CHEMISTRY LETTERS, pp. 55-58, 1983.

MECHANISM OF THE PHOTOINDUCED REARRANGEMENT OF 5α-ANDROSTAN-17β-OL HYPOIODITE TO 13α- AND 13β-FORMYLOXY-16-IODO-13,16-SECO-D-NOR-5α-ANDROSTANE IN THE PRESENCE OF HgO AND I_2 —— AN ^{18}O LABELING STUDY(1)

Hiroshi SUGINOME,* Shinji YAMADA, and Norio MIYAURA
Organic Synthesis Division, Department of Chemical Process Engineering,
Faculty of Engineering, Hokkaido University, Sapporo 060

An ^{18}O labeling study indicates that the title rearrangement involves a novel intramolecular combination between a carbonyl oxygen and a carbon radical which are generated by a β-scission of an oxyl radical.

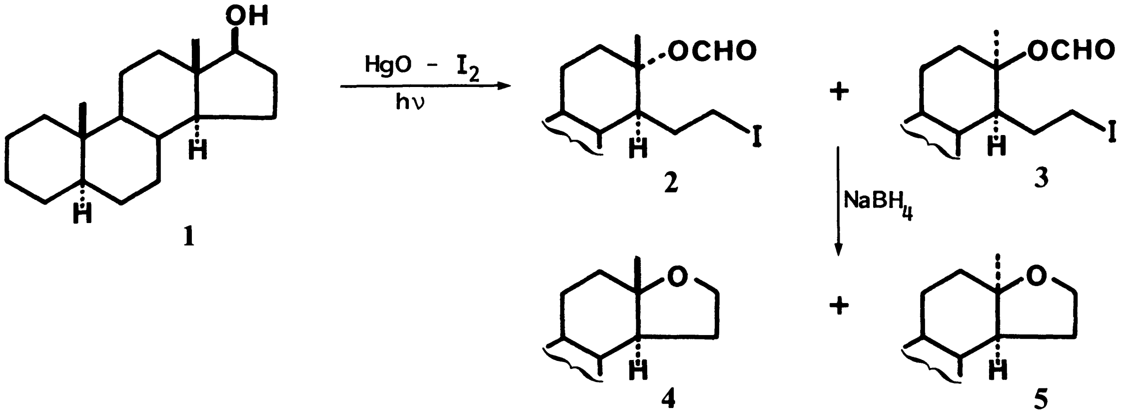
In our previous paper(1), we reported a new method for the transformation of hydroxysteroids into oxasteroids. Mercury(II) oxide-iodine(2) was used as an effective reagent for the formation of hypoiodites from hydroxysteroids(3) in this transformation and the reaction involved a novel photoinduced reaction of the hypoiodite into a formate, which can be cyclized to oxasteroids, in the presence of an excess of the reagent. 5α-Androstan-17β-ol(1), for example, could be converted into 17-oxa-5α-androstane(4) and its 13α-epimer(5) *via* 13β-formyloxy-16-iodo-13,16-seco-D-nor-5α-androstane(2) and its 13α-epimer(3) by this method (Scheme 1).

An initial intermediate in this transformation is a carbon radical [e.g., (8)] formed by a β-scission of the corresponding oxyl radical [e.g., (7)] (Scheme 2). A probable pathway, by which the formates(2) or (3) are formed from this intermediate, has already been suggested in our previous paper(4).

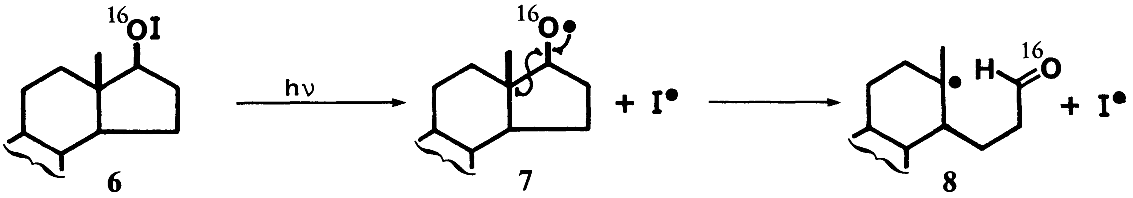
Three paths (a), (b), and (c), however, are possible for the formation of the formates from the carbon radical intermediate (8), as depicted in Scheme 3. Thus, in the most plausible path (a), the carbon radical (8) combines intramolecularly with the carbonyl oxygen to form a tetrahydropyranyl radical (9) which reacts with iodine oxide or ·OI to generate a new hypoiodite. This hypoiodite may generate a second oxyl radical (10) by irradiation which generates the observed formate [e.g., (11)] by a β-scission. Alternatively, iodine oxide or ·OI may combine with the carbon radical (8) directly to form a second hypoiodite (13). This then generates the corresponding oxyl radical [e.g., (14)] by irradiation, which intramolecularly attacks the carbonyl carbon of the aldehyde to form a new oxyl radical [e.g., (15)]. The β-scission gives the observed formates [e.g., (16)]. In a third pathway (c), ·OI reacts with the carbonyl carbon of the carbon radical intermediate (8) to form a hypothetical species such as (18). This species may rearrange to another hypoiodite [e.g., (19)] under the conditions as depicted and the successive reactions *via* [e.g., (20)] may give formate [e.g., (21)] (Scheme 2).

Which of these three paths is operative can be distinguished by experiments which use ^{18}O labeled mercury(II) oxide as a source of $I_2{}^{18}O$.

We now wish to report the results of an ^{18}O labeling study which confirms that



Scheme 1



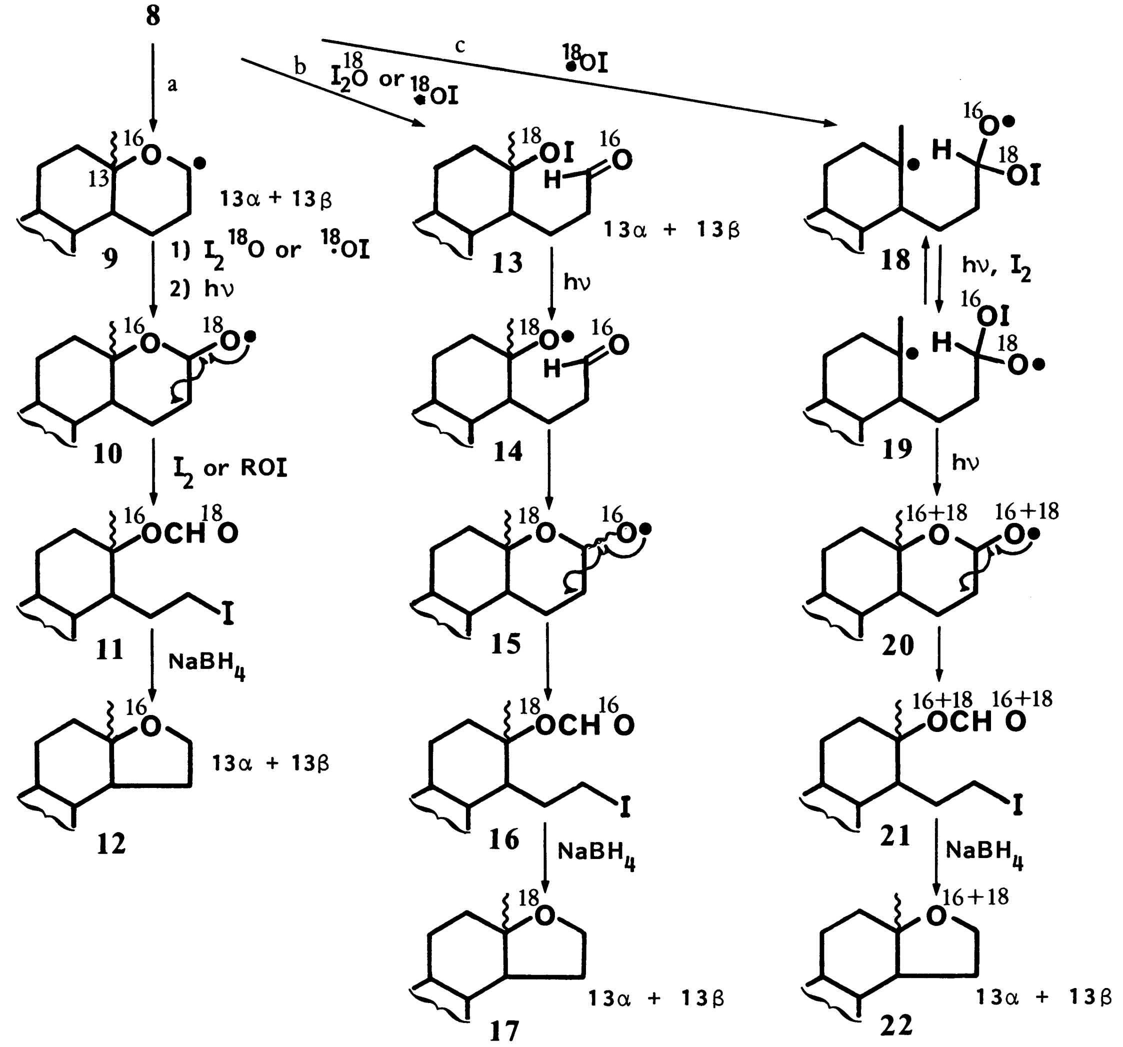
Scheme 2

the formates (2) and (3) arise by path (a) and not by path (b) or (c).

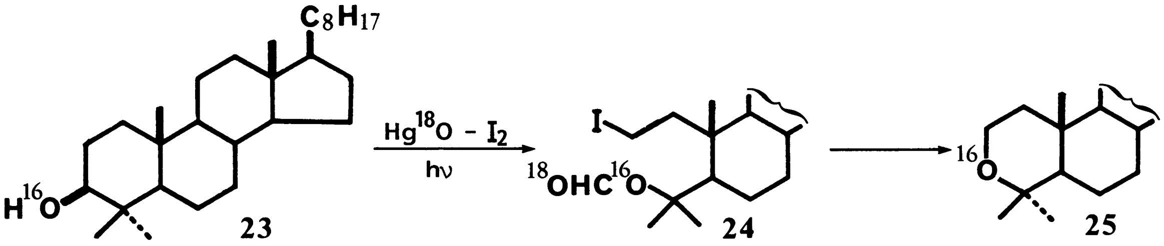
Thus, 5α-androstan-17β-ol(1) was transformed into a mixture of formates (2) and (3) with mercury(II) oxide-^{18}O (48.9 atom% ^{18}O)$^{5)}$ and iodine under the conditions described in our previous paper.$^{1)}$ The mixture of the formates was transformed into a mixture of oxasteroid (4) and its 13α-isomer (5). This mixture was separated to its components (4) and (5) as reported previously. The extent of incorporation of ^{18}O into oxasteroids (4) and (5) was then analyzed by mass spectrometry. This analysis proved no incorporation of ^{18}O in oxasteroids (4) and (5). Similarly, 4,4-dimethyl-5α-cholestan-3β-ol(23) was converted into formate(24) with mercury(II) oxide-^{18}O and iodine and 4,4-dimethyl-3-oxa-5α-cholestane(25) obtained by the cyclization was analyzed by mass spectrometry. This again indicated no incorporation of ^{18}O in the oxasteroid (Scheme 4).

These isotopic labeling experiments provide conclusive evidence that the oxygen atom in the oxasteroids is derived from the hydroxy group of the starting alcohols and not from the oxygen of mercury(II) oxide and that the formates arise by path (a) since ^{18}O should wholly or partly be incorporated in the 17-oxygen of oxasteroids (4) or (5) if they are formed _via_ path (b) or (c). It should be noted that the rearrangement of oxyl radical (7) to tetrahydropyranyl radical (9) can not be a concerted process but passes through a discrete carbon radical (8) in the path (a) since epimeric formates (2) and (3) are formed in the reaction of 5α-androstan-17β-ol hypoiodite(6).

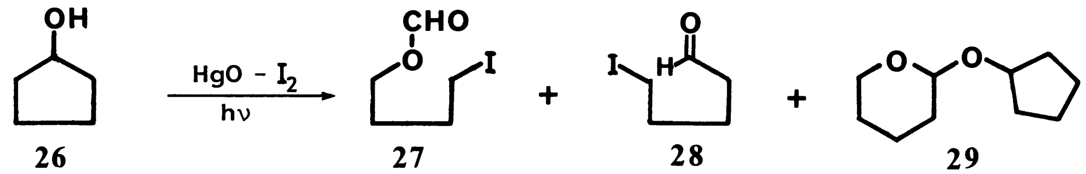
When cyclopentanol(26) was subjected to the above reaction, three products, 4-iodobutyl alcohol formate(27) (16%), 5-iodopentanal(28) (8%), and cyclopentyl



Scheme 3



Scheme 4



Scheme 5

tetrahydropyranyl ether(29) (7%) were obtained. The formation of an acetal(29) fully supports the intervention of a discrete tetrahydropyranyl radical [e.g., (9)] in path (a) (Scheme 5).

A carbon radical intermediate equivalent to (8) is also generated in the photolysis of a nitrite corresponding to hypoiodite(6)$^{6)}$. In nitrite photolysis, however, the tertiary carbon radical center of (8) combines with nitric oxide instead of with the carbonyl oxygen of the formyl group in the molecule. In hypoiodite photolysis, the combination of bulky ·OI or I_2O with the tertiary carbon radical center of (8) may be sterically hindered and thus intramolecular combination with the carbonyl oxygen is the preferred course of the reaction.

The formation of the tetrahydropyranyl radical from a carbon radical represents a novel intramolecular combination of a carbonyl oxygen with a carbon radical. An analogous intramolecular interaction between a carbonyl oxygen and a carbon radical has been reported to be involved in the formation of 2-phenyltetrahydrofuran in the reduction of γ-chlorobutyrophenone with tributyltin hydride.$^{7)}$

References

1) Photo-induced Transformations. Part LXVII. Part LXVI. H. Suginome and S. Yamada, Chem. Lett., 1982, 1233.
2) A. A. Petrov, J. Gen. Chem., U.S.S.R., 10, 819 (1940); Chem. Abstr., 35, 2112 (1941); M. Akhtar and D. H. R. Barton, J. Am. Chem. Soc., 86, 1528 (1964).
3) For a general review, see J. Kalvoda and K. Heusler, Synthesis, 1971, 501.
4) H. Suginome, A. Furusaki, K. Kato, N. Maeda, and F. Yonebayashi, J. Chem. Soc, Perkin Trans. 1, 1981, 236.
5) HgO-^{18}O 48.9 at.% ^{18}O was prepared by the reaction of mercury(II) chloride in water-^{18}O [prepared by diluting water-^{18}O (Merck Sharp and Dohme Canada Ltd., 97 at.% ^{18}O) with water] with sodium hydroxide-water-^{18}O. C. H. Rogers "Inorganic Pharmaceutical Chemistry" (1930), p.403.
6) C. H. Robinson, O. Gnoj, A. Mitchell, E. P. Oliveto, and D. H. R. Barton, Tetrahedron, 21, 743 (1965); H. Suginome, N. Yonekura, T. Mizuguchi, and T. Masamune, Bull. Chem. Soc. Jpn., 50, 3010 (1977).
7) L. W. Menapace and H. G. Kuivila, J. Am. Chem. Soc., 86, 3047 (1964).

(Received October 26, 1982)