Tetrahedron Letters No. 15, pp 1323 - 1326.
©Pergamon Press Ltd. 1979. Printed in Great Britain.

0040-4039/79/0408-1323$02.00/0

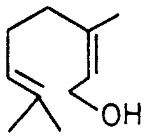
REACTION OF NEROL WITH THALLIUM(III) PERCHLORATE

Yasuji Yamada*, Hidenao Sanjoh, and Kazuo Iguchi
Tokyo College of Pharmacy, Horinouchi 1432-1, Hachioji, Tokyo 192-03, Japan

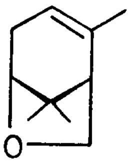
Summary: Reaction of nerol (1) with thallium(III) perchlorate gave 6-oxabicyclo[3.2.1]octane derivatives (2) and (3), and 6,9-dioxabicyclo[3.3.1]nonane derivatives (4a-d) as the cyclization products.

In the course of our investigation[1)] on the thallium(III) induced reactions of 1,5-dienes, we reported a new type of olefinic cyclization[1a)] of geraniol with thallium(III) perchlorate leading predominantly to the five-membered carbocyclic products. This finding prompted us to investigate a thallium(III) induced reaction of nerol (1)[(Z)-3,7-dimethyl-2,6-octadien-1-ol] which is a geometrical isomer of geraniol. Here we wish to describe that the reaction of 1 with thallium(III) perchlorate under the similar condition used for the reaction of geraniol gave the cyclization products; two isomeric 6-oxabicyclo[3.2.1]octane derivatives (2) and (3), and four diastereomeric 6,9-dioxabicyclo[3.3.1]nonane derivatives (4a-d). This reaction is remarkably different from our previous result of the thallium(III) induced cyclization of geraniol.

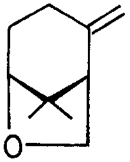
Treatment of nerol (1) (5 g) in methylene chloride (65 ml) with the diluted thallium(III) perchlorate solution[2)] (224 ml, ca. 2 equiv.) at room temperature for 2 h with extremely vigorous stirring gave pale-yellow oil (4.1 g). Silica gel column chromatography of the oil using n-hexane-ethyl acetate (1:4) as an eluent gave two fractions; the formerly eluted fraction (2.6 g) containing cyclic products and the later eluted fraction (1.0 g) which consisted of acyclic products[3)]. Repeated preparative gas chromatography of the former fraction gave six



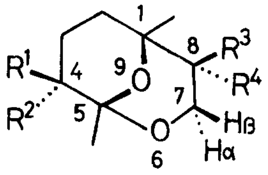
1



2



3



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

cyclization products4) in order of elution, 2, 3, 4a, 4b, 4c and 4d (the ratio, 45:15:20:10:5:5), respectively.

The compound (3) is karahana ether5) which is a monoterpene isolated from Japanese hop, and the spectral data of 3 coincided in every respect with those of the natural products, except for the optical rotation. Comparison of the spectral data of 26) with those of 3 led to the structure (2) which is a positional isomer of the olefin (3).

The diastereomeric relations between 4a-d were apparently indicated by the spectroscopic properties as shown in the Table. The presence of the cyclic ketal moiety for 4a was clearly shown by the ^{13}C-NMR signals; δ 109.7(s,C-5), 81.3(d,C-8), 80.3(s,C-1) and 63.7(t,C-7)ppm. These spectroscopic behaviour reasonably led to the 6,9-dioxabicyclo[3.3.1]nonane structures for 4a-d. The stereochemistry at C-4 position was assigned by comparison of the ^{1}H-NMR chemical shifts of the secondary methyl signals of 4a-d with those of the corresponding methyl signals of the related bicyclic compounds7). The stereochemistry at C-8 position was based on the analysis of the splitting patterns of the ^{1}H-NMR signals of C-7 and C-8 protons.

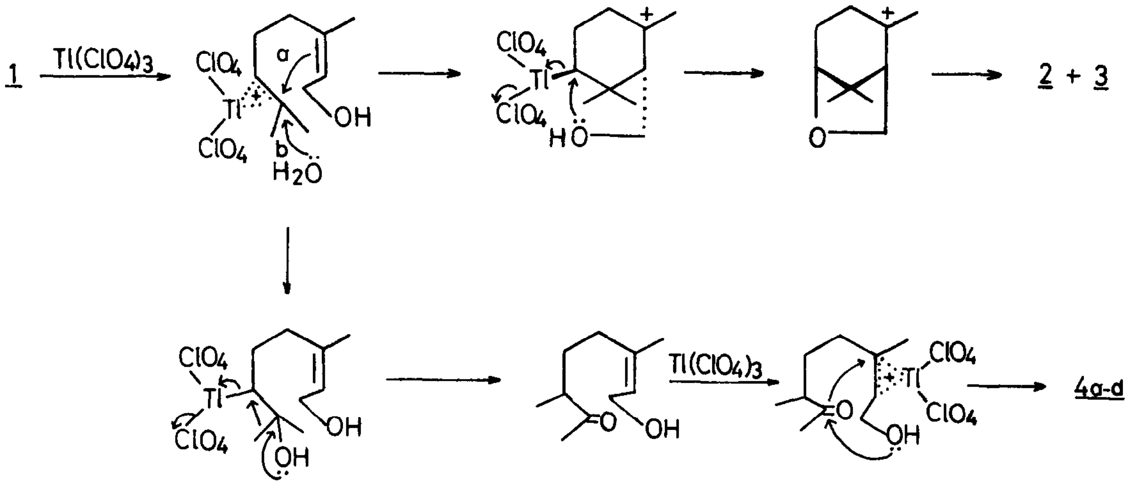
The possible reaction path-way for the formation of these cyclization products is illustrated in the Scheme. Karahana ether (3) and its isomer (2) are derived by the action of thallium(III) perchlorate to the double bond at C-6 position. The 6,9-dioxabicyclo[3.3.1]nonane derivatives (4a-d) are apparently formed by the further action of the reagent on the primarily formed rearranged

Table Spectroscopic Data of 4a-d

	Molecular formula	IR($CHCl_3$) cm^{-1}	^{1}H-NMR($CDCl_3$,100 MHz) δ ppm
4a	$C_{10}H_{18}O_3$	3550, 3300	0.89(3H,d,J=6.0), 1.27(3H,s), 1.39(3H,s) 3.52(1H,d,J=6.5,C_7-Hα), 3.54(1H,d,J=4.0,C_8-Hβ) 3.89(1H,dd,J=6.5,4.0,C_7-Hβ)
4b	$C_{10}H_{18}O_3$	3550, 3400	1.02(3H,d,J=7.0), 1.27(3H,s), 1.40(3H,s) 3.51(1H,d,J=6.5,C_7-Hα), 3.52(1H,d,J=4.5,C_8-Hβ) 3.91(1H,dd,J=6.5,4.5,C_7-Hβ)
4c	$C_{10}H_{18}O_3$	3590	0.88(3H,d,J=7.5), 1.29(3H,s), 1.35(3H,s) 3.72(1H,m), 3.96(1H,m), 4.24(1H,d,J=8.0)
4d	$C_{10}H_{18}O_3$	3590	0.99(3H,d,J=7.5), 1.36(3H,s), 1.37(3H,s) 3.82(1H,m), 4.05(1H,m), 4.27(1H,dd,J=8.0,1.5)

intermediate. However, no five-membered carbocyclic product which was the major product in the reaction of geraniol was detected in the present reaction.

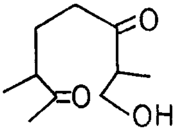
The reason why the thallium(III) induced reaction is dependent on the geometry of the carbon-carbon double bond is currently under investigation.



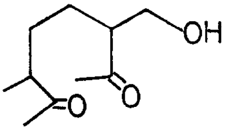
Scheme

REFERENCES AND NOTES

1. a) Y.Yamada, H.Sanjoh and K.Iguchi, J.Chem.Soc.Chem.Commun., 997(1976);
   b) Y.Yamada, A.Shibata, H.Sanjoh and K.Iguchi, Tetrahedron Lett., 2407(1977);
   c) Y.Yamada, H.Sanjoh and K.Iguchi, Tetrahedron Lett., in press.
2. The reagent solution was prepared by dissolving Tl_2O_3 (91 g) in 70 % perchloric acid (206 ml) at 120-130°C followed by dilution with water (1100 ml) in order to prevent acid-catalyzed side reactions. The reaction of geraniol by using this reagent solution gave the same result as the previous report[1)]
3. The following acyclic diketones (5) and (6) were isolated, and characterized by the following spectral data: 5 IR($CHCl_3$) 3550, 1705 cm^{-1}, ^1H-NMR($CDCl_3$) δ 1.08(3H,d,J=7.0), 1.10(3H,d,J=7.0), 2.14(3H,s), 3.65(1H,dd,J=11.5,2.0) and 3.71(1H,dd,J=11.5,8.5)ppm; 6 IR($CHCl_3$) 3300, 1730 and 1708 cm^{-1}, ^1H-NMR ($CDCl_3$) δ 1.09(3H,d,J=7.5), 2.14(3H,s), 2.20(3H,s) and 3.74(2H,d,J=6.0)ppm.



5



6

4. The retention times (15 % PEG-20M, column temp. 195°C, He) are shown below; 2 (4.2 min), 3 (4.5 min), 4a (18.8 min), 4b (19.7 min), 4c and 4d (24-25 min) respectively. The compounds (4c) and (4d) were separated by preparative thin-layer chromatography (n-hexane-AcOEt =4:1, developed seven times).
5. Y.Naya and M.Kotake, Tetrahedron Lett., 1645(1968). The present reaction provides a synthesis of (±)-karahana ether from nerol.
6. All new compounds gave correct elemental analyses /or high resolution mass measurements. 2, ^1H-NMR($CDCl_3$) δ 1.08(6H,s), 1.68(3H,m), 3.68(1H,br), 3.79 (1H,d,J=7.5), 4.04(1H,dd,J=7.5,4.0) and 5.15(1H,br)ppm.
7. W.E.Gore, G.T.Pearce and R.M.Silverstein, J.Org.Chem., 40, 1705(1975); ibid, 41, 603(1976).

(Received in Japan 12 January 1979)