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INTENTIONAL SYNTHESES OF UTAHIN, A CONIFER CONSTITUENT OF A C_{20}-DITROPONOFURAN, VIA THE OXIDATIVE CONDENSATION

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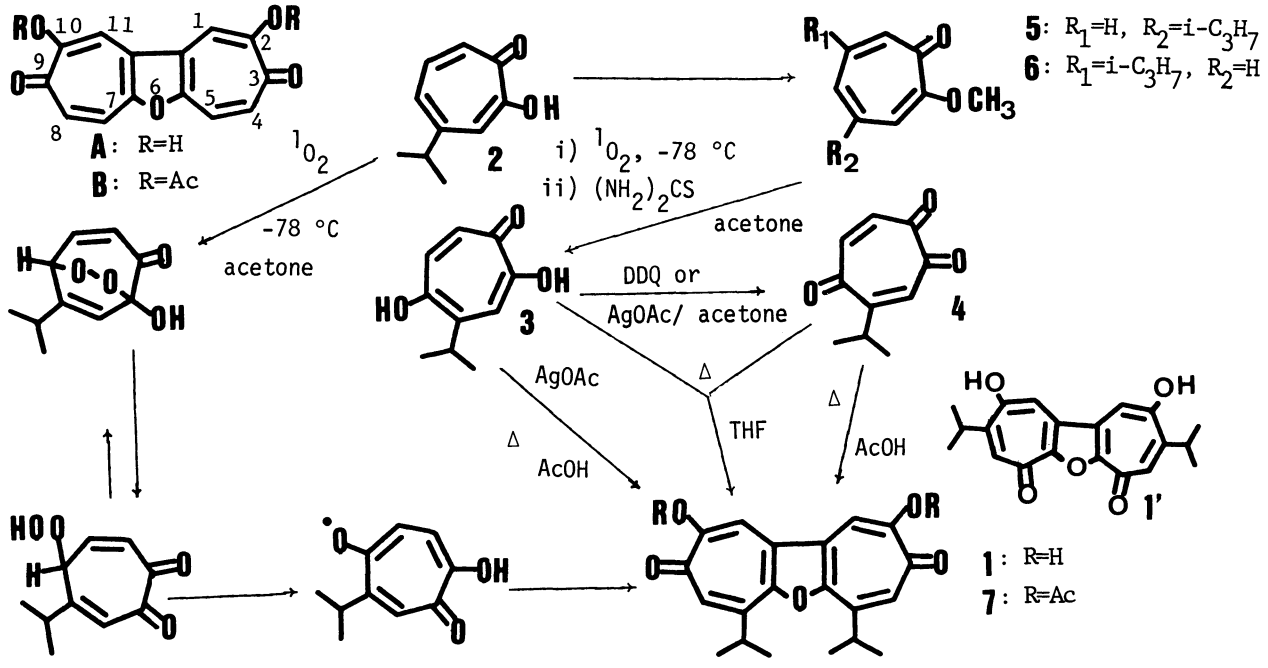
Utahin, previously characterized as a constituent of *Juniperus utahensis*, has been prepared by a biomimetic oxidation of hinokitiol in addition to the coupling reactions of 4-isopropyl-*p*-tropoquinone with 5-hydroxyhinokitiol.

Recently, we have reported an oxidative dimerization of 5-hydroxytropolone derivatives to ditroponofurans, 2,10-dihydroxy-3*H*,9*H*-dicycloheptafuran-3,9-dione(A) and its derivatives.[1] The mode of the formation belongs to "the oxidative coupling of phenolic compounds"[2] that is a common biogenetic path for the condensed phenolic natural products. Since there are reports on the isolation and structure elucidation of a dimeric tropolone, utahin(1), from *Juniperus utahensis Lemm.*,[3,4] and this seems to be identical with the dimeric condensate obtained by several oxidation reactions with hinokitiol(4-isopropyltropolone, 2) derivatives,[5,6] we thought that 1[6] might be biomimetically prepared from 5-hydroxyhinokitiol(3) and 4-isopropyl-*p*-tropoquinone(4), or even from 2 under certain mild conditions. Herein the findings will be described.

At first, 2 was methylated with CH_2N_2 to 4-and 6-isopropyl-2-methoxytropones (5 and 6),[7] which were easily separable by means of silica-gel column or high-



pressure liquid chromatography (μ-Polasil/ EtOAc), but there was not much difference in the reactivity toward singlet oxygen($^1O_2$). Consequently, 3 was prepared by tetraphenylporphyrin-sensitized photooxygenation of a 1:1-mixture of 5 and 6 in acetone at -78 °C and following reduction of resultant endoperoxides by thiourea as pale yellow needles, mp 191-192 °C[δ(CD_3OD):[8)] 1.22(6H, d, J=7 Hz), 3.56(1H, sept, J=7 Hz), 7.06(1H, d, J=12 Hz), 7.17(1H, d, J=12 Hz), and 7.44(1H, s)], 43% yield. The recovered methyl ether, 18%, was a 1:1-mixture of 5 and 6. The DDQ-dehydrogenation of 3 gave 4, yellow needles, mp 49.5-50 °C[δ: 1.16(6H, d, J=7 Hz), 3.24(1H, sept, J=7 Hz), 6.69(1H, s), 6.73(1H, d, J=13 Hz), and 6.90(1H, d, J=13 Hz). δ(C): 21.9, 30.7, 130.1, 132.6, 140.9, 158.4, 185.7, 187.0, and 188.8], 35% yield. The AgOAc-oxidation of 3 in acetone at 15-20 °C for 20 min similarly gave 4 in a 10% yield.[1)]

When a 1:1-mixture of 3 and 4, thus formed, was stirred in THF for 12 h at 15-20 °C, 1, pale yellow prisms, mp>300 °C[δ: 1.45(12H, d, J=7 Hz), 3.75(2H, sept, J=7 Hz), 7.45(2H, s), and 7.65(2H, s). δ(C): 22.5, 31.5, 105.0, 126.5, 127.8, 148.5, 150.6, 158.3, and 178.3], 13%, has been formed together with 3, 15%. Identity of 1 with natural utahin was assured by comparisons with reported figures of UV, IR, H-NMR, and mass spectra.[4)] With Ac_2O, 1 gave the diacetate(7),[9)] pale yellow needles, mp 202-203 °C(lit.[4)] 207 °C). In addition, heating of 4 alone in AcOH gave 1, 13%, with accompanied evolution of CO_2, and although the conversion ratio was small (3%), the AgOAc-oxidation of 3 in refluxing AcOH for 3 h gave 1.

Furthermore, occurrence of 1 was shown in the $^1O_2$-oxidation of 2 in acetone solution at -78 °C for 24 h; a methanol insoluble fraction of the reaction mixture gave 1 in a 21% yield by a simple recrystallization from chloroform.

The formation of 1 by the $^1O_2$-oxidation of 2, which is carrying no substituent on C-5 position, is particularly interesting; up to date, 3 has not been found in nature. Probably, 2 itself can serve as the precursor of 1 *in-vivo*.

References

1) H. Takeshita, T. Kusaba, and A. Mori, *Chem. Lett.*, 1982, 701.

2) T. Kametani and K. Fukumoto, "The Phenol Oxidations," Gihodo Publ., Tokyo (1970), pp. 1-74; J. Mann, "Secondary Metabolism," Oxford University Press, Oxford (1978), p. 50.

3) J. Runeberg, *Acta. Chem. Scand.*, 14, 797 (1960).

4) K. H. Baggaley and T. Norin, *Chem. Commun.*, 1968, 233.

5) T. Nozoe, S. Seto, S. Itô, M. Sato, and T. Katono, *Proc. Jpn. Acad.*, 28, 488 (1952).

6) According to ref. 4, identity of 1 with the Nozoe's sample seems not to be fully settled.

7) The NMR data of 5[δ: 1.28(6H, d, J=7 Hz), 2.86(1H, sept, J=7 Hz), 3.96(3H, s), 6.67(1H, br. s), 6.76(1H, br. m), and 7.0-7.2(2H, m). δ(C): 23.4, 38.9, 56.0, 113.9, 124.5, 134.7, 136.9, 154.1, 164.4, and 179.9] and 6[δ: 1.23(6H, d, J=7 Hz), 2.78(1H, sept, J=7 Hz), 3.91(3H, s), 6.62(1H, dd, J=9.5, 1.5 Hz), 6.76(1H, dt, J=11, 1.5 Hz), 7.00(1H, dd, J=11, 9.5 Hz), and 7.16(1H, d, J=1.5 Hz). δ(C): 23.0, 38.4, 56.1, 111.5, 129.3(2C), 131.6, 157.7, 164.8, and 180.2] are herein recorded.

8) The NMR spectra were measured in $CDCl_3$ solutions otherwise stated, and the chemical shifts were expressed in the δ unit from the internal standard, Me_4Si.

9) The ^{13}C-NMR spectral comparison of 7[δ(C): 20.7, 22.3, 31.4, 118.2, 122.2, 134.1, 146.4, 153.1, 153.3, 168.4, and 178.0] with B[1)] eliminated the alternative structure of 1, 1'.[4)]

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