BUTENOLIDE SYNTHESIS USING ACYL COBALT COMPLEXES

Marie E. Krafft^{*1} and Jacek Pankowski Department of Chemistry, Florida State University, Tallahassee, FL 32306-3006

Summary: Acylcobalt tetracarbonyls react with alkynes to give rise to butenolides in high yields.

The insertion of unsaturated functional groups, i.e. alkenes, alkynes and carbon monoxide, into transition metal-carbon bonds is an important step in a variety of transition metal mediated carbon-carbon bond forming processes.² Acyl cobalt carbonyl complexes have been shown to react with alkenes³ and alkynes⁴ to give rise to more functionalized organic compounds. One example is the butenolide ring system. Not only are butenolides contained in a variety of natural products,⁵ but, they are useful building blocks themselves.⁶

Several transition metal mediated butenolide syntheses have been reported.⁷⁻¹² Insertion of an alkyne into a metal acyl bond followed by carbonylation and cyclization, in a formal 2+2+1 addition (eq 1), appears to be a



general mechanistic pathway.⁷⁻¹⁰ Heck^{4a} reported several examples of the reaction of a disubstituted alkyne with an acyl cobalt carbonyl complex to give a π -allyl lactonyl complex¹³ in moderate yield. Our attempts to generalize the reaction and functionalize the π -allyl system have yielded a butenolide synthesis which results from protonation of the metal carbon bond (eq 2).



We found that acyl cobalt tetracarbonyls, prepared in ethyl ether solution according to Heck,¹⁴ reacted with disubstituted alkynes to give rise to π -allyl lactonyl complexes which, upon protonation with an ethereal solution of anhydrous HCl, gave low to moderate yields of 3,4,5-trisubstituted 3-buten-2-olides. The yields were much lower when THF was substituted for ethyl ether. However, dramatic improvements in the yield were observed when toluene or methylene chloride was used as the solvent. The reaction is quite general and results of reactions with several different acid halides are listed in Table I. In a typical experiment, sodium tetracarbonyl cobaltate (2 mmol) was suspended in methylene chloride (20 mL) at 0 °C. After addition of propionyl chloride (1.6 mmol) and 3-hexyne (2 mmol) a red-brown solution was formed. Stirring was continued for 6-8 h at 0 °C, and then the reaction was quenched with ethylenediamine (0.4 mL, 6 mmol) and the resulting lactone, 3,4,5-triethyl-3-buten-2-olide, was isolated by silica gel chromatography in 77% yield (entry 2, Table I). Decomposition of the presumed π -

lactoryl intermediate with a solution of DCl in D_2O gave complete deuterium incorporation at the γ -position (entry 11, Table I). With more hindered acid chlorides, such as trimethylacetyl (entry 6) or 3,3-dimethylbutyryl chloride (entry 7), reaction times of 10 - 15 h were necessary for complete reaction. Perfluoro acyl cobalt carbonyls were very reactive and gave rise to high yields of butenolides after short reaction times (1-2 h).

TABLE I						
	Entry	Alkyne	Acid Halide	Butenolide	Isolated yield	
			0			
	1	Cirk - Cirk		$\mathbf{R} = \mathbf{CH}_3$	71%	
	2			$\mathbf{R} = \mathbf{C}_2\mathbf{H}_5$	77%	
	3			$R = n - C_3 H_7$	92%	
	4	CI		R = CL	80%	
	5			R = n-octyl	85%	
	6			$\mathbf{R} = t - \mathbf{C_4} \mathbf{H_9}$	64%	
	7		۲	$\mathbf{R} = t - \mathbf{C_4} \mathbf{H_9} \mathbf{C} \mathbf{H_2}$	56%	
	8			R = Ph	69%	
	9	[$R = PhCH_2$	75%	
	10	((C ₂ F ₅ CO) ₂ O	$R = C_2 F_5$	99%	
	11				76%	
	All re	All reactions were carried out in CH ₂ Cl ₂ .				

Analogous reactions with unsymmetrically substituted alkynes are shown in Table II. Reactions of unsymmetrically substituted internal alkynes, in which the substituents at each end of the alkyne are sterically similar, gave rise to mixtures of regioisomers. For example, propionylcobalt tetracarbonyl reacted with 2-hexyne to give a 1:1 mixture of regioisomeric butenolides (entry 1, Table II). In contrast, 2,2-dimethyl-3-pentyne underwent the same reaction to give predominantly one regioisomer (entry 5, Table II) in 91% yield. Steric interactions during the insertion of the alkyne should be responsible for directing the acyl group migration to the less hindered end of the alkyne. However, the reaction of 1-phenylpropyne was even more selective and yielded only one regioisomer.



Terminal alkynes are known to react with acyl metal complexes but, under the present reaction conditions gave rise to complicated mixtures of products. In an attempt to modify the reactivity of terminal alkynes in the reaction, 1-trimethylsilyl and 1-phenylthio substituted alkynes were prepared and subjected to the standard conditions. The reaction of propionylcobalt tetracarbonyl with 1-phenylthio-1-butyne did not lead to the desired butenolide. Limited success was achieved upon reaction of propionylcobalt tetracarbonyl with 1-trimethylsilyl-1-butyne. The α -trimethylsilyl substituted butenolide was obtained as the predominant regioisomer (30:1, Table II, entry 6) in only 28% yield when the reaction was quenched with an ethereal solution of anhydrous HCl but not when quenched with ethylenediamine.

The mechanism (Scheme) most likely involves insertion of the least sterically hindered end of the alkyne into the cobalt acyl bond of complex 1 to give the vinyl cobalt carbonyl 2. Subsequent carbonylation would be expected to lead to 3. Addition of the ketone oxygen to the acylcobalt carbonyl would then lead to the zwitterionic intermediate 4 which is set up for a 1,2 shift to give π -allyl complex 5.¹⁵

Work is in progress toward controlling the regioselectivity in reactions of unsymmetrical alkynes. These results will be reported in due course.

Acknowledgments: We acknowledge partial support of this work from the National Science Foundation (CHE-8704933), the National Institutes of Health (GM-40693), the Sloan Foundation and the Camille and Henry Dreyfus Foundation.



REFERENCES and NOTES

- 1. Fellow of the A.P. Sloan Foundation, 1989-1991. Camille and Henry Dreyfus Teacher Scholar 1989 1994.
- 2. For leading references, see: a) Wender, I.; Pino, P. "Organic Syntheses via Metal Carbonyls" Vol 1, Wiley Interscience, New York, NY 1968. b) Wender, I.; Pino, P. "Organic Syntheses via Metal Carbonyls" Vol 2, Wiley Interscience, New York, NY 1977. Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. "Principles and Applications of Organotransition Metal Chemistry" 2nd Ed., University Science Books, Mill Valley, CA, 1987. c) Schore, N. E. Chem. Rev. 1989, 89, 1081. d) Davies, S. G. "Organotransition Metal Chemistry: Applications to Organic Synthesis" Pergamon, Oxford, 1982. e) Heck, R. F. Accts Chem. Res. 1969, 2, 10.
- Hegedus, L. S.; Perry, R. J. J. Org. Chem. 1984, 49, 2570. Hegedus, L. S.; Inoue, Y. J. Am. Chem. Soc. 1982, 104, 4917. Heck, R. F. J. Am. Chem. Soc. 1963, 85, 3116. Heck, R. F. J. Am. Chem. Soc. 1963, 85, 3383. Heck, R. F. J. Am. Chem. Soc. 1963, 85, 3381. Heck, R. F. J. Am. Chem. Soc. 1965, 87, 4727.
- a) Heck, R. F. J. Am. Chem. Soc. 1964, 86, 2819. b) Alper, H.; Currie, J. K.; Abbayes, H. D. J. Chem. Soc. Chem. Comm. 1978, 311. c) Heck, R. F. in "Advances in Organometallic Chemistry" F. G. A. Stone and R. West, Eds., Academic, NY, Vol 4, 1966, p.243. d) ref 2a.
 ApSimon, J. Ed. "The Total Synthesis of Natural Products" Wiley, New York, NY, Vol 5, 1983.
- Heathcock, C. H. in "The Total Synthesis of Natural Products" ApSimon, J. Ed. Wiley, New York, NY, Vol 2, 1973.
- 6. For examples, see: Ochiai, M.; Shiro, M. J. Org. Chem. 1989, 54, 5211. and references cited therein. Kennedy, R. M.; Kim, H. B.; Krafft, M. E.; Holton, R. A. J. Am. Chem. Soc. 1987, 109, 1597-1600. Posner, G. H.; Kogan, T. P.; Haines, S. R.; Frye, L.L. Tetrahedron Lett. 1984, 25, 2627. Rao, Y. S. Chem. Rev. 1976, 76, 625.
- 7. Rh: Hong, P.; Mise, T.; Yamazaki, H. Chem. Lett. 1981, 989.
- 8. Mn: DeShong, P.; Sidler, D. R.; Rybczynski, P. J.; Slough, G. A.; Rheingold, A. L. J. Am. Chem. Soc. 1988. 110. 2575.
- 9. Co: 5-hydroxy-3-butenolides: Ref 4b. Arzoumanian, H.; Petrignani, J-F. Tetrahedron Lett. 1986, 27, 5979.
- 10. Ni: Carmona, E.; Gutierrez-Puebla, E.; Monge, A.; Marin, J. M.; Paneque, M.; Poveda, M. L. Organometallics 1989, 8, 967. Cassar, L.; Chiusoli, G. P. Tetrahedron Lett. 1966, 2805.
- 11. Pd: Cowell, A.; Stille, J. K. J. Am. Chem. Soc. 1980, 102, 4193. Kasahara, A.; Izumi, T.; Sato, K.; Maemura, M.; Hayasaka, T. Bull. Chem. Soc. Jpn. 1977, 50, 1899.
- 12. Zr: Buchwald, S. L.; Fang, Q.; King, S. M. Tetrahedron Lett. 1988, 29, 3445.
- 13. Similar allyl molybdenum complexes have been reported: Green, M.; Nyathi, J. Z.; Scott, C.; Stone, F.G.A.;
- Welch, A. J.; Woodward, P. J. Chem. Soc. Dalton Trans. 1978, 1067.
 Heck, R. F. J. Am. Chem. Soc. 1963, 85, 3116. For the preparation of NaCo(CO)₄, see: Edgell, W. F.; Lyford, J. Inorganic Chemistry 1970, 9, 1932. The cobaltate was titrated according to the procedure reported by Wender: Sternberg, H. W.; Wender, I.; Orchin, M. Analytical Chemistry 1952, 174. The sodium tetracarbonyl cobaltate was prepared in THF. For reactions carried out in other solvents, the THF was completely removed on a vacuum line and the appropriate solvent was added to the remaining solid.
- 15. For a partial discussion of the mechanism, see Ref 4a. The step in which a zwitterionic intermediate is formed (i.e. 3-4) has been proposed in a similar molybdenum catalyzed reaction, see ref 13.

(Received in USA 17 May 1990)