ORGANIC LETTERS

2001
Vol. 3, No. 5
763−764

Addition Reaction of Dialkyl Disulfides to Terminal Alkynes Catalyzed by a Rhodium Complex and Trifluoromethanesulfonic Acid

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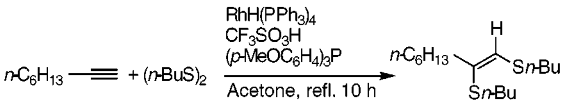
Received January 6, 2001

ABSTRACT



Addition of dialkyl disulfides to terminal alkynes is catalyzed by a rhodium–phosphine complex and trifluoromethanesulfonic acid giving (*Z*)-bis(alkylthio)olefins stereoselectively.

Metal-catalyzed cis-addition reaction of disulfides to alkynes was first reported by Ogawa and Sonoda.[1] Although high yields are obtained in the case of aromatic disulfides, aliphatic disulfides are not studied in detail. A method involving the metal-catalyzed addition of bis(triisopropylsilyl) disulfide followed by alkylation was developed for the synthesis of the alkyl derivatives.[2] Several related transformations are also known. Alkyl disulfides add to alkynes via photoinitiated free radical mechanism giving isomeric mixtures of the products.[3] 1,4-Dithiepines are obtained by the cleavage of 1,2-dithiolanes with acetylides.[4] As an extension of our recent investigations on the catalytic use of transition metal complexes and sulfuric acid derivatives in organic synthesis,[5] we describe here that the direct cis-addition of dialkyl disulfides to terminal alkynes can be catalyzed by a rhodium−phosphine complex and trifluoromethanesulfonic acid.

When 1-octyne is treated with dibutyl disulfide (1 equiv) in the presence of $RhH(PPh_3)_4$ (3 mol %), tris(*p*-methoxyphenyl)phosphine (12 mol %), and trifluoromethanesulfonic acid (3 mol %) in refluxing acetone for 10 h, (*Z*)-1,2-bis(butylthio)-1-octene is obtained in 95% yield (Table 1, entry 11). The (*Z*)-stereochemistry of the double bond is determined by NOE, and no trace of its isomer is detected by NMR analysis of the crude product. The rhodium complex and trifluoromethanesulfonic acid are essential for the addition, and no reaction occurs in the absence of either of the reagents (entries 1, 2, and 3). Addition of a triphenylphosphine, especially that with electron-donating substituents, improves the yield (entries 4−9). Bidentate phosphines (entries 12−15), tributylphosphine (entry 16), and triphenyl phosphite (entry 17) are not very effective. The catalytic activities of $RhCl(PPh_3)_3$,[6] $[RhCl(cod)]_2$, $Rh^+(cod)$-BF_4^-, $Pd_2(dba)_3$, $Pd(PPh_3)_4$,[6] $Pd(OAc)_2$, $PdCl_2(PPh_3)_2$, $RuClH(CO)(PPh_3)_3$, and $NiCl_2$(dppp) are very low even in the presence of trifluoromethanesulfonic acid and tris(*p*-

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[2] Gareau, Y.; Orellana, A. *Synlett* **1997**, 803.

[3] Heiba, E. I.; Dessau, R. M. *J. Org, Chem*. **1967**, *32*, 3837. Also see the followings for the addition of diselenides to alkynes. Ogawa, A.; Yokoyama, H.; Yokoyama, K.; Masawaki, T.; Kambe, N.; Sonoda, N. *J. Org. Chem*. **1991**, *56*, 5721. Back, T. G.; Krishna, M. V. *J. Org. Chem*. **1988**, *53*, 2533.

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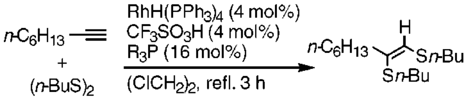
[5] Addition of phosphine to alkyne: Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc*. **2000**, *122*, 2387. Arisawa, M.; Yamaguchi, M. *Adv. Synth. Cat*. **2001**, *343*, 27. Beckmann rearrangement: Arisawa, M.; Yamaguchi, M. *Org. Lett*. **2001**, *3*, 311.

[6] $RhCl(PPh)_3$ and $Pd(PPh_3)_4$ are not effective for the addition of dibutyl disulfide to 1-octyne under the reaction conditions reported by Ogawa and Sonoda.[1]

10.1021/ol015521l CCC: $20.00

Table 1. Effect of Phosphine on the Rh-Catalyzed Addition of Dibutyl Disulfide to 1-Octyne



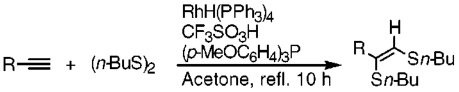
entry	R_3P	yield (%)
1[a]	none	-
2[b]	none	-
3	none	10
4	PPh_3	20
5	$(C_6F_5)Ph_2P$	-
6	(p-Tol)$_3$P	35
7	(p-$MeOC_6H_4$)Ph_2P	21
8	(p-$MeOC_6H_4$)$_2$PhP	31
9	(p-$MeOC_6H_4$)$_3$P	49
10[c]	(p-$MeOC_6H_4$)$_3$P	86
11[d]	(p-$MeOC_6H_4$)$_3$P	95
12	dppe[e]	-
13	dppp[f]	-
14	dppb[g]	6
15	dppf[h]	22
16	n-Bu_3P	-
17	$(PhO)_3P$	-

[a] In the absence of CF_3SO_3H. [b] In the absence of Rh complex. [c] The reaction time: 10 h. [d] The reaction was conducted in refluxing acetone for 10 h in the presence of 3 mol % of $RhH(PPh_3)_4$, 12 mol % of (p-$MeOC_6H_4$)$_3$P, and 3 mol % of CF_3SO_3H. [e] 1,2-Bis(diphenylphosphino)ethane. [f] 1,3-Bis(diphenylphosphino)propane. [g] 1,4-Bis(diphenylphosphino)butane. [h] 1,1′-Bis(diphenylphosphino)ferrocene.

methoxyphenyl)phosphine (cod = 1,5-cyclooctadiene, dba = dibenzylideneacetone, dppp = 1,3-bis(diphenylphosphino)-propane).

The rhodium-catalyzed addition of dibutyl disulfide to various alkynes are summarized in Table 2.[7] The yields are generally high, and bulky alkyl substituents as well as aryl substituents on 1-alkynes do not interfere with the addition (entries 3, 4, 5, 13, and 14). Functional groups such as hydroxy (entries 6 and 7), *tert*-butyldimethylsilyloxy (entry 8), ester (entry 9), and nitrile (entry 10) are unaffected. It may be interesting to note that trimethylsilylethyne is also converted to the bissulfide (entry 15). All the addition reactions proceed stereoselectively giving the (Z)-isomers. The addition reaction of the dialkyl disulfide to the internal acetylene such as 4-octyne, however, does not take place.

Table 2. Rh-Catalyzed Addition of Dibutyl Disulfide to Alkynes[a]

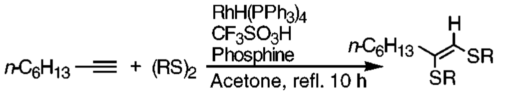


entry	R	yield (%)
1	n-C_6H_{13}	95
2	n-C_8H_{17}	98
3	cyclohexyl	83
4	1-ethylpentyl	85
5	t-butyl	91
6	$HO(CH_2)_2$	96
7	$HO(CH_2)_4$	100
8	t-$BuMe_2SiO(CH_2)_2$	95
9	$PhCO_2(CH_2)_3$	75
10	$NC(CH_2)_3$	73
11	$Ph(CH_2)_2$	99
12	$PhCH_2$	99
13	C_6H_5	62
14	p-MeC_6H_4	77
15	Me_3Si	64

[a] See ref 7 for the reaction conditions.

The rhodium-catalyzed addition of several disulfides to 1-octyne are summarized in Table 3. Even a cystine derivative adds to the alkyne, giving the 1,2-bis(thio)alkene in 48% yield (entry 4). The reactions of protected bis(2-hydroxyethyl) disulfide is effectively conducted in the presence of tris(p-chlorophenyl)phosphine rather than tris-(p-methoxyphenyl)phosphine (entries 6−8). The addition of diaryl disulfides to the alkyne also takes place under the present conditions provided that dppf is used for the ligand (entries 10−12). It may be interesting to note that the presence of a small amount of acid dramatically changes the reactivity of the rhodium complex.

Table 3. Rh-catalyzed Addition of Disulfides to 1-octyne[a]



entry	R	phosphine	yield (%)
1	C_2H_5	(p-$MeOC_6H_4$)$_3$P	93
2	n-C_3H_7	(p-$MeOC_6H_4$)$_3$P	96
3	n-C_4H_9	(p-$MeOC_6H_4$)$_3$P	95
4	(R,R)-$MeO_2CCH(NHCOPh)CH_2$	(p-$MeOC_6H_4$)$_3$P	48[b]
5	$PhCH_2$	(p-$MeOC_6H_4$)$_3$P	53
6	$PhCO_2(CH)_2$	(p-$MeOC_6H_4$)$_3$P	24
7		(p-ClC_6H_4)$_3$P	65
8	t-$BuCO_2(CH_2)_2$	(p-ClC_6H_4)$_3$P	61
9	Ph	(p-$MeOC_6H_4$)$_3$P	42
10[c]		dppf	99
11[d]		dppf	91
12[c]	p-MeC_6H_4	dppf	100

[a] See ref 7 for the reaction conditions. [b] $[\alpha]^{23}_{D}$ 120 (c 1, $CHCl_3$). [c] The reaction was conducted in refluxing $(ClCH_2)_2$ for 3 h in the presence of 1 mol % of $RhH(PPh_3)_4$, 2 mol % of dppf, and 1 mol % of CF_3SO_3H. [d] The reaction was conducted in 4 mmol scale using 0.6 mol % of $RhH(PPh_3)_4$, 1.2 mol % of dppf, and 0.6 mol % of CF_3SO_3H in $(ClCH_2)_2$.

Acknowledgment. M.A. expresses her thanks to JSPS for a Grant-in-Aid for Encouragement of Young Scientists (No. 11771374).

Supporting Information Available: Spectroscopic data for all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) In a two-necked flask equipped with a reflux condenser were placed tetrakis(triphenylphosphine)hydriderhodium (3 mol %, 17.3 mg), tris(p-methoxyphenyl)phosphine (12 mol %, 21.1 mg), trifluoromethanesulfonic acid (3 mol %, 1.4 μL), 1-octyne (0.5 mmol, 73.8 μL), and dibutyl disulfide (0.5 mmol, 95.1 μL) in acetone (1.0 mL) under an argon atmosphere, and the solution was heated at reflux for 10 h. Then, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel giving (Z)-1,2-bis(butylthio)-1-octene (137 mg, 95%).