

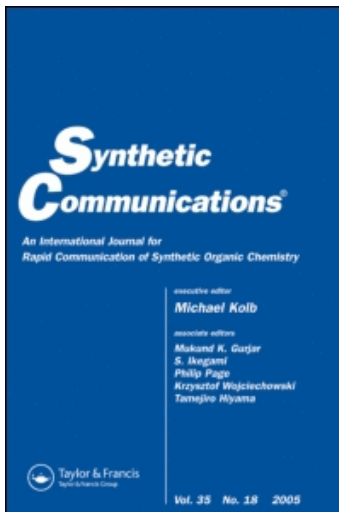
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An Improved Procedure for the Oxidation of Alkynols to Alkynoic Acids

B. C. Holland ^a; N. W. Gilman ^a

^a Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey

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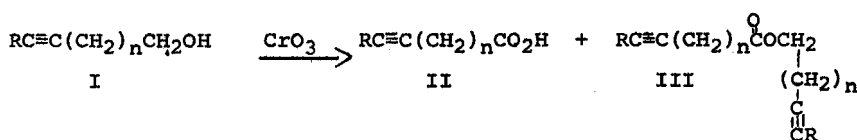
AN IMPROVED PROCEDURE FOR THE OXIDATION
OF ALKYNOLS TO ALKYNIC ACIDS

B.C. Holland and N.W. Gilman

Chemical Research Department, Hoffmann-La Roche Inc.

Nutley, New Jersey 07110

The chromic acid oxidation of alkynols I to the corresponding alkynic acids II is a well known process.¹ However, in most cases, the yield of the desired acid is poor to moderate (20-50%) due to the formation of the ester III as a by-product.

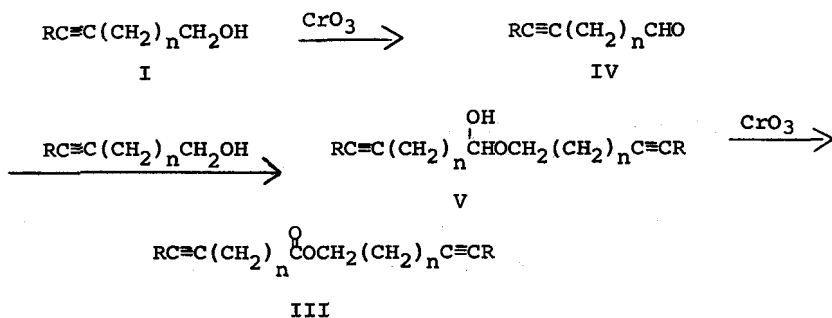


R=alkyl

n=any number

The ester III presumably is formed by the oxidation of a hemi-acetal V which is formed from the intermediate aldehyde IV and alcohol I, as shown².

As part of an investigation involving the synthesis of acetylenic acids, we also found that the chromic acid oxidation procedure gave substantial yields of unwanted esters.

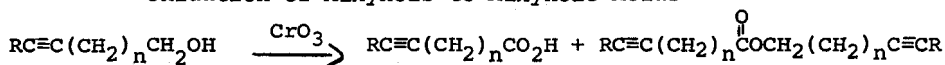


The oxidations were carried out by the addition of a solution of chromic anhydride in sulfuric acid to the alcohol in acetone. The crude reaction mixture was separated into acidic and neutral fractions which were purified by recrystallization and/or distillation; see Table I:

In order to improve the yields of the desired alkynoic acids, an inverse addition method (alcohol added to chromic acid) was developed. Presumably, this type of addition inhibits the formation of the hemi-acetal since the amount of

Table I

Oxidation of Alkynols to Alkynoic Acids



<u>R</u>	<u>n</u>	<u>Yield %</u>	<u>Yield %</u>
H	2	48 ^a	33
CH ₃ (CH ₂) ₆	1	32	42
CH ₃ (CH ₂) ₈	1	43	24

a) Yields are for purified products.

OXIDATION OF ALKYNOLS TO ALKYNIC ACIDS

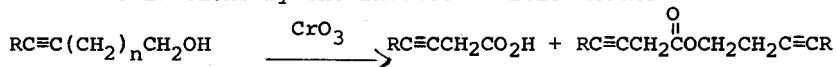
unoxidized alcohol present in the reaction mixture is kept at a minimum. The results obtained by this method are shown in Table II.

A limited study on the effect of acid strength, rate of addition and alcohol concentration on the oxidation reaction showed that the use of 10N H₂SO₄ with a slow rate of addition of the alcohol in acetone gave the best yields of alkynoic acids, see Table III.

Experimental: All melting points are corrected. IR spectra were determined on a PE-137 instrument and NMR spectra were determined as CDCl₃ solutions, using tetramethylsilane as an internal standard, on a Varian T-60 instrument. The microanalysis were performed by Dr. F. Scheidl of our Physical Chemistry Department. The oxidations of 4-pentyn-1-ol and of 3-undecyn-1-ol by both the standard and inverse addition methods are given as representative experiments. The CrO₃ was dried over P₂O₅ before use.

Table II

Oxidations by the Inverse Addition Method



<u>R</u>	<u>n</u>	<u>Yield, %</u>	<u>Yield, %</u>
H	2	78	<1
CH ₃ (CH ₂) ₆	1	73	12
CH ₃ (CH ₂) ₈	1	78	12

Table III
Effect of Acid Strength and Addition Time On
the Inverse Addition Oxidation of

Alkynols to Alkynoic Acids

<u>Alcohol</u>	<u>Concentration Alcohol/Acetone</u>	<u>Acid Strength</u>	<u>Addition Time</u>	<u>% Yield Acid Ester</u>
$\text{CH}_3(\text{CH}_2)_6\text{C}\equiv\text{CCH}_2\text{CH}_2\text{OH}$	1.0 M	3 N ^a	4 hr	> 50
$\text{CH}_3(\text{CH}_2)_6\text{C}\equiv\text{CCH}_2\text{CH}_2\text{OH}$	1.0 M	10 N	2 hr	18
$\text{CH}_3(\text{CH}_2)_6\text{C}\equiv\text{CCH}_2\text{CH}_2\text{OH}$	0.1 M	10 N	7 hr	73

a) The CrO_3 concentration was 1.0 M.

Based on all of the oxidations studied, the best yields of acids are obtained by the slow rate of addition of a dilute solution of the alcohol in acetone to a 1.0 M solution of CrO_3 in 10 N H_2SO_4 .

OXIDATION OF ALKYNOLS TO ALKYNIC ACIDS

Normal Addition Oxidations

4-Pentyn-1-ol³: To a stirred solution of 21 g (240 mmol) of 4-pentyn-1-ol in 125 ml of acetone, cooled to 5°, a solution of 50 g (500 mmol) of CrO₃ in 250 ml of 13 N H₂SO₄ was added slowly at such a rate that the internal temperature was maintained between 5 and 15°. After the addition was complete, the reaction mixture was stirred at 5-10° for 1.5 hr and then at room temperature for 1 hr. After concentration under reduced pressure (rotary evaporator), the residue was dissolved in H₂O and extracted with six 100 ml portions of ether. The ether extracts were combined, washed with H₂O, dried (Na₂SO₄) and concentrated to give a mixture of neutral and acidic products. The residue was dissolved in ether and extracted with two 150 ml portions of 3 N NaOH. The basic extracts were washed with a small amount of ether which was combined with the original ether phase. The combined ether solutions were dried (Na₂SO₄), and concentrated to give 8.3 g of crude product which was distilled to yield 6.7 g (33%) of 4-pentynyl-4-pentynoate as a colorless liquid, b.p. 70-72°/0.33 mm.^{1a} IR (neat): 3300 (sharp C≡C-H band), 1750 (strong C=O), and 1170 cm⁻¹; there was no hydroxyl absorption. NMR: δ 1.53-2.63 (overlapping m, 8 H, methylene protons), 2.62 (s, 2 H, ≡CH), 4.25 (t, 2 H, OCH₂). Found: C, 72.90; H, 7.33 (Calcd. for C₁₀H₁₂O₂: C, 73.15; H, 7.37)

The basic solutions were cooled, acidified with 3 N HCl and extracted well with ether. The ether extracts were

washed with brine, dried (Na_2SO_4) and concentrated to give 11.8 g (48%) of 4-pentynoic acid. Recrystallization of a small sample from ether/pet. ether gave the analytical sample, m.p. $54.5 - 56.5^\circ$ (lit., ^{1a}m.p. $57-58^\circ$). IR (KBr): 3280 ($\text{C}\equiv\text{C}-\text{H}$), 3500-2500 (broad OH), 1725 cm^{-1} ($\text{C}=\text{O}$). NMR: δ 1.97 (t, $J = 2$ cps, 1 H, $\text{C}\equiv\text{CH}$), 2.53 (t, $J = 2$ cps, 4 H, CH_2-CH_2), 11.13 (s, 1 H, OH). Found: C, 61.08; H, 5.89 (Calcd. for $\text{C}_5\text{H}_6\text{O}_2$: C, 61.22; H, 6.17).

3-Undecyn-1-ol⁴

The oxidation of 3-undecyn-1-ol (17.6 g, 105 mmol), was carried out as described above, and the crude product separated into neutral and acidic fractions.

The acidic fraction (7.9 g) was distilled to give 5.1 g (32%) of 3-undecynoic acid, b.p. $123-128/0.4$ mm. A small amount was recrystallized from pet. ether to give the analytical sample, m.p. $41-42.5^\circ$. IR (CHCl_3): 3600-2350 (broad OH), 1720 cm^{-1} (strong $\text{C}=\text{O}$). NMR: δ 0.90 (distorted t, 2 H, $\text{CH}_2\text{C}\equiv\text{C}$), 3.33 (t, 2 H, CH_2CO_2), 11.53 (s, 1 H, CO_2H). Found: C, 72.53; H, 9.91 (Calcd. for $\text{C}_{11}\text{H}_{18}\text{O}_2$: C, 72.49; H, 9.96).

The neutral fraction was chromatographed on silica gel using 4% ether in hexane as the eluting solvent. From the column 7.24 g (42%) of 3-undecynyl-3-undecynoate was collected as a faint yellow oil. A sample was bulb to bulb distilled to give the analytical sample. IR (neat): 2900 ($\text{C}=\text{C}-\text{H}$), 1750 ($\text{C}=\text{O}$), 1170 cm^{-1} . NMR: δ 0.88 (distorted t, 6 H, CH_3), 1.28

(m, 20 H, $-(\text{CH}_2)_5$), 1.87 - 2.67 (m, 6 H, $\text{CH}_2\text{C}\equiv\text{C}$), 3.23 (t, 2 H, CH_2CO), 4.17 (t, 2 H, OCH_2). Found: C, 79.78, 79.49; H, 11.15, 11.06 (Calcd. for $\text{C}_{22}\text{H}_{36}\text{O}_2$: C, 79.46; H, 10.91).

Inverse Addition Oxidations

4-Pentyn-1-ol: A solution of 8.4 g (100 mmol) of 4-pentyn-1-ol in 100 ml of acetone was added dropwise to a cooled solution of 20 g (200 mmol) of CrO_3 in 250 ml of 10 N H_2SO_4 , maintaining an internal temperature of $5-10^\circ$. The addition required 2 hr, and then stirring was continued for 1.5 hr. The typical workup procedure gave 52 mg (<1%) of 4-pentynyl-4-pentynoate and 7.65 g (78%) of 4-pentynoic acid.

3-Undecyn-1-ol: To a cooled solution of 10 g (100 mmol) of CrO_3 in 100 ml of 10 N H_2SO_4 , was added over 7 hr., a solution of 8.4 g (50 mmol) of 3-undecyn-1-ol in 500 ml of acetone. The internal temperature was maintained at $3-5^\circ$. The usual workup gave 1.1 g (12%) of 3-undecynyl-3-undecynoate and 6.7 g (73%) of 3-undecynoic acid.

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