8-Methyl-5,6,7,8-tetrahydrocoumarin

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Acid-catalysed cyclodehydration of β-(2-keto-3-methylcyclohex-3-enyl)propionic acid proceeded efficiently to 8-methyl-5,6,7,8-tetrahydrocoumarin.

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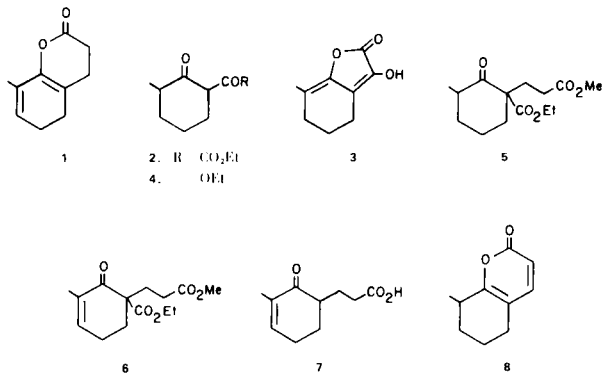
We were interested in the possible participation of the enol lactone (**1**) in Diels-Alder addition reactions. Other enol esters have been shown to be successful diene components in these reactions (1).

Acylation of 2-methylcyclohexanone with ethyl oxalate gave the glyoxylate (**2**) together with the enol lactone (**3**) (2). Thermal decarbonylation of **2** gave **4** which added to methyl acrylate to give the keto diester (**5**). Bromination of **5** and dehydrobromination of the product gave **6**, the nmr spectrum of which showed the presence of a vinyl proton centered at ~ δ 6.6. The infrared spectrum had carbonyl absorptions at 1740 and 1675 cm^{-1} for the ester and α,β-unsaturated keto functions, respectively. Hydrolysis of this keto diester followed by decarboxylation gave β-(2-keto-3-methylcyclohex-3-enyl)propionic acid (**7**). Attempted formation of the enol lactone (**1**) by acid catalysed dehydration of **7** gave a product whose nmr spectrum showed an AB quartet characteristic of α-pyrones (3). The signal ascribed to the methyl function appeared as a doublet (J = 7 Hz) at δ 1.27 indicating that double bond migration had occurred. The infrared spectrum of the product showed absorption at 1740 cm^{-1} with a shoulder at 1730 cm^{-1} in accord with reported α-pyrone carbonyl absorptions (4).

Hence dehydration of **7** was accompanied by isomerization to give the tetrahydrocoumarin (**8**). This unexpected and extensive rearrangement was evidently a very favoured process as no reaction conditions could be found under which intermediate dehydration products could be detected.

The sequence described represents an efficient synthesis of 5,6,7,8-tetrahydrocoumarins, few methods of preparation of which exist in the literature (5).



1 2. R = CO_2Et 4. R = OEt 3 5 6 7 8

EXPERIMENTAL

Melting points were determined on a Kofler block. Infrared spectra were measured as solutions in carbon tetrachloride on a Perkin Elmer Infracord 137G. Mass spectra were determined with a Varian MAT-CH7 spectrometer at 70 eV while nmr spectra were measured using a Varian A60A instrument. Elemental analyses were performed by the Australian Microanalytical Service, Melbourne.

Methyl β-(1-Ethoxycarbonyl-2-keto-3-methylcyclohexyl)propionate (**5**).

Acylation of 2-methylcyclohexanone (224 g.) with ethyl oxalate (292 g.) according to the literature (2) gave the crude glyoxylate (**2**) (400 g.). Distillation of the product from ground soda glass gave ethyl 2-keto-3-methyl-cyclohexane carboxylate (**4**) as a yellow oil (156 g.), b.p. 80°/0.5 mm. (lit. (2) b.p. 115°/12 mm.).

Crystallization of the pot residue from benzene gave the enol lactone (**3**) as needles, m.p. 141° (lit. (2) m.p. 141°); nmr (deuteriochloroform) δ: 1.88 (s, 3, CH_3); 1.50-2.04 (m, 2, CH_2); 2.07-2.50 (m, 2, C=C-CH_2); 2.58 (br t, J = 6.5 Hz, 2, C=C-CH_2); 7.00 (br s, 1, OH).

The keto ester (**4**) (123 g.) was added to potassium (1.6 g.) in *t*-butyl alcohol (250 ml.) under nitrogen. A solution of methyl acrylate (58 g.) in *t*-butyl alcohol (100 ml.) was then added dropwise and the solution was stirred at room temperature for 12 hours then poured into 1% hydrochloric acid and extracted with chloroform. The chloroform extract was washed with water, dried and evaporated to give the keto diester (**5**) as an oil (183.6 g.) b.p. 150°/2.5 mm; nmr (carbon tetrachloride) δ: 0.99 (d, J = 6.5 Hz, 3, CH_3); 1.28 (t, J = 7.5 Hz, 3, $CO_2CH_2CH_3$); 1.35-2.60 (m, 11, CH_2 and CH); 3.62 (s, 3, OCH_3); 4.18 (q, J = 7.5 Hz, 2, CO_2CH_2).

Methyl β-(1-Ethoxycarbonyl-2-keto-3-methylcyclohex-3-enyl)propionate (**6**).

A solution of bromine (109 g.) in carbon tetrachloride (300 ml.) was added rapidly to a stirred solution of the keto diester (**5**) (183.6 g.) in carbon tetrachloride (1000 ml.) at -10°. The solution was allowed to warm to room temperature and after the colour had dissipated, solid sodium bicarbonate was added then the solution was poured into water (1000 ml.). The organic layer was separated, washed with water, dried and evaporated to give methyl β-(3-bromo-1-ethoxycarbonyl-2-keto-3-methylcyclohexyl)-propionate as a pale yellow oil (222 g.); nmr (carbon tetrachloride) δ: 1.27 (t, J = 7.5 Hz, 3, $CO_2CH_3CH_3$); 1.82 (br s, 3, CH_3); 1.68-2.76 (m, 10, CH_2); 3.61 (s, 3, OCH_3); 3.90-4.34 (m, 2, CO_2CH_2); ir ν: 1720 (ketone carbonyl); 1740 cm^{-1} (ester carbonyl).

The crude bromo ketone (222 g.) was dissolved in dimethylformamide (1000 ml.) under nitrogen and a mixture of lithium chloride (81.1 g.) and lithium carbonate (141 g.) was added. The mixture was stirred at 100° for 5 hours then poured into water (1000 ml.) and extracted with ether. The extract was washed with 2% hydrochloric acid, then with water, dried and evaporated to give a dark oil (156.3 g.). Distillation of this oil gave methyl β-(1-ethoxycarbonyl-2-keto-3-methylcyclohex-3-enyl)propionate (**6**) as

an oil (140 g.), b.p. 126-128°/0.05 mm.; nmr (carbon tetrachloride) δ: 1.22 (t, J = 7.5 Hz, 3, $CO_2CH_2CH_3$); 1.73 (br d, J = 2 Hz, 3, C=C-CH_3); 1.84-2.61 (m, 8, CH_2); 3.60 (s, 3, OCH_3); 4.15 (q, J = 7.5 Hz, 2, CO_2CH_2); 6.48-6.77 (m, 1, C=CH); ir ν: 1675 (ketone carbonyl); 1740 cm^{-1} (ester carbonyl).

Anal. Calcd. for $C_{14}H_{20}O_5$: C, 62.7; H, 7.5. Found: C, 62.5; H, 7.4.

β-(2-Keto-3-methylcyclohex-3-enyl)propionic Acid (**7**).

A solution of potassium hydroxide (5 g.) in water (25 ml.) was added to a solution of the keto diester (**6**) (10 g.) in ethanol (25 ml.) under nitrogen. The mixture was refluxed for 48 hours then acidified with 10% hydrochloric acid and extracted with ether. The extract was washed with water, dried and evaporated to give β-(2-keto-3-methylcyclohex-3-enyl)propionic acid (**7**) as an oil (6.8 g.). The analytical sample was distilled, b.p. 100°/0.5 mm; nmr (carbon tetrachloride) δ: 1.74 (br d, J = 2 Hz, 3, C=C-CH_3); 1.47-2.69 (m, 9, CH_2 and CHCO); 6.60-6.83 (m, 1, C=CH); 13.03 (s, 1, OH); ir ν: 1670 (ketone carbonyl); 1710 (acid carbonyl); 3250 cm^{-1} (OH).

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.8; H, 7.6. Found: C, 65.9; H, 7.7.

The *p*-bromophenacyl ester of this acid crystallized from aqueous methanol melted at 74.5-75°.

Methyl β-(2-Keto-3-methylcyclohex-3-enyl)propionate.

The keto acid (**7**) (2 g.) was treated with an excess of ethereal diazomethane to give methyl β-(2-keto-3-methylcyclohex-3-enyl)-propionate as an oil (2 g.), b.p. 72°/0.01 mm; nmr (carbon tetrachloride) δ: 1.72 (br d, J = 2 Hz, 3, C=C-CH_3); 1.80-2.61 (m, 9, CH_2 and CHCO); 3.64 (s, 3, OCH_3); 6.50 (m, 1, C=CH); ir ν: 1680 (ketone carbonyl); 1740 cm^{-1} (ester carbonyl).

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.3; H, 8.2. Found: C, 67.2; H, 8.2.

8-Methyl-5,6,7,8-tetrahydrocoumarin (**8**).

A solution of the keto acid (**7**) (1 g.) and *p*-toluenesulphonic acid (0.4 g.) in benzene (40 ml.) was refluxed with continuous removal of water using a Dean and Stark apparatus. The cooled mixture was washed successively with saturated sodium bicarbonate solution and water, then evaporated to give 8-methyl-5,6,7,8-tetrahydrocoumarin (**8**) as an oil (0.85 g.), b.p. 63°/0.01 mm; nmr (carbon tetrachloride) δ: 1.27 (d, J = 7 Hz, 3, CH_3); 1.38-2.88 (m, 7, CH_2 and C=C-CH); 5.95 (d, J = 10 Hz, 1, H3); 7.05 (d, J = 10 Hz, 1, H4); ir ν: 1740, 1730 (sh) cm^{-1} (carbonyl); ms m/e (relative abundance): 164 (100), 136 (83), 121 (100), 108 (60%). $C_{10}H_{12}O_2$ requires M^+ 164.0837; Found: M^+ 164.0837.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.1; H, 7.4. Found: C, 72.6; H, 7.3.

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