Phytochemistry, Vol. 22, No. 8, pp. 1757–1759, 1983.
Printed in Great Britain.

0031-9422/83$3.00 + 0.00

FOUR ALIPHATIC ESTERS OF *CHAMAEMELUM FUSCATUM* ESSENTIAL OIL

J. DE PASCUAL-T., E. CABALLERO, C. CABALLERO, J. ANAYA and M. S. GONZALEZ

Department of Organic Chemistry, Salamanca University, Salamanca, Spain

(*Received* 29 *October* 1982)

Key Word Index—*Chamaemelum fuscatum*; Compositae; essential oil; aliphatic esters.

Abstract—Four new aliphatic esters were isolated from the essential oil of *Chamaemelum fuscatum*. Three are esters of methacrylic acid with 2-methyl-2*E*-butenol, 2-hydroxy-2-methyl-3-butenol and 2-hydroxy-2-methyl-3-oxobutanol. The other is neryl isovalerate obtained in addition to known compounds. The structures were determined by spectral measurements and by synthesis.

INTRODUCTION

The chemical investigation of the roots of *Chamaemelum fuscatum* (syn. *Anthemis fuscata* Brot.) was carried out by Bohlmann in his systematic research on polyines [1, 4]. The infusion of inflorescences of the plant (known as 'bitter chamomile') has a pleasant aroma as well as healing properties. For this reason, the study of the aerial part of plant was carried out and a report is made of the essential oil components.

Among known compounds two sesquiterpenes with a bisabolene skeleton were isolated: (−)-*ar*-curcumene (**1**) [5] and bisabolen-1,4-endoperoxide (**2**) [6]; an acetylenic thiophene derivative, methyl-*trans*-5-(2-thienyl)pent-4-in-2-enoate (**3**) [3] and 2-methylallyl isobutyrate (**4**) [7]. Four esters were isolated as new natural products, neryl isovalerate (**5**) and three methacrylates of different isoprene alcohols (**6**–**8**). During this study, some novel aliphatic esters of low MW were found in *Anthemis nobilis* similar to those found in *A. fuscata* by us [8].

RESULTS AND DISCUSSION

The isolation of the products was carried out by chromatography (see Experimental). Compound **5** was isolated as a fragrant oil with the ^{1}H NMR spectrum showing among others, three methyls on trisubstituted double bonds and a doublet at δ4.50 assignable to an allylic methylene geminal with oxygen. The IR spectrum indicated the presence of an ester group, while the mass spectrum gave an M^+ at *m/z* 238 in agreement with $C_{15}H_{26}O_2$. The presence of an isovalerate residue was supported by the fragments $[M-C_4H_9COO\cdot]^+$ and $[C_4H_9CO\cdot]^+$. Saponification of **5** with 10% methanolic potassium hydroxide gave nerol (**9**) and isovaleric acid.

Compound **6** is an oil with an intense odour. The mass spectrum has an M^+ at *m/z* 154 in agreement with the molecular formula $C_9H_{14}O_2$. The IR spectrum shows the presence of an unsaturated ester (1730 cm^{-1}). The ^{1}H NMR exhibits the presence of a methacrylate and a trisubstituted double bond (Table 1). The *E*-configuration was assigned on the basis of methyl and olefinic proton displacements [10]. With these data, we have identified this product as 2-methyl-2*E*-butenyl methacrylate (**6**).

Compound **7** is a fragrant oil. It shows in the IR spectrum absorptions for a hydroxyl group and an unsaturated ester, while the mass spectrum gave $[M-Me]^+$ and $[M-H_2O]^+$ at *m/z* 155 and 152 in agreement with the molecular formula $C_9H_{14}O_3$. The ^{1}H NMR spectrum indicated the presence of a methyl group attached to a carbon bearing a hydroxyl and vinylic protons. The singlet at δ3.99 was attributed to the C-1′ methylene. Furthermore, it showed the same signals of the methacrylate group present in **6**, and was identified as 2-hydroxy-2-methyl-3-butenyl methacrylate (**7**).

The IR spectrum of **8** shows absorptions of an ester (1730 cm^{-1}), a carbonyl group (1710 cm^{-1}) and a hydroxyl group (3340 cm^{-1}, weak intensity) that suggests a hydrogen bond association. The ^{1}H NMR spectrum was very similar to that of **7**. The major differences were the absence of the vinyl double bond and the presence of a three-proton singlet at δ2.05 assigned to a methyl ketone. This substance was identified as 2-hydroxy-2-methyl-3-oxobutyl methacrylate (**8**).

The synthesis of **6** was achieved by esterification of 2-methyl-2*E*-butenol with methacrylic acid chloride in the presence of pyridine [11]. The spectroscopic data of the synthesized product were identical to those of the natural one.

The reaction with $^1O_2$ of **6** following triphenylphosphite reduction gave **7** and **9**. Spectroscopic data of **7** were identical with those of the natural product and those of **9** are shown in Table 1.

Compound **4** was identified from its spectroscopic properties and confirmed by synthesis. It was obtained by esterification of 2-methylallyl alcohol with isobutyric acid chloride.

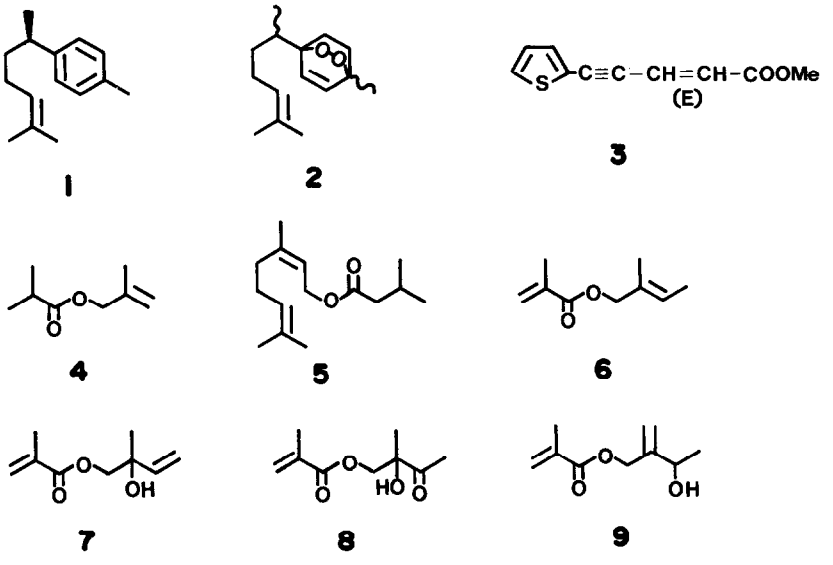
EXPERIMENTAL

MS were operated at 70 eV with the ion source at 180°. ^{1}H NMR spectra were recorded at 60 MHz using TMS as int. standard. IR spectra were run as liquid films. Analytical TLC was performed on Si gel G (Merck 7731), prep. TLC on Si gel $PF_{234-336}$ (Merck 7748) and CC on Si gel 60 (Merck 7734).

Extraction and separation of compounds. The hexane extract of the air-dried plant material (4 kg) [*Chamaemelum fuscatum* (Brot)

Table 1. ^{1}H NMR chemical shifts (δ-values from TMS) and multiplicities (J values, in Hz, in parentheses) of **6–9** measured in carbon tetrachloride

	6	7	8	9
H-3	5.49 *brs* 6.05 *brs*	5.50 *brs* 6.05 *brs*	5.50 *brs* 6.05 *brs*	5.50 *brs* 6.05 *brs*
H-4	1.95 *d* (2)	1.91 *d* (2)	1.91 *d* (2)	1.91 *d* (2)
H-1′	4.50 *s*	3.99 *s*	4.70 *s*	4.50 *s*
H-3′	5.50 *m*	5.84 *dd* (16,10)	4.32 *q* (7)	—
H-4′	1.62 *d* (7)	4.99 *dd* (10,2) 5.20 *dd* (16,2)	1.35 *d* (7)	2.05 *s*
H-5′	1.67 *s*	1.31 *s*	5.15 *s* 5.25 *s*	1.20 *s*



Vasc.] collected at the end of May, in Zarza de Granadilla (Cáceres, western Spain), was steam distilled and yielded 5.4 g (0.13%) of essential oil. The oil was chromatographed over a Si gel column using hexane with gradually increasing proportions of Et_2O as eluent. The first fraction (hexane) gave (−)-*ar*-curcumene (**1**, 500 mg). The second fraction (hexane–Et_2O, 19:1) gave **6** (150 mg), **4** (30 mg), bisabolen-1,4-endoperoxide (**2**, 35 mg), methyl-*trans*-5-(2-thienyl)pent-4-in-2-enoate (**3**, 90 mg) and **5** (170 mg). The third fraction (hexane–Et_2O, 4:1) gave **8** (90 mg) and **7** (450 mg).

2-Methylallyl isobutyrate (**4**). IR ν_{max} cm^{-1}: 3060, 1740, 1640, 1390, 1380, 1165, 900. ^{1}H NMR: δ1.17 (6H, *d*, J = 7 Hz), 1.71 (3H, *d*, J = 1.5 Hz), 2.40 (1H, *m*), 4.37 (2H, *s*, H-1′), 4.81 (2H, *br s*, $W_{1/2}$ = 8 Hz, H-3′).

Synthesis of **4**. Compound **4** was prepared by esterification of 2-methylallyl alcohol (400 mg) with isobutyric acid chloride (500 mg) in dry dimethylaniline (3.5 ml) and yielded 480 mg. It had identical spectra with those of the natural product.

Neryl isovalerate (**5**) IR ν_{max} cm^{-1}: 3010, 1735, 1670, 1180, 830. ^{1}H NMR: δ0.94 (6H, *d*, J = 6 Hz), 1.58 (3H, *s*), 1.64 (3H, *s*), 1.72 (3H, *s*), 4.50 (2H, *d*, J = 7 Hz, H-1′), 5.00 (1H, *m*, H-6′), 5.30 (1H, *t*, J = 7 Hz, H-2′). MS m/z (rel. int.): 238 [M]$^+$ (1), 153 (3), 137 (4), 85 (36), 69 (100), 57 (33).

The saponification of **5** with 10% KOH–MeOH afforded isovaleric acid and nerol (IR and ^{1}H NMR and comparison with authentic products).

2-Methyl-2E-butenyl methacrylate (**6**). IR ν_{max} cm^{-1}: 3040, 3015, 1730, 1680, 1640, 970, 815, 790. ^{1}H NMR: (Table 1). MS m/z (rel. int.): 154 [M]$^+$ (2), 139 (1), 113 (3), 105 (7.5), 85 (25), 71 (29.5), 69 (100), 41 (16.5).

Synthesis of **6**. (a) *Preparation of 2-methyl-2E-butenol.* To a mixture of 2-butanone (10 g) and a soln of NaCN (5.7 g) in H_2O (14 ml) at 15°, 40% H_2SO_4 (24 ml) was added with stirring. The addition lasted 30 min and after 15 min the organic layer was extracted with Et_2O. The Et_2O soln was distilled under red. pres. and 2-cyano-2-butanol (6.8 g) bp 74–76° (8 mm Hg) was obtained. IR ν_{max} cm^{-1}: 3430, 2250, 1470, 1390, 1170, ^{1}H NMR: δ1.05 (3H, *t*, J = 7 Hz), 1.52 (3H, *s*), 1.72 (2H, *c*, J = 7 Hz). The cyanohydrin (6.8 g) was added slowly with vigorous stirring to 96% H_2SO_4 (21.2 g) and maintained at 75–80°. The mixture was heated for 1 hr at 125–130° with vigorous stirring. To this product, MeOH (28 ml) and H_2O (2 ml) were added and the soln boiled under reflux for 24 hr. All the volatile material was distilled and methyl tiglate (2.8 g) was separated. Extraction with Et_2O, which was subsequently distilled, then afforded methyl tiglate (3.1 g) (bp 138–139°). IR ν_{max} cm^{-1}: 3010, 1720, 1665, 1260, 1130, 1070, 805. ^{1}H NMR: δ1.75 (3H, *d*), 1.77 (3H, *s*), 3.63 (3H, *s*), 6.75 (1H, *m*). The reduction of methyl tiglate (3 g) with $LiAlH_4$ (1.5 g)

in Et_2O afforded 2-methyl-2*E*-butenol (2 g). IR ν_{max} cm^{-1}: 3300, 3015, 1670, 1005, 830. ^1H NMR: δ1.60 (3H, *d*), 1.62 (3H, *s*), 3.88 (3H, *s*), 5.32 (1H, *m*).

(b) *Esterification.* Methacrylic acid chloride (5.1 g) [prepared by addition of Cl_2SO (14 ml) to a soln of methacrylic acid (7 g) in C_6H_6 (28 ml), C_5H_5N (2 ml) and hydroquinone (150 mg) under N_2] was added slowly to a soln of 2-methyl-2*E*-butenol (2 g) and C_5H_5N (2.6 ml) and stirred at room temp. for 3 hr. It afforded 1.5 g of product which by CC gave pure 2-methyl-2*E*-butenyl methacrylate (**6**, 220 mg).

2-Hydroxy-2-methyl-3-butenyl methacrylate (**7**). $[\alpha]_D^{22} = 0°$ ($CHCl_3$; *c* 1.5). IR ν_{max} cm^{-1}: 3480, 3060, 3010, 1725, 1640, 1160, 990, 950, 910, 815. ^1H NMR: (Table 1). MS *m/z* (rel. int.): 155 $[M-Me]^+$ (16), 152 $[M-H_2O]^+$ (7), 137 (11), 111 (16), 101 (18), 85 (65), 71 (69), 69 (65), 43 (100).

Synthesis of **7** *from* **6**. To a soln of **6** (200 mg) in *iso*-PrOH (20 ml) Rose Bengal (6 mg) was added, stirred for 8 hr and exposed to sunlight. When the *iso*-PrOH had been evaporated, Et_2O (12 ml) and Ph_3P (238 mg) were added and the stirring continued for another 30 min. Evaporation of the solvent gave 120 mg of product, which by CC gave a mixture (50%) of **7** and **9** (30 mg).

2-Hydroxy-2-methyl-3-oxobutyl methacrylate (**8**). IR ν_{max} cm^{-1}: 3400, 3050, 1730, 1710, 1640, 1160, 1130, 950, 810. ^1H NMR: (Table 1).

Acknowledgements—We are grateful to Dr. B. Casaseca Mena of the Faculty of Biological Sciences, Salamanca University, for identification of plant material, and to Dr. J. M. Hernández of our laboratory for the mass spectra.

REFERENCES

1. Bohlmann, F., Kap-Herr, W. V., Fanghänel, L. and Arndt, Ch. (1965) *Chem. Ber.* **98**, 1411.
2. Bohlmann, F., Kleine, K. H., Arndt, Ch. and Köhn, S. (1965) *Chem. Ber.* **98**, 1616.
3. Bohlmann, F. and Zdero, Ch. (1970) *Chem. Ber.* **103**, 2856.
4. Bohlmann, F. and Zdero, Ch. (1971) *Chem. Ber.* **104**, 1375.
5. Damodaran, N. P. and Sukh, D. (1968) *Tetrahedron* **24**, 4113.
6. Bohlmann, F., Jakupovic, J. and Zdero, Ch. (1978) *Phytochemistry* **17**, 2034.
7. Thomas, A. F. (1981) *Helv. Chim. Acta* **64**, 2397.
8. Klimes, I., Lamparsky, D. and Scholz, E. (1981) *Helv. Chim. Acta* **64**, 2338.
9. Yukawa, Y., Hanafusa, T. and Fujita, K. (1964) *Bull. Chem. Soc.* **37**, 158.
10. Bates, R. B., Gale, D. H. and Gruner, D. J. (1963) *J. Org. Chem.* **28**, 1086.
11. Buckles, R. E. and Mock, G. V. (1950) *J. Org. Chem.* **15**, 680.