REFERENCES

1. Asakawa, Y. (1982) *Progress in the Chemistry of Organic Natural Products* (Herz, W., Grisebach, H. and Kirby, G. W., eds) Vol. 42, p. 1. Springer, New York.
2. Asakawa, Y., Tokunaga, N., Toyota, M, Takemoto, T. and Suire, C. (1979) *J. Hattori Bot. Lab.* **45**, 395.
3. Suire, C., Asakawa, Y., Toyota, M. and Takemoto, T. (1982) *Phytochemistry* **21**, 349.
4. Asakawa, Y. (1987) *Farumashia* **23**, 455.
5. Barlow, L. and Pattenden, G. (1976) *J. Chem. Soc. Perkin I* 1029.
6. Nishimura, K., Shinoda, N. and Hirose, Y. (1969) *Tetrahedron Letters*, 3097.
7. Nishida, K., Horibe, I. and Tori, K. (1973) *Tetrahedron* **29**, 271.

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# MANDASSIDIONE AND OTHER SESQUITERPENIC KETONES FROM *CYPERUS ARTICULATUS*

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**Key Word Index**—*Cyperus articulatus*; Cyperaceae; sesquiterpenes; mandassidione; mustakone; isopatchoulenone.

**Abstract**—A new monocyclic sesquiterpenic diketone, mandassidione, was isolated from the rhizomes of *Cyperus articulatus*, along with mustakone and isopatchoul-4(5) en-3-one. The structures were established from spectroscopic and chemical evidence.

## INTRODUCTION

*Cyperus articulatus* known in Cameroon as 'mandassi' is a tropical sedge widely used in traditional medicine. It is also used as perfume by traditional healers. Earlier studies on the essential oils from *Cyperus articulatus* led to the isolation of a bicyclic ketone named articulone, the structure of which was later revised and renamed cypernone, then finally isopatchoul-4 (5) en-3-one, **1** [1–5]. Recently we described the isolation and structural elucidation of corymbolone and α-corymbolol from the *n*-hexane extract of *C. articulatus* [6]. We now report on the structural determination of a new compound, mandassidione **2**, isolated from the same extract together with known isopatchoulenone **1** and mustakone **3**.

## RESULTS AND DISCUSSIONS

The *n*-hexane extract of *C. articulatus* rhizomes was fractionated by column chromatography on silica gel with *n*-hexane–ethyl acetate mixture (EtOAc) of increasing polarity. Part of fraction eluted with (hexane–EtOAc: 19:1) was further purified by CC and preparative TLC to give mustakone **3** as a colourless oil ($[\alpha]_D^{25}$ −42.5°). The remaining part was converted into 2,4-dinitrophenylhydrazone derivatives from which two 2,4-DNP hydrazone derivatives were further separated by fractional crystallization. The first was determined as 2,4-DNP hydrazone of mustakone (**4**) from a spectroscopic study, while the second was identified as 2,4-DNP hydrazone of isopatchoulenone (**5**) by comparison of its physical and spectral data with that already published [2–5].

As the structure of mustakone was previously assigned mainly by chemical means [7, 8] its spectral data will be briefly described here. We observed the molecular ion of mustakone in its El mass spectrum at *m/z* 218, in agreement with the molecular formula $C_{15}H_{22}O$. The IR spectrum was indicative of an α,β-unsaturated ketone ($\nu$ 1673 $cm^{-1}$). The $^{13}C$ NMR spectrum showed the signals of the 15 carbon atoms among which that of the carbonyl group (δ203.47) and those of the double bond (δ121.39 and 169.5 *s*). Assignments of the $^1H$ NMR spectrum were made by using 2D COSY and led to the structure **3** of mustakone. We observed the large value (6.7 Hz) of the $^4J_{HH}$ coupling constant between H-1 and H-5, characteristic of *cis* protons located on opposite vertices of a cyclobutane ring [9].

The fraction eluted with mixture (hexane–EtOAc: 9:1) yielded corymbolone, while that of eluent mixture (hexane–EtOAc 4:1) yielded a mixture of α-corymbolol and mandassidione which were further separated by CC.

Mandassidione **2**, ($[\alpha]_D^{25}$ −9.1°) was obtained as a colourless oil and analysed for $C_{15}H_{22}O_2$ from mass spectral data. This molecular formula implied five unsaturated sites in a monocyclic structure since the

$^{13}$C NMR spectrum revealed two carbonyl functions ($\delta$ 209.52 and 209.07), two $sp_2$ carbon atom signals typical of an isopropenyl group ($\delta$ 146.54 *s* and 112.52 *t*), and two fully substituted $sp_2$ carbon atoms ($\delta$ 171.06 *s* and 138.95 *s*) [10, 11]. The IR spectrum was in agreement with the presence of an isopropenyl chain ($\nu$ 3071, 1656 and 891 cm$^{-1}$) and was indicative of an aliphatic ketone ($\nu$ 1703 cm$^{-1}$) and an $\alpha,\beta$-unsaturated carbonyl ($\nu$ 1698 and 1643 cm$^{-1}$), that was located in a strained cyclopentenone ring, as suggested by these last values.

Proton systems from the $^1$H NMR spectrum were analysed by $^1$H–$^1$H COSY techniques, and the $^{13}$C NMR assignments were made by $^1$H–$^{13}$C COSY. The two geminal protons $\alpha$ to the conjugated carbonyl group appeared at $\delta$ 2.47 and were coupled with the methylene protons at $\delta$ 2.32. The results defined the ring as an $\alpha,\beta$-disubstituted cyclopentenone.

Further examination of $^1$H NMR spectrum of **2** indicated the presence of a vinyl methyl group ($\delta$ 2.01) which was thus a ring substituent, an acetyl group ($\delta$ 2.09), and an isopropenyl group ($\delta$ Me 1.68, $\delta$ $CH_2$ 4.57 and 4.68). Evidence that the methine at $\delta$ 2.27 was simultaneously attached to the isopropenyl chain and to two methylene groups at $\delta$ 2.23 and 1.58 was obtained by coupling information. The former ($\delta$ 1.58) was adjacent to a deshielded methylene ($\delta$ 2.35), linked to the acetyl carbonyl. The latter ($\delta$ 2.23) was directly bound to the ring double bond and terminated the $C_9$ chain.

The remaining problem was to place the methyl group ($\delta_H$ 2.01) and the $C_9$ chain respectively on the $\alpha$ and $\beta$ positions of the cyclic enone. Expected chemical shifts for an $\alpha$ methyl substituent (−5) are $\delta_H$ 1.7 and $\delta_C$ 12.0, while those for the $\beta$ isomer are $\delta_H$ 2.0 and $\delta_C$ 17.0 [12, 13]. In this later situation the deshielding of the $\delta_H$ is due to conjugation with the carbonyl group while the shielding of the $\delta_C$ arises from weaker gauche interaction.

The observed values (Table 1) are in agreement with the location of the methyl group in $\beta$ while the $C_9$ chain is thus linked $\alpha$ to the carbonyl group, leading to structure **2** for mandassidione, which is in good agreement with the mass spectral fragmentations (Fig. 1).

From a biosynthetic point of view, mandassidione may arise from an oxidative cleavage of the C-1, C-10 bond of a guaiatriene precursor as shown in Fig. 2.

Mustakone and mandassidione were observed to inhibit the growth of the fungus *Penicilium crustosum* when tested by using the disk method.

## EXPERIMENTAL

The air-dried rhizomes of *C. articulatus* harvested in Kribi (South Cameroon, December 1984), were powdered and extracted with *n*-hexane. The hexane was evaporated under red. pres. and the oily residue obtained (60 g) was chromatographed over silica gel column 1 with a mixture of *n*-hexane and increasing proportion of EtOAc (hexane–EtOAc) as eluent. Fractions eluted with hexane–EtOAc (19:1) yielded fraction $A_1$ (5 g) which was further purified over silica gel column in similar way to give fraction $A_2$ (800 mg). Part of fraction $A_2$ yielded **3** (40 mg) on purification by prep. TLC on silica gel. From the remaining portion of $A_2$, isopatchoulenone and mustakone were isolated as their 2,4-DNPH derivatives (13 and 17 mg) with hexane–EtOAc (9:1) yield corymbolone [6]. Further elution of column 1 with hexane–EtOAc (4:1) yielded a mixture, which on repeated chromatography over silica gel with $CH_2Cl_2$–EtOAc as eluent gave mandassidione (37 mg), from ($CH_2Cl_2$–EtOAc 9:1) fractions and $\alpha$-corymbolol (40 mg), from ($CH_2Cl_2$–EtOAc 17:3) fractions.

*Mandassidione* (**2**). Oil $[\alpha]_D^{25}$ −9.1° ($CHCl_3$; *c* 0.74). IR $\nu_{max}$ cm$^{-1}$: 3071, 2936, 1698, 1643, 1443, 1410, 1383, 1180, 1162, 1074, 891. MS (CI, $NH_4^+$) *m/z*: 235 $(M+H)^+$ MS (EI, 70 eV, 200°) *m/z* (%): 234 (4) $M^+$, 219 (15), 217 (20), 216 (15),

Table 1. $^1$H (500.13 MHz) and $^{13}$C (62.8 MHz) NMR spectral data of compounds **2** and **3** ($CDCl_3$, TMS as int. ref.)

| | Mandassidione **2** | | Mustakone **3** | |
|---|---|---|---|---|
| C | $\delta_C$ | $\delta_H$ multiplicity | $\delta_C$ | $\delta_H$ multiplicity, *J*(Hz) |
| 1 | *209.07 *s* | | 56.55 *d* | 2.646 (1H) *dd* (6.7; 1.3) |
| 2 | 31.70 *t* | 2.47 (2H) *sl* | 203.47 *s* | |
| 3 | 34.33 *t* | 2.32 (2H) *m* | 121.39 *d* | 5.707 (1H) *ddq* (0.9; 1.3; 1.4) |
| 4 | 171.06 *s* | | 169.51 *s* | |
| 5 | 138.96 *s* | | * 55.91 *d* | 1.958 (1H) *dd* (6.7; 0.9) |
| 6 | 27.79 *t* | 2.23 (2H) *m* | * 54.55 *d* | 2.636 (1H) *s* |
| 7 | 45.34 *d* | 2.26 (1H) *m* | 45.41 *d* | 1.7 (1H) *m* |
| 8a | 26.40 *t* | 1.58 (2H) *m* | 21.92 *t* | 1.499 (1H) *ddd* (2.8; 10.5; 10.5) |
| 8e | | | | 1.7 (1H) *m* |
| 9a | 41.63 *t* | 2.36 (2H) *m* | 36.70 *t* | 1.847 (1H) *m* |
| 9e | | | | 1.7 (1H) *m* |
| 10 | *209.52 *s* | | 57.03 *s* | |
| 11 | 146.54 *s* | | 31.73 *d* | 1.487 (1H) *dd* (6.5; 6.5) |
| 12 | 112.52 *t* | 4.68 (1H) *m* | ** 19.44 *q* | 0.827 (3H) *d* (6.5) |
| | | 4.57 (1H) *m* | | |
| 13 | 18.16 *q* | 1.68 (3H) *s* | ** 19.85 *q* | 0.814 (3H) *d* (6.5) |
| 14 | 17.64 *q* | 2.01 (3H) *s* | 20.21 *q* | 1.976 (3H) *d* (1.4) |
| 15 | 30.12 *q* | 2.09 (3H) *s* | 23.48 *q* | 0.942 (3H) *s* |

***May be reversed within the same column.

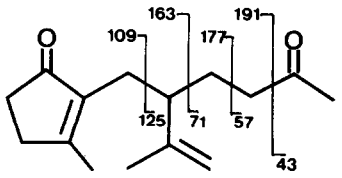



Fig. 1. Main mass spectrum fragmentations of mandassidione **2**.

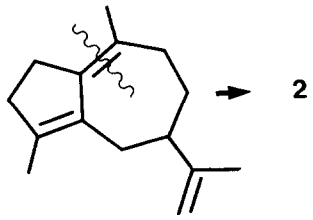
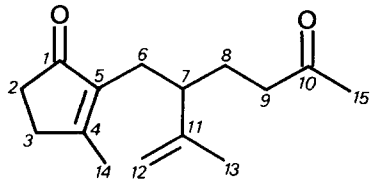
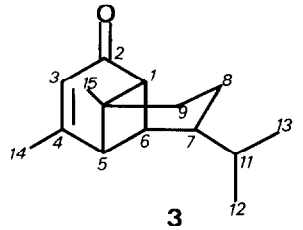



Fig. 2. Hypothetical guaiatriene precursor of mandassidione **2**.



**2**



**3**

203 (17), 201 (31), 191 (19), 189 (15), 177 (45), 175 (27), 173 (28), 163 (25), 161 (34), 159 (48), 149 (43), 147 (40), 145 (34), 135 (45), 133 (46), 125 (39), 123 (46), 121 (49), 119 (53), 110 (79), 109 (71), 107 (70), 95 (79), 93 (63), 83 (69), 81 (80), 71 (71), 69 (79), 57 (76), 43 (100).

*Mustakone* (**3**). Oil, $[\alpha]_D^{25} - 42.5°$ ($CHCl_3$; *c* 1.85) IR $\nu_{max}$ $cm^{-1}$: 3020, 2995, 1673, 1643, 1376, 1235, 887. MS (El, 70 eV, 200°) *m/z* (%): 218 (31) $M^{+}$, 203 (23), 175 (37), 161 (22), 147 (34), 135 (26), 121 (23), 109 (28), 105 (31), 93 (40), 91 (28), 81 (37), 69 (48), 55 (80), 43 (100).

2,4-*DNP of mustakone* (**4**). Mp 141–142° (EtOH). IR $\nu_{max}$ $cm^{-1}$: 3435, 3310, 3150, 2950, 2868, 1614, 1588, 1517, 1463, 1425, 1368, 1332, 1309, 1251, 1220, 1131, 1070, 952, 919, 830, 740, 708, 683, 633, MS (El, 70 eV, 200°) *m/z* (%): 399 (21), 398 (91) $M^{+}$, 383 (13), 381 (18), 363 (35), 355 (29), 321 (29), 307 (44), 293 (29), 281 (55), 267 (35), 216 (44), 172 (84), 159 (71), 157 (93), 119 (75), 93 (100). $^1$H NMR (250 MHz, $CDCl_3$, TMS), $\delta$(ppm): 11.4 (1H, *sl*), 9.11 (1H, *d*, *J* = 2.6 Hz), 8.25 (1H, *dd*, *J* = 2.6 and 9.4 Hz), 7.93 (1H, *d*, *J* = 9.4 Hz), 6.27 (1H, *d*, *J* = 1.4 Hz), 2.93 (1H, *dd*, *J* = 1.5 and 6.7 Hz), 2.40 (1H, *s*), 2.06 (3H, *d*, *J* = 1.4 Hz), 2.01 (1H, *d*, *J* = 6.7 Hz), 1.84 (2H, *m*), 1.68 (4H, *m*), 0.91 (3H, *s*), 0.90 (6H, *d*, *J* = 6.3 Hz).

2,4-*DNP of isopatchoul-4(5)-en-3-one* (**5**). Mp 226–227° (EtOH), lit. 226.5–227.5° [2, 5]. IR $\nu_{max}$ $cm^{-1}$: 3304, 3111, 2917, 1625, 1587, 1517, 1500, 1415, 1333, 1309, 1254, 1128, 842, 743. MS (El, 70 eV. 200°) *m/z* (%); 399 (24), 398 (100) $M^{+}$, 383 (11), 381 (13), 363 (26), 356 (12), 355 (13), 321 (15), 307 (22), 293 (14), 281 (55), 267 (16), 255 (16), 216 (93), 200 (48), 186 (25), 172 (53), 160 (80), 159 (83), 157 (90), 146 (78), 134 (89), 133 (78). $^1$H NMR (250 MHz, $CDCl_3$, TMS), $\delta$(ppm): 10.94 (1H, *sl*), 9.11 (1H, *d*, *J* = 2.5 Hz), 8.27 (1H, *dd*, *J* = 2.5 and 9.6 Hz), 7.97 (1H, *d*, *J* = 9.6 Hz), 2.50 (1H, *m*), 2.33 (1H, *d*, *J* = 16.6 Hz), 2.23 (1H, *d*, *J* = 16.6 Hz), 2.16 (1H, *m*), 2.03 (1H, *m*), 1.89 (3H, *s*), 1.59 (2H, *m*), 1.44 (1H, *m*), 1.12 (3H, *s*), 0.86 (2H, *m*), 0.77 (3H, *s*), 0.63 (3H, *d*, *J* = 6.4 Hz).

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## REFERENCES

1. Couchman, F. M., Pinder, A. R. and Bromham, N. H. (1964) *Tetrahedron* **20**, 2037.
2. Nigam, I. C. (1965) *J. Pharm. Sci.* **54**, 1823.
3. Hikino, H., Aota, K. and Takemoto, T. (1965) *Chem. Pharm. Bull.* **13**, 628.
4. Nerali, S. B., Kalsi, P. S., Chakravarti, K. K. and Bhattacharyya, S. C. (1965) *Tetrahedron Letters* 4053
5. Neville, G. A., Nigam, I. C. and Holmes, J. L. (1968) *Tetrahedron* **24**, 3891.
6. Nyasse, B., Ghogomu Tih, R., Sondengam, B. L., Martin, M. T. and Bodo, B. (1988) *Phytochemistry* **27**, 179.
7. Kapadia, V. H., Nagasampagi, B. A., Naik, V. G. and Dev, S. (1963) *Tetrahedron Letters* 1933.
8. Kapadia, V. H., Nagasampagi, B. A., Naik, V. G. and Dev, S. (1965) *Tetrahedron* **21**, 607.
9. Abraham, R. J., Cooper, M. A., Salmon, J. R. and Whittaker, D., *Org. Magn. Reson.* 489.
10. Levy, G. C. and Nelson, G. L. (1972) *Carbon-13 Nuclear Magnetic Resonance for Organic Chemists*. Wiley, New York.
11. Breitmaier, E. and Voetter, W. (1978) $^{13}$C *NMR Spectroscopy*, 2nd Edn. Verlag Chemie, Weinheim.
12. Kueh, J. S. H., Mellor, M. and Pattenden, G. (1981) *J. Chem. Soc. Perkin Trans. I.* 1052.
13. Herz, W. and Sharma, R. P. (1975) *J. Org. Chem.* **40**, 2557.