Photo-bromination of 4,4-Dimethyl-Δ^5-steroids†

By H. de Nijs, W. N. Speckamp,* and H. O. Huisman

(*Laboratory of Organic Chemistry, University of Amsterdam, Nieuwe Achtergracht 129, Amsterdam, the Netherlands*)

Summary Irradiation of a mixture of 1 equiv. of a 4,4-dimethyl-Δ^5-steroid with 2 equiv. of *N*-bromosuccinimide gives a 4,4-dimethyl-7,7-dibromo-Δ^5-steroid, which can be converted into a 4,4-dimethyl-7-bromo-$\Delta^{5,7}$-steroid or into a 4,4-dimethyl-7-oxo-Δ^5-steroid.

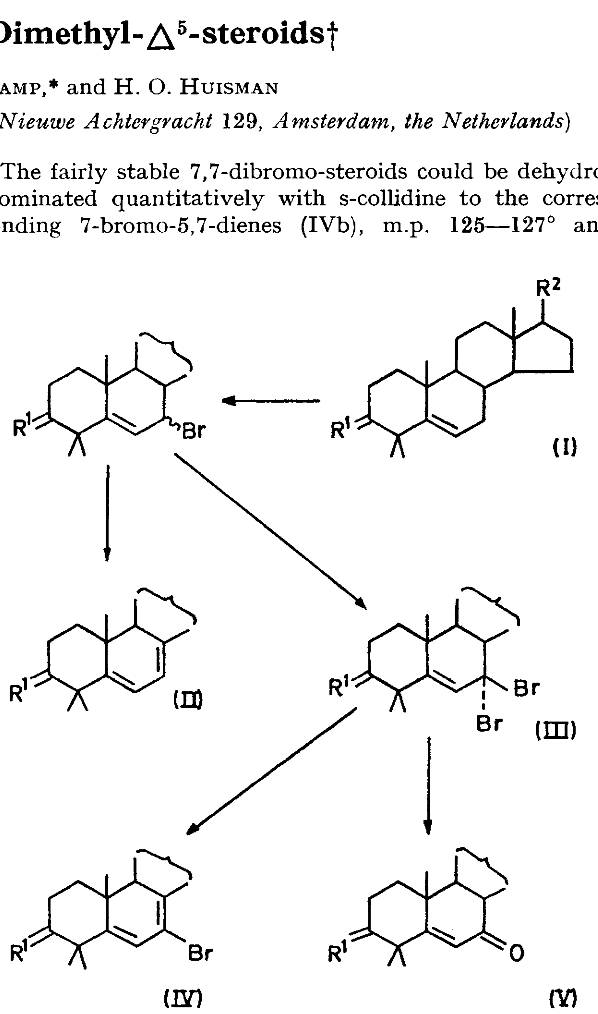
Allylic and benzylic methylene groups are reported to be oxidized to the corresponding unsaturated ketones by irradiation in the presence of excess of *N*-bromosuccinimide in moist solvents[1] or under influence of either mercury(II) bromide or *N*-bromosuccinimide in cyclohexane in the presence of air.[2] A versatile method for introduction of Δ^7-unsaturation into a Δ^5-steroid consists of irradiation in the presence of *N*-bromosuccinimide followed by elimination of HBr from the allylic mono-bromide in the presence of base,[3] but, unexpectedly, a 7-oxo-Δ^5-steroid has not to our knowledge been isolated in this reaction.

The addition of dimethyl diazodicarboxylate to a series of 4,4-dimethyl-$\Delta^{5,7}$-steroids has been studied, and some observations connected with the preparation of this series are related to the recently described oxidation procedures.[1,2]

Irradiation of a mixture of *N*-bromosuccinimide (1 equiv.) and (Ia) (1 equiv.) and dehydrobromination with s-collidine gave (IIa) (65%). However, the mother liquor contained a second product, the bromo-diene (IVa), m.p. 146—148° albeit in low yield (<5%). No trace of the 7-oxo-Δ^5-compound was detected.

The formation of the bromodiene was assumed to take place *via* a dibromo-compound, which lost HBr to give (IVa). The experiment was repeated in the presence of *N*-bromosuccinimide (2 mol. equiv.); solvent was removed *in vacuo* after u.v. irradiation for 2 min, to give the 7,7-dibromo-compound (IIIa)‡ (45%), m.p. 124–126° (from hexane). This photo-bromination was extended to (Ib) and (Ic), which reacted similarly to afford the 7,7-dibromo-compounds (IIIb), m.p. 130—132°, and (IIIc), m.p. 123—125° (66 and 67%, respectively after recrystallization).

The fairly stable 7,7-dibromo-steroids could be dehydrobrominated quantitatively with s-collidine to the corresponding 7-bromo-5,7-dienes (IVb), m.p. 125—127° and



a; $R^1 = O$, $R^2 = C_8H_{17}$
b; $R^1 = \beta\text{-OAc,H}$, $R^2 = C_8H_{17}$
c; $R^1 = O$, $R^2 = \beta\text{-OAc,H}$

---

† H. de Nijs, Thesis, University of Amsterdam.

‡ The alternative 5ξ,7-dibromo-Δ^6-structure was rejected on n.m.r. spectroscopic grounds, neither the 4,4-Me_2 singlet nor the C(19)-Me singlet being significantly affected by introduction of the two bromine atoms.

(IVc), m.p. 116—118°. As expected, the u.v. spectra did not differ much from those of the corresponding dienes: (IVa), λ_{max} 278 (ϵ 8050), 283 (8200), and 297 (4700) nm; (IVb), 278 (7500), 283 (7050), and 297 (6150) nm; (IVc), 276 (8200), 283 (8250), and 295 (4910) nm.

However, when a benzene solution of (IIIa) was shaken with aqueous Na_2CO_3, the ketone (Va), m.p. 163—165°, λ_{max} 237 (ϵ 11,800) was obtained (80%). Similar treatment of (IIIb) and (IIIc) gave the corresponding ketones (Vb), m.p. 152—154·5°, λ_{max} 238 (ϵ 12,300) and (Vc) (after acylation with Ac_2O–pyridine), m.p. 156—159°, λ_{max} 257 (ϵ 11,550), in yields of > 80%. Our experimental data are in accord with the earlier statement[2] on the limited possibility of application of the *N*-bromosuccinimide oxidation to sterically less accessible Δ^5-steroids.§

Finally the method allows the easy preparation of the hitherto unknown 7-bromo-$\Delta^{5,7}$-steroidal dienes as well as the corresponding 7-oxo-Δ^5-steroids.

(*Received*, 29*th December* 1971; *Com.* 2196.)

---

§ Application of the method to Δ^5-steroids gave a series of mostly non-identifiable products from which small amounts (<5%) of Δ^5-7,7-dibromo-steroids could be isolated.

[1] B. W. Finucane and J. B. Thompson, *Chem. Comm.*, 1969, 1220.

[2] N. Friedman, M. Gorodetsky, and Y. Mazur, *Chem. Comm.*, 1971, 874.

[3] (a) R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1957, 1131; (b) M. Fétizon and M. Golfier, *Bull. Soc. chim. France*, 1966, 850; (c) P. Johnston, R. C. Sheppard, C. E. Stehr, and S. Turner, *J. Chem. Soc.*, 1966, 1847.

[4] A. v.d. Gen, J. Lakeman, M. A. M. P. Gras, and H. O. Huisman, *Tetrahedron*, 1964, **20**, 2521; J. Lakeman, W. N. Speckamp, and H. O. Huisman, *Tetrahedron Letters*, 1967 ,**38**, 3699; *Tetrahedron*, 1968, **24**, 5151.