Facile Stereoselective Synthesis of 4-Alkylidene-2-oxo-1,3-oxathiolanes from 2-Alkyn-1-ols, Carbon Monoxide, and Sulfur

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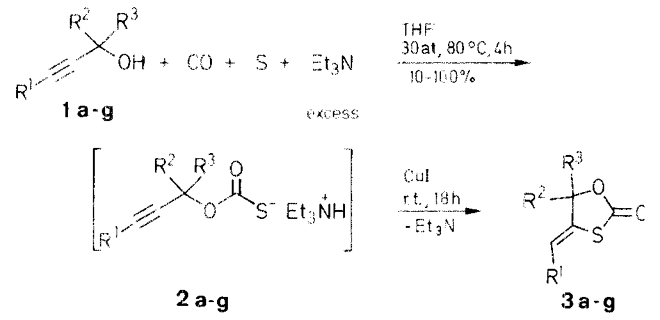
4-Alkylidene-2-oxo-1,3-oxathiolanes were synthesized in moderate to high yields by reaction of 2-alkyn-1-ols with carbon monoxide, sulfur, and triethylamine and copper(I)-catalyzed cyclization of the resultant triethylammonium *O*-(2-alkynyl)carbonothioates.

Recently, we reported a convenient method for the preparation of amine salts of carbonothioic acids from alcohols, carbon monoxide, and sulfur in the presence of amines.[1] During our investigation on the utilization of these salts, we found that triethylammonium *O*-(2-alkynyl)carbonothioates **2**, obtained from the reaction of 2-alkyn-1-ols **1** with carbon monoxide, sulfur, and triethylamine in the presence of copper(I) iodide as catalyst readily cyclized to 4-alkylidene-2-oxo-1,3-oxathiolanes **3**. We here report a novel synthesis of 4-alkylidene-2-oxo-1,3-oxathiolanes **3** which is based on these findings.[2,3]

Several transition metal compounds were examined in the cyclization of **2a** (Table 1). Catalytic amounts of copper(I) iodide gave the best yields of 4-methylene-2-oxo-1,3-oxathiolane (**3a**); high activities were also found for cobalt and zinc salts.

A variety of 4-alkylidene-2-oxo-1,3-oxathiolanes **3a–g** were thus prepared synthesized in moderate to high yields under similar conditions using copper(I) iodide as catalyst (Table 2).



1–3	R¹	R²	R³	1–3	R¹	R²	R³
a	H	H	H	**e**	Ph	H	H
b	CH_3	H	H	**f**	H	CH_3	H
c	CH_2OH	H	H	**g**	H	CH_3	CH_3
d	CH_2CH_3	H	H				

Table 1. Activity of Various Catalysts in the Cyclization of Triethylammonium *O*-(2-Propynyl)carbonothioate (**2a**) to 4-Methylene-2-oxo-1,3-oxathiolane (**3a**)

Catalyst[a]	Yield[b] (%)	Catalyst[a]	Yield[b] (%)
CuCl	74	$CoCl_2$	61
$CuCl_2$	47	$CoBr_2$	67
CuBr	81	$CoI_2 \cdot 2H_2O$	0
$CuBr_2$	45	$NiCl_2$	0
CuI	100	$ZnCl_2$	90
$CuSO_4$	70	$ZnBr_2$	86
$FeCl_2 \cdot 4H_2O$	0	ZnI_2	78
$FeCl_3$	3	$PdCl_2$	0

[a] 1.0 equiv of catalyst was used.

[b] Yields were determined by GLC analysis of the crude reaction product and are based on **1a**.

Table 2. 4-Alkylidene-2-oxo-1,3-oxathiolanes **3** Prepared

Product	CuI (equiv)	Yield[a] (%)	mp[b] (°C) (solvent)	Molecular Formula[c]	MS (70 eV, EI)[d] *m/z* (%)	IR (neat or KBr)[e] ν(cm⁻¹)	¹H-NMR ($CDCl_3$/TMS)[f] δ, *J* (Hz)	¹³C-NMR ($CDCl_3$)[f] δ
3a	0.2 1.0 0.5 0.1 0	96; 99[g] 100[g] 100[g] 26[g] 0[g]	oil	$C_4H_4O_2S$ (116.1)	116 (M^+, 100); 71 (87)	1750 (C=O); 1630 (C=C)	5.04 (t, 2H, *J* = 2); 5.24–5.36 (m, 2H)	73.0, 106.6, 138.1, 170.3
3b	0.2	83	oil	$C_5H_6O_2S$ (130.2)	130 (M^+, 75); 71 (100)	1750 (C=O); 1670 (C=C)	1.75 (dt, 3H, *J* = 7, 3); 4.99 (dq, 2H, *J* = 2, 2); 5.67 (qt, 1H, *J* = 7, 2)	16.2, 72.7, 117.1, 129.8, 170.1
3c	0.2	55	48.5 (benzene)	$C_5H_6O_3S$ (146.2)	146 (M^+, 14); 71 (100)	3450 (OH); 1710, 1690 (C=O); 1665 (C=C)	3.02 (s, 1H); 4.23 (dt, 2H, *J* = 5, 2); 5.07 (dt, 2H, *J* = 2, 2); 5.71–5.88 (m, 1H)	60.5, 73.0, 120.3, 130.0, 171.6
3d	0.2	57	oil	$C_6H_8O_2S$ (144.2)	144 (M^+, 100); 58 (58)	1755 (C=O); 1665 (C=C)	1.05 (t, 3H, *J* = 7); 2.08 (qd, 2H, *J* = 7, 7); 4.98 (dt, 2H, *J* = 2, 2); 5.61 (tt, 1H, *J* = 7, 2)	12.9, 24.7, 72.7, 124.0, 128.5, 170.2
3e	0.2	24	106.1 (Et_2O/benzene)	$C_{10}H_8O_2S$ (192.2)	192 (M^+, 26); 147 (100)	1755 (C=O); 1630 (C=C)	5.17 (d, 2H, *J* = 2); 6.58 (t, 1H, *J* = 2); 7.16–7.52 (m, 5H)	74.1, 121.4, 121.5, 127.9, 128.7, 134.6, 170.2
3f	0.2	90	oil	$C_5H_6O_2S$ (130.2)	130 (M^+, 57); 71 (100)	1750 (C=O); 1630 (C=C)	1.61 (d, 3H, *J* = 6); 5.18–5.45 (m, 3H)	20.6, 81.5, 106.4, 143.4, 168.9
3g	0.2	10	oil	$C_6H_8O_2S$ (144.2)	144 (M^+, 33); 85 (100)	1740 (C=O); 1640, 1620 (C=C)	1.64 (s, 6H); 5.16 (d, 1H, *J* = 2); 5.24 (d, 1H, *J* = 2)	27.8, 89.8, 105.3, 147.9, 167.8

[a] Yield of isolated product, based on 2-propyn-1-ols used.

[b] Uncorrected, measured with a Mettler-FP5 apparatus.

[c] Satisfactory microanalyses (determined with a Yanaco CHN recorder MT-3): C ±0.31, H ±0.10

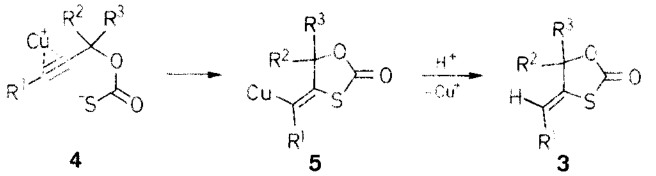
[d] Recorded a JEOL DX303-HF spectrometer.

[e] Recorded on a JASCO A-3 Infrared spectrophotometer.

[f] Measured using a JEOL FX90Q spectrometer.

[g] Yield determined by GLC.

However, in the case of 1,1-dimethyl-2-propyn-1-ol (**1g**), the yield was lowered due to steric hindrance by the two methyl groups. The reaction of the 2-alkyn-1-ols **1b–e** gave exclusively a single isomer. Comparison of the observed olefinic proton shifts in the ^{1}H-NMR spectrum with the calculated values[4] showed the highly selective formation of *Z*-isomers. (The ^{13}C-NMR data also indicate the formation of only one isomer). This stereoregulation can be explained by backside attack of the thiolate anion in the copper complex **4** to form an organocopper intermediate **5**, which on reaction with a proton gives the *Z*-isomer stereoselectively. Similar stereoregulation to give the *Z*-isomer has been observed in the cyclization of alkynoic acids in the presence of palladium,[5] mercury,[6] or rhodium[7] catalysts.



Because of its practical simplicity, the good yields, the high stereoselectivity, and the use of easily available reagents, the present method may provide a useful route to 4-alkylidene-2-oxo-1,3-oxathiolanes **3**.

All reactions were carried out using a 100 mL stainless steel autoclave (SUS-316) purchased from Taiatsu Glass Kogyo Co. Tetrahydrofuran was dried over Na wire and was freshly distilled before use. 2-Alkyn-1-ols **1a–c, f, g** were purchased from Tokyo Kasei Kogyo Co., dried (K_2CO_3), and distilled. 2-Pentyn-1-ol (**1d**) was prepared from 2-propyn-1-ol and EtBr according to Lit.[8] 3-Phenyl-2-propyn-1-ol (**1e**) was prepared by Grignard reaction of phenylacetylene with formaldehyde. Triethylamine was purified by distillation from KOH. The transition metal catalysts were purchased from Nacalai Tesque Co. and used without further purification. Powdered sulfur (99.5%) from Yoneyama Chem. Co. and carbon monoxide (99.9%) from Seitetsu Chem. Co. were also used as purchased.

4-Methylene-2-oxo-1,3-oxathiolane (3a); General Procedure:
In a 100 mL stainless-steel autoclave, 2-propyn-1-ol (**1a**; 0.58 mL, 10 mmol), powdered sulfur (0.96 g, 30 mmol), Et_3N (7.0 mL, 50 mmol), and THF (20 mL) are placed under N_2. The autoclave is flushed several times with CO and finally charged with carbon monoxide (30 at) at r.t., and then heated at 80 °C for 4 h with stirring. Thereafter, CO is evacuated, CuI (0.38 g, 2 mmol) is added, and the mixture is stirred for 18 h at ambient temperature and pressure. The mixture is then filtered to remove CuI, poured into 1 N aq. HCl (100 mL), and extracted with Et_2O (3 × 100 mL). The extract is dried ($MgSO_4$) and evaporated. The residual oil is purified by fractional distillation; yield of **3a**: 1.11 g (96%); bp 119 °C/22 Torr.

This work was supported in part by a Grant-in-Aid for General Scientific Research (61430020) from the Ministry of Education, Science, and Culture, Japan.

Received: 10 February 1989; revised: 1 June 1989

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(4) The calculated olefinic proton shifts are: **3b** *Z*: $\delta = 5.66$, *E*: $\delta = 5.41$; **3c** *Z*: $\delta = 5.89$, *E*: $\delta = 5.64$; **3d** *Z*: $\delta = 5.66$, *E*: $\delta = 5.41$; **3e** *Z*: $\delta = 6.57$, *E*: $\delta = 6.32$; see: Pascal, C., Meier, J., Simon, W. *Helv. Chim. Acta* **1966**, *49*, 164.

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