Tetrahedron Letters No. 13, pp 1161 - 1164, 1974. Pergamon Press. Printed in Great Britain.

HYPOIODITE REACTION OF N-ACETYLJERVINE: AN UNPRECEDENTED RADICAL ADDITION TO A CARBONYL GENERATED BY β-CLEAVAGE OF ALKOXYL RADICAL (1)

Hiroshi Suginome*, Kimitoshi Kato, and Tadashi Masamune
Department of Chemistry, Faculty of Science, Hokkaido University
Sapporo, Japan

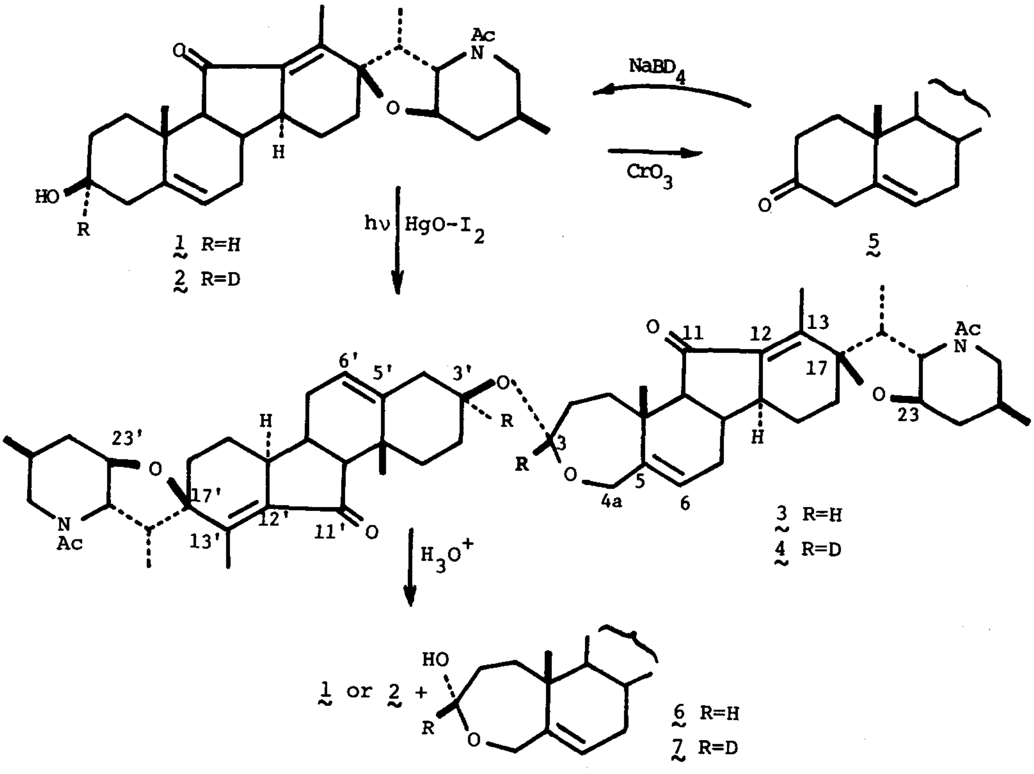
(Received in Japan 16 January 1974; received in UK for publication 12 February 1974)

Our recent investigation disclosed that the products of the hypoiodite reaction of steroids with 3-hydroxy-Δ^5 system are 4-iodo-3,4-seco-steroid-5-en-3-als and oxidomethylene-3α,5α-*A*-norsteroids. (2)

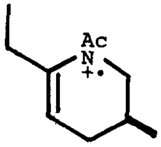
We wish to report on the results of hypoiodite reaction of *C*-nor-*D*-homosteroid with 3-hydroxy-Δ^5 system as the part structure. An unexpected variation between steroids and *C*-nor-*D*-homosteroids with regard to the type of the products was found.

Thus, the irradiation of N-acetyljervine **1** (3) (800 mg) in benzene (60 ml) in the presence of HgO and I_2 (each 3 equivalents) through pyrex for 12 hr by a 100-W high pressure Hg arc lamp under an argon atmosphere afforded a mixture of products separated by the preparative t.l.c. to afford five new compounds. The structure of a major product **3**, m.p. 216-218°, (25% yield) is described in the present paper, and the structures of the remainder and the probable sequences of the formations of all five products are discussed in the following paper.

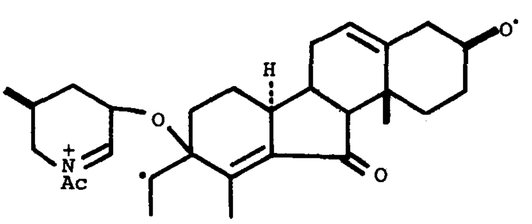
The molecular formula of **3** was found to be $C_{58}H_{80}O_8N_2$ by elemental analysis and the molecular weight determination by the osmometric method. (4) (Found; 918 Calcd for $C_{58}H_{80}O_8N_2$, 933.28). The i.r., u.v. and ^{1}H n.m.r. spectra of 3 confirmed that the C, D and the heterocyclic rings of **1** are not altered by the photolytic procedure. Thus, the presence of the α,β-unsaturated carbonyl group in **3** was confirmed by the i.r. spectrum (Nujol, 1633 and 1713 cm^{-1}) and by the u.v. spectrum ($\lambda_{max}^{CHCl_3}$ 253 nm, ε31,100). In the ^{1}H n.m.r. spectrum (100 MHz, $CDCl_3$), the N-acetyl, the 18- and the 19-methyl groups appeared as the three 6-



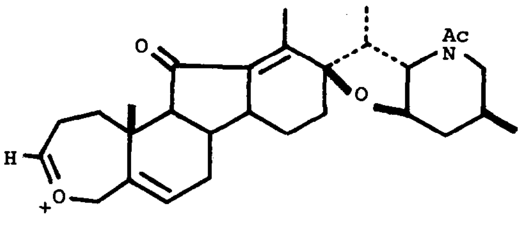
Scheme



8 m/e 167 (100%)



9 m/e 465 (2%)



10 m/e 466 (1%)

proton singlets at τ7.89 at τ7.73 and at τ8.98, as well as the 21- and the 26-methyl groups as the two 6-proton doublets at τ8.95 (J=9.0 Hz) and at τ9.11 (J=8.3 Hz).

The clue for the structure of 3 was given by the presence of very characteristic four one-proton signals at τ4.39 (diffused doublet, J=4.0 Hz), at τ4.63 (diffused doublet, J=4.0 Hz), at τ5.10 (triplet, J=5.8 Hz) and at τ5.65 (doublet, J=13.0 Hz) in the ^{1}H n.m.r. spectrum.

Decoupling experiments showed that two signals at τ4.39 and at τ4.63 collapsed to two clear singlets on double irradiation at τ7.5 ± 0.1 ppm while a triplet at τ5.10 was only partially decoupled. The properties of the two signals at τ4.39 and at τ4.63 in this double irradiation is reminiscent of those of C-6 olefinic proton of steroids and suggests the presence of a couple of protons, both of which are in a similar environment to C-6-olefinic proton of steroids. The diffused triplet at τ5.10 was also partially decoupled to broad singlet (W_H=7.0 Hz) on irradiation at τ8.3. This proton which is responsible for this triplet was confirmed to be derived from the C-3α-H of N-acetyljervine since this signal is absent in the spectrum of the product 4, m.p. 220-222° obtained from 3α-deuterio-N-acetyljervine 2, m.p. 224.5-226.5° prepared by the Jones oxidation of N-acetyljervine to N-acetyljerva-5,12(13)-diene-3,11-dione 5, m.p. 172.5-174.5°, followed by $NaBD_4$ reduction.

The chemical shift and double irradiation also confirmed that the doublet at τ5.65 should be attributable to geminal coupling of isolated oxygen-bearing methylene protons; on irradiation of the centre of a doublet at τ6.46 (J=13.0 Hz) this doublet collapsed to a singlet, and the irradiation at τ5.65 caused a collapse of a doublet at τ6.46 without alteration of the signals at τ4.39, at τ4.63 and at τ5.10.

Hydrolysis of either 3 or 4 in THF with dilute aqueous HCl at room temperature affords a couple of alcohols, N-acetyljervine and amorphous alcohol 6 or 3β-deuterio-N-acetyljervine and deuterated 7.

The ^{1}H n.m.r. spectrum (100 MHz, $CDCl_3$) of 6 revealed that, besides the signals due to the N-acetyl, the 18-, 19-, 21- and 26-methyl groups, a series of one-proton signals at τ4.41 (diffused doublet, J=3.9 Hz), at τ4.86 (triplet, J=

6.1 Hz) and at τ5.59 (doublet J=13.3 Hz), which showed remarkable similarity to the signals of 3 in the coupling patterns, the chemical shifts and behaviours for the decoupling of each signals. However, the spectrum of 6 lacked a signal corresponding to a diffused signal at τ4.63 in 3. The i.r. and u.v. spectra of 6 indicated the presence of α,β-unsaturated ketone function of jervine type. These coupled with the formation of N-acetyljervine in this hydrolysis, prove the signal at τ4.63 in 3 is due to the C-6-H of N-acetyljervine unit in the compound 3.

All results on 3 above can now be reconciled with perfect consistency in terms of the dimeric structure formulated in the Scheme.

The mass spectrum of 3 revealed no M^+ peak and the highest fragments at 465 (M^+-467) and at 466 with the base peak at m/e 167. These fragment peaks are assignable to species 8, 9 and 10. The ^{13}CFT n.m.r. and ^{1}H off reasonance spectra of 3 ($CDCl_3$, 25.1 MHz, ppm from TMS) fully supported the assigned formula 3. Except C-17, C-17′, N-Ac, N′Ac and C-23, C-23′which appeared respectively as the coincident singlets at 172.97, 85.42 and 72.68, all the resonances due to SP^2 carbon atoms and oxygen-bearing carbon atoms appeared as a pair of signals. The assignments of these signals are as follows; C-11-CO and C-11′CO (206.28 and 206.65), C-5 and C-5′(145.79 and 146.28), C-13 and C-13′(142.46 and 144.22), C-6 and C-6′ (120.67 and 125.95), C-3 of oxepane ring (99.08), C-3′(75.72).

The probable sequence of the formation of 3 together with those of other products will be the subject of an accompanying Communication, but it is noted that the present reaction is a rare example in which radicals combine with a polar π bond generated by β-cleavage of an alkoxyl radical.

REFERENCES AND NOTES

(1) Part XXVI of the series "Photoinduced Transformation". Paper XXV. H. Suginome, H. Ono, M. Kuramoto, and T. Masamune, *Tetrahedron Letters*, 4147 (1973).
(2) H. Suginome and K. Kato, *Tetrahedron Letters*, 4139 (1973).
(3) K. Saito, Harusada Suginome and M. Takaoka, *Bull. Chem. Soc. Japan*, 11, 172 (1936).
(4) Hitachi 115 instrument was used, using benzene as the solvent.

ACKNOWLEDGEMENT: We are grateful to the Ministry of Education of Japan for financial assistance. ^{13}CFT nmr spectra of 3 were measured by Mr. K. Matsushita of Japan Electron Optics Laboratory Co., Ltd., and ^{1}H nmr and the spin decoupling by Mrs. S. Araki and Miss T. Okayama. We thank them for these measurements.