Unusual Photochemical Behaviour of the Enone Chromophore of the Insect Moulting Hormone 20α-Hydroxyecdysone

(The late) Luigi Canonica, Bruno Danieli,* Giordano Lesma, and Giovanni Palmisano

Dipartimento di Chimica Organica e Industriale, Facoltà di Scienze, Università degli Studi di Milano, Via Venezian 21, 20133 Milano, Italy

U.v. irradiation of the most representative insect moulting hormone 20α-hydroxyecdysone (1) in water follows two unusual pathways affording the reduction products (2) and (4) (path a) together with the ketone (5) and the cyclobutanol (6) (path b).

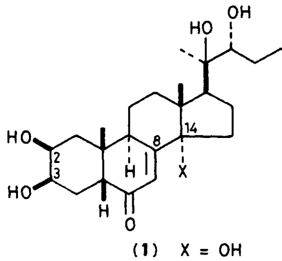
The utility of insect moulting hormones as specific pest controlling agents is dependent upon many factors among which inactivation under environmental conditions plays an important role.[1] As part of a comprehensive study on degradation of ecdysteroids,[2] we report here the characterisation of products from the photolysis in water of the most representative ecdysteroid 20α-hydroxyecdysone (**1**). These results highlight the unusual photochemical behaviour of the enone chromophore in (**1**).[3]

When a 10^{-3} M solution of (**1**) in water (pH 7.1) was irradiated with a 125 W high-pressure mercury lamp through a Pyrex filter (λ >290 nm) for 12 h under argon, (**1**) was completely consumed (h.p.l.c.). After removal of the solvent, the residual mixture was chromatographed on silica gel to give (**2**) (15% isolated yield), (**4**) (35%), (**5**) (23%), and (**6**) (18%).†

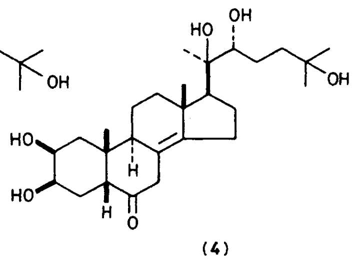
The major photoproduct was shown to be the $\Delta^{8,14}$ ketone (**4**)‡ from its ^{1}H and ^{13}C n.m.r. spectra [δ_H 2.60 and 3.01 (2H, ABq, *J* 14.2 Hz), diastereotopic 7-H$_2$; δ_C 122.8 (C-8), 150.6 (C-14), and 212.4 (C-6)]. Consistent with the proposed structure, haematoporphyrin-sensitised photo-oxygenation[4] of (**4**) in dry pyridine, followed by thiourea reduction, led to (**1**) in almost quantitative yield.

The structure of the less polar compound was established as 14α-deoxy-20α-hydroxyecdysone (**2**)‡ from its n.m.r. data [δ_H 2.88 (1H, ddd, *J* 11.0, 5.2, and 2.5 Hz, 9-H) and 5.86 (1H, dd, *J* 2.5 and 2.5 Hz, 7-H); δ_C 13.7 (C-18) and 57.1 (C-14)]. The coupling constants $^4J_{7,9}$ and $^4J_{7,14}$ for 7-H were in agreement with a 14*S* (H-α) configuration.[5]

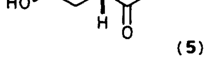
The third photoproduct was identified as the *abeo*-13 (14 → 8) derivative (**5**)‡ from its ^{13}C n.m.r. spectrum and from the 300 MHz ^{1}H n.m.r. spectrum of its 2,3;20,22-diacetonide. The ^{13}C n.m.r. spectrum of (**5**) showed significant changes compared to (**1**) in the signals attributable to



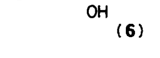
(**1**) X = OH
(**2**) X = H
(**3**) X = OOH



(**4**)



(**5**)



(**6**)

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† Occasionally, in addition to (**2**) and (**4**)—(**6**), an unexpected 14α-hydroperoxy derivative (**3**)[2d] was isolated in low and erratic yields although great care was taken to remove the residual oxygen from the argon purge.

‡ Selected spectroscopic data for (**4**): (M^+ + H) *m/z* 465 [positive xenon fast-atom bombardment mass spectrometry (f.a.b.m.s.)], i.r. 1695 cm^{-1}, Raman 1670 cm^{-1} (tetrasubstituted alkene); δ_H (200 MHz, C$_5$D$_5$N) 0.80 (s, 19-Me), 0.93 (s, 18-Me), 4.17 (br dt, *J* 11.0 and 3.5 Hz, 2-H), and 4.59 (m, $W_{\frac{1}{2}}$ 7 Hz, 3-H); (**2**): (M^+ + H) *m/z* 465 (f.a.b.m.s.); u.v. 247 nm (log ε 4.13); c.d. (dioxane) $\Delta\varepsilon$(nm) 1.02(349), 1.03(335), 0(311), −0.75(280), and −8.73(252); δ_H (200 MHz, C$_5$D$_5$N) 0.97 (s, 18- and 19-Me) and 2.88 (ddd, *J* 11.0, 5.2, and 2.5 Hz, 9-H); δ_C (25.2 MHz, C$_5$D$_5$N) 121.7 (C-7), 163.2 (C-8), and 202.0 (C-6); (**5**): (M^+ + H) *m/z* 481 (f.a.b.m.s.); i.r. 1715 cm^{-1}; δ_H (200 MHz, C$_5$D$_5$N) 3.17 (d, *J* 16.1 Hz, 7α-H), 4.17 (ddd, *J* 3.5, 3.5, and 3.5 Hz, 2-H), and 4.26 (br. dt, *J* 10.1 and 3.5 Hz, 3-H); δ_C (C$_5$D$_5$N) 210.3 (C-6) and 215.5 (C-14); (**5**) 2,3;20,22-diacetonide: ($M^{+\cdot}$) *m/z* 560.7750; δ_H (300 MHz, CDCl$_3$) 0.95 (s, 18-Me), 1.25 (s, 19-Me), 1.98 and 2.81 (ABq, *J* 13.5 Hz, 7β- and 7α-H), 4.04 (ddd, *J* 5.5, 4.5, and 2.1 Hz, 2-H), and 4.35 (ddd, *J* 9.5, 6.8, and 5.5 Hz, 3-H); (**6**): (M^+ + H) *m/z* 481 (f.a.b.m.s.); i.r. 1698 cm^{-1}; δ_C (C$_5$D$_5$N) 69.9 (C-2), 29.6 (C-4), 47.3 (C-5), 42.9 (C-7), 63.6 (C-8), and 214.0 (C-14).

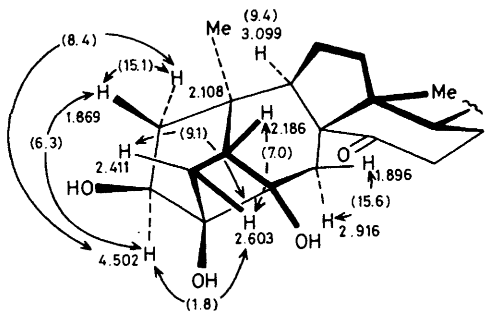


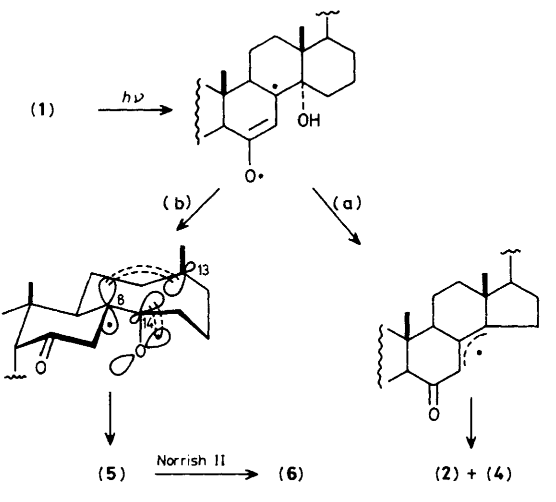
Figure 1. ^1H Chemical shifts and coupling constants (*J*/Hz) for the A–B rings in (**6**).

C-14 [δ_C 215.5(s) *vs.* 84.2(s)], C-8 [δ_C 65.4(s) *vs.* 165.7(s)], and C-7 [δ_C 41.1(t) *vs.* 121.6(d)]. The stereochemistry at the newly formed centres, 8*R* and 13*S*, was established by difference nuclear Overhauser enhancement (n.O.e.) studies. In particular, irradiation of the high-field 18-Me (δ_H 0.95) produced significant enhancement only in the signals of 7α-H (24%), 7β-H (16%), 22-H (15%), 12β-H (18%), and 16β-H (25%). In contrast to (**1**), irradiation of 9-H (δ_H 2.85) led to an n.O.e. of 19-Me (8%) and 1β-H (22%), but not 2-H. This evidence suggests for (**5**) a 'non-steroid' all-chair *cis*-fused A–B conformation in which 9-H, 1β-H, and 19-Me are *syn* and in close proximity, thus relieving the dramatic non-bonding interaction between angular methyl groups. As a consequence of this conformational change, the 3-H proton moves in proximity to the deshielding cone of the C-6 carbonyl group, experiencing a downfield shift (0.14 p.p.m.).

The structure of the more polar photoproduct (**6**) was proved by its ^1H n.m.r. spectra (600 MHz). From the values of the coupling constants, as corroborated by extensive ^1H–{^1H} homonuclear decoupling experiments and n.O.e. studies, the (^1H,^1H) connectivity pattern of the A–B rings of (**6**) could be assigned (see Figure 1). A feature of the ^1H n.m.r. data is the signal at δ 4.502 assigned to 2-H which showed ^4J 1.8 Hz with 4α-H (W path). Further support for the cyclobutane ring came from the ^{13}C n.m.r. spectrum with singlets attributable to C-3 [δ_C 79.3 *vs.* 67.5 (d) in (**5**)] and C-6 [δ_C 78.8 *vs.* 210.3 (s)].

On the basis of minimal mechanistic information, we propose the following tentative explanation. The photobehaviour of (**1**) upon irradiation with Pyrex-filtered light is strongly retarded in an oxygen atmosphere, implying a triplet intermediate of the enone chromosphere, presumably of n–π* type (Scheme 1). The initially produced diradical would then undergo homolytic cleavage of the C(14)–O bond to give photoreduced products (**2**) and (**4**) (path a) or an internal hydrogen transfer (path b) to form a 14α-oxyl radical. This would collapse *via* regiocontrolled β-fission[6] of the 13–14 bond and fast transannular recombination to give (**5**). Although the stereochemistry of the reaction (**1**) → (**5**) is correct for a concerted process, the observed stereospecificity could be a result more of steric than electronic factors.

Finally, the cyclobutanol derivative (**6**) would arise from the secondary photolysis of (**5**) through a typical Norrish type II process in which 3-H is held by the preferred conformation (*vide supra*) in an ideal position for the γ-hydrogen abstraction by the excited C-6 carbonyl oxygen atom.[7] No fragmentation was encountered presumably because of the unsuitable orientation of the 4–5 bond in the 1,4-diradical.



Scheme 1

None of the photoproducts showed biological activity comparable to that of (**1**) in *Calliphora* bioassay, thus giving a plausible rationale for the photoinactivation of (**1**).

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