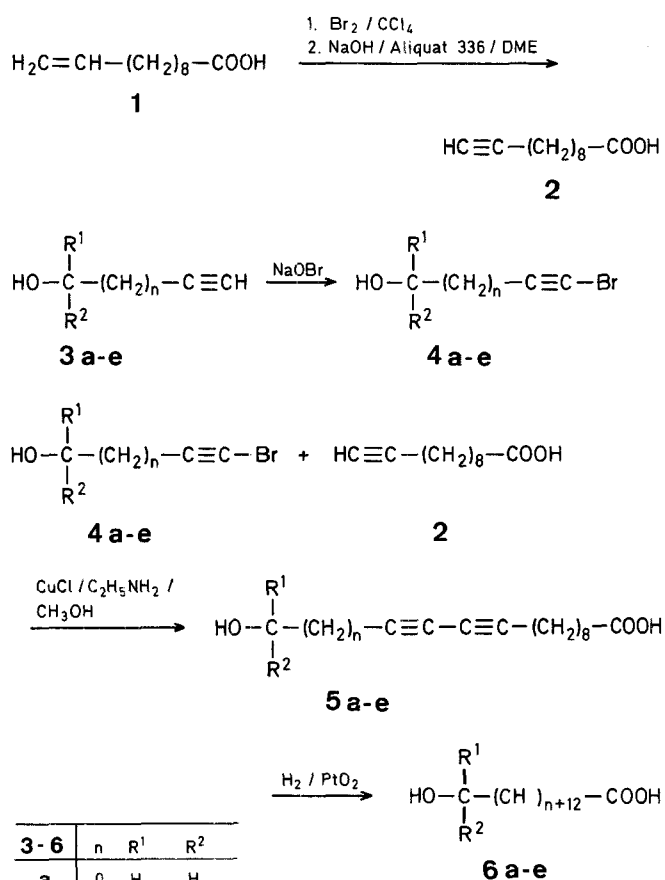


decynoic acid (**2**). This unsymmetrical coupling reaction between undecynoic acid (**2**) and the bromoacetylenic alcohols **4** is particularly suitable for hydrophilic acetylenes.

Undecynoic acid (**2**) was prepared from commercially available undecenoic acid (**1**) by bromination and debromination<sup>10</sup> under phase transfer conditions. The bromoacetylenic alcohols **4** were obtained by aqueous sodium hypobromite oxidation of the acetylenic alcohols **3**. Compounds **2** and **4** were coupled together in a methanol/ethylamine mixture using copper(I) chloride as catalyst at room temperature. The resulting  $\omega$ -hydroxydiynoic acids **5** were then catalytically hydrogenated to  $\omega$ -hydroxyalkanoic acids **6** (Table). The overall yield is high and the reaction is manipulatively simple.



### A New Synthesis of $\omega$ -Hydroxyalkanoic Acids via Copper Catalysis

Didier VILLEMEN, Paul CADIOT, Mikem KUÉTEGAN

Laboratoire de recherche de chimie organique ENSCP, 11, Rue Pierre et Marie Curie, F-75231 Paris Cedex 05, France

$\omega$ -Hydroxyalkanoic acids are important as models in order to test new methods of lactonisation<sup>1</sup> for the synthesis of antibiotic macrolides. Some  $\omega$ -hydroxyalkanoic acids like 12-hydroxydodecanoic acid (sabinic acid – wax of conifers)<sup>2</sup>, 15-hydroxypentadecanoic acid (angelica refracta) and 16-hydroxyhexadecanoic acid (juniperic acid – wax of conifers)<sup>2</sup> occur in nature. The lactones derived from these hydroxy acids with 15–17 carbon atoms have a musk odour and are important in perfumery, e.g., Exaltolide<sup>®4</sup> from 15-hydroxypentadecanoic acid and dihydroambretolide<sup>5</sup> from 16-hydroxyhexadecanoic acid. Baeyer-Villiger oxidation of cycloalkanones<sup>6</sup> is a method of choice for the preparation of macrocyclic lactones, when the cycloalkanones themselves are easy to prepare, e.g. cyclododecanone. New methods based on organometallic chemistry have been recently developed<sup>7</sup> in order to replace inefficient and multistep classical synthesis<sup>8</sup>.

We report here a convenient method for the synthesis of  $\omega$ -hydroxyalkanoic acids **6** utilising the Cadiot-Chodkiewicz reaction<sup>9</sup> for a rapid chain extension from the easily available un-

The acetylenic alcohols **3a-d** are commercially available, the pentyn-4-ol (**3e**) was prepared by an adaption of Ref.<sup>11</sup>. The bromoacetylenic alcohols **4** were prepared from the alcohols **3a-e** as reported<sup>12,13</sup>.

#### Undecynoic Acid (**2**):

A mixture of 10,11-dibromoundecanoic acid<sup>14</sup> (34.4 g, 0.1 mol), Aliquat 336 (0.46 ml, 0.001 mol) and pulverized sodium hydroxide (16 g, 0.4 mol) in 1,2-dimethoxyethane (100 ml) is stirred under reflux for 12 h. After careful neutralisation with concentrated hydrochloric acid, the mixture is extracted with ether (3 × 150 ml) and the ether phase is dried with magnesium sulfate. Evaporation of the solvent gives a brown oil, which is distilled using a Kugelrohrfen; b.p. 140°C/0.05 torr. The distillate is crystallised from pentane; yield: 14.74 g (81%); m.p. 42°C (Ref.<sup>12</sup>, m.p. 42°C). The debromination can also be carried out using powdered potassium hydroxide in hexane; yield: 12.09 g (65%).

<b>3-6</b>	n	R <sup>1</sup>	R <sup>2</sup>
<b>a</b>	0	H	H
<b>b</b>	0	H	CH <sub>3</sub>
<b>c</b>	0	CH <sub>3</sub>	CH <sub>3</sub>
<b>d</b>	1	H	H
<b>e</b>	2	H	H

Table.  $\omega$ -Hydroxydiynoic Acids **5a-e** and their Hydrogenation to  $\omega$ -Hydroxyalkanoic Acids **6a-e**<sup>a</sup>

Diynoic Acid	Yield [%]	m.p. [°C] (solvent)	Molecular formula <sup>b</sup>	Alkanoic Acid	Yield [%]	m.p. [°C] (solvent)	Molecular formula <sup>b</sup> or Lit. m.p. [°C]
<b>5a</b>	75	84° (cyclohexane)	C <sub>14</sub> H <sub>20</sub> O <sub>3</sub> (236.3)	<b>6a</b>	98	91° (cyclohexane)	91 <sup>6a</sup> 93-95 <sup>6b</sup>
<b>5b</b>	48	36.5-37.5° (pentane)	C <sub>15</sub> H <sub>22</sub> O <sub>3</sub> (250.3)	<b>6b</b>	95	85° (pentane)	C <sub>15</sub> H <sub>30</sub> O <sub>3</sub> (258.4)
<b>5c</b>	88	46° (pentane)	C <sub>16</sub> H <sub>24</sub> O <sub>3</sub> (264.3)	<b>6c</b>	97	81° (pentane)	C <sub>16</sub> H <sub>32</sub> O <sub>3</sub> (272.4)
<b>5d</b>	87	62° (pentane)	C <sub>15</sub> H <sub>22</sub> O <sub>3</sub> (250.3)	<b>6d</b>	98	81° (toluene)	82 <sup>6a</sup> 85 <sup>6d</sup>
<b>5e</b>	81	60° (pentane)	C <sub>16</sub> H <sub>24</sub> O <sub>3</sub> (264.3)	<b>6e</b>	98	95° (toluene)	91-93 <sup>6a</sup> 94 <sup>6b</sup>

<sup>a</sup> All products reported in this Table were characterised by their I.R., <sup>1</sup>H-N.M.R. and Mass spectra.

<sup>b</sup> Satisfactory microanalyses obtained: C  $\pm$  0.30%, H  $\pm$  0.25%.

#### 14-Hydroxytetradeca-10,12-diynoic Acid (**5a**); Typical Procedure:

3-Brompropyn-1-ol (**4a**; 1.7 ml, 0.19 mmol) is added dropwise to a stirred solution of copper(I) chloride (10 mg), hydroxylamine hydrochloride (50 mg) and undecynoic acid (**2**; 3.64 g, 20 mmol) in methanol (10 ml)/ethylamine (9 ml) mixture cooled in a water bath. If the solution turns blue, more hydroxylamine hydrochloride is added to reduce copper(II). After 15 min, the pale solution is extracted with ether (1  $\times$  20 ml) and the aqueous phase is acidified with 5 normal hydrochloric acid (25 ml). The hydroxy acid **5a** formed is collected by suction and recrystallised from cyclohexane; yield: 3.54 g (75%); m.p. 84°C.

C<sub>14</sub>H<sub>20</sub>O<sub>3</sub>      calc.      C 71.9      H 8.7  
(236.3)              found      71.8      8.7

I.R. (Film):  $\nu$  = 3150 (OH), 2600 (OH), 1680 cm<sup>-1</sup> (C=O).

U.V. (C<sub>2</sub>H<sub>5</sub>OH):  $\lambda_{\max}$  = 233 ( $\epsilon$  = 267), 245.6 ( $\epsilon$  = 407), 258.9 nm ( $\epsilon$  = 420).

<sup>1</sup>H-N.M.R. (CCl<sub>4</sub>):  $\delta$  = 1.4 (m, 12 H, CH<sub>2</sub>); 2.4 (m, 2 H, CH<sub>2</sub>-C $\equiv$ C); 2.25 (m, 2 H, CH<sub>2</sub>-COOH); 4.4 (s, 2 H, CH<sub>2</sub>OH); 8.0 (s, 1 H, OH); 14.0 ppm (s, 1 H, COOH).

M.S. (70 eV):  $m/e$  = 236 (M<sup>+</sup>).

#### 14-Hydroxytetradecanoic Acid (**6a**); Typical Procedure:

A solution of 14-hydroxytetradeca-10,12-diynoic acid (**5a**; 1.18 g, 5 mmol) in methanol (30 ml) is hydrogenated in the presence of platinum oxide (200 mg) as catalyst at 1 atmosphere pressure. After total absorption of hydrogen is over (about 1 h), the platinum is recovered by filtration and the methanol is evaporated to give **6a**; yield: 2.39 g (98%); m.p. 91°C (cyclohexane) (Ref.<sup>7a</sup>, m.p. 91°C).

I.R. (Film):  $\nu$  = 3400 (OH), 2600 (OH), 1700 cm<sup>-1</sup> (C=O).

<sup>1</sup>H-N.M.R. (CDCl<sub>3</sub>):  $\delta$  = 1.45 (m, 22 H, CH<sub>2</sub>); 2.5 (m, 2 H, CH<sub>2</sub>COOH); 3.7 (s, 2 H, CH<sub>2</sub>OH); 5.85 (s, 1 H, OH); 13.85 ppm (s, 1 H, COOH).

M.S. (70 eV):  $m/e$  = 213 (M<sup>+</sup> - CH<sub>2</sub>OH).

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