Pergamon

0031-9422(93)E0131-W

Phytochemistry, Vol. 36, No. 1, pp. 159–161, 1994
Copyright © 1994 Elsevier Science Ltd
Printed in Great Britain All rights reserved
0031-9422/94 $6.00 + 0.00

STRUCTURE REVISION OF CUCURBITACIN Q_1

HOSNY ABD EL-FATTAH

Pharmacognosy Department, Faculty of Pharmacy, Mansoura University, Mansoura, Egypt

(*Received in revised form* 13 *August* 1993)

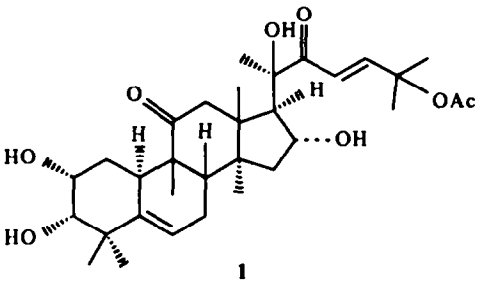
Key Word Index—*Cucumis*; Cucurbitaceae; cucurbitacin Q_1; cucurbitacin F 25-*O*-acetate.

Abstract—Structure revision of curcurbitacin Q_1 is discussed on the basis of spectroscopic data. The stereochemistry of ring A is evaluated and the compound is corrected to be cucurbitacin F 25-*O*-acetate.

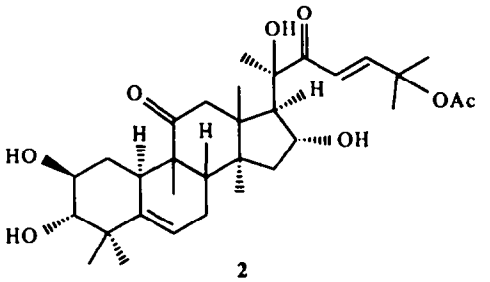
INTRODUCTION

Cucurbitacins are a special group of triterpenoids having a cucurbitane skeleton [1]. Most of the cucurbitacins are tetracyclic, but some representatives have an extra ring due to formal cyclization between C-16 and C-24 (cucurbitacins S and T) [2, 3]. Certain cucurbitacins have been discovered in the form of glycosides and some of them lack C-11 carbonyl function [4]. Biologically, they exhibit a wide range of activities including cytotoxicity and antitumour effects [5–11]. Chemically, cucurbitacins are classified according to the functionalities in ring A and C, side chain modifications, as well as stereochemical considerations.

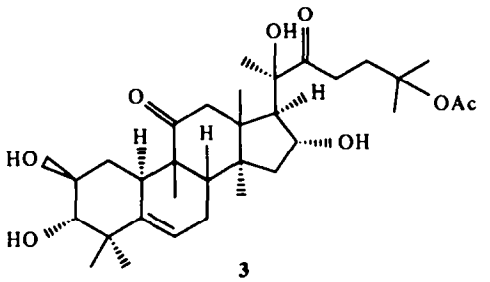
Cucurbitacin Q_1 was formerly isolated by Atta-Ur-Rahman *et al.* [12] and later by Abd El-Fattah *et al.* [13] from some *Cucumis* species. Chemotaxonomically, the genus *Cucumis* is characterized by the presence of cucurbitacins A–F, dihydro-F–I and K in addition to Q_1 [1, 14]. Atta-Ur-Rahman *et al.* [12] elucidated the structure of cucurbitacin Q_1 to have the trans-configuration at the C-23/C-24 double bond on the basis of direct comparison with the reported data of cucurbitacin Q (**1**) which was originally isolated by Kupchan *et al.* [15] from *Brandegea bigeloii*. The stereochemistry of ring A is still confused and the ^{13}C NMR data are not available. The present study describes the structure revision of cucurbitacin Q_1 to cucurbitacin F 25-*O*-acetate (**2**).



1



2



3

RESULTS AND DISCUSSION

The high resolution ^1H NMR (Table 1) revealed three oxymethine protons at δ5.05 (*dd*, $J = 7.49, 7.49$ Hz), 4.03 (*m*) and 3.42 (*d*, $J = 8.99$ Hz). ^1H–^1H COSY and a series of spin–spin decoupling experiments indicated that the signals at δ4.03 and 3.42 were mutually coupled and they were assigned to H-2 and H-3, respectively, showing a $CH(OH)_{eq}$–$CH(OH)_{eq}$ system. The magnitude of the coupling constants observed for H-2 and H-3 ($J_{2,3} = 8.99$ Hz) required that the hydroxyl groups be placed as a 2β,3α-diol confirming a diaxial coupling [16–18]. The remaining oxymethine at δ5.05 was assigned to H-16 [16]. The ^1H NMR spectrum also showed signals attributed to eight methyls attached to quaternary carbons (δ1.20–1.69), a pair of doublets at δ2.84 and 3.31 ($J = 14.43$ Hz) indicative for H-12, an upfield singlet at δ1.89 assigned to the 25-*O*-acetate group and a pair of doublets in the olefinic region at δ7.40 and 7.33 which comprised an AB system ($J = 15.78$ Hz) characteristic of a *trans*-double bond (23–24 α,β-unsaturated ketone) [12,

Table 1. ^{1}H NMR data of cucurbitacin Q_1 (δ values in pyridine-d_5 and TMS as internal standard)

Proton no.	δ(ppm)
H-1α(eq)	2.41 (*ddd*, $J = 12.34_{(1\alpha,1\beta)}$, $3.08_{(1\alpha,2\alpha)}$, $3.8_{(1\alpha,10)}$ Hz)
H-1β(ax)	s.o.*
H-2α(ax)	4.07 (*m*)
H-3β(ax)	3.42 (*d*, $J = 8.99_{(2\alpha,3\beta)}$ Hz)
H-6	5.73 (*d*, $J = 5.49_{(6,7\beta)}$ Hz)
H-7α	2.35(*m*)
H-7β	s.o.*
H-8	1.93 (*d*, $J = 7.81_{(7\alpha,8)}$ Hz)
H-10	2.72 (*br d*, $J = 12.73_{(1\beta,10)}$ Hz)
H-12α	3.31 (*d*, $J = 14.43$ Hz)
H-12β	2.84 (*d*, $J = 14.43$ Hz)
H-15α	s.o.*
H-15β	1.73 (*d*, $J = 12.83$ Hz)
H-16	5.05 (*dd*, $J = 7.49_{(15\alpha,16)}$, $7.49_{(16,17)}$ Hz)
H-17	3.02 (*d*, $J = 7.49_{(16,17)}$ Hz)
H-23	7.40 (*d*, $J = 15.78_{(23,24)}$ Hz)
H-24	7.33 (*d*, $J = 15.78_{(23,24)}$ Hz)
2-OHβ(eq)	6.08 (*d*, $J = 4.74$ Hz)
3-OHα(eq)	6.32 (*d*, $J = 4.74$ Hz)
16-OH	6.23 (*s*)
Methyls	
	1.20 (*s*)
	1.24 (*s*)
	1.29 (*s*)
	1.47 (*s*)
	1.52 (*s*)
	1.56 (*s*)
	1.57 (*s*)
	1.69 (*s*)
25-OAc	1.89 (*s*)

*s.o.; Signals totally obscured by other signals.

Table 2. ^{13}C NMR and DEPT data of cucurbitacin Q_1 (δ values in pyridine-d_5 and TMS as internal standard)

Carbon no.	δ(ppm)	DEPT
1	34.6	CH_2
2	70.8	CH
3	79.8	CH
4	42.8	C
5	142.5	C
6	118.8	CH
7	24.2	CH_2
8	34.5	CH
9	48.6	C
10	43.3	CH
11	213.2	C=O
12	49.1	CH_2
13	48.9	C
14	51.1	C
15	46.4	CH_2
16	71.0	CH
17	59.6	CH
18	19.2*	Me
19	20.5*	Me
20	79.8	C
21	25.4*	Me
22	204.3	C=O
23	122.5	CH
24	150.1	CH
25	79.7	C
26	24.2*	Me
27	26.2*	Me
28	26.6*	Me
29	25.4*	Me
30	20.4*	Me
OCOMe	169.8	C=O
OCOMe	22.4	Me

*Assignments may be interchanged in vertical column.

13, 16]. The shift values and coupling pattern of other protons fit with that reported in the literature for cucurbitacin F [16, 19]. All assignments and spin–spin coupling interactions were confirmed through 2D ^{1}H–^{1}H COSY measurements and selective decoupling experiments. The ^{13}C NMR data (Table 2) supported assignments of an unsaturated, tetracyclic, triterpene nucleus.

The polarization transfer experiments (DEPT) confirmed the cucurbitacin nucleus and indicated the presence of nine (CH), four (CH_2), eight (Me), seven quaternary carbons, two ketonics and one acetate function (Table 2). The signals at δ70.8, 79.8 and 71.0 were assigned to three secondary oxygenated functionalities attributable to C-2, C-3 and C-16, respectively. A final confirmation of the structure was obtained by hydrogenation of cucurbitacin Q_1 over 10% Pd/C which yielded, after TLC purification, 23,24-dihydrocucurbitacin F 25-*O*-acetate 3 (identified by mp, IR, ^{1}H NMR, ^{13}C NMR) [16, 19]. In accordance with the previous evidence, cucurbitacin Q_1 must now be corrected to cucurbitacin F 25-*O*-acetate.

Cucurbitacin F 25-*O*-acetate was previously isolated in the form of its 2-*O*-β-D-glucoside from *Cigarrilla mexicana* [20], but no physical or spectroscopic data were available.

EXPERIMENTAL

^{1}H NMR and ^{1}H–^{1}H COSY data were recorded at 400 MHz in pyridine-d_5 using TMS as int. standard. ^{13}C NMR and DEPT spectra were recorded at 100 MHz on a Bruker NMR spectrometer in pyridine-d_5 using TMS as int. standard. Cucurbitacin Q_1 was isolated from *Cucumis callosus* (Rottl) Cong [13] and compared with standard authentic sample from *Cucumis prophetarum* L.

Catalytic hydrogenation of cucurbitacin Q_1 [20]. To a soln of 15 mg of cucurbitacin Q_1 in 5 ml EtOH was added 5 mg of 10% Pd/C. The mixt. was stirred under H_2 for 45 min. The resulting product was filtered and purified by prep. TLC on silica gel GF_{254} using $CHCl_3$–MeOH (95:5) solvent system which afforded 10 mg of 23,24-dihydrocucurbitacin F 25-*O*-acetate.

REFERENCES

1. Lavie, D. and Glotter, E. (1971) *Fortschr. Chem. Org. Naturstoffe*, **29**, 307.

2. Hylands, P. J. and Mansour, E. S. (1982) *Phytochemistry* **21**, 2703.
3. Gamlath, C. B., Leslie Gunatilaka, A. A., Alvi, K. A., Ur-Rahman, A. and Balasubramaniam, S. (1988) *Phytochemistry* **27**, 3225.
4. Stuppner, H., Muller, E. P. and Wagner, H. (1991) *Phytochemistry* **30**, 305.
5. Cassady, J. M. and Suffness, M. (1980) in *Anticancer Agents Based on Natural Products Models* (Cassady, J. M. and Douros, J. D., eds), pp. 201–269. Academic Press, New York.
6. Naik, V. R., Agshikar, N. N. and Abraham, G. S. S. (1980) *Pharmacology* **20**, 52, 56.
7. Yesilada, E., Tamaka, S., Sezik, E. and Tabata, M. (1988) *J. Nat. Prod.* **51**, 504.
8. Shohat, B., Beecher, A. M., Gitter, S. and Lavie, D. (1972) *Experientia* **28**, 1203.
9. Hu, R., Peng, Y., Chen, B. and Hou, X. (1982) *Zhongcaoyao* **13**, 445.
10. Metcalf, R. L., Metcalf, R. A. and Rhoades, A. M. (1980) *Proc. Natl Acad. Sci. U.S.A.* **77**, 3769.
11. Nielsen, J. K., Larsen, L. M. and Sorensen, H. (1977) *Phytochemistry* **16**, 1519.
12. Atta-Ur-Rahman, Ahmed, V. U., Khan, M. A. and Zehra, F. (1973) *Phytochemistry* **12**, 2741.
13. Abd El-Fattah, H., Zaghloul, A. M., Halim, A. F. and Waight, E. S. (1989) *Acta Pharm. Jugosl.* **39**, 137.
14. Rizk, A. M. (1986) in *The Phytochemistry of The Flora of Qatar*, p. 115. Scientific and Applied Research Center, University of Qatar, Qatar.
15. Kupchan, S. M., Smith, R. M., Aynehchi, Y. and Maruyama, M. (1970) *J. Org. Chem.* **35**, 2891.
16. Che, C. T., Fang, X., Phoebe, C. H., Kinghorn, A. D., Farnsworth, N. R., Yellin, B. and Hecht, S. M. (1985) *J. Nat. Prod.* **48**, 429.
17. Provan, G. J. and Waterman, P. G. (1988) *Phytochemistry* **27**, 3841.
18. Hattori, M., Kuo, K., Shu, Y., Tezuka, Y., Kikuchi, T. and Namba, T. (1988) *Phytochemistry* **27**, 3975.
19. Fang, X., Phoebe, C. H., Jr, Pezzuto, J. M., Fong, H. H. S., Farnsworth, N. R., Yellin, B. and Hecht, S. M. (1984) *J. Nat. Prod.* **47**, 988.
20. Mata, R., Castaneda, P., Camacho, M. and Delgado, G. (1988) *J. Nat. Prod.* **51**, 839.