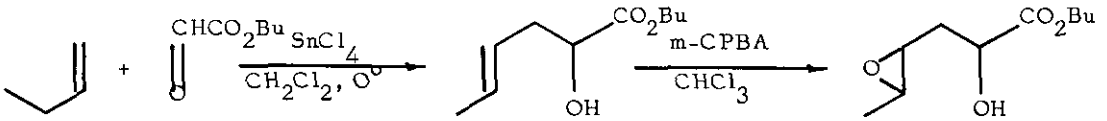
THE INTRAMOLECULAR OPENING OF THE OXIRANE RING IN BUTYL 4,5-EPOXY-2-HYDROXYHEXANOATE. A NEW SIMPLE SYNTHESIS OF RACEMIC ALLOMUSCARINE

Marek Chmielewski and Piotr Guzik
Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw, Poland

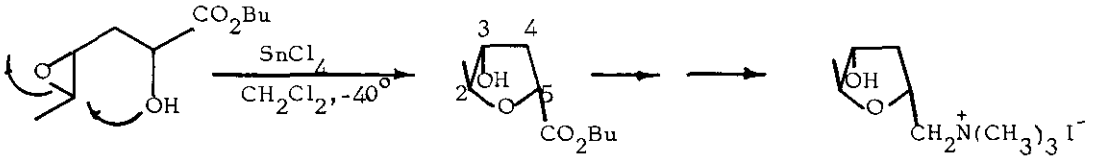
Abstract - The new simple synthesis of racemic allomuscarine via the intramolecular opening of the trans substituted epoxide ring in butyl 4,5-epoxy-2-hydroxyhexanoate is described.

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]



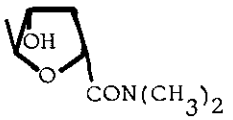
1

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,$J_{44'}$=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).

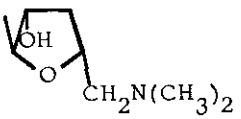


1 2 3

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, -CHH N<), 3.71(dd,1H,J_{vic}=8.8Hz, -CHH N<), 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.

ACKNOWLEDGEMENT The authors are indebted to Professor A.Zamojski for help in carrying this work, and to the Polish Academy of Sciences for a Grant No MR-I.12.1.1.1.

REFERENCES

1. M.Chmielewski, Tetrahedron 1980, 36, 2345.
2. The configuration of 2 was proved by its transformation into racemic allomuscarine. Micro-analytical (combustion) data for 2 and all subsequent products (3 - 5) are in full accord with the proposed structures.
3. E.Schleusener and C.H.Eugster, Helv.Chim.Acta, 1970, 53, 130.
4. S.Wilkinson Quart.Rev., 1961, 15, 153, and references cited therein; J.Whiting, Y.-K.An-Young and B.Belleau, Can.J.Chem., 1972, 50, 3322; G.Fronza, C.Fuganti and P.Grasselli, Tetrahedron Lett., 1978, 3941; S.Pochet and T.Huynh-Dinh, J.Org.Chem., 1982, 47, 193.
5. The experiment was performed with cooperation of Dr. J.Jurczak according to the known procedure [M.Pietraszkiewicz, P.Sałański and J.Jurczak, J.Chem.Soc.,Chem.Commun., in press].
6. C.H.Eugster, F.Hafliger, R.Denss and E.Girod, Helv.Chim.Acta, 1958, 41, 583.

Received, 6th July, 1983