Tetrahedron Letters No. 26, pp. 2373-2376, 1971. Pergamon Press. Printed in Great Britain.

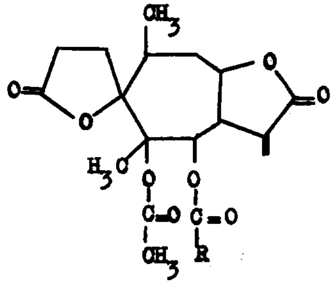
REVISED STRUCTURE OF ENHYDRIN*

B.S. Joshi, V.N. Kamat and H. Fuhrer†

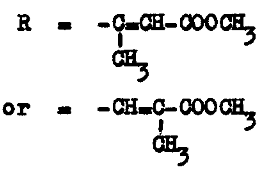
CIBA Research Centre, Goregaon, Bombay 63, India.

(Received in UK 10 May 1971; accepted in UK for publication 26 May 1971)

Recently Seshadri *et al*. reported the isolation[1] of a new sesquiterpene enhydrin from the leaves of *Enhydra fluctuans* (Fam. Compositae) and formulated it as (I)[2]. We wish to report here degradative and spectroscopic evidence which leads to the gross structure (II) for enhydrin.

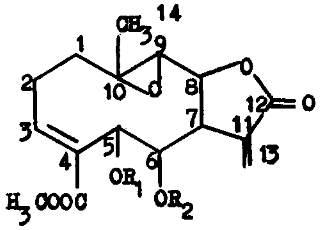


I



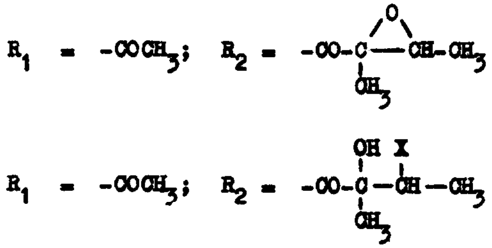
$R = -\underset{\displaystyle CH_3}{C}=CH-COOCH_3$

or $= -CH=\underset{\displaystyle CH_3}{C}-COOCH_3$



II : $R_1 = -COCH_3;\ R_2 = -CO-\underset{\displaystyle CH_3}{C}\overset{O}{\diagdown\!\!\diagup}CH-CH_3$

IV : $R_1 = -COCH_3;\ R_2 = -CO-\underset{\displaystyle CH_3}{\overset{OH}{C}}-\overset{X}{CH}-CH_3$



Enhydrin $C_{23}H_{28}O_{10}$, m.p. 185°, $[\alpha]_D$ - 55°, M^+ at m/e 464, exhibited UV and IR spectra typical for the presence of α,β-unsaturated-γ-lactones. The most useful evidence came from the NMR spectrum (Fig.1). Double resonance experiments showed that H_7 proton was coupled with H_6, H_8 and the H_{13} methylene protons.

---

[*] Contribution No.240 from CIBA Research Centre

† CIBA-GEIGY Limited, Basle, Switzerland

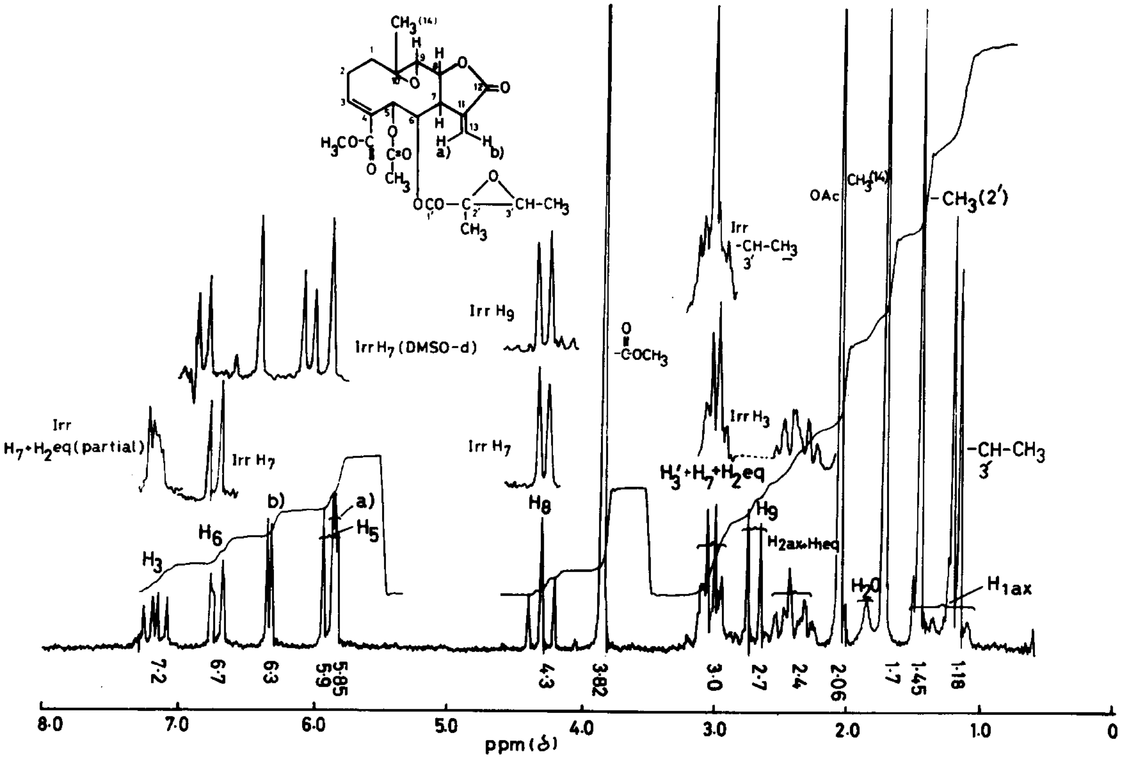
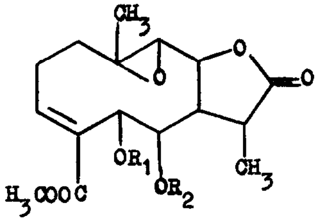
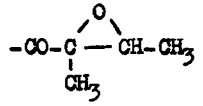


FIG.1. 100 Mc NMR Spectrum of enhydrin (II) in $CDCl_3$

Irradiation of the H_9 proton collapsed the H_8 proton triplet to a doublet. Similarly, irradiation of the H_3 vinyl proton quartet at 7.2 δ affected the signals in the methylene region. Hydrogenation of enhydrin with PtO_2 in acetic acid gave dihydroenhydrin (III), m.p. 198°, $[\alpha]_D$ - 38°, M^+ at m/e 466. The presence of a methylene group conjugated with a γ-lactone was also shown by the formation of a pyrazoline, m.p. 245°.



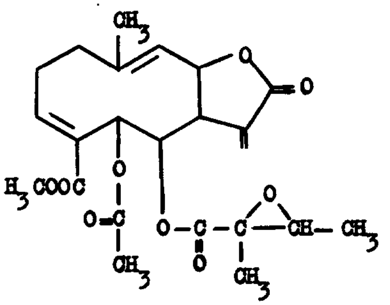
III : R_1 = $-COCH_3$; R_2 =



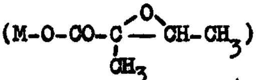
$-CO-\underset{CH_3}{C}(O)-CH-CH_3$

V : R_1 = R_2 = H

VI : R_1 = R_2 = $-COCH_3$



VII

On treatment with conc. HCl in methanol, enhydrin gave the chlorohydrin (IV; X = Cl), m.p. 219°, $[\alpha]_D$ - 48°, M^+ at $^m/e$ 501 by opening of the epoxide ring in the side chain. Similarly the bromohydrin (IV; X = Br), m.p. 214°, was obtained by reaction with 40% HBr in methanol. These formulations were supported by their NMR spectra. The mass spectrum of (II) shows the peaks at $^m/e$ 433 ($M-OCH_3$), 405 ($M-OCOCH_3$), 349  $(M-O-CO-\underset{CH_3}{C}\overset{O}{—}CH-CH_3)$ and these are increased by two units in the mass spectrum of dihydroenhydrin (III). The compound (III) on hydrolysis with sodium methoxide in methanol gave the diol (V), m.p. 210°, which was acetylated to the diacetate (VI), m.p. 255-257°. The ambiguity of assigning the acetyl and the α-methyl- α, β-epoxybutyryl group at positions 5 and 6 had remained.

Attempts were made to partially hydrolyse (II) or (III) without success. While this work was in progress, Herz et al reported[3] the structure elucidation of uvedalin (VII) isolated from Polymnia uvedalia (L.) L. and preparation of dihydrouvedalin by sodium borohydride reduction. Both these compounds were converted to the corresponding epoxides m.p. 218-220° and m.p. 213-215°, $[\alpha]_D$ - 73.6° formulated as (II) and (III) respectively. From the NMR data we suspected enhydrin to be identical with uvedalin epoxide although their m.ps were different. A comparison of the TLC, IR (KBr) and NMR spectra of enhydrin with uvedalin epoxide kindly carried out by Professor Herz showed that they are identical. However, dihydroenhydrin (III) differed from dihydro uvedalin epoxide, prepared by sodium borohydride reduction of uvedalin and subsequent epoxidation.

Acknowledgements : The authors thank Professor T.R. Govindachari for his interest in the work, Professor Werner Herz for comparison of the samples and Dr. S. Selvavinayakam for analytical and spectral data.

REFERENCES

1. N.R. Krishnaswamy, T.R. Seshadri and B.R. Sharma, Curr. Sci., 37, 94 (1968).

2. N.R. Krishnaswamy, T.R. Seshadri and T.N.C. Vedantam, Curr. Sci., 38, 284 (1969).

3. W. Herz and S.V. Bhat, J. Org. Chem., 35, 2605 (1970).