COMMUNICATIONS

Synthesis of 2-Oxo-3-hydroxy-Δ^4-alkenes (Unsaturated Acyloins)

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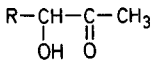
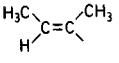
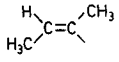
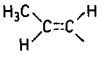
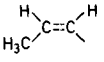
For a study of spin delocalization in unsaturated semidiones the precursors **1a–j** were required[1].

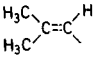


1a R = $H_2C{=}CH-$ **1f** R = 

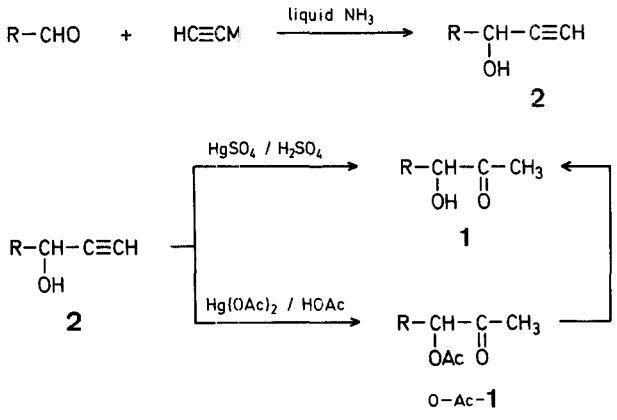
b R =  **g** R = 

c R =  **h** R = 

d R =  **i** R = $H_3C-C{\equiv}C-$

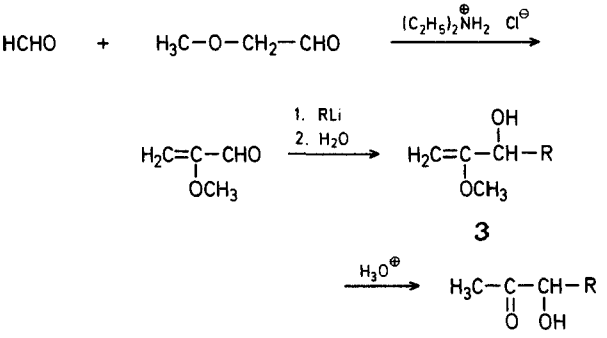
e R =  **j** R = $HC{\equiv}C-CH_2-$

The general synthesis of Scheme **A** had been used previously for the synthesis of **1h**[2] and the acetates of **1a** and **1c**[3]. We were able to extend this synthesis to **1b** and **1f** but it could not be used to prepare **1d** or **1g** (aldehydes unknown) or **1i** and **1j**.



Scheme **A**

Acyloins **1g**, **i**, **j** (and **1d** by partial hydrogenation of **1i**) were prepared by a new method (Scheme **B**) wherein the substituent R is introduced as an organometallic reagent.

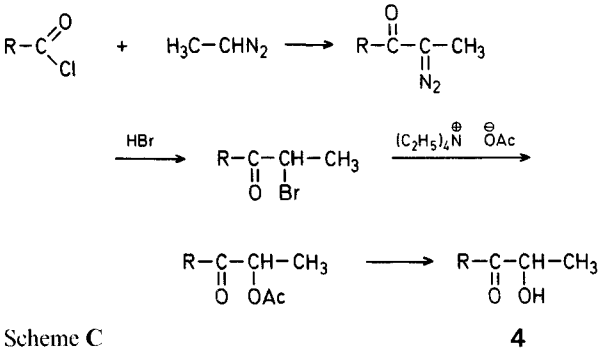


Scheme **B**

Since the hydrolysis **1**-acetate to **1** is often difficult, Scheme **B** is usually preferable to Scheme **A** if the underivatized acyloin is desired. However, in the case of R = vinyl the yield of **1** from Scheme **B** was < 15% and **1** was difficult to isolate in pure form.

The table lists analytical data for **1a–j**.

The synthesis of 2-hydroxy-3-oxo-Δ^4-alkenes (**4**) by Scheme **C** was briefly investigated.



Scheme **C**

1. $HOCH_2-CH_2OH$ / Tos-OH / $HC(OCH_3)_3$
2. KOH / $HOCH_2-CH_2OH$
3. $H_3O^{\oplus}$

Although the method worked for the synthesis of **4e** it failed for other unsaturated acyloins. Moreover, acyloins **4** (e.g. **4a**[6]) when treated with strong base were less efficient than the acyloins **1** as precursors to semidiones, possibly because of the base-catalyzed elimination of water.

3-Acetoxy-4-methyl-2-oxopent-2-ene (1 b-Acetate):
3-Hydroxy-4-methyl-pent-4-en-1-yne[8] (44.7 g, 465 mmol) in acetic acid (30 ml) was added (15 min) to a solution of yellow

mercuric oxide (8.65 g, 40 mmol) in acetic acid (130 ml) at 90° with stirring. After 3.5 hr, the mixture was filtered, neutralized with conc. aqueous potassium carbonate at 0°, and then extracted with ether (5 × 100 ml). The extract was washed with aqueous sodium hydrogen carbonate, water, aqueous sodium chloride, and dried with Molecular Sieves before distillation through a Vigreux column to yield the acetate.

E-3-Hydroxy-4-methyl-2-oxohex-4-ene (1f):
Reaction of tigaldehyde and sodium acetylenide in ammonia solution gave E-3-hydroxy-4-methyl-hex-4-en-1-yne. The acetylenic alcohol (15 g, 138 mmol) in methanol (40 ml) was added (15 min) to a stirred mixture of yellow mercuric oxide (7.0 g, 324 mmol), water (150 ml), methanol (100 ml), and conc. sulfuric acid (15 ml) at 10°. The mixture was warmed to 60° (1 hr), filtered, and extracted with ether (5 × 100 ml). The extract was washed with water, 10% aqueous sodium carbonate, water, and saturated aqueous sodium chloride, dried with Molecular Sieves, and vacuum-distilled through a Vigreux column.

3-Hydroxy-2-oxo-4-methylpent-1-ene (1b):
The acetate of **1b** (12.7 g, 81 mmol) was heated to 150° (1 hr) with ethylene glycol (15.7 g), triethyl orthoformate (29.5 g), dioxane (20 ml), and *p*-toluenesulfonic acid[10] (1 g). A solution of potassium hydroxide (8 g) in ethylene glycol (30 ml) was added and the resultant mixture stirred for 15 hr at 150° before hydrolysis with ice water (150 g) followed by extraction with ether (5 × 50 ml). The ether was evaporated and to the residue dissolved in methanol (20 ml) there was added a mixture of 50% aqueous sulfuric acid (20 ml) and methanol (20 ml). After 15 min, water (150 ml) was added and the solution neutralized with 20% aqueous sodium hydroxide. Extraction with ether (5 × 50 ml) followed by washing with water and saturated aqueous sodium chloride gabe **1b** after drying with Molecular Sieves and distillation.

2-Methoxyacrolein[11]:
An improved synthesis utilized a 500 ml 4-necked flask equipped with a stirrer, dropping funnel, and the electrodes of a pH meter. A mixture of diethylamonium chloride (109.6 g, 1 mol), 37% formaldehyde (81 g, 1 mol), and water (50 ml) was stirred for 30 min at 25° and then neutralized to pH 7.0 with 10% aqueous sodium hydrogen carbonate. Methoxyacetaldehyde (1 mol) in aqueous solution (analyzed by the oximination method) containing hydroquinone (0.4 g) was then introduced at 25° over 50 min with constant control of the pH at 7.0. After 90 min at 60°, the solution was cooled, saturated with sodium chloride,

Table. Properties of Acyloins

Acyloin	Yield %	b.p./torr[a]	Mol. Wt. calc.	measured[b]	^{1}H-N.M.R. (CCl_4) δ =
1a, acetate	86 (Scheme A)[c]	90–93°/21	142.063	142.063	2.08 (s, 3H), 2.11 (s, 3H), 5.12–5.81 (m, 4H)
1b, acetate	85 (Scheme A)[c]	84–85°/14	156.079	156.080	1.72 (d, 3H, J = 1.5 Hz), 2.08 (s, 6H), 5.00–5.25 (m, 2H), 5.27 (broad s, 1H)
1b[7]	32[d]	40–43°/5	114.068	114.068	1.57 (d of d, 3H, J = 1.50, 0.92 Hz), 2.14 (s, 3H), 3.84 (broad s, 1H), 4.41 (m, 1H), 5.05 (p, 1H, J = 1.50), 5.16 (d of q, 1H, J = 1.50, 0.92 Hz)[e]
1c, acetate	60[e]	97–100°/19	156.079	156.078	1.75 (d of m, 3H, J = 6.2 Hz), 2.03 [s, 6H; split by Eu(fod)$_3$], 5.23 (d of m, 1H, J = 7.4 Hz), 5.39 (d of d of q, 1H, J = 16, 7,4, 1.4 Hz), 5.91 (d of q, 1H, J = 16, 6.2 Hz)[e]
1c	15[d]	53–55°/4.5	114.068	114.068	1.77 (d of m, 3H, J = 6.5 Hz), 2.14 (s, 3H), 3.60 (m, 1H), 4.41[d of m (with D_2O), 1H, J = 7 Hz], 5.36 (d of d, 1H, J = 15, 7 Hz) 5.91 (d of q, 1H, J = 15, 6.5 Hz)[e]
1d	80[f]	35–37°/1	114.068	114.068	1.80 (d of d, 3H, J = 7.0, 1.6 Hz), 2.07 (s, 3H), 3.86 (broad s, 1H), 4.78 (d of m, 1H, J = 9.0 Hz), 5.09 (d of d of q, 1H, J = 10.5, 9.0, 1.6 Hz), 5.76 (d of q of d, 1H, J = 10.5, 7.0, 1 Hz)[e]
1f, acetate	80[e]	70–73°/3	170.094	170.096	1.57 (m, 3H, J ~ 1.5 Hz), 1.69 (d of m, 3H, J = 7, ~ 1.5 Hz), 2.05 (s, 3H), 2.07 (s, 3H), 5.21 (s, 1H), 5.71 (q of m, 1H, J = 7 Hz)[e]
1f	51[d]	53–55°/4	128.084	128.081	1.45 (p, 3H, J = 1.2 Hz), 1.70 (d of q, 3H, J = 6.8, 1.2 Hz), 2.08 (s, 3H), 3.63 (m, 1H), 3.46 (m, 1H), 5.68 (q of m, 1H, J = 6.8 Hz)[e]
1g	30[g]	52–54°/5.5	128.084	128.082	1.48 (p, 3H, J = 1.4 Hz), 1.80 (d of q, 3H, J = 6.8, 1.4 Hz), 2.08 (s, 3H), 3.37 (broad s, 1H), 4.93 (s, 1H), 5.50 (q of m, 1H, J = 6.8 Hz)
1h, acetate	75[e]	117–119°/5.5	196.110	196.112	1.4–2.2 [m (s at 2.06), 14H], 5.20 (s, 1H), 5.86 (m, 1H)
1h	60[e]	77–78°/1.6	154.099	154.102	1.4–2.3 [m (s at 2.11), 11H], 3.54 (m, 1H), 4.35 (m, 1H), 5.86 (m, 1H)
1i	44[g]	63–65°/3	112.052	112.051	1.87 (d, 3H, J = 2.7 Hz), 2.30 (s, 3H), 4.32 (broad s, 1H), 4.66 (q, 1H, J = 2.7 Hz)
1i, acetate	62[h]	61–62°/0.7	154.063	154.064	1.92 (d, 3H, J = 2.7 Hz), 2.11 (s, 3H), 2.21 (s, 3H), 5.50 (q, 1H, J = 2.7 Hz)
1j	46[g]	73–74°/10	112.052	112.053	2.04 (t, 1H, J = 2.5 Hz), 2.24 (s, 3H), 2.59 (d of d, 2H, J = 5.5, 2.5 Hz), 3.87 (m, 1H), 4.25 [t (with D_2O), 1H, J = 5.5 Hz)
4e, acetate	47[i]	76–78°/13	170.094	170.094	1.31 (d, 3H, J = 7 Hz), 1.93 (broad s, 3H) 2.15 (broad s, 3H), 2.08 (s, 3H), 4.94 (q, 1H, J = 7 Hz), 6.2 (m, 1H)

[a] Uncorrected.
[b] High-resolution mass spectrometry (MS-902).
[c] From acetylenic alcohol, Scheme A.
[d] From the acetate.
[e] 100 MHz spectra.
[f] Hydrogenation of **1i**.
[g] From 2-methoxyacrolein, Scheme B.
[h] Esterification of **1i**.
[i] From acid chloride, Scheme C.

and extracted with ether (10×60 ml). The extract was washed with saturated aqueous sodium chloride, dried with Molecular Sieves, and distilled through a Vigreux column; yield: 51.1 g (59%); b.p. 37–40°/20 torr.

^{1}H-N.M.R. (CCl_4): $\delta = 3.68$ (s, 3H), 5.05 (s, 2H), 9.38 (s, 1H).

3-Hydroxy-2-oxo-4-hexyne (1i):
Under nitrogen, a suspension of propynyllithium (25.8 g, 560 mmol; Foote Mineral Co.) in purified tetrahydrofuran (500 ml, distilled from benzophenone ketyl) was stirred at −35°. Methoxyacrolein (47.1 g, 545 mmol) in tetrahydrofuran (100 ml) was added during 30 min at −35°. The temperature was allowed to slowly rise to 10° before hydrolysis with ice (200 g) and 3 *N* hydrochloric acid. The tetrahydrofuran was removed with a rotary evaporator and the residue extracted with ether (5×80 ml). The extract was washed with saturated aqueous sodium chloride, dried with Molecular Sieves, and distilled through a Vigreux column; yield: 26.9 g. The product readily dimerized to a solid from which the acyloin can be partially recovered by distillation.

3-Acetoxy-2-oxo-4-hexyne:
To acyloin **1i** (4.86 g, 43.5 mmol) in ether (40 ml) at 0° was added pyridine (3.56 g, 45 mmol) followed by acetyl chloride (3.55 g, 45 mmol) in benzene (40 ml) over an 8 min period. The mixture was stirred at 25° for 12 hr before filtration, followed by washing with water, 10% aqueous sulfuric acid, water, and saturated aqueous sodium chloride. The solution was dried with magnesium sulfate and distilled through a Vigreux column; yield: 4 g of **1i**-acetate.

3-Hydroxy-2-oxo-*cis*-hex-4-ene (1d):
Acyloin **1i** was hydrogenated in methanol (100 ml) in a low-pressure vortex hydrogenator in the presence of 10% palladium-on-charcoal (200 mg) and quinoline (200 ml). Distillation yielded **1d**.

***Z*-3-Hydroxy-4-methyl-2-oxohex-4-ene (1g):**
Z-2-Bromo-2-butene[12] was converted to the lithium reagent[13] which was added to methoxyacrolein in ether at −30°. After hydrolysis, **1g** was isolated by distillation.

3-Hydroxy-2-oxo-5-hexyne (1j):
3-Hydroxy-2-methoxyhex-1-en-5-yne (**3j**): The Grignard reagent from propargyl bromide[14] (42 g, 353 mmol) in ether (300 ml) was cooled to −40° and a solution of methoxyacrolein (30 g, 350 mmol) in ether (70 ml) was added over 20 min. The mixture was stirred an additional 30 min at −40°, hydrolyzed with water (60 ml) at a temperature below −30°, and then allowed to warm to 25°. The mixture was filtered, the solid washed with ether (5×80 ml), and the filtrate distilled through a Vigreux column; yield: 33 g (75%); b.p. 70–74°/8 torr.

^{1}H-N.M.R. (CCl_4): $\delta = 1.89$ (t, 1H, $J = 2.5$ Hz), 2.43 (d of m, 2H, $J = 6$ Hz), 2.65 (m, 1H), 3.52 (s, 3H), 4.6 (m, 1H), 3.98 (d, 1H, $J = 2.5$ Hz), 4.18 (d, 1H, $J = 2.5$ Hz).

Mass spectrum: M^+ at $m/e = 126.070$ (calc. for $C_7H_{10}O_2$, 126.068).

3-Hydroxy-2-oxo-5-hexyne: Hydrolysis of the enol ether was accomplished by stirring with 5% sulfuric acid at 0° for 1 hr. The solution was then saturated with sodium chloride, and extracted with ether 6×40 ml). The extract was washed, dried (Molecular Sieves), and distilled; yield: 61%.

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