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# BASE-CATALYZED SKELETAL ISOMERIZATION OF 6-ENDO-HYDROXY-9-THIABICYCLO-[3.3.1]NONA-3,7-DIEN-2-ONE WITH THE EPIMERIZATION OF THE HYDROXY GROUP

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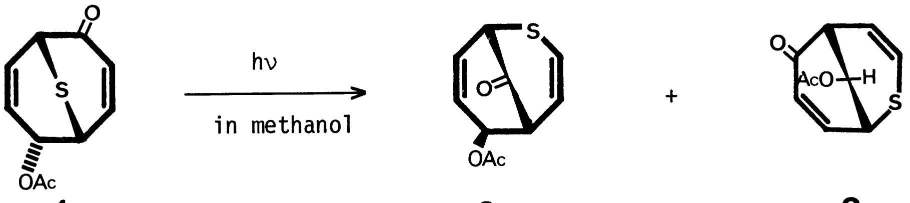
Studies on the base-catalyzed skeletal isomerization of (4) to (5) and (6) and the base-catalyzed epimerization of the hydroxy group in (5) and (6) are reported. The most plausible mechanism for the skeletal isomerization of (4) and the epimerization in (5) and (6) involves retro-aldol cleavages of (4), (5) and (6) to give an enolate (7) as the common intermediate.

When 6-*endo*-acetoxy-9-thiabicyclo[3.3.1]nona-3,7-dien-2-one (1)[1] was irradiated in methanol,[2] formal 1,3-acyl[3] and carbon[4] shifts take place to give the isomeric compounds, 6-*exo*-acetoxy-2-thiabicyclo[3.3.1]nona-3,7-dien-9-one (2) (27%)[5] and 9-*endo*-acetoxy-2-thiabicyclo[3.3.1]nona-3,7-dien-6-one (3) (9%)[6], respectively.

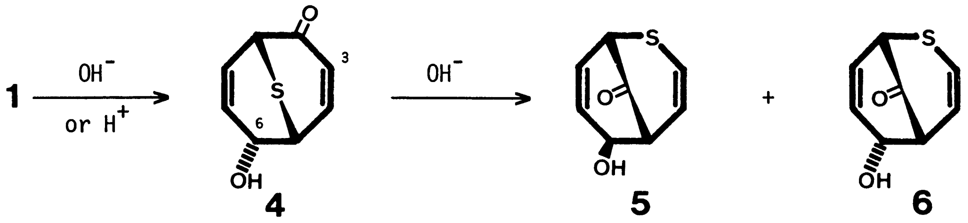


**1** **2** **3**

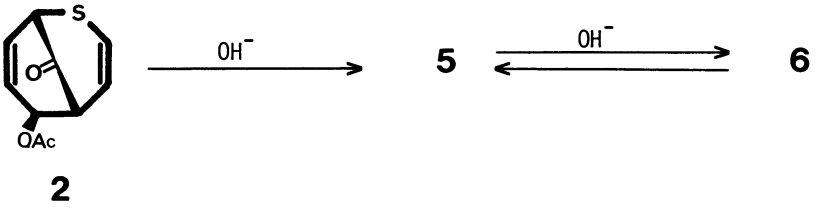
In connection with the photochemical isomerization of (1) to (2), we found that a similar, but non-photochemical, skeletal isomerization takes place during hydrolysis of (1) by potassium carbonate in aqueous methanol solution. We wish to report here the remarkably smooth base-catalyzed isomerization of (1) with the epimerization of the hydroxy group to give a mixture of 6-*exo*- and 6-*endo*-hydroxy-2-thiabicyclo[3.3.1]nona-3,7-dien-9-ones (5 and 6).

The keto acetate (1) was synthesized from 2,6-dihydroxy-9-thiabicyclo[3.3.1]nona-3,7-diene[7] by acetylation followed by oxidation with active $MnO_2$. The structural determination and the stereochemical assignment to (1) were derived unequivocally by the nmr spectrum.[1]

The keto acetate (1) upon hydrolysis with dilute acid afforded 6-endo-hydroxy-9-thiabicyclo-[3.3.1]nona-3,7-dien-2-one (4)[8] in 90% yield. On the other hand, the keto acetate (1) when treated with potassium carbonate in aqueous methanol solution at room temperature for 4 hr furnishes, upon work-up without acidification, a mixture of (5) and (6) with a ratio of 1 : 1 in 80% yield. Both (5) and (6) exhibit the strong carbonyl absorption at 1725 $cm^{-1}$, indicating the non-conjugate carbonyl group. The structures of (5) and (6) were established by chemical evidence that both (5) and (6) gave 2-thiabicyclo[3.3.1]nona-3,7-dien-6,9-dione[3] and stereochemical assignments to (5) and (6) were derived from their nmr spectra.[9,10] The real intermediacy of the alcohol (4) for the rearrangement of (1) to (5) and (6) was proved by evidence that (4) afforded a mixture of (5) and (6) under the same conditions.



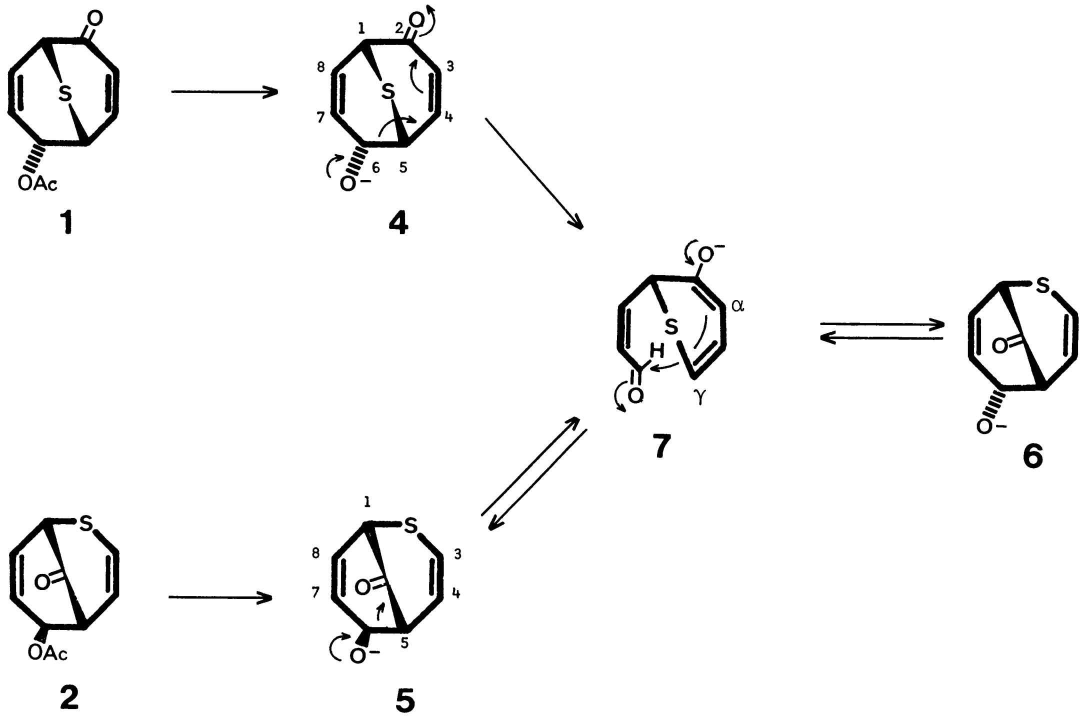
It was also found that the photo-rearrangement product (2) undergoes no skeletal isomerization such as (4) → (5) and (6) under the same conditions, but instead resulted in the formation of a mixture of (5) and (6). Furthermore, base-catalyzed equilibration between (5) and (6) was observed when (5) and (6) were independently treated with potassium carbonate in aqueous methanol solution.



The skeletal isomerization of (4) to give (5) and (6) can be formally explained by a 1,3-sigmatropic rearrangement of the anionic oxy-Cope system[11] incorprated within (4) which involves non-stereospecific $C_6$-carbon migration to the $C_3$-position. Evidence that 2,6-dihydroxy-9-thiabicyclo[3.3.1]nona-3,7-diene did not undergo such an isomerization, however, requires the ketone function at the $C_2$-position for this formal 1,3-sigmatropic rearrangement of (4) to (5) and (6).

Combining these data, the rearrangement of (4) and the epimerization reactions of (5) and (6) can be well rationalized by the retro-aldol mechanism shown in Scheme I. Base-catalyzed retro-aldol cleavages[12] of (4), (5) and (6) involve an enolate (7) as the common intermediate. High negative charge density at the α-position of an enolate (7) relative to the γ-position furnishes the reversible aldol mechanism for (5) and (6), but the irreversible one for (4).

(Scheme I)



## References and Notes

1) (1) : $\nu_{max}^{neat}$, 1740, 1685 cm$^{-1}$; $\lambda_{max}^{EtOH}$, 234 (4700), 295 (600), 358 (300 sh) nm; m/e, 210 ($M^+$), 194, 179, 178, 150, 97, 48, 28 (100%); nmr (δ in $CDCl_3$), 2.15 (3H, s), 3.55 ($C_1$-H, d, $J_{1,8}$=6.5Hz), 5.95 ($C_3$-H, d, $J_{3,4}$=10.5Hz), 6.85 ($C_4$-H, dd, $J_{4,5}$=6.5Hz), 3.75 ($C_5$-H, dd, $J_{5,6}$=6.0Hz), 5.95 ($C_6$-H, m), 5.75 ($C_7$-H, dd, $J_{6,7}$=2.0, $J_{7,8}$=10.5Hz), 6.15 ($C_8$-H, ddd).

2) Irradiation of (1) in benzene afforded two thiolactones together with (2) and (3). Detail studies on the photochemistry of (1) will be reported elsewhere.

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4) D. Gravel and J. Gauthier, Tetrahedron Lett., 5489 (1968).

5) (2) : $\nu_{max}^{CHCl_3}$, 1740 cm$^{-1}$; $\lambda_{max}^{EtOH}$, 229 (7750), 300 (590 sh), 320 (380 sh) nm; m/e, 210 ($M^+$), 168, 150, 139, 97, 89, 73, 45 (100%); nmr (δ in $CDCl_3$), 2.08 (3H, s), 3.75 ($C_1$-H, d, $J_{1,8}$=5Hz),

6.14 ($C_3$-H, d, $J_{3,4}$=9.5Hz), 5.68 ($C_4$-H, dd, $J_{4,5}$=5.0Hz), 3.20 ($C_5$-H, ddd, $J_{5,6}$=3.0Hz), 5.52 ($C_6$-H, ddd, $J_{6,7}$=5.0Hz), 6.18 ($C_7$-H, dd, $J_{7,8}$=9.5Hz), 6.08 ($C_8$-H, dd); mp 91°C.

6) (3) : $\nu_{max}^{KBr}$, 1745, 1680 $cm^{-1}$; $\lambda_{max}^{EtOH}$, 217 (6000), 245 (1000 sh), 252 (970 sh), 291 (800), 350 (400sh); m/e, 210 ($M^+$), 167, 150, 139, 123, 122, 97, 43 (100%); nmr (δ in $CDCl_3$), 2.10 (3H, s), 3.80 ($C_1$-H, m, $J_{1,8}$=5.5, $J_{1,9}$=3.5Hz), 6.25 ($C_3$-H, d, $J_{3,4}$=10.0Hz), 5.70 ($C_4$-H, dd, $J_{4,5}$=7.0Hz), 3.35 ($C_5$-H, m, $J_{5,9}$=3.5Hz), 6.30 ($C_7$-H, d, $J_{7,8}$=10.0Hz), 6.70 ($C_8$-H, ddd, $J_{8,9}$=2.0Hz), 5.40 ($C_9$-H, m); mp 103°C.

7) F. Lautenschlaeger, J. Org. Chem., 33, 2627 (1968).

8) (4) : $\nu_{max}^{neat}$, 3400, 1680 $cm^{-1}$; $\lambda_{max}^{EtOH}$, 232 (4720), 298 (870), 360 (310 sh) nm; m/e, 168 ($M^+$), 150, 139, 123 (100%), 111, 97, 84, 79; nmr (δ in $CDCl_3$), 3.50 ($C_1$-H, d, $J_{1,8}$=6.5Hz), 5.95 ( $C_3$-H, d, $J_{3,4}$=10.5Hz), 7.00 ($C_4$-H, dd, $J_{4,5}$=7.0Hz), 3.66 ($C_5$-H, dd, $J_{5,6}$=6.0Hz), 4.96 ($C_6$-H, m, $J_{6,8}$=2.0, $J_{6,7}$=2.0Hz), 5.80 ($C_7$-H, dd, $J_{7,8}$=10.5Hz), 6.16 ($C_8$-H, ddd).

9) (5) : $\nu_{max}^{KBr}$, 3200, 1725 $cm^{-1}$; $\lambda_{max}^{EtOH}$, 231 (4200), 310 (400 sh) nm; m/e, 168 ($M^+$), 139, 123, 111, 107, 97, 84, 79; nmr (δ in $CDCl_3$), 1.84 (1H, s), 3.72 ($C_1$-H, d, $J_{1,8}$=5.0Hz), 6.08 ($C_3$-H, d, $J_{3,4}$=9.5Hz), 5.65 ($C_4$-H, dd, $J_{4,5}$=5.0Hz), 3.20 ($C_5$-H, m, $J_{5,6}$=3.0Hz), 4.65 ($C_6$-H, dd, $J_{6,7}$=5.0Hz), 6.25 ($C_7$-H, dd, $J_{7,8}$=9.5Hz), 6.00 ($C_8$-H, dd); mp 143°C.

10) (6) : $\nu_{max}^{neat}$, 3400, 1725 $cm^{-1}$; $\lambda_{max}^{EtOH}$, 230 (3130), 318 (190) nm; nmr (δ in $CDCl_3$), 1.70 (1H, s), 3.66 ($C_1$-H, d, $J_{1,8}$=5.0Hz), 6.24 ($C_3$-H, d, $J_{3,4}$=9.5Hz), 5.88 ($C_4$-H, dd, $J_{4,5}$=5.0Hz), 3.24 ( $C_5$-H, dd, $J_{5,6}$=5.0Hz), 4.88 ($C_6$-H, m, $J_{6,7}$=2.0, $J_{6,8}$=2.0Hz), 6.08 ($C_7$-H, dd, $J_{7,8}$=9.5Hz), 5.84 ($C_8$-H, ddd).

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12) S. Swaminathan, J. P. John, and S. Ramachandran, Tetrahedron Lett., 729 (1962); K. G. Srinivasan and S. Swaminathan, Tetrahedron, 25, 2661 (1969), 26, 1453 (1970); M. Akhtar and P. F. Hunt, Chem. Comm., 199 (1965); J. D. Connolly, R. Henderson, and R. McCrindle, J. Chem. Soc., 6935 (1965); J. MacMillan and R. J. Pryce, J. Chem. Soc. (C), 740 (1967); D. Gravel and J. Gauthier, Tetrahedron Lett., 5489 (1968).

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