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PENTACYCLIC TRITERPENE SYNTHESIS. III. PREPARATION OF AN OPTICALLY ACTIVE SYNTHON FOR RINGS A AND B

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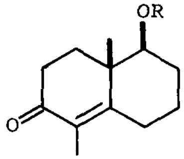
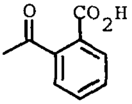
In previous communications, we have outlined syntheses of decalinic substances which are synthons for the AB[1] and DE[2] rings of the pentacyclic triterpene β-amyrin, and which may be used in a convergent synthesis of the terpene. One feature of a convergent synthesis in which both major building blocks are chiral is the necessity that the sub-units be resolved prior to coupling. In this communication, we report the resolution of 5β-hydroxy-1,4aβ-dimethyl-4,4a,5,6,7,8-hexahydro-2(3H)-naphthalenone (1), a substance which, in racemic form, has already been converted into a potential precursor for rings A and B of β-amyrin, as well as other triterpenes of the oleane, ursane, or lupane families.[1]



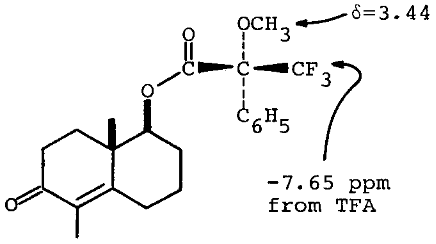
1: R = H

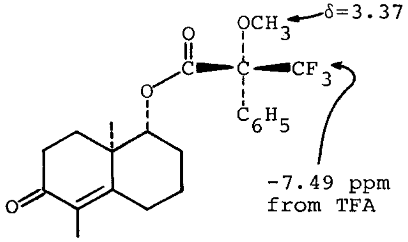
2: R =



Racemic 1 (m.p. 88-89°)[1] is allowed to react with 1.2 equivalents of phthalic anhydride in anhydrous pyridine to afford the racemic half-phthalate ester 2 (m.p. 186-190°) in 83% yield. Compound 2 is treated with brucine and the resulting salt crystallized 3-4 times from acetone to obtain a crystalline "insoluble" brucine salt ($[\alpha]_D^{25°}$ = +20.98 (2.02, $CHCl_3$)) and a non-crystalline "soluble" brucine salt. The two brucine salts are dissolved in hot acetone, then poured into cold 5% aqueous HCl. After stirring at room temperature, the solid phthalate ester is collected by filtration. The crystalline salt yields a dextrorotatory ester and the non-crystalline residual salts yield a levoratatory phthalate ester. The two phthalates are recrystallized to give (+)-2 (m.p. 190-192.5°; $[\alpha]_D^{25°}$ = 172.6 (2.01, $CHCl_3$)) in 89% yield and (-)-2 (m.p. 190-192.5°; $[\alpha]_D^{25°}$ = -174.5 (2.02, $CHCl_3$)) in 79% yield.

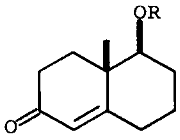
Compound (+)-2 is treated with 25% aqueous KOH at 25° while being continuously extracted with ether to obtain oily (+)-1 ($[\alpha]_D^{25°}$ + 162.6 (2.17, $CHCl_3$)) in 100% yield. Similar treatment of (-)-2 affords (-)-1 ($[\alpha]_D^{25°}$ -164.6 (2.16, $CHCl_3$)) in 100% yield. The solution ir and nmr spectra of (+)-1 and (-)-1 are identical to those of the racemic hydroxy ketone. The overall resolution yields are 75% for (+)-1 and 67% for (-)-1. Optical purities were determined by Mosher's method using (R)-2-phenyl-2-methoxy-3,3,3-trifluoropropanoyl chloride.[3] Enantiomeric analysis was accomplished by using the methoxy resonance in the ^{1}H-nmr spectrum or the CF_3 resonance in the ^{19}F-nmr spectrum.



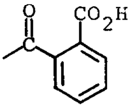


The optical purity of (+)-1 was found to be ≥93% and that of (-)-1 was found to be ≥93%.

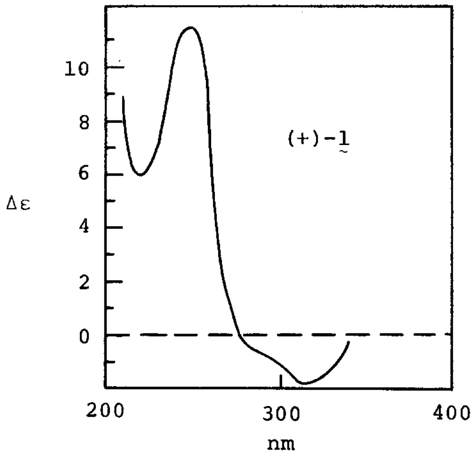
Absolute configurations were assigned by comparing the CD curves of (+)-1 and (-)-1 with those of the enantiomeric 5β-hydroxy-4aβ-methyl-4,4a,5,6,7,8-hexahydro-2(3H)-naphthalenones (3),[4] whose absolute stereostructures have been



3: R = H

4: R = 

rigorously established.[5] The CD curve of optically pure (+)-1 is shown below.



On the basis of these comparisons, (+)-1 is assigned the 4aS,5S configuration and (-)-1 the 4aR,5R configuration.

The present resolution was patterned after the previously reported resolution of compound 3.[4] However, the modifications outlined here result in much higher material and optical yields than were realized by the previous workers.

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