S}$)-**3**, prepared[2)] by the Sharpless kinetic resolution of the racemate, to a synthesis of (+)-disparlure. We are currently investigating further applications of an optically active 2-furylcarbinol to the synthesis of other natural products.

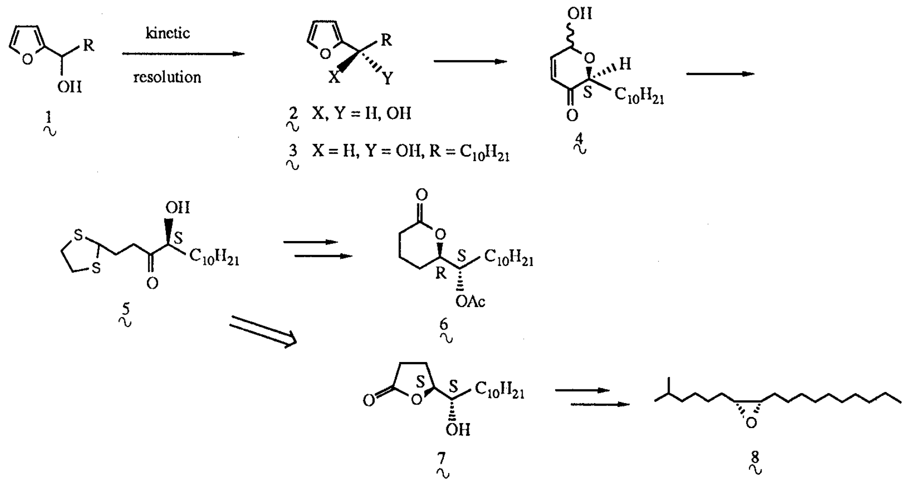


Chart 1

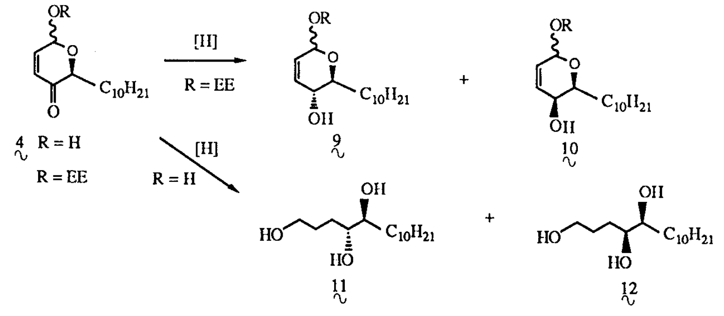
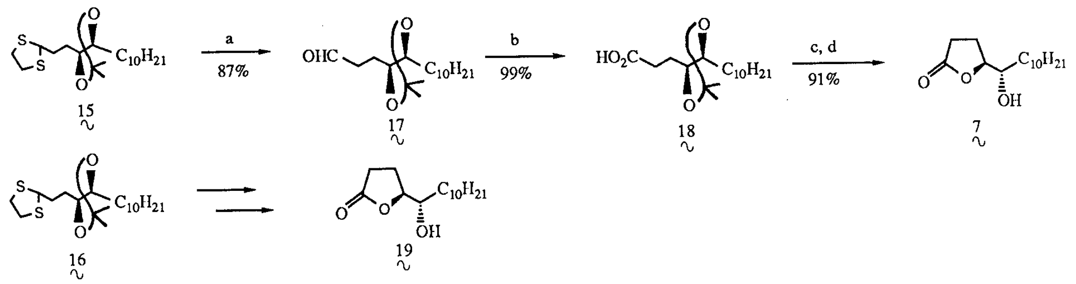


Chart 2



a) red HgO, $BF_3 \cdot OEt_2$, aq. THF; b) $NaClO_2$, 2-methyl-2-butene, tert-BuOH, KH_2PO_4, H_2O; c) $AcOH$-H_2O, 100°C; d) benzene, p-TsOH, reflux

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LICORICE-SAPONINS A3, B2, C2, D3, AND E2, FIVE NEW OLEANENE-TYPE TRITERPENE OLIGOGLYCOSIDES FROM CHINESE GLYCYRRHIZAE RADIX

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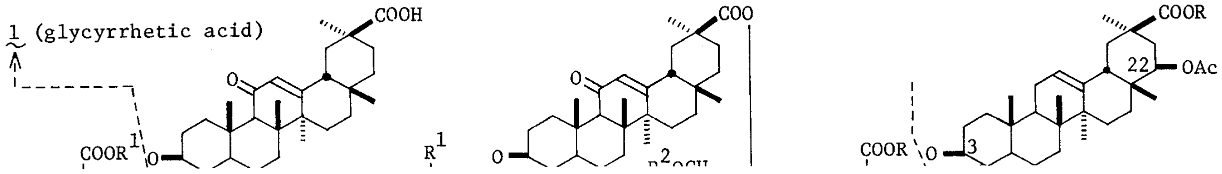
Ten new oleanene-type triterpene oligoglycosides were isolated from Chinese Glycyrrhizae Radix, the dried root of Glycyrrhiza uralensis Fischer [Tohoku-Kanzo (in Japanese) from China], and the structures of five oligoglycosides, named licorice-saponins A3 (3), B2 (5), C2 (7), D3 (9), and E2 (12), have been determined on the basis of chemical and physicochemical evidence.

KEYWORDS —— Glycyrrhizae Radix; Glycyrrhiza uralensis; licorice-saponin A3; licorice-saponin B2; licorice-saponin C2; licorice-saponin D3; licorice-saponin E2; oleanene-type triterpene oligoglycoside

Glycyrrhizae Radix (licorice root, the root of Glycyrrhiza sp.) is a Chinese



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10) The specific rotation of the enantiomer of **19** was also reported by S. Iwaki et al.8) $[\alpha]_D^{20} = +14.8^\circ$ (c=1.2, $CHCl_3$).

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