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PHOTO-INDUCED REARRANGEMENT OF WIDDROL HYPOIODITE

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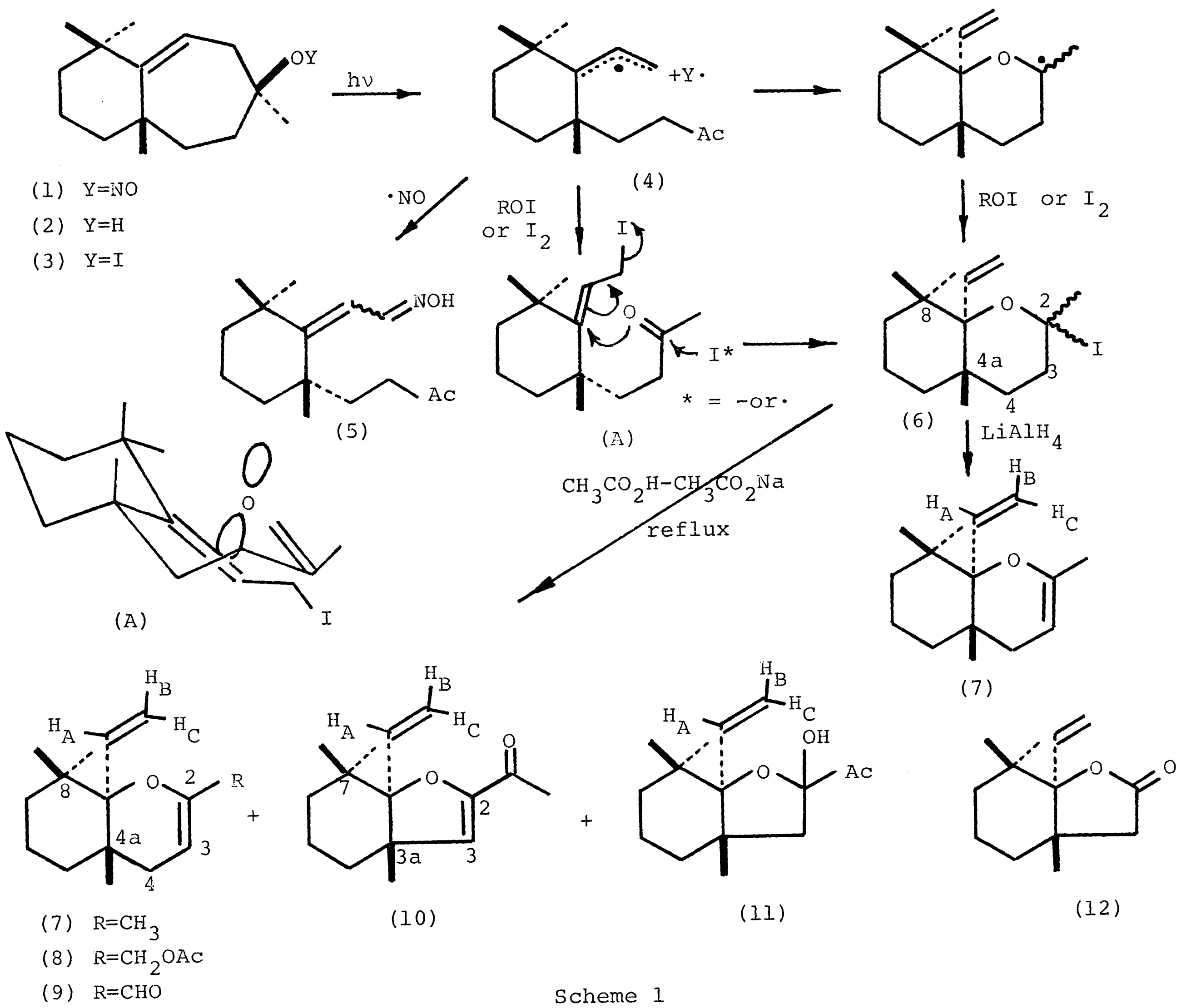
Hypoiodite of widdrol, a sesquiterpene, underwent a rearrangement to 5,6,7,8-tetrahydro-2ξ-iodo-2ξ,4aβ,8,8-tetramethyl-8aα-vinylchroman on irradiation. Reflux in acetic acid containing sodium acetate transformed it into several compounds resulting from elimination of hydrogen iodide and reactions with generated iodine.

We recently reported$^{1)}$ that irradiation of the nitrite ester (1) of a sesquiterpene widdrol (2), a seven-membered cyclic homoallyl alcohol, in benzene through Pyrex afforded a mixture of four isomeric α,β-unsaturated ketone oximes (5) resulting from a β-scission of the corresponding oxyl radical.

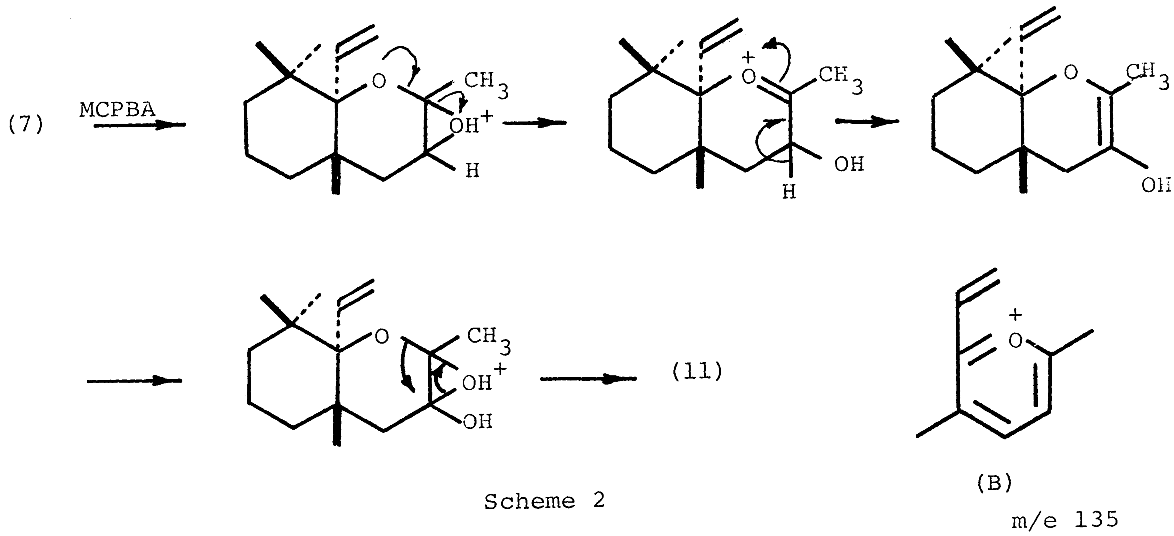
In this paper, we wish to report the results of the photolysis of hypoiodite (3) of widdrol. It was found that the allyl radical intermediate (4) reacted in a manner distinct from that formed in the nitrite photolysis and a six-membered cyclic ether (6) was formed as virtually an exclusive product.

Irradiation of widdrol (2) in cyclohexane containing iodine (1.5 mol equiv.) and mercuric oxide$^{2)}$ (2.0 mol equiv.) with a 100-W Hg arc for 45 min afforded an oily product (6) having an iodine in 75% yield. Its structure as a cyclic ether was deduced on the basis of the following physical and chemical evidence as well as some mechanistic considerations.

The NMR spectrum ($CDCl_3$, TMS, τ) showed three singlets (each 3H) at 9.13, 9.00, and 8.91 assignable to three tertiary methyl groups attached to the C-4a and the C-8 and singlet (3H) at 7.96 assignable to a methyl attached to a carbon bearing an iodine. It also showed three double doublets centred at 5.07 (1H, J = 16 and 3 Hz), 4.86 (1H, J = 11 and 3 Hz) and 4.15 (1H, J = 16 and 11 Hz) assignable to a vinyl group. The IR spectrum (neat) showed bands at 922 (vinyl) and 1050 cm^{-1} (C-O-C). Treatment of product (6) with $LiAlH_4$ afforded a compound, mp 105 -107 °C, (haxane), the spectral properties of which were consistent with a dihydropyran structure (7) resulting from the elimination of HI. [m/e 220 (20.6%, M^+), 205 (11.5%, M^+-CH_3) and 135 (84.6%, ion (B) formulated); ν_{max}^{KBr} 1703 (enol ether) and 924 cm^{-1}; 9.08, 8.97, and 8.88 (each 3H, s, C-8 gem dimethyl and C-4a methyl), 8.25 (3H, s, C-2 methyl), 5.70 (1H, d, J = 5.0 Hz, C-3-H), 5.00 (1H, dd, J = 16 and 3 Hs, H_A), 4.86 (1H, dd, J = 3 and 11 Hz, H_B), and 4.10 (1H, dd, J = 11 and 16



Scheme 1



Scheme 2

Hz, H_C)].

Two plausible paths leading to (6) are depicted in Scheme 1. Between these, a path via intramolecular combination of the allyl radical (4) with carbonyl oxygen at the tertiary radical centre is less likely since allyl radical (4) generated in the nitrite photolysis rapidly traps nitric oxide at the primary radical center1) and iodine and iodides are proved to be good radical scavengers comparable to nitric oxide.3) Thus, iodide (6) is presumably produced via ionic or radical cyclization of an intermediate (A). Although no spectral evidence was available for the configuration of a vinyl substituent at the C-5, the vinyl substituent is likely to be α-oriented since the cyclization of allyl radical (4) would take place from a more stable conformation depicted. Several other examples of the formation of oxygen rings in photolysis of steroidal homoallyl alcohol hypoiodites have been reported recently.4,5)

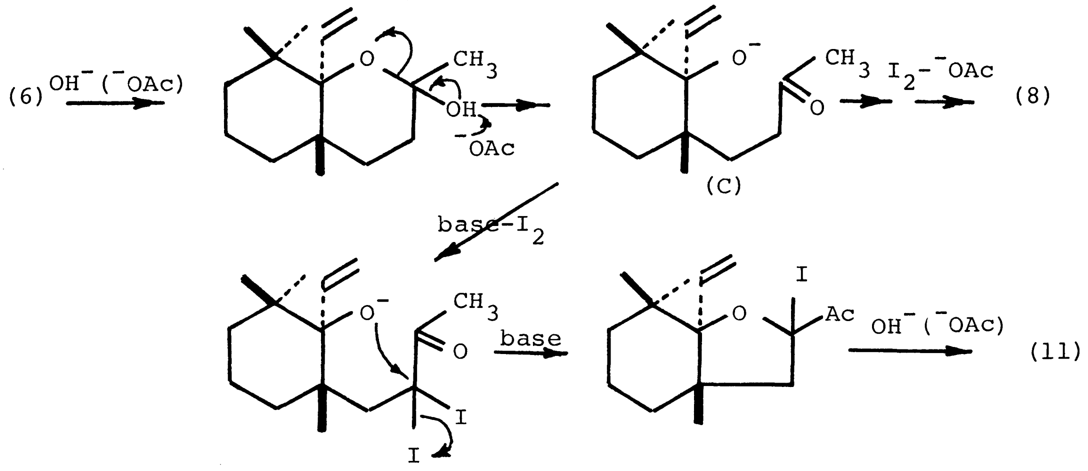
When cyclic ether (6) in acetic acid containing an excess of sodium acetate hydrate was refluxed for 1 h, a mixture of products was formed, from which dihydropyran (7), (15%), and the following four products, (8) (30%), (9), mp 111-113 °C, (hexane) (8%), (10) (8%), and (11), mp 129-131 °C, (hexane) (12%), were isolated by column chromatography in order of decreasing mobility.

Compound (8); after spectral identification [9.10, 8.97 and 8.83 (each 3H, s, C-8 gem dimethyl and C-4a methyl), 7.93 (3H, s, $OCOCH_3$), 5.50 (2H, broad s, C-2-CH_2O-), 5.33 (1H, dd, J = 2 and 6 Hz, C-3-H), 4.88 (1H, dd, J = 3 and 17 Hz, H_A), 4.82 (1H, dd, J = 9 and 3 Hz, H_B), and 4.15 (1H, dd, J = 9 and 17 Hz, H_C); ν_{max} (neat) 1739 (OAc) and 1223 cm^{-1} (C-O-C)], the structure was confirmed by its preparation from compound (9) by reduction with $NaBH_4$ followed by acetylation.

Compound (9); the structure was confirmed as an aldehyde by IR, ^{1}H NMR and spin-decoupling and ^{13}C NMR [8.96, 8.94, and 8.77 (each 3H, s, C-8 gem dimethyl and C-4a methyl), 8.31 (1H, dd, J = 19.4 and 5.7 Hz, C-4-H), 7.86 (1H, dd, J = 19.4 and 3.0 Hz, C-4-H), 4.25 (1H, dd, J = 3.0 and 5.7 Hz, C-3-H), 5.03 (1H, dd, J = 1.8 and 17.3, H_A), 4.83 (1H, dd, J = 10.8 and 1.8, H_B), 3.12 (1H, dd, J = 10.8 and 17.3 Hz, H_C), and 0.87 (1H, s, C-2-CHO); ν_{max} (Nujol), 1689 and 1650 cm^{-1} (C=C-CHO); ^{13}C NMR ($CDCl_3$, TMS, PPM), 8.57 (s, C-8a), 116.3 and 131.4 (d and t, CH = CH_2), 121.0 (d, C-3), 149.9 (s, C-2), and 186.1 (d, CHO)] and by reverting back to compound (7) by Wolff-Kishner reduction in 55% yield.

Compound (10); the spectral data were fully consistent with the dihydrofuran structure [m/e 414 (57.5%, M$^+$), 399 (40.0%, M$^+$-CH_3), and 55 (100%); ν_{max} (neat), 1687 and 1617 cm^{-1} (C=C-C=O); 9.01, 8.95, and 8.74 (each 3H, s, C-7 gem dimethyl and C-3a methyl), 7.70 (3H, s, Ac), 4.35 (1H, s, C-3-H), 4.85 (1H, dd, J = 3 and 10 Hz, H_B), 4.75 (1H, dd, J = 3 and 17 Hz, H_A), and 4.11 (1H, dd, J = 10 and 17 Hz, H_C)].

Compound (11); on the basis of the spectral data [m/e 252 (0.6%, M$^+$), 209 (79.2%, M$^+$-Ac) and 69 (100%); 9.05 (6H, s) and 8.60 (3H, s, C-7 gem dimethyl and C-3a methyl), 8.64 (3H, s, Ac), 4.62 (1H, dd, J = 4 and 10 Hz, H_B), 4.32 (1H, dd, J = 4 and 17 Hz, H_A), and 3.77 (1H, dd, J = 10 and 17 Hz, H_C); ν_{max}^{KBr} 3435 (OH) and 1707 cm^{-1} (Ac)], as well as its transformation into a γ-lactone (12), mp 128-131 °C [ν_{max} (neat) 1778 (γ-lactone); 9.05, 8.93, and 8.74 (each 3H, s, C-7 gem dimethyl and C-3a methyl), 8.06 (1H, d, J = 16 Hz, C-3-H), and 7.39 (1H, d, J = 16



Scheme 3

Hz, C-3-H)], by oxidation with lead tetraacetate, the product was formulated as an α-hydroxytetrahydrofuran (11). We found that compound (11) can be obtained by oxidation of (7) with 2.5 mol equivalent of *m*-chloroperbenzoic acid in 80% yield. This ring contraction reaction seems a new type and may proceed as rationalized in Scheme 2.[6)]

The active species which transforms photoproduct (6) into a series of compounds (8), (9), (10), and (11) is believed to be iodine resulting from iodide (6). Thus, the formation of acetate (8) and α-hydroxytetrahydrofuran (11) can be envisioned as indicated in Scheme 3. A methylketone (C) would be a common intermediate for the formation of (8) and (11). A base-catalyzed iodination at either methyl or methylene group of (C), followed by a base-catalyzed cyclization and substitution of iodides with $^-$OAc would result in the formation of (8) and (11). It was found that acetate (8) can be oxidized to aldehyde (9) in the presence of sodium acetate and iodine in acetic acid, indicating the formation of (9) from (8). Moreover, dihydrofuran (10) is formed from α-hydroxytetrahydrofuran (11) as proved by the transformation of (11) into (10) by treatment with sodium acetate in acetic acid in 90% yield.

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