THE INTRAMOLECULAR OPENING OF THE OXIRANE RING IN BUTYL 4,5-EPOXY-2-HYDROXYHEXANOATE. A NEW SIMPLE SYNTHESIS OF RACEMIC ALLOMUSCARINE

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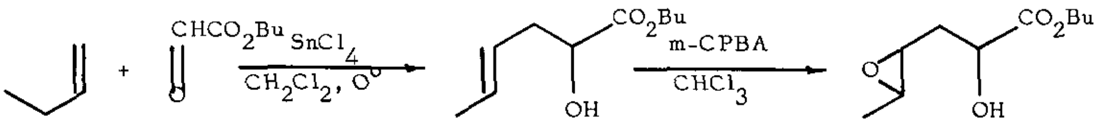
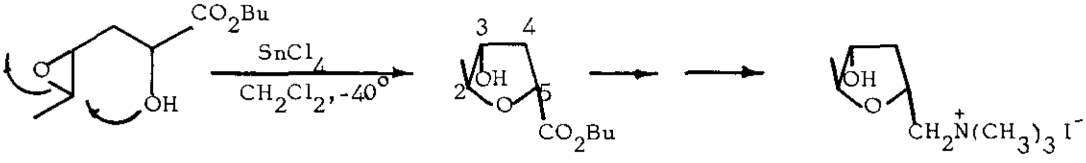
Abstract - The new simple synthesis of racemic allomuscarine via the intramolecular opening of the trans substituted epoxide ring in butyl 4,5-epoxy-2-hydroxyhexanoate is described.

The intramolecular opening of the epoxide ring in esters of 4,5-epoxy-2-hydroxyhexanoic acid by the hydroxyl group to a tetrahydrofuran derivative is a new way to C-glycofuranosides. The model β-hydroxyepoxide grouping 1 can be obtained via an ene reaction between butyl gloxylate and but-1-ene followed by the epoxidation of the double bond with m-chloroperoxybenzoic acid.[1]



1

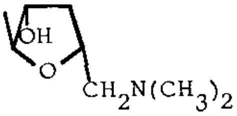
The mixture of diastereomeric epoxides 1 (6:4) treated with 0.5 equiv. of stannic chloride in methylene chloride at -40°C undergoes intramolecular opening of the epoxide ring to afford 2[2] as the major product (40%); ^{1}H NMR ($CDCl_3$):0.8-1.9(m,7H,C_3H_7),1.19(d,3H,CH_3), 2.11(m,1H,$J_{44'}$=14.0, J_{34}=2.6, J_{45}=3.6Hz,H_4), 2.50(m,1H,$J_{4'5}$=8.9, $J_{34'}$=5.8Hz,$H_{4'}$), 4.01(m,1H,H_3), 4.1-4.4(m,3H, H_2,CH_2), 4.63(dd,1H,H_5).



1 2 3

To demonstrate the potential synthetic value of the presented reaction we have performed a new simple synthesis of racemic allomuscarine 3. The synthesis of racemic and natural D-(-)-allomuscarine which occurs in *Amanita muscaria*[3] *has been attempted several times in the past.*[4] The ester 2 was treated with freshly prepared dimethylamide magnesium bromide in THF solution to yield amide 4 (90%), mp 74-75°C; ^{1}H NMR ($CDCl_3$):1.19(d,3H,CH_3), 2.1-2.6(m,2H,H_4,$H_{4'}$), 3.06, 3.25[2s,6H,$N(CH_3)_2$], 4.03(m,1H,H_3), 4.27(dq,1H,J_{23}=1.7Hz,H_2), 5.03(dd,1H,J_{45}=2.8, $J_{4'5}$=7.4Hz,H_5).

4



5

Reaction of 4 using LAH in boiling THF solution for 1 h gave dimethylamino derivative 5 (95%); ^{1}H NMR ($CDCl_3$):1.08(d,3H,CH_3), 1.75(bd,1H,$J_{44'}$=13.5Hz,H_4), 2.2-2.8(m,3H,$H_{4'}$,$CH_2N\!<$), 2.48[s,6H,$N(CH_3)_2$], 3.94(bd,1H,$J_{34'}$=5.5Hz,H_3), 4.22(bq,1H,H_2), 4.42(dq,1H,H_5).Quaternization of 5 was performed using the high pressure technique which allows to obtain a pure crystalline quaternary salt with almost quantitative yield.[5] Treatment of 5 with eqiuv. of methyl iodide in acetone solution under 11 kbar at room temperature for 16 h afforded allomuscarine iodide 3, mp 131-132°C (lit.131-132°C [6]); ^{1}H NMR (D_2O):1.22(d,3H,CH_3), 1.67(dt,1H,$J_{44'}$=11.8,J_{34}+J_{45}=9.8Hz,H_4), 2.61(dq,1H,$J_{34'}$+$J_{4'5}$=13Hz,$H_{4'}$) 3.23[s,9H,$N(CH_3)_2$], 3.46(dd,1H,J_{gem}=13.0, J_{vic}=2.3Hz, -C$\underline{H}$H N$\leq$), 3.71(dd,1H,J_{vic}=8.8Hz, -CH$\underline{H}$N$\leq$), 4.10(m,2H,H_2H_3), 4.73(m,1H,H_5). The ^{1}H NMR data of 3 are identical with those published ones.[4] Further studies on the intramolecular opening of the oxirane ring in 1 are currently in progress.

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