Tetrahedron Letters, Vol.22, No.37, pp 3649 - 3652, 1981
Printed in Great Britain

0040-4039/81/373649-04$02.00/0

# THE REVISED STRUCTURE OF AN OXIDATION PRODUCT FROM THE REACTION OF AN α-TOCOPHEROL MODEL COMPOUND, 2,2,5,7,8-PENTAMETHYLCHROMAN-6-OL, WITH POTASSIUM SUPEROXIDE; 6-HYDROXY-2,2,6,7,8-PENTAMETHYLCHROMAN-5(6H)-ONE[1]

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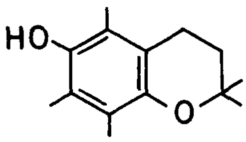
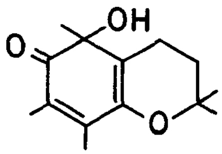
ABSTRACT: The previously reported structure of an oxidation product obtained from the reaction of an α-tocopherol model compound(1) with $KO_2$ is revised to 6-hydroxy-2,2,6,7,8-pentamethylchroman-5(6H)-one(3) on the basis of the X-ray crystallographic and $^{18}O$-labeling studies.

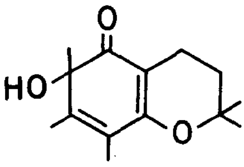
An oxidation product has been obtained from the reaction of 2,2,5,7,8-pentamethylchroman-6-ol(1)(an α-tocopherol model compound) with potassium superoxide($KO_2$) in tetrahydrofuran(THF) under an oxygen atmosphere, and assumed to be 5-hydroxy-2,2,5,7,8-pentamethylchroman-6(5H)-one(2)[2]. However, we report here that its structure should be revised to 6-hydroxy-2,2,6,7,8-pentamethylchroman-5(6H)-one(3) on the basis of results of the X-ray crystallographic analysis and $^{18}O$-labeling experiments described below; the revised structure is the one that the ketonic and α-hydroxyethylidene groups in 2 are interchanged in position.



1



2



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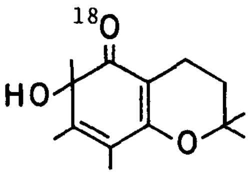


4

A prismatic crystal of 3 suitable for an X-ray diffraction study was obtained by recrystallization from hexane. The crystal data are as follows 3; $C_{14}H_{20}O_3$, MW 236.3, monoclinic, space group C2/c, Z=8, $D_c$=1.192 gcm$^{-3}$, a=18.869(9), b=8.377(5), c=16.731(8) Å, β=95.04(5)°, V=2634 Å$^3$. Intensities were measured on a Philips four-circle diffractometer using graphite-monochromated Cu-$K_\alpha$ radiation, and 2401 reflections were observed as above the 3σ(I) level out of 3100 within the 2θ range of 6°-156°. The structure was solved by the direct method and refined by the method of block-diagonal matrix least-squares. The final R value was 0.064 including all hydrogen atoms except for one phenolic hydrogen, H($O_{15}$). The X-ray crystal structure of 3 is shown in Fig. 1. As shown in Fig. 1, there are no abnormal bond lengths and angles found in the molecule. The conjugation of the double bonds extends along the bonds $O_{14}$-$C_5$-$C_{4a}$-$C_{8a}$-$C_8$-$C_7$. The average standard deviations were estimated as σ(C-C)=0.003 Å, σ(C-C-C)= 0.2° [3].

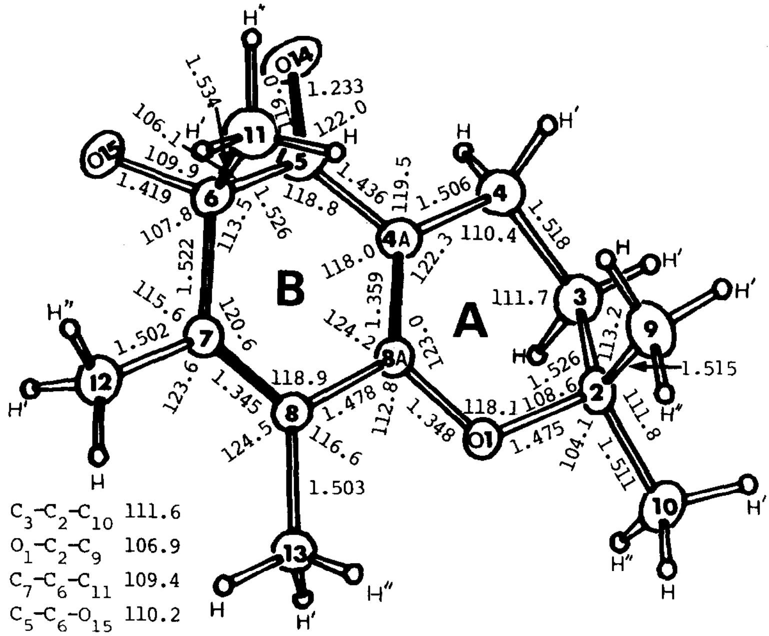


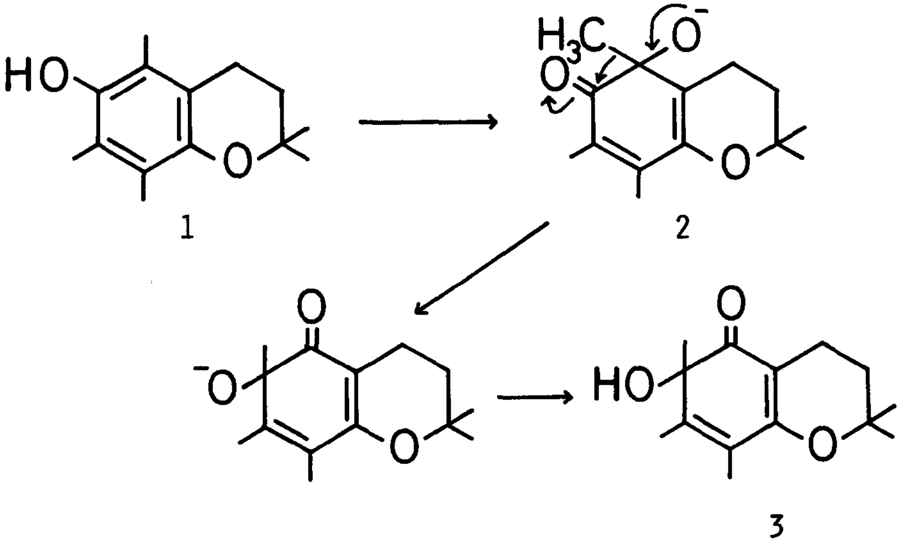
Fig. 1. The X-ray crystal structure of 3 together with bond lengths (Å) and bond angles (°) for non-hydrogen atoms. The black bonds represent double bonds.

In order to examine the reaction mechanism for the formation of 3, 1 was treated with $KO_2$ in $^{18}O_2$-saturated THF (99 atom % excess $^{18}O$, The British Oxygen Company Ltd., London, U.K.) under the conditions similar to those described in the previous paper[2]. The product obtained was 4 in which a ketonic oxygen was labeled with an $^{18}O$-atom (mass-spectroscopic analysis; 85 % $^{18}O$ incorporation). The introduction of an $^{18}O$-atom into the molecule was established on the basis of the difference of two mass units between the m/e's of the molecular ions of 3 ($M^+$;236) and 4 (238). The presence of an $^{18}O$-labeled ketonic group in 4 was demonstrated by the utilization of $^{18}O$-isotope effects in infrared(IR) and $^{13}C$ nuclear magnetic resonance($^{13}C$-NMR) spectroscopy. In the IR spectrum of 4, the observed C=O stretching absorption band (1613 $cm^{-1}$, KBr) appeared 26 $cm^{-1}$ lower than the corresponding band (1639 $cm^{-1}$) of 3. The magnitude of the $^{18}O$-induced shift is consistent with that of the corresponding shifts (20-40 $cm^{-1}$) found for the compounds containing a $C={}^{18}O$ group[4]. In the $^{13}C$-NMR spectrum of the 1:1 mixture of 3 and 4 , the $^{13}C$ resonance of the ketonic group was split into two peaks with the space of 0.038 ppm. This shows that the signal of the ketonic carbon atom in 4 ($\delta^{CDCl_3}_{TMS}$ 202.925 ppm) was shifted upfield 0.038 ppm relative to that in 3 (202.963 ppm). The $^{18}O$-induced upfield shift is very similar to the shifts observed for [$^{18}O$]acetone (0.050 ppm) and [$^{18}O$]benzophenone (0.045 ppm)[5].

It appears that the oxygenation at $C_5$ and the migration of a methyl group from $C_5$ to $C_6$ in 2 take place to yield 3. The rearrangement of an alkyl group in α-hydroxyketone is known as the acyloin rearrangement[6]. It consists in the conversion of a hydroxyketone (or hydroxyaldehyde), usually catalyzed by acid or base, into an isomeric hydroxyketone with the concomitant interchange of the oxygen functions and migration of an alkyl group to the adjacent carbon atom. In consideration of the structure of 2 and the basic property of superoxide anion[7], the acyloin rearrangement is presumed to involve in the formation of 3. Thus, the reaction of the formation of 3 may take a course shown in Scheme 1. We can testify the validity of the hypothetical scheme by determining whether 2 is quantitatively convered to 3 under the conditions employed here. Further work is underway to prepare 2.

Acknowledgment: The present work was partially supported by Grants-in-Aid for Scientific Research No. 457086 & 577896 from the Ministry of Education, Science and Culture of Japan.

Scheme 1



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(Received in Japan 4 July 1981)