Tetrahedron Letters No. 5, pp 423 - 424.
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0040-4039/79/0129-0423$02.00/0

A NOVEL SYNTHESIS OF 6,8-DIOXABICYCLO[3.2.1]OCTANE DERIVATIVES BY THE REACTION OF CITRAL WITH THALLIUM(III) PERCHLORATE

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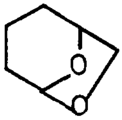

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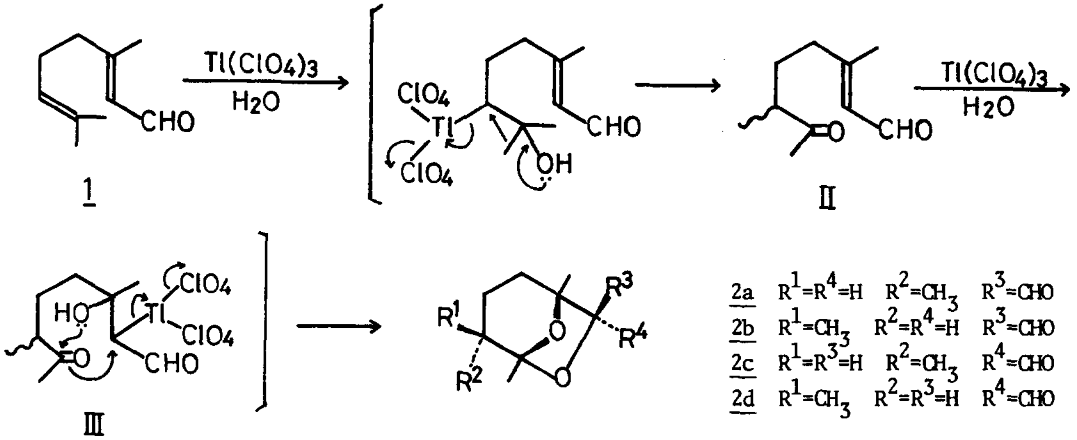
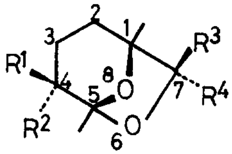
Recently attention has been given to the natural products[1)] having a 6,8-dioxabicyclo[3.2.1]octane skeleton I owing to their pheromone activities against bark beetles. In connection with these biological importance, the syntheses of the pheromones were extensively studied[2)]. In the course of our investigation on the thallium(III) induced cyclization[3)] of 1,5-dienes, we have found that the reaction of citral 1, trans-3,7-dimethyl-2,6-octadienal, with thallium-(III) salts gave directly 6,8-dioxabicyclo[3.2.1]octane derivatives in high yield. Here we wish to describe a novel synthesis of 6,8-dioxabicyclo[3.2.1]octane derivatives 2a-d by the reaction of 1 with thallium(III) perchlorate.

Treatment of citral 1(1.63 g) in methylene chloride(40 ml) with the diluted thallium(III) perchlorate solution[4)](100 ml, ca. 3 equiv.) at room temperature for 6 hr with extremely vigorous stirring gave a diastereomeric mixture of the aldehydes 2a-d (1.55 g, 80 % yield); the ^{1}H-NMR signals(δ 9.50-10.0 ppm) and the IR absorptions(1720-1724 cm^{-1}) of the mixture clearly showed the presence of an aldehyde group. Glc analysis[5)] of the mixture showed four peaks with the ratio of 12:11:37:20 corresponding to 2a, 2b, 2c and 2d, respectively. For the purpose of separation and structure elucidation, the aldehydes mixture was submitted to



2a $R^1=R^4=H$ $R^2=CH_3$ $R^3=CHO$
2b $R^1=CH_3$ $R^2=R^4=H$ $R^3=CHO$
2c $R^1=R^3=H$ $R^2=CH_3$ $R^4=CHO$
2d $R^1=CH_3$ $R^2=R^3=H$ $R^4=CHO$

Table ^{1}H-NMR and ^{13}C-NMR Chemical Shifts of 3a-d.



	R^1	R^2	R^3	R^4	^{1}H-NMR($CDCl_3$,100 MHz) δ ppm	^{13}C-NMR($CDCl_3$,25.0 MHz) δ ppm
3a	H	CH_3	CH_2OH	H	0.80(3H,d,J=6.0) 1.20(3H,s) 1.36(3H,s) 3.5-4.0(3H,m)	16.5(q) 22.6(q) 22.9(q) 27.2(t) 31.6(t) 37.3(d) 61.0(t) 79.8(s) 85.3(d) 109.5(s)
3b	CH_3	H	CH_2OH	H	0.98(3H,d,J=8.0) 1.20(3H,s) 1.35(3H,s) 3.5-4.2(3H,m)	16.4(q) 22.9(q) 23.1(q) 25.6(t) 27.0(t) 35.6(d) 61.0(t) 80.9(s) 84.4(d) 109.7(s)
3c	H	CH_3	H	CH_2OH	0.89(3H,d,J=6.0) 1.28(3H,s) 1.40(3H,s) 3.54(2H,m) 3.90(1H,dd,J=6.0,4.0)	16.6(q) 19.9(q) 22.9(q) 26.8(t) 36.6(t) 38.0(d) 63.7(t) 80.3(s) 81.3(d) 109.7(s)
3d	CH_3	H	H	CH_2OH	1.04(3H,d,J=7.0) 1.28(3H,s) 1.41(3H,s) 3.56(2H,m) 3.92(1H,dd,J=6.0,4.0)	15.8(q) 20.0(q) 23.4(q) 25.1(t) 31.6(t) 35.9(d) 63.7(t) 80.5(d) 81.4(s) 109.8(s)

the reduction with sodium borohydride(EtOH, 30 min) giving quantitatively the corresponding alcohols 3a-d$^{6)}$, which were separated by repeated preparative thin-layer chromatography. The structures of diastereomeric 7-hydroxymethyl-1,4,5-trimethyl-6,8-dioxabicyclo[3.2.1]octanes for 3a-d were fully elucidated by the spectral data as shown in the Table. Thus the structures of the initially formed aldehydes were apparently represented as 2a-d.

The formation of 2a-d is well explained by the reaction path way as illustrated. Initially the ketoaldehyde II is formed by oxythallation of 1 followed by rearrangement of the methyl group. Subsequently oxythallation of the remaining C-C double bond of II takes place to give an intermediate III, which finally undergoes intramolecular ketalization giving the unique 6,8-dioxabicyclo[3.2.1]octane skeleton.

References and Notes

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4. The reagent solution was prepared by dissolving Tl_2O_3(91 g) in 70 % perchloric acid(206 ml) at 120-130° followed by dilution with water(1100 ml) in order to prevent acid catalyzed side reactions.
5. The retention times of 2a, 2b, 2c and 2d (1.5 % SE-30 on Chrom W, column temp. 100°, He) are 8.4, 9.0, 9.9 and 10.6 min, respectively.
6. Satisfactory elemental analyses and/or high resolution mass measurements were obtained for these new compounds.

(Received in Japan 8 November 1978)