A new synthesis of (±) and (+)-2,6,7,7a-tetrahydro-1β-hydroxy-4-formyl-7αβ-methylindenes

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Abstract. A new method for the preparation of the synthon (±)-2,6,7,7a-tetrahydro-1β-hydroxy-4-formyl-7αβ-methylindene (1,a) for the total synthesis of steroids in both (±) and (+) forms, starting from the known β-ketoester, (±)-methyl 1β-t-butoxy-5,6,7,7a-tetrahydro-7αβ-methyl-5-keto-4-indanscarboxylate (2,a) has been described. An alternative route to (1,a) has been investigated. Although the compound, (±)-1β-hydroxy-5,6,7,7a-tetrahydro-7αβ-methyl-5-keto-4-methoxymethylindan (2,b) could not be prepared, interesting pathways leading to two unexpected products, (±)-5,6,7,7a-tetrahydro-4,7α-dimethyl-5H-indene-1,5-dione and (±)-2,6-diketo-3-methyltricyclo-(5,2,1,0)decan-8-ol (3 and 4), were encountered during an attempted annelation reaction of the ketone, N-diethylamino-5-methoxypentan-3-one (6), with 2-methylcyclopentan-1,3-dione (5). Trapping of the intermediate, (±)-3α,4,5,6,7,7a-hexahydro-3α-hydroxy-4-methylene-7αβ-methylindene-1,5-dione (7), through the formation of the adduct, (±)-3α,4,5,6,7,7a-hexahydro-3α-hydroxy-4,1' 3'-diketo-2'-methylcyclopentano-2'-methylene)-7αβ-methylindene-1,5-dione (8), established the mechanism of the formation of the products (3 and 4).

Keywords. New synthesis; racemic and asymmetric synthesis; steroid synthone.

1. Introduction

The syntheses of (±) and (+)-2,6,7,7a-tetrahydro-1β-hydroxy-4-formyl-7αβ-methylindenes (1,a) were reported earlier by us (Banerjee et al 1976, 1983), the yield in the last oxidation step being moderate and inconsistent, depending upon the brand of the reagent used. This prompted us to look for alternative routes.

2. New synthesis of (±) and (+)-2,6,7,7a-tetrahydro-1β-hydroxy-4-formyl-7αβ-methylindenes

2.1 Synthesis of (±)-2,6,7,7a-tetrahydro-1β-hydroxy-4-formyl-7αβ-methylindene

Our starting material of choice for this synthesis was the diketoester (9, b or c), which has been earlier prepared by Collins and Tomkins (1977) and Ellis et al (1974). With the view to improving upon the yields obtained by the above workers, we utilized the β-ketoacid (2, c), prepared by Micheli et al (1975) from the enedione (10) which was prepared earlier by Boyce and Whitehurst (1959) in 70%
Chart 1.