UNUSUAL PUMMERER REARRANGEMENT OF 3-METHOXY-16-THIA-D-HOMOESTRA-1,3,5(10),8,14-PENTAEN-17a-OL SULFOXIDES[1]

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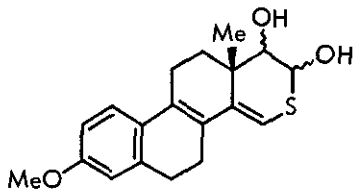
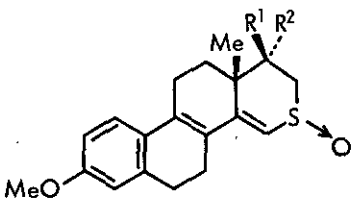
The reaction of acetic anhydride with the title steroidal sulfoxides leading to an unusual rearrangement is described.

In an attempt to prepare 3-methoxy-16-thia-D-homoestra-1,3,5(10),8,14-pentaene-17,17a-diols 1, we had occasion to examine the Pummerer reaction of sulfoxides 2 and 3. However, we found that these reactions gave no expected Pummerer products and led to an unusual rearrangement induced by double bond migration.

The reaction of excess acetic anhydride with the above sulfoxides catalyzed by a trace of p-toluenesulfonic acid was carried out at room temperature (1.5 hr). The products, after treatment with lithium aluminum hydride, were separated by chromatography. In neither case were any products of type 1 detected. In the reaction of 2 (α-oxide), only compounds 4 (9.7%), 5 (14.4%), and 6a (8.3%) were isolated.

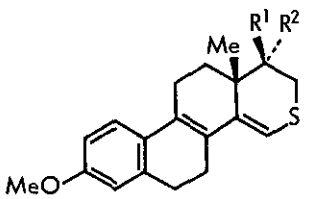


1



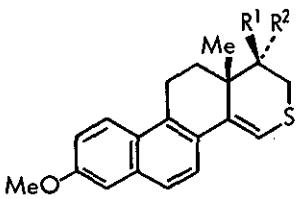
2, R^1 = H, R^2 = OH

3, R^1 = OH, R^2 = H



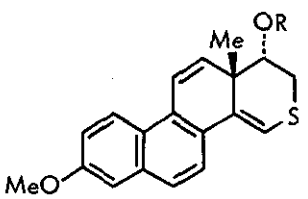
4, R^1 = H, R^2 = OH

7, R^1 = OH, R^2 = H



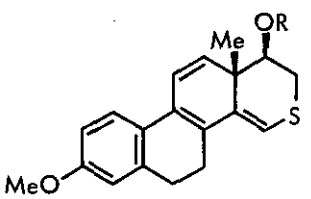
5, R^1 = H, R^2 = OH

8, R^1 = OH, R^2 = H



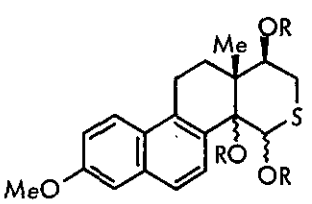
6a, R = H

6b, R = Ac



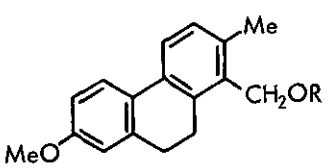
9a, R = H

9b, R = Ac



10a, R = H

10b, R = Ac



11a, R = H

11b, R = Ac

Other polar components were not pursued further at that time. The reaction products were examined in more detail for the similar acetic anhydride reaction of 3 (a mixture of α- and β-oxides). After hydride reduction, we obtained compounds 7 (19.2%), 8 (5.8%), 9a (4.1%), 10a (34.0%), and 11a (8.4%). Among the products from the above reactions, 4 and 7 were identified as corresponding parent sulfides and 5 and 8 were identical with their known authentic samples.[2] The structural assignment of other new compounds (6a, 9a, 10a, and

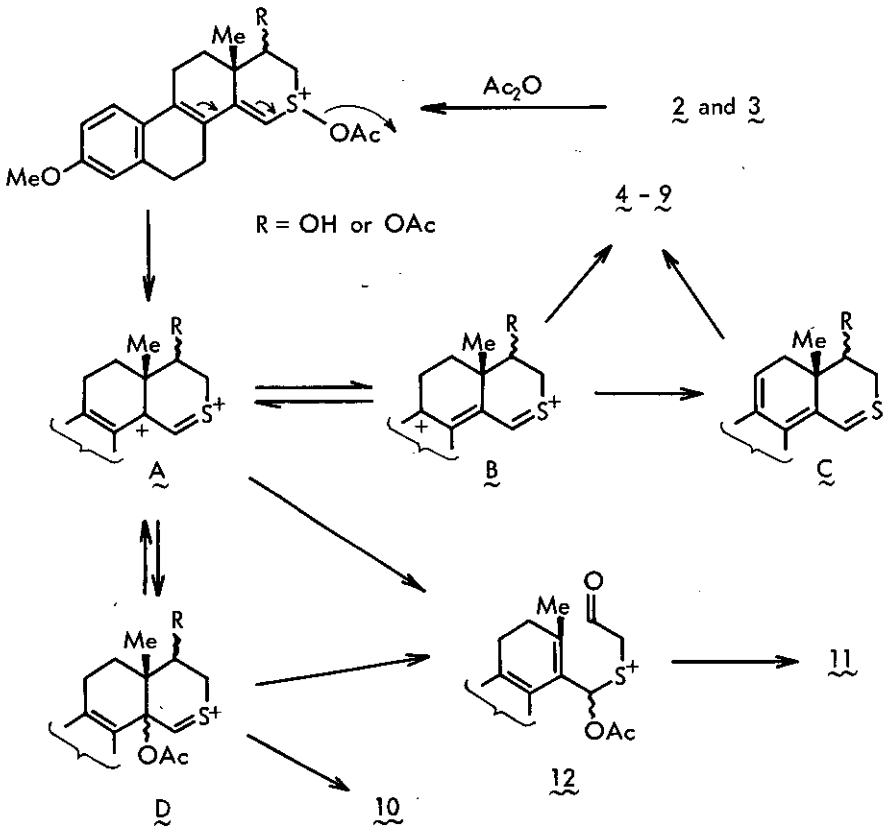


TABLE I. Physical and Spectral Data of Compounds 6 and 9-11

6a: mp 197-198°; m/e 310 (M^+); $\lambda_{max.}$ (EtOH) 245, 278, 300 sh nm (ε 30400, 30900, 20900).

6b: mp 164-166°; $\nu_{max.}$ ($CHCl_3$) 1729 cm^{-1}; δ($CDCl_3$) 1.22 (3H, s, 13-Me), 2.06 (3H, s, OAc), 3.90 (3H, s, OMe), 5.25 (1H, q, J 2, 4Hz, 17a-H), 5.88 (1H, d, J 10 Hz, 12-H), 6.58 (1H, s, 15-H), 7.17 (1H, d, J 10 Hz, 11-H), 7.1-7.3 (4H, m, 1-, 2-, 4-, 7-H), 7.98 (1H, d, J 8 Hz, 6-H).

9a: mp 242-243°; δ($CDCl_3$) 0.82 (3H, s, 13-Me), 3.93 (3H, s, OMe), 5.78 (1H, s, 15-H), 6.6-7.8 (5H, m, Arom. H).

9b: mp 243-246°; m/e 354 (M^+); $\lambda_{max.}$ (EtOH) 228, 243, 276, 282, 306 nm (ε 22600, 20800, 22300, 22100, 18400); $\nu_{max.}$ ($CHCl_3$) 1743, 1726 cm^{-1}: δ($CDCl_3$) 0.87 (3H, s, 13-Me), 2.18 (3H, s, OAc), 3.89 (3H, s, OMe), 4.86 (1H, q, J 4.5, 9.5 Hz, 17a-H), 5.73 (1H, s, 15-H), 6.5-7.3 (4H, m, Arom. H), 7.06 (1H, d, J 9 Hz, 12-H), 7.53 (1H, d, J 9 Hz, 11-H).

10a: Viscous syrup; m/e 346 (M^+).

10b: mp 105-106.5°; m/e 472 (M^+); $\lambda_{max.}$ (EtOH) 236.5, 265, 275 sh, 287 sh, 318, 332.5 nm (ε 59600, 12300, 9800, 6500, 1600, 1800); $\nu_{max.}$ ($CHCl_3$) 1760 sh, 1735 cm^{-1}; δ($CDCl_3$) 1.12 (3H, s, 13-Me), 1.96 (2H, t, 12-CH_2), 2.00 (3H, s, OAc), 2.16 (3H, s, OAc), 2.42 (3H, s, OAc), 3.90 (3H, s, OMe), 4.15 (2H, t, 11-CH_2), 5.27 (1H, q, J 3.5, 6 Hz, 17a-H), 5.98 (1H, s, 15-H), 7.0-7.4 (3H, m, 2-, 4-, 7-H), 7.58 (1H, d, J 9 Hz, 1-H), 7.63 (1H, d, J 10 Hz, 6-H).

11a: mp 123.5-124°; m/e 254 (M^+); $\lambda_{max.}$ (EtOH) 279, 310 sh nm (ε 22200, 5600); δ($CDCl_3$) 2.42 (3H, s, Me), 2.87 (4H, s, CH_2CH_2), 3.83 (3H, s, OMe), 4.74 (2H, s, CH_2O), 6.7-7.8 (5H, m, Arom. H).

11b: mp 134.5-137°; $\nu_{max.}$ ($CHCl_3$) 1732 cm^{-1}; δ($CDCl_3$) 2.05 (3H, s, OAc), 2.42 (3H, s, Me), 2.86 (4H, s, CH_2CH_2), 3.82 (3H, s, OMe), 5.26 (2H, s, CH_2O), 6.7-7.8 (5H, m, Arom. H).

11a) was based on spectral data, coupled with those of their acetates (6b, 9b, 10b, and 11b) (Table I).

The formation of these products may be rationalized in the following way. The initially formed acetoxysulfonium salt must undergo facile migration of the double bond with expulsion of the acetate ion to generate ionic intermediates A and B, and then C. Further deprotonation of these species would logically lead to 5, 8, and 9. Disproportionation may account for the simultaneous formation of 4 and 6. Based on the result from 3, however, 4 as well as 7 could have only resulted from the unrearranged substrate. Thus, concomitant oxidation may have caused B-aromatization of 9 to 6. A nucleophilic attack of acetate ions on the ion A and concomitant aromatization probably lead to the major product 10 via an intermediate D. A possible pathway for the formation of 11 may involve an initial ring cleavage of A or D to 12 and successive aromatization followed by reductive workup.

REFERENCES

1 Totally Synthetic Steroid Heterocycles. Part 6. — Part 5, T. Terasawa, T. Okada, preceding paper.

2 T. Terasawa and T. Okada, J.C.S. Perkin I, 576 (1978).

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