

HALOGEN CATALYZED ACETYLENIC OXY-COPE REARRANGEMENT
IN N-METHYL-2-PYRROLIDONE SOLVENT
A NEW INDUSTRIAL PROCESS FOR PSEUDOIONONE AND ITS ANALOGUES

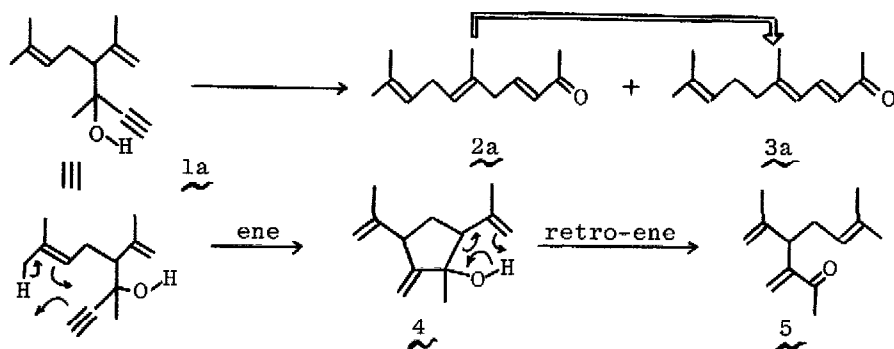
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Summary. Selective synthesis of pseudoionone was achieved by the acetylenic oxy-Cope rearrangement of 4-isopropenyl-3,7-dimethyl-6-octen-1-yn-3-ol (1) in N-methyl-2-pyrrolidone solvent containing a trace of hydrochloric acid, hydrobromic acid, iodine, ammonium bromide and ammonium chloride catalysts.

Recently we have developed a new industrial process for production of pseudoionone via acetylenic oxy-Cope rearrangement of 1a²⁾. As illustrated below, the thermolysis of 1a in neat system at 165°C for 5 hr under nitrogen atmosphere afforded a mixture of 2a+3a only in 45% yield (2a/3a=80/20). The main side reactions were the ene-reaction to yield 4 (25%) and the continued retro-ene reaction to yield 5 (5%). The previously reported modifications of 1,5-hexadien-3-ol system, such as siloxy-Cope³⁾ or anionic process⁴⁾ were of no use for increasing the yield of pseudoionone. The use of N-methyl-2-pyrrolidone (NMP) or DMSO solvent increased the yield of 2a+3a up to 68% and 72% respectively, with predominant formation of 2a. Unfortunately, however, the yield of ionone from 2a via acid catalyzed cyclization was extremely lower (50%) than from 3a (85%), which made it necessary to employ additional isomerization process of 2a→3a. In this report we wish to describe a selective one-pot synthesis of 3a from 1a via simultaneous acetylenic oxy-Cope rearrangement and double bond migration using NMP as solvent containing a trace of halogen catalysts.



Rearrangement of 1a⁵⁾ (0.1 mol) [165°C, 4 hr] in NMP solvent (twice by weight v.s. 1a) containing nickelacetylacetonate (1 mmol) which has been shown to be an excellent catalyst for isomerization of 2a→3a⁶⁾ resulted in failure (2a/3a=15/85; 40%) with accompaniment of high boiling products. Then we investigated the reaction by using various halogen catalysts which have been reported to be efficient for double bond conjugation⁷⁾. As represented in Table 1, the halogen catalyzed isomerization of 2a→3a proceeded selectively to give an equilibrium mixture of 2a/3a=3/97. Furthermore, the thermolysis of 1a (10 g) in NMP (30 g) containing 1N-HCl (0.35 ml) at 165°C for 5 hr afforded pseudo-ionone (2a/3a=3/97) in ca. 73% selectivity. Time-variation of the ratio of 2a/3a clearly indicated that double bond migration proceeded concurrently with the rearrangement. Similar results were also obtained by using other halogen catalysts (Table 2).

Table 1. Halogen catalyzed isomerization of 2a→3a.

Catalyst (mol % v.s. <u>2a</u>)	Solvent ^{a)}	Reaction condition	Conversion of <u>2a</u> ^{b)} ; %	Selectivity of <u>3a</u> ^{b)} ; %	Ratio of <u>2a</u> / <u>3a</u>
I ₂ (1.0)	CH ₃ OH	reflux 5 hr	97	100	3/97
(0.4)	NMP	165°C, 1hr	95	98	6/94
(0.2)	NMP	165°C, 5 hr	82	98	20/80
NH ₄ I (1.0)	NMP	165°C, 3 hr	85	82	30/70
NH ₄ Br (6.0)	C ₂ H ₅ OH	reflux 2 hr	45	95	57/43
1N-HCl (0.5)	NMP	165°C, 5 hr	98	99	4/96
0.4N-HBr (0.2)	NMP	165°C, 3 hr	96	98	6/94

a) Ratio of 2a/solvent=5/15 (g).

b) Conversion and selectivity were determined by G.L.C. Selectivity=[yield of 3a]/[conversion of 2a].

Table 2. Halogen catalyzed acetylenic oxy-Cope rearrangement of 1a).

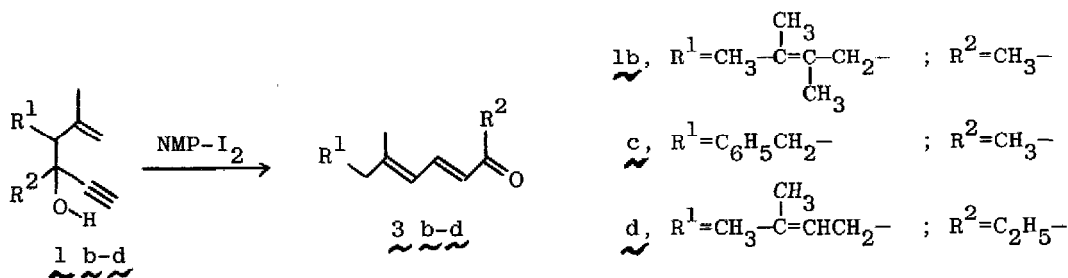
<u>1</u> Catalyst	Reaction time (hr)	Conversion of <u>1</u> ; %	Selectivity of <u>2+3</u> ; % ^{b)}	Ratio of <u>2/3</u>
<u>a</u> 1N-HCl (0.35 ml)	1	62	—	37/63
	3	90	75	13/87
	5	95	73 (65) ^{c)}	3/97
0.4N-HBr (0.27 ml)	1	66	—	26/74
	3	92	71	3/97
I ₂ (50 mg)	4	92	70 (64) ^{c)}	4/96
NH ₄ Cl (100 mg)	5	96	72	8/92
NH ₄ Br (100 mg)	4	94	70	5/95
<u>b</u> I ₂ (50 mg)	4	96	83 (76) ^{c)}	3/97
<u>c</u> I ₂ (50 mg)	4	94	70 (65) ^{c)}	5/95
<u>d</u> I ₂ (50 mg)	4	96	69 (62) ^{c)}	5/95

a) A mixture of 1 (10 g) in NMP (30 g) solvent was heated at 165°C.

b) Selectivity=[yield of 2+3]/[conversion of 1].

c) Isolated yield after distillation.

This is the first example for selective one-pot synthesis of $\alpha\beta,\gamma\delta$ -unsaturated carbonyl compound via acetylenic oxy-Cope rearrangement⁸⁾, and the synthetic utility was confirmed by large scale production of pseudoionone 3a and by applications to the other systems of 1b-d.



References and Notes

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