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REACTION OF ESTRONE WITH THALLIUM(III) PERCHLORATE. REMOTE OXIDATION AT C-11 POSITION

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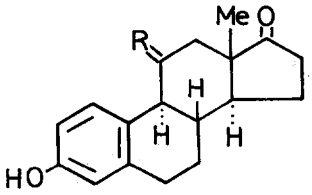
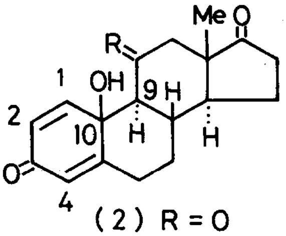
Recently thallium(III) salts have been recognized as excellent oxidizing agents[1)] for some phenolic compounds. In the previous paper[1d)], we reported the reaction of simple p-alkyl phenols with thallium(III) perchlorate leading regioselectively to the corresponding p-quinols. Coombs and Jones[1b)] reported that the reaction of estrone (1) with thallium(III) trifluoroacetate gave a p-quinol derivative (3) after the hydrolysis of the reaction product. In contrast to this report, we have found an interesting result that a remotely oxidized 11-keto-p-quinol (2) was yielded as a major product in addition to (3) when (1) was reacted with thallium(III) perchlorate.



(1) R=H_2
(4) R=O

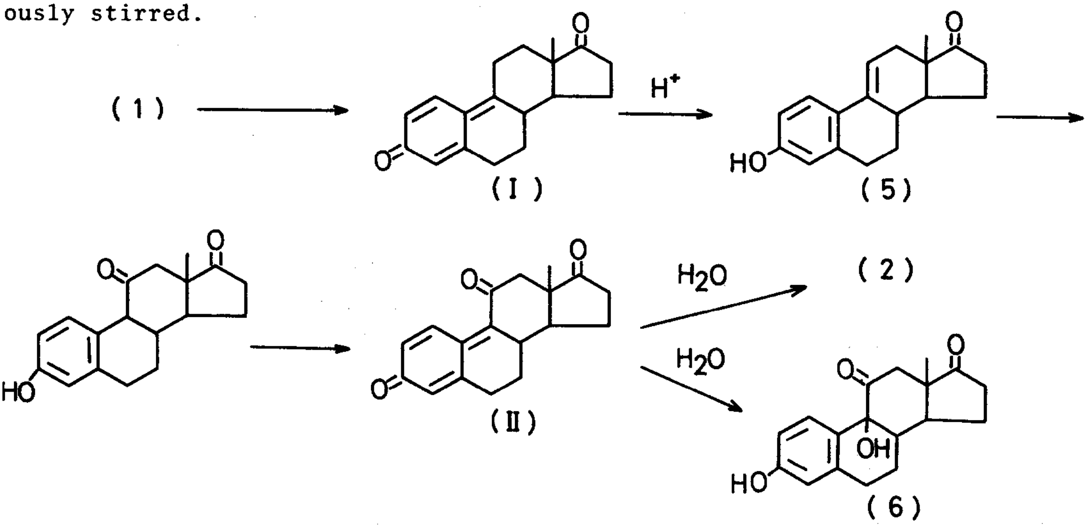


(2) R=O
(3) R=H_2

The reaction of (1)(270 mg, 1 mmole) in CH_2Cl_2(80 ml) with thallium(III) perchlorate in perchloric acid solution(24 ml, 4 equiv.)[2)] at 25° for 20 min with vigorous stirring gave (2)[40 % yield, m.p. 207°. $[\alpha]_D^{22}$ +178°(c 0.45, $CHCl_3$)] and (3)[1b,3)][20 %, m.p. 211°, $[\alpha]_D^{22}$ +57.5°(c 0.43, $CHCl_3$)], after separation by chromatography on silica gel.

The p-quinol structure of the ring A in (2) was elucidated by its characteristic spectral data [IR($CHCl_3$) 3525, 1673, 1640 cm^{-1}, UV(EtOH) 230(19,260), 260(9,800) nm, ^1H NMR($CDCl_3$) δ 6.05(1H,d,J=2 Hz,H-4), 6.12(1H,dd,J=2,10 Hz, H-2), 7.42(1H,d,J=10 Hz,H-1) ppm] as compared with those of the p-quinol (3). The ^{13}C NMR spectrum($CDCl_3$) of (2) clearly showed the presence of three carbonyl groups [δ 216.0(C-17), 211.3(C-11), 185.8(C-3) ppm], and the position of the newly arisen carbonyl group at C-11 was established by the remarkably downfield ^1H NMR chemical shift(δ 7.42 ppm) of the H-1 proton as compared with that (δ 7.07 ppm) of the corresponding proton in (3). The intramolecular hydrogen bonding between the hydroxyl group and the C-11 carbonyl group enabled the stereochemistry at both C-9 and C-11 positions to be assigned. Furthermore the structure of (2) was confirmed by transforming (2) into 11-ketoestrone (4)[4] by Zn-AcOH reduction.

The 11-keto-p-quinol (2) was presumably formed by the reaction path way as illustrated. The possibility that (2) was formed from the minor p-quinol (3) was apparently excluded, since (2) could not be detected on treating (3) with thallium(III) perchlorate under the same condition. On the other hand, 9,11-dehydroestrone (5)[5] which may be derived from the initial quinone methide intermediate (I), was transformed into (2) on the same condition. The presence of the intermediate (II) was suggested by the fact that 9-hydroxy-11-keto-estrone (6)[4] (20 % yield) was obtained together with (2) (10 % yield) and (3) (50 % yield) when the reaction was carried out in the mild condition: the reagent used above was diluted by adding ten-fold volume of water, 25°, 10 hr, vigorously stirred.



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2) The reagent was prepared[1d] by dissolving Tl_2O_3(6.0 g) in 60 % perchloric acid(100 ml), followed by dilution with a half volume of water.

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