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SIMPLE SYNTHESES OF PROSTANOID SYNTHONS

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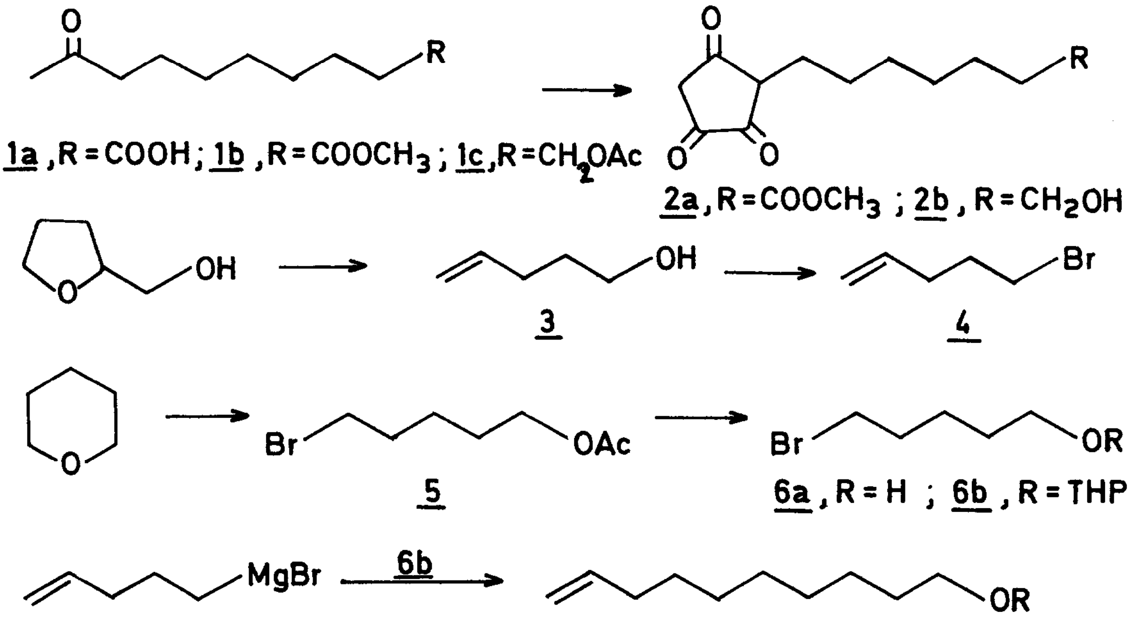
9-Oxodecanoic acid (1a) is a key intermediate in the synthesis of prostanoid synthons (2a & 2b)[1-3]. We wish to report here, a simple synthetic route (as shown below) for the preparation of this keto-acid via 9-decenol (7b). The acetate of this olefin alcohol was also used for the synthesis of the trione alcohol (2b) in high yield. The procedure is based on the Grignard coupling reaction and oxidation of the terminal olefin to methyl ketone.



1a, R = COOH; 1b, R = COOCH$_3$; 1c, R = CH$_2$OAc

2a, R = COOCH$_3$; 2b, R = CH$_2$OH

3

4

5

6a, R = H ; 6b, R = THP

7a, R = THP ; 7b, R = H ; 7c, R = Ac

4-Penten-1-ol (3) was prepared from tetrahydrofurfuryl alcohol by the known procedure[4]. The reaction of 3 with PBr$_3$-pyridine[5] gave 1-bromo-4-pentene (4) in 84% yield.

The C$_5$ bromoalcohol (6a) was obtained by the ring opening of tetrahydropyran[6] with acetyl bromide followed by the hydrolysis of the intermediate bromoacetate (5)[7]. The alcohol group of 6a was protected using dihydropyran by the usual method to afford 6b. Coupling of the Grignard reagent prepared from bromopentene (4) in tetrahydrofuran with 6b was carried out at -5° via organo-copper (I) intermediate using catalytic quantities (ca. 0.3%) of dilithium tetrachlorocuprate[8] to give 7a which on hydrolysis of the protecting group (p-toluenesulphonic acid in aqueous methanol, Δ, 2h) afforded 9-decenol (7b) in 65% yield [b.p. 108°/8 mm (reported[9] 80-82°/0.8 mm); I.R. ν max (film): 3390 (OH), 1665, 995, 915 (-CH=CH$_2$) cm^{-1}; NMR (CDCl$_3$) δ : 2.51 (s, 1H, -OH, D$_2$O exchangeable), 3.63 (t, J = 6Hz, 2H, -CH$_2$OH), 4.85-6.13 (m, 3H, -CH=CH$_2$)]. The Jones oxidation of 7b, catalysed by mercuric acetate[10], to methyl ketone was also accompanied by the oxidation of the primary alcohol to give the desired intermediate (1a) in 72% yield [m.p. 48° (reported[11] 47.5-48.5°); NMR (CDCl$_3$) δ ; 2.10 (s, 3H, CH$_3$-CO-), 10.83 (s, 1H, -COOH, D$_2$O exchangeable)].

Acetylation of 9-decenol (7b) by the usual method furnished 7c in quantitative yield [b.p. 60-65°/8 mm (frothing); I.R. ν max (film): 1750, 1240 (acetate), 1645, 995, 915 (-CH=CH$_2$) cm^{-1}; NMR (CDCl$_3$) δ : 2.02 (s, 3H, -O-CO-CH$_3$), 4.05 (t, J = 6.5Hz, 2H, -CH$_2$OCOCH$_3$), 4.75-6.10 (m, 3H, -CH=CH$_2$)]. This terminal olefin acetate when subjected to oxidation[10] as mentioned above yielded the required key intermediate 9-oxodecanol acetate (1c) [b.p. 144-146°/6 mm, I.R. ν max (film): 1740, 1245 (acetate), 1715 (ketone) cm^{-1}; NMR (CDCl$_3$) δ : 2.02 (s, 3H, -O-CO-CH$_3$), 2.13 (s, 3H, CH$_3$-CO-), 4.05 (t, J = 6.5Hz, 2H, -CH$_2$-OCOCH$_3$)] for the synthesis of the trione alcohol (2b).

The conversion of the methyl ketones (1b) and (1c) to the corresponding triones (2a) and (2b) was accomplished in 70% yield[12] by condensation with diethyl oxalate in the presence of sodium ethoxide by known procedure[1]. The physical data of these compounds are in good agreement with those described in literature[1,3].

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12. The trione alcohol (2b) was reported[3] in 31% yield from 9-oxodecanol.