

Studies Related to Naturally Occurring Acetylene Compounds. X. The Synthesis of some Hydro- genated Relatives of Matricaria Ester

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From the essential oil of various plants belonging to the family of the Compositae the following closely related highly unsaturated derivatives of methyl caprate¹⁻³ amongst others have been isolated:

- I. $\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{CH}=\text{CH}-\text{COOCH}_3$ Lachnophyllum ester
- II. $\text{H}_3\text{C}-\text{CH}=\text{CH}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{CH}=\text{CH}-\text{COOCH}_3$ Matricaria ester
- III. $\text{H}_3\text{C}-\text{CH}=\text{CH}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{COOCH}_3$ Dehydro matricaria ester

Further investigation in this plant family made it probable that this series might be extended in the hydrogenated direction (compare the preceding paper of Stavholt-Baalsrud *et.al.*⁴).

For purpose of comparison the following new members of the hydrogenated series have been synthesized through oxidative coupling according to Glaser.

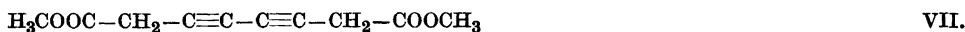
	m.p.	
	Methyl ester	Free acid
IV. $\text{CH}_3-\text{CH}=\text{CH}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{CH}_2-\text{CH}_2-\text{COOCH}_3$	liq.	60.5°
	15.5°	144°
V. $\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{CH}_2-\text{CH}_2-\text{COOCH}_3$	liq.	92°
VI. $\text{CH}_3-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{CH}_2-\text{COOCH}_3$	»	53°

The preparations of IV to VI, and the unavoidable by-products, are given in the experimental part.

It turned out that the 8-*cis*- α,β -dihydromatricaria ester IV is identical with an ester rather widely distributed in nature (compare⁴).

The 2 : 8-tetrahydro matricaria ester (V) and methyl deca-3 : 5-diyne-1-oate (VI) only show very weak selective absorption in U.V. below 2700 ÅU corresponding to dialkyl diacetylenes. The esters themselves will be very difficult to detect through the U.V. spectroscopy of natural essential oils, even when present in high concentrations as, at least most, composite oils contain small amounts of strong chromophors which will hide the spectrum of these esters completely. So far no indications have been found of the occurrence of V and VI in nature.

In the synthesis of VI by Glaser coupling dimethyl octa-3 : 5-diyne-1 : 8-dioate (VII)



results as a by-product in fair yield. This substance shows the interesting property of turning beautifully violet-red on standing. The coloration accelerates in light, but some crystals remain colourless, so obviously some catalysing impurities are co-responsible for the colour development. The red material is insoluble in organic solvents, unchanged VII is extracted by attempts of recrystallization. These secondary crystalline fractions repeat the curious colouration. A similar colouration was discovered by Castille ⁵ in 1939 with the acetylenic fatty acids from *Ongokea Klaineana* Pierre. The true nature of the component of the *Ongokea* acids responsible for their colouration is not known. Castille's formula for the main acid, which he on account of this colour development named erythrogenic acid, is — as was emphasized first by professor E. R. H. Jones ⁶ — obviously not in accordance with its spectral properties. None of our synthetic or natural acetylenic compounds with an isolated diyne or enediyne grouping have shown this colouration phenomenon.

The red material has the unchanged composition $(\text{C}_5\text{H}_5\text{O}_2)_x$. This fact in connection with its extreme insolubility points to a polymeric nature. The beautiful colour necessitates conjugation in the polymer material. In analogy with the deeply coloured polyenes, which Eisler *et.al.*⁷ recently have synthesized from cyclopentadiene, formula VIII, is put forward as a working hypothesis.



Finally it should be mentioned that we have tried to synthesize methyl deca-2 : 4-diyne-1-oate through the coupling of *n*-hept-1-yne with propiolic acid

methyl ester. We were not able to isolate any amount of the desired asymmetric coupling product; besides tetradeca-6 : 8-diyne a colourless compound, m.p. 54,5°, was isolated in the same yield as when n-heptyne is omitted from the reaction. The elementary composition corresponds to $C_8H_8O_6$. Since dimethyl adipate is generated by catalytic hydrogenation with consumption of about 4 Mol H_2 this compound must originate by a Glaser coupling of the ester of propiolic acid with, formally, addition of water and one atom of oxygen.

Shortening the reaction time in the Glaser coupling gave a mixture of $C_8H_8O_6$ with a new compound $C_8H_8O_5$.

We are returning later to the investigation of the constitution of these compounds. The tendency of diacetylene dicarboxylic acid to add water might be one of the reasons for the difficulty which different investigators have met when trying to repeat the classical condensations of A. v. Bayer.

EXPERIMENTAL

a,β-Dihydromatricaria ester (IV). Pent-3-en-1-yne was prepared according to Eglinton and Whiting⁸ and fractionated as described in⁹. Methyl pent-4-yn-1-oate was prepared from tribromopropane and ethyl acetoacetate according to T. E. Gardner and W. H. Perkin jr.¹⁰.

cis Isomer: 4 ml pent-3-en-1-yne b.r. 46–48° and 4 ml methyl pent-4-yn-1-oate were coupled under the experimental conditions worked out for the analogous synthesis of the matricaria esters. By the distillation at 10^{-4} mm Hg the hydrocarbon fraction passed into the trap, the desired dihydromatricaria ester was distilled over until the temperature reached 65° air bath and redistilled slowly, b.p. 50–53° Yield 1.1 g. The *cis* isomer is an oil m.p. < -17°.

$C_{11}H_{12}O_2$ (176.2)	Calc.	C 74.97	H 6.86
	Found	» 75.09, 74.82	» 6.80, 6.75
	$n_D^{20} = 1.0017$	$n_D^{20} = 1.5450$	$M_D = 55.6$
	M_D calc. $C_{11}H_{12}O_2$	$2 \sqrt{=} , 1 \sqrt{=} = 50.14$	

Table 1. Dispersion of *cis a,β-dihydro-matricaria ester*.

$$R_{\lambda, \text{ calc.}} = \frac{52.817 \cdot \lambda^2}{\lambda^2 - 1.7393 \cdot 10^6}, (\lambda_0 = 1319 \text{ \AA})$$

λ	n_{λ}^{20}	$R_{\lambda, \text{ obs.}}$	$R_{\lambda, \text{ calc.}}$
5895.9	1.54500	55.61	55.60
5790.7	1.54618	55.71	55.71
5460.7	1.55092	56.11	56.09
4358.3	1.57458	58.09	58.14

U.V.-absorption, in hexane, Fig. 1 curve 1.

$\epsilon_{\max.}$	11350	15140	11100	4900	2400	
$\lambda_{\max.}$	2810	2650	2514	2381	2275	ÅU
$\nu_{\max.} \cdot 10^{-12}$	1067.6	1132.1	1193.3	1260.0	1318.7	
$\Delta\nu \cdot 10^{-12}$	64.5	61.2	66.7	58.7		

Catalytic hydrogenation: 59 mg *cis*-ester was hydrogenated with Pt in alcoholic solution. Calc. $2 \sqrt{=}$, $1 \sqrt{=}$ 20°, 740 mm 41.3 ml. Found 41.2 ml H₂. The perhydroester = methyl caprate was distilled $n_D^{20} = 1.4288$, methyl caprate 1.4265. The hydrogenation product, which had the characteristic strawberry odour of methyl caprate, was saponified and the free capric acid isolated in the usual way; m.p. and mixed m.p. with authentic capric acid 31° C.

cis- α,β -Dihydromatricaria acid. The *cis* methyl ester was saponified under nitrogen as in (9) and recrystallized from petroleum ether, m.p. = 60.5°. Re-esterification with diazo-methane gave the liquid methyl ester with unchanged U.V.-spectrum.

trans-Isomer. 2 ml Pent-3-en-1-yne b.r. 52–53° and 3 ml methyl pent-4-yn-1-oate were coupled as above. The crude distillate, b.r. < 61° at 10⁻⁴ mm Hg (0.86 g), was recrystallized from petroleum ether as colourless leaflets, m.p. 15.5° C.

C₁₁H₁₂O₂ (176.2) Calc. C 74.97 H 6.86
 Found » 74.76, 75.09, 75.11 » 6.67, 6.87, 6.68
 $d_4^{20} = 0.9940$ $n_D^{20} = 1.5496$ $M_D, \text{obs.} = 56.14$ $M_D, \text{calc.} = 50.14$ $2 \sqrt{=}$, $1 \sqrt{=}$

Table 2. Dispersion of *trans*- α,β -dihydromatricaria ester.

$$R_{\lambda, \text{calc.}} = \frac{53.545 \cdot \lambda^2}{\lambda^2 - 1.78 \cdot 10^6}, (\lambda_0 = 1334 \text{ ÅU})$$

λ	n_{λ}^{20}	$R_{\lambda, \text{obs.}}$	$R_{\lambda, \text{calc.}}$
5895.9	1.54963	56.44	56.44
5790.7	1.55112	56.56	56.55
5460.7	1.55577	56.96	56.94
4358.3	1.58063	59.04	59.08

UV.-absorption in hexane. Fig. 1 curve 2.

$\epsilon_{\max.}$	17780	22650	16600	10720
$\lambda_{\max.}$	2814	2653	2510	2390
$\nu_{\max.} \cdot 10^{-12}$	1066.1	1130.8	1195.2	1255.2
$\Delta\nu_{\max.} \cdot 10^{-12}$	64.7	64.4	60.0	

Catalytic hydrogenation: 81.45 mg *trans*-ester was hydrogenated with a Pt-catalyst in alcoholic solution. Calc. 18.5°, 738 mm 57.0 ml. Found 58.6 ml H₂, that is 5.14 $\sqrt{=}$. The perhydroester had the characteristic strawberry odour and showed $n_D^{20} = 1.4284$ (methyl caprate $n_D^{20} = 1.4265$). Saponification gave the free acid m.p. and mixed m.p. with authentic capric acid 31° C.

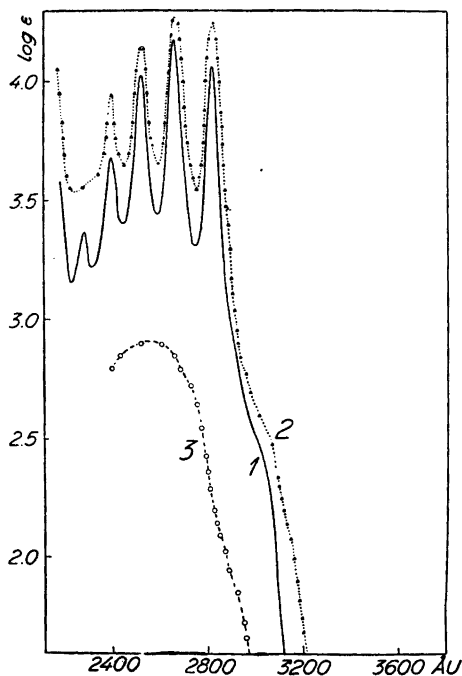


Fig. 1. Ultraviolet absorption of hexane solutions of:

- Curve 1. *8-cis- α,β -dihydromatricaria ester.*
 » 2. *8-trans- α,β -dihydromatricaria ester.*
 » 3. $C_8H_8O_6$ from *propionic acid methyl ester E* $\frac{1}{1\%}$ $\frac{1}{1\text{cm}}$.

trans- α,β -Dihydromatricaria acid. The *trans* ester was saponified cautiously under nitrogen according to the usual procedure. Crystallization from petroleum ether gave colourless prisms m.p. 144° (corr.).

Re-esterification with diazomethane gave the *trans* ester m.p. 15.5° . The U.V.-absorption spectrum of this regenerated ester has the data given above. In the U.V.-spectrum of the *trans* ester isolated primarily from the Glaser coupling a weak band occurred, maximum 3112 \AA ($\log \epsilon = 2.92$). This impurity could not be eliminated through recrystallization. The four main maxima were in identical positions, the extinction coefficients of the regenerated ester lying some 10 % higher.

Dimethyl deca-4 : 6-diyne-1 : 10dioate [$(H_3COOC-CH_2-CH_2-C\equiv C-C\equiv C-CH_2-CH_2-COOCH_3)$.] The residues from the distillation of the *cis*- and *trans* dihydroesters above solidified on cooling and were recrystallized from petroleum ether, m.p. 37.5° .

$C_{12}H_{14}O_4$ (222.2)	Calc.	C 64.84	H 6.35
	Found	» 64.79, 64.62	» 6.21, 6.22

U.V.-absorption in hexane:

$\epsilon_{\text{max.}}$	380	560	660	840
$\lambda_{\text{max.}}$	2814	2662	2515	2392
$\nu_{\text{max.}} \cdot 10^{-12}$	1066.1	1127.0	1192.8	1254.2
$\Delta\nu_{\text{max.}} \cdot 10^{-12}$	60.9	65.8	61.4	

Catalytic hydrogenation: 69.6 mg in alcoholic solution with a Pt-catalyst. $C_{12}H_{14}O_4$, $2 \sqrt{\text{calc.}}$ 19°, 740 mm 30.8 ml. Found 30.4 ml H_2 . The hydrogenation product was saponified, and the crystalline acid recrystallized from alcohol. M.p. and mixed m.p. with authentic sebacic acid, 134°.

Methyl deca-4 : 6-diyne-1-oate (= 2 : 8-tetrahydromatricaria ester (V)). 3.4 g Pent-1-yne prepared according to (11), and 3.6 g methyl pent-4-yn-1-oate prepared according to (12) were added to 112 g ammonium chloride, 70 g cuprous chloride and 2 ml 2 N ammonia in 250 ml water. The suspension was shaken mechanically for 2 hours without additional introduction of air. The reaction mixture was distilled at 10^{-4} , the hydrocarbon fraction passing into the trap. 1.73 g Tetrahydromatricaria ester distilled between 55–58° in the air-bath. Colourless liquid m.p. $< -12^\circ$.

$C_{11}H_{14}O_2$ (178.2) Calc. C 74.11 H 7.92
 Found » 73.7 » 7.8
 $n_D^{20} = 1.5000$, $d_4^{20} = 0.9792$, M_D , obs. = 53.87, M_D , calc. $C_{11}H_{14}O_2$, $2 \sqrt{\text{calc.}}$ = 50.65

U.V.-spectrum in hexane:

$\epsilon_{\text{max.}}$	235	425	495
$\lambda_{\text{max.}}$	2530	2386	2256
$\nu_{\text{max.}} \cdot 10^{-12}$	1185.8	1257.3	1329.8
$\Delta\nu_{\text{max.}} \cdot 10^{-12}$		71.5	72.5

Catalytic hydrogenation: 41.5 mg in alcoholic solution with PdO-catalyst, 19°, 760 mm. Calc. $2 \sqrt{\text{calc.}}$ 23.2 ml, found 21.7 ml H_2 .

2 : 8-Tetrahydromatricaria acid. The methyl ester was saponified at 0° under nitrogen and worked up as above. The free acid was recrystallized from petroleum ether as colourless leaflets m.p. 92°.

Methyl deca-3 : 5-diyne-1-oate VI. *n*-Hex-1-yne was prepared according to (13). For the synthesis of methyl but-3-yn-1-oate ethylene oxide was reacted with sodium acetylide according to Henne and Greenlee¹⁴ to give but-3-yn-1-ol, which was oxidized with chromic acid to but-3-yn-1-oic acid according to the procedure given by Heilbron, Jones and Sondheimer¹⁵. This acid was esterified with the calculated amount of diazomethane in anhydrous ether and the liquid ester distilled, b.p. 28° at 8 mm Hg. 4.1 g *n*-Hexyne and 4.9 g methyl-but-3-yn-1-oate were added to a solution of 112 g ammonium chloride, 70 g cuprous chloride and 2 ml. 2 N ammonia in 286 ml water and the suspension shaken in a flask for 1 hour mechanically, then one hour more by hand with connection to the air. The reaction mixture was distilled at 10^{-4} mm Hg and the fractions 50–70° and 90–100° C redistilled slowly. Methyl deca-3 : 5-diyne-1-oate distilled at 55°/10⁻⁴ mmHg as a liquid mp. $< -18^\circ$ C.

$C_{11}H_{14}O_2$ (178.2) Calc. C 74.11 H 7.92
 Found » 73.9 » 7.93
 $n_D^{20} = 1.4978$, $d_4^{20} = 0.9478$, M_D , obs. = 55.09, M_D , calc. $C_{11}H_{14}O_2$, $2 \sqrt{\text{calc.}}$ = 50.65

Catalytic hydrogenation: PdO₂ catalyst, alcoholic solution, 60.7 mg 740 mm, 17.5° C. Calc. 33.4 ml, Found 33.8 ml H_2 , that is 2.02 $\sqrt{\text{calc.}}$. –264.4 mg, 745 mm, 21.5° C. Calc. 146.0, Found 144 ml, that is 1.96 $\sqrt{\text{calc.}}$. The hydrogenated ester was isolated in the usual way and distilled, $n_D^{20} = 1.4291$; methyl caprate 1.4265. The hydrogenated ester was saponified and the free acid isolated m.p. and mixed m.p. with authentic capric acid 31° C.

Deca-3 : 5-diyne-1-oic acid. The methyl ester was saponified under pure nitrogen at 0° C. The free acid formed colourless leaflets m.p. 53°.

Dimethyl octa-3:5-diyne-1:8-dioate $\text{H}_3\text{COOC}-\text{CH}_2-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{CH}_2-\text{COOCH}_3$. The fraction boiling range $90-100/10^{-4}$ solidified and was recrystallized from petroleum ether. In the light about one half of the crystals turned a beautiful violet-red. The m.p. of both the colourless and the red crystals was 54°C .

$\text{C}_{10}\text{H}_{10}\text{O}_4$ (194.2)	Calc.	C 61.84	H 5.19
	Found	» 61.55, 62.05	» 5.06, 5.21

Catalytic hydrogenation: PdO_2 , in alcoholic solution.

229.3 mg,	745 mm,	$t = 19.5^\circ\text{C}$	Calc. 2	$\frac{1}{\text{ml}}$ 116	ml,	Found 114	ml
37.6 »	740 »	$t = 20^\circ\text{C}$	» 2	» 19.15	»	» 19.6	»

The hydrogenation product was a colourless liquid m.p. = $-6--5.5^\circ\text{C}$. Synthetic dimethyl suberate melted at $-6.5--6^\circ\text{C}$, mixed m.p. $-6-5.5^\circ\text{C}$.

$\text{C}_{10}\text{H}_{18}\text{O}_4$ (202.2)	Calc.	C 59.40	H 8.97
	Found	» 59.5	» 8.93

Glaser coupling of propiolic acid methyl ester. 4.2 g Propiolic acid methyl ester prepared according to ^{13,14} was added to a solution of 112 g ammonium chloride, 70 g cuprous chloride and 1 ml 2 N ammonia in 250 ml H_2O . The suspension was shaken mechanically for 1 hour and then stirred by a stream of air for 2 hours. The reaction mixture was worked up as usual and distilled at 10^{-3} mm Hg. The main fraction, boiling about 62° (air bath temperature), solidified and was recrystallized from 100 ml petroleum ether. Yield 0.8 g colourless needles m.p. 54.5°C .

$\text{C}_8\text{H}_8\text{O}_6$ (200.1)	Calc.	C 48.0	H 4.03
	Found	» 47.5, 47.7	» 3.47, 3.58

Ultra violet absorption, Fig. 1 curve 3.

Catalytic hydrogenation: PdO_2 in alcoholic solution.

39.4 mg,	745 mm,	$t = 21^\circ\text{C}$	Consumed 18.5 ml H_2 ,	Calc. 4 Mol H_2	19.4
40.4 »	745 »	»	» 18.9 »	» 4 »	» 19.9

The hydrogenation product was not homogeneous. On distillation at 10^{-3} mm there passed over a main fraction at about 45°C as a colourless liquid,

$\text{C}_8\text{H}_{14}\text{O}_4$ (174.2)	Calc.	C 55.15	H 8.10
	Found	» 54.9, 55.6	» 8.06, 8.17

The hydrogenation product was saponified and the free acid isolated, m.p. 149° , authentic adipic acid 150.5° , mixed m.p. 150° .

Second fraction, b.r. $70-80/10^{-3}$, colourless liquid.

$\text{C}_8\text{H}_{14}\text{O}_5$ (190.2)	Calc.	C 50.52	H 7.42
	Found	» 50.3	» 7.13

Shortening of coupling time: Experimental conditions as above, but the aeration time cut down to $1\frac{1}{2}$ hour. The reaction mixture was isolated as usual and distilled at 10^{-3} mm. The fraction of b.p. about 45° (air bath temperature) (450 mg) solidified at room temperature. It crystallized from petroleum ether, as colourless needles, m.p. $37-41^\circ\text{C}$.

$\text{C}_8\text{H}_8\text{O}_5$ (184.1)	Calc.	C 52.19	H 4.38
	Found	» 52.7, 52.7	» 4.04, 4.01

No selective absorption in U.V., but stepping out below 2700 \AA .

SUMMARY

The following unsaturated derivatives of methyl caprate has been synthesized by means of Glaser coupling of their acetylenic moieties:

α,β -Dihydromatricaria ester (IV) 8-*cis* and 8-*trans*

Methyl deca-4 : 6-diyne-1-oate (V)

Methyl deca-3 : 5-diyne-1-oate (VI)

So far only the 8-*cis* α,β -dihydromatricaria ester has been found in nature.

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