DIEPOXYMONTIN, A NOVEL ACETOGENIN FROM *ANNONA MONTANA*[1]

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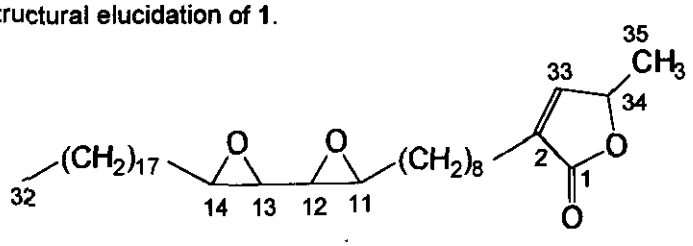
Abstract -Tandem mass spectrometry has been used to elucidate the structure of diepoxide α, β – unsaturated -γ -lactonic acetogenin, diepoxymontin, which is the first example of acetogenin having an adjacent epoxides in place of tetrahydrofuran moiety.

In the previous papers, [2,3] we have reported the presence of some cytotoxic acetogenins from the leaves of Formosan *Annona reticulata*. As part of our continuing investigation on the acetogenins of Formosan Annonaceous plants, we have isolated several acetogenins from the chloroform extract of fruits of *A. montana*.[4] One of these, diepoxymontin(**1**), presents a novel structure in which the tetrahydrofuran systems are replaced by adjacent epoxy groups. We report herein the structural elucidation of **1**.



Diepoxymontin (**1**)

Compound (1) was obtained as white amorphous powder. The strong absorption at 1745 cm^{-1} in the ir spectrum and a positive Kedde's reaction suggest the presence of an α, β -unsaturated γ - lactone , which is confirmed by comparison of the ^{1}H and ^{13}C nmr data with those of previously isolated acetogenins [5] and 2D nmr experiment. Along with the signals corresponding to the γ – lactone moiety, the ^{1}H and ^{13}C nmr spectra show characteristic chemical shifts for a long aliphatic chain (δ 1.26) with a terminal methyl group (δ 0.88). No carbinol methine protons and carbons are present indicating the absence of hydroxyl groups. Similarly, no typical signals for THF rings are present. ^{1}H Nmr of **1** shows four epoxymethine protons as a multiplet around δ 3.0 indicating the presence of two epoxide groups. This has been confirmed by a ^{1}H-^{13}C HETCOR nmr spectrum showing two intense signals at δ 56.9 and 57.8. These signals are attributed to two epoxide groups with identical stereochemistry, which can be established as *cis* by considerations of general chemical shift and by comparison with the nmr spectral data of diepomuricanin containing two epoxide groups. [6,7] A ^{1}H-^{1}H COSY spectrum reveals that protons of both epoxide groups only correlate to four protons of C-10 and C-15 can prove the both epoxide groups are adjacent.

In the high resolution electron impact mass spectrum m/z 546.4644 (Calcd 546.4648) ion is got to confirm the formula $C_{35}H_{62}O_4$ of diepoxymontin. Various ionization methods of mass experiments such as EI, CI, FAB and linked scan MS/MS were carried out to localize the adjacent bis-epoxyl moiety on the aliphatic chain. The molecular ion M^+ or protonated molecular ion $(M+H)^+$ of $C_{35}H_{62}O_4$ in EI, CI and FAB mass spectra were observed at m/z 546 (R.A. 5%), 547(R.A. 100%) and 547(R.A. 100%), respectively. From the EI mass spectrum, two major fragment ions at m/z 295 (R.A. 100%) and m/z 251(R.A. 20 %) can be used to conclude that the weakest position of diepoxymontin is at between two epoxides. The fragment pathways of diepoxymontin are concluded from EI mass spectrum and daughter spectra experiments as in Figure 1. This shows the following daughter ions resulting from the fragmentation of the diepoxymontin M^+ parent ion at m/z 546. Two major fragment ions at m/z 295 and 251 indicate fragmentation on the bond between C-12 and C-13. This result also can be confirmed from which then lose a water to form the stable ions at m/z 277 and 233. Through α - cleavage followed by loss of carbon monoxide and hydrogen transfer is another important decomposition pathway for ions at m/z 295 and 251. The proposed fragmentation scheme for diepoxymontin is figured out in Figure 1.

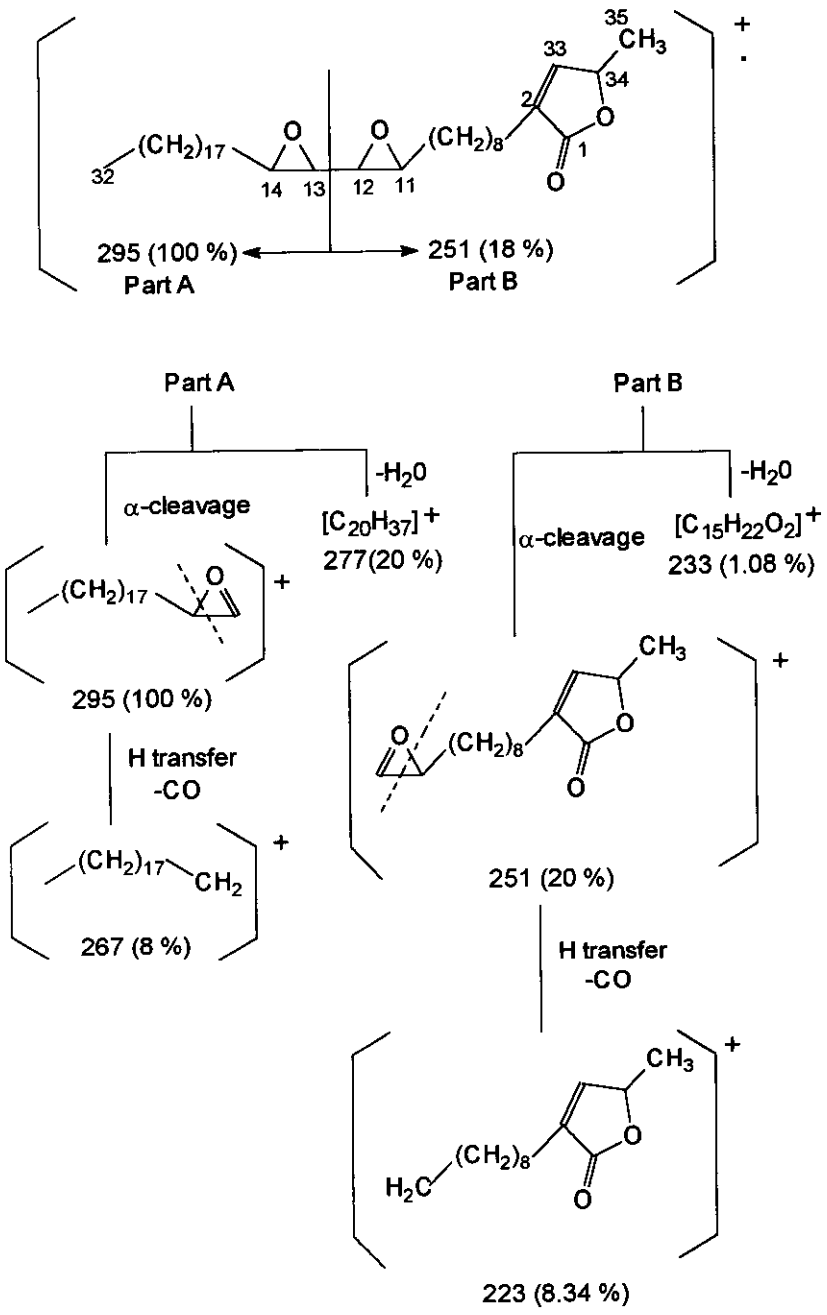


Figure 1. The proposed fragmentation scheme for diepoxymontin.

From the above data, we can conclude that the structure of diepoxymontin is as illustrated for **1** with the absolute and certain relative stereochemistry remaining undefined. Diepoxymontin(**1**) is the first example of an acetogenin containing the adjacent epoxy groups in place of tetrahydrofuran moiety and unfortunately it doesn't like most of acetogenins exhibiting cytotoxic property.

ACKNOWLEDGEMENT

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REFERENCES AND NOTES

1. Part 3 in the series " Studies on the Acetogenins of Formosan Annonaceous Plants." For part 2, see ref. 3.
2. Y. C. Wu, F. R. Chang, C. Y. Duh, and S. K. Wang, *Heterocycles*, 1992, **34**, 667.
3. F. R. Chang, Y. C. Wu, C. Y. Duh, and S. K. Wang, *J. Nat. Prod.*, 1993, **56**, 1688.
4. *A. montana* was collected from Chie Shan, Kaohsiung Hsien, Taiwan, in June, 1992. A voucher specimen is deposited in the school of Pharmacy, Kaohsiung Medical College, Kaohsiung, Taiwan, R.O.C..
5. X. P. Fang, M. J. Rieser, Z. M. Gu, G. X. Zhao, and J. L. McLaughlin, *Phytochemistry Analysis*, 1993, **4**, 27.
6. A. Hisham, U. Sreekala, L Pieters, T. D. Bruyne, H. V. D. Heuvel, and M. Claeys, *Tetrahedron*, 1993, **49**, 6913.
7. F. Roblot, T. Laugel, M. Lebceuf, A. Cave, and O. Laprevote, *Phytochemistry*, 1993, **34**, 281.
8. The mass spectra were recorded on a Jeol JMS-SX/SX 102A and nmr spectra were obtained on a Varian Gemini-200 spectrometer with TMS as internal standard. Diepoxymontin : ^{1}H nmr ($CDCl_3$, 200 MHz) δ : 0.88(3H, t, J 6.4, 32-Me), 1.26(m, aliphatic CH_2), 1.39(3H, d, J 6.8, 35-Me), 1.69(4H, m, 10- and 15-CH_2), 2.26(2H, td, J 7.4;1.6, 3-CH_2), 2.95(4H, m, 11-14 CH), 4.99(1H, qtd, J 6.8;1.6;1.4, 34-CH), 6.98(1H, td, J 1.6; 1.4, 33-CH); ^{13}C nmr($CDCl_3$, 50.3 MHz) δ : 14.5(C-32), 19.4(C-35), 25.4 (C-10 and C-15), 25.6(C-3), 26- 32(aliphatic CH_2), 56.9 and 57.8(C 11-14), 77.8 (C- 34), 134.8(C-2), 149.3(C-33), 174.3(C-1).

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