Cleavage of α-Ketoacetals by Catalysis with the Solid Superacid Nafion-H®

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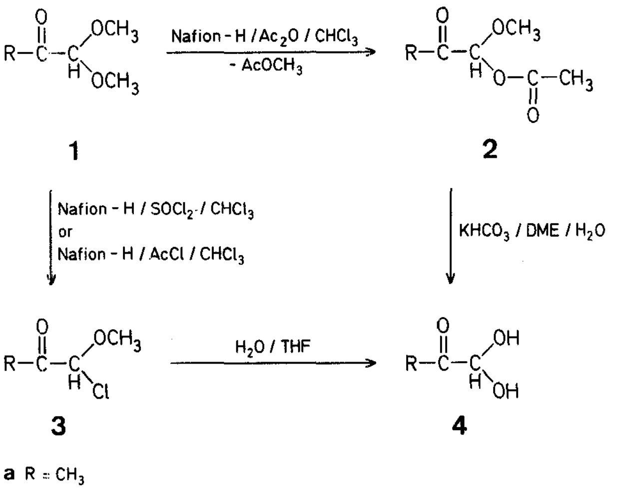
The acid hydrolysis of α-ketoacetals proceeds with great difficulty and does not constitute a practical method for the preparation of the unstable α-ketoaldehydes from their acetals. The destabilization of the required carbenium ion intermediate by the neighboring keto group accounts for this phenomenon[1].

Olah et al.[2,3] have demonstrated the utility and practicality of the perfluorinated solid superacid resin Nafion-H® for the preparation of acetals and thioacetals. We now report that Nafion-H can catalyze the cleavage of α-ketoacetals (**1**) to α-acetoxy-α-methoxymethyl ketones (**2**) and α-chloro-α-methoxymethyl ketones (**3**) in 90–100% yield.



a R = CH_3
b R = C_6H_5–CH=CH–

Not only does the use of the resin make for a simple procedure, but attempts to utilize soluble acids for these reactions led to destruction of the very sensitive α-ketoaldehydes **4**. Compounds **2** and **3** are readily converted into the α-ketoaldehyde hydrates **4**, the former by hydrolysis with potassium hydrogen carbonate in tetrahydrofuran/water, the latter by solvolysis with water. The two steps constitute the formal hydrolysis of α-ketoacetals.

Small-scale distillations (< 100 mg) were performed using a cold-finger apparatus, larger-scale distillation using a 10 in Vigreux column. All samples showed a single spot on T.L.C. on silica gel except methyl- and styrylglyoxal, which form mixtures with their hydrates. ^{1}H-N.M.R. spectra were performed on a Chicago-built 500 MHz Instrument.

α-Acetoxy-α-methoxyacetone (2a):

A solution of pyruvaldehyde 1-(dimethyl acetal) (**1a**, α,α-dimethoxyacetone; 93 mg, 0.78 mmol) and acetic anhydride (0.3 ml, 3.15 mmol) containing powdered Nafion-H (37.0 mg, 0.077 mmol) in deuteriochloroform (0.5 ml) is vigorously stirred at 25 °C under argon for 18 h. The solution is filtered, the catalyst washed with methanol (5 × 0.5 ml), and the combined solutions allowed to remain at 25 °C for 3 h. Water (3 ml) is then added and the mixture extracted with ether (3 × 2 ml). The combined organic phases are washed with pH 7.0 phosphate buffer (3 × 5 ml) and with water (2 × 5 ml) and are dried with sodium sulfate. The solvent is removed and the residual crude product **2a** (100 mg) is purified by distillation in vacuo; yield: 89 mg (79%); b.p. 80–80.5 °C/20 torr.

$C_6H_{10}O_4$	calc.	C 49.32	H 6.85
(146.1)	found	49.60	7.09

M.S.: $m/e = 146$ (M^+), 114 ($M - OCH_3$).

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 5.72$ (s, 1 H); 3.57 (s, 3 H); 2.29 (s, 3 H); 2.22 ppm (s, 3 H).

4-Acetoxy-4-methoxy-1-phenylbuten-3-one (2b):

Styrylglyoxal 1-(Dimethyl Acetal) (**1b**, *4,4-Dimethoxy-1-phenylbuten-3-one*): A solution of styrylglyoxal[2] (590 mg, 3.69 mmol) in methanol (4 ml) is refluxed with Nafion-H (200 mg) for 10 h. The catalyst is filtered, washed with methanol (4 × 1 ml) and the combined deep-yellow filtrates evaporated to dryness in vacuo, leaving a light brown oil (670 mg, 94%). A small amount of colored impurity is removed by filtration of its solution in hexane/ethyl acetate (3 : 2) through a bed of silica gel (2 g).

$C_{12}H_{14}O_3$ (206.2)

M.S.: $m/e = 175$ ($M - OCH_3$).

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 7.72$ (d, 1H, $J = 16$ Hz); 7.6–7.2 (m, 5H); 7.01 (d, 1H, $J = 16$ Hz); 4.76 (s, 1H); 3.49 ppm (s, 6H).

4-Acetoxy-4-methoxy-1-phenylbuten-3-one (**2b**): A solution of acetal **1b** (446 mg, 2.2 mmol) and acetic anhydride (0.70 ml, 7.38 mmol) in deuteriochloroform (1.5 ml) containing Nafion-H (150 mg) is treated and worked up as described for **2a**; yield of **2b**: 461 mg (90%); b.p. 50–70°C (bath)/0.05 torr.

$C_{13}H_{14}O_4$	calc.	C 66.67	H 5.98
(234.25)	found	66.89	6.18

M.S.: $m/e = 235$ ($M + 1$); 191 ($M - CO—CH_3$); 175 ($M - O—CO—CH_3$).

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 7.70$ (d, 1H, $J = 15$ Hz); 7.57–7.26 (m, 5H); 6.98 (d, 1H, $J = 15$ Hz); 6.04 (s, 1H); 3.63 (s, 3H); 2.25 ppm (s, 3H).

α-Chloro-α-methoxyacetone (3a):

Pyruvaldehyde 1-(dimethyl acetal) (**1a**; 3.5 g, 25.3 mmol), thionyl chloride (6.5 ml, 89.4 mmol), and Nafion-H (0.95 g, 0.79 mmol) are stirred in chloroform (10 ml) under dry nitrogen at 25°C for 10 h. The mixture is filtered, the catalyst washed with chloroform, and the mixture subjected to fractional distillation under atmospheric pressure; yield: 3.3 g (91%); b.p. 139–140°C/770 torr.

$C_4H_7ClO_2$	calc.	C 39.18	H 5.71	Cl 28.93
(122.6)	found	38.93	5.89	29.17

M.S.: $m/e = 122$, 124 (M^+); 87 ($M - Cl$).

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 5.50$ (s, 1H); 3.63 (s, 3H); 2.34 ppm (s, 3H).

4-Chloro-4-methoxy-1-phenylbuten-3-one (3b):

Styrylglyoxal 1-(dimethyl acetal) (**1b**; 537 mg, 2.6 mmol), thionyl chloride (0.40 ml, 5.5 mmol), and Nafion-H (200 mg) are stirred in deuteriochloroform (2.2 ml) till completion of the reaction as monitored by ^{1}H-N.M.R. Chloroform (10 ml) is then added, the solution washed with water (3 x 5 ml), and dried with sodium sulfate. Evaporation of the solvent in vacuo furnishes crude **3b** as a brown oil; yield: 521 mg. The product may be purified by distillation in vacuo; yield of pure **3b** from 66 mg of crude **3b**: 41 mg (corresponding to 59% yield based on **1b**).

$C_{11}H_{11}ClO_2$ (210.65)

M.S.: $m/e = 210$, 212 (M^+); 175 ($M - Cl$).

^{1}H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 7.79$ (d, 1H, $J = 16$ Hz); 7.61–7.24 (m, 5H); 7.07 (d, 1H, $J = 16$ Hz); 5.80 (s, 1H); 3.72 ppm (s, 3H).

The distilled chlorides **3a, b** are stable for long periods of time when stored under argon. The thionyl chloride may be replaced by an equivalent amount of acetyl chloride (freed from free acids by shaking with dry potassium carbonate).

Styrylglyoxal and its Hydrate (4b):

From Compound **3b**: A solution of 4-chloro-4-methoxy-1-phenylbuten-3-one (**3b**; 15.9 mg, 0.08 mmol) in tetrahydrofuran/water (3 : 1; 0.33 ml) is heated at 65 °C for 6.5 h. The solution is then diluted with water (3 ml) and extracted with ether (3 x 2 ml), the ether washed with water (3 x 5 ml) and dried with sodium sulfate. Removal of the solvent furnishes a yellow oil (15 mg) which (according to ^{1}H-N.M.R. comparison with authentic material) consists of a 1+4 mixture of styrylglyoxal and its hydrate (**4b**).

From Compound **2b**: A solution of 4-acetoxy-4-methoxy-1-phenylbuten-3-one (**2b**; 25.0 mg, 0.11 mmol) in 0.15 molar potassium hydrogen carbonate in 1,2-dimethoxyethane/water (2/1; 2 ml) is stirred at 25 °C for 4 h. The mixture ist then diluted with water (2 ml) and extracted with ether (3 x 3 ml). The ether extracts are washed with water (2 x 5 ml) and dried with sodium sulfate. Removal of the solvent in vacuo leaves a nearly colorless oil (20.1 mg, 100%), whose ^{1}H-N.M.R. spectrum shows it to be mainly the hydrate **4b**. When the hydrolysis is conducted in dioxan/water or acetonitrile/water the product contains up to 25% of the free aldehyde.

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