Catalytic Conversion of β-Hydroxy Carboxylic Acids to Olefins by Tungsten(VI) Complexes: A New Acyl Group Transfer Catalyst

Tomoya Tanzawa and Jeffrey Schwartz*

Department of Chemistry, Princeton University, Princeton, New Jersey 08544-1009

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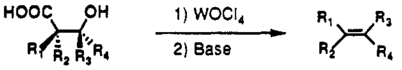
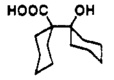
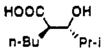
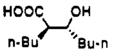
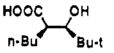
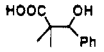
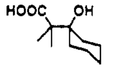
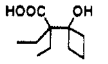
Summary: Oxotungsten tetrachloride catalyzes the conversion of β-hydroxy carboxylic acids to olefins, in the presence of base. The reaction proceeds in high yield, stereospecifically, and with high catalyst turnover. Examination of the likely stoichiometric steps for β-hydroxy carboxylic acid activation shows the formation of intermediate chelates, structures of which were studied by ^{1}H NMR. The role of the base was probed by using both ^{1}H and ^{183}W NMR, and it was shown that base simply deprotonates the chelate; base does not coordinate to the W center. β-Lactones were the initial products of this sequence from which decarboxylation occurred to give the olefinic product.

Catalytic conversion of easily available starting materials to a desirable organic product lends efficiency to a synthetic transformation and makes it practical. Examining the chemistry of tungsten analogues of vanadium-complex-based conversion of 3-hydroxy carboxylic acids to olefins,[1] we discovered an efficient, stereospecific reagent system: in contrast to the vanadium species which yield olefins directly, this tungsten-based route converts the 3-hydroxy acid to the corresponding β-lactone, which then yields olefin thermally. It is, therefore, analogous to known procedures involving mixed organic anhydride intermediates[2,3] with one major difference: unlike these other, purely organic, *stoichiometric* reagents, the metallic product of lactone synthesis, likely an in situ generated WO_2^{2+} equivalent, *catalyzes* acyl-transfer dehydration of the "aldol" acid to the β-lactone.[4]

Table I. Yields of Olefins for Tungsten-Complex-Catalyzed Reactions of 3-Hydroxy Acids

1  2

		conditions			
		equiv W	equiv base[a]	°C, h	yield, %[b]
1a		0.1	0.5	140, 8	98[c]
		0.01		130, 38	22[d]
		0.01	0.1	130, 38	70[e]
		0.01	0.3	130, 38	69[c]
		0.001	0.1	135, 77	68[c]
		0.001	0.5	135, 77	59[c]
		0.0001	0.1	135, 96	36[c]
		0.0001		135, 72	43[c]
		10^{-6}		135, 72	18[c]
		control		135, 72	13[c]
1b		0.1		140, 20	66*E*, 2*Z*[f]
		0.1 (WCl_6)	0.1[g]	140, 30	66*E*, 2*Z*
		0.2 (WCl_4)	0.1[g]	140, 7	60*E*, 2*Z*
		0.1 (WO_2Cl_2)	0.1[g]	140, 60	56*E*, 5*Z*
		0.1 (W[NPh]-Cl_4)	0.1[g]	140, 20	62*E*, 2*Z*
1c		0.1		140, 20	62*E*, 3*Z*
1d		0.1		140, 20	51*Z*, 7*E*
1e		0.1	0.1[g]	135,[h] 96	80[i]
1f		0.1	0.5	140, 8	76
1g		0.1	0.5	140, 8	65[j]

[a] All reactions were run in acetonitrile with Proton Sponge unless otherwise indicated. [b] Determined by GC. [c] No other products were detected. [d] In the absence of base, an isomer, likely (1-cyclohexyl)cyclohexene by NMR, was formed (11%). [e] This same isomer was formed in 0.1% yield. [f] No olefin was formed in the absence of catalyst for this acid. [g] TMEDA was used as base. [h] Reaction run in chlorobenzene. [i] Benzaldehyde (17%) was also formed; in acetonitrile, benzaldehyde increased to 39%. [j] Control yielded 14% olefin.

In a typical procedure, a catalytic amount of $WOCl_4$ was dissolved in acetonitrile to which was added the β-hydroxy carboxylic acid and 0–0.5 mol equiv of base (either TMEDA or Proton Sponge). The vessel was sealed under reduced pressure, and the reaction mixture was heated to 140 °C. Products were analyzed by quantitative GC and GC/MS. For example, **1a** (45.2 mg, 0.2 mmol) reacted with 6.8 mg (0.1 equiv) of $WOCl_4$ and 21.4 mg (0.5 equiv) of Proton Sponge in 1 mL of acetonitrile to give olefin **2a**, 98%, 9.8 turnovers, in 8 h. Interestingly, the requirement for added base decreased with decreasing concentration of the catalyst. Thus, **1a** reacted with 10^{-4} equiv of the catalyst and no added base to give 43% **2a** in 72 h. Other examples of catalyzed olefin synthesis using $WOCl_4$ or other simple W(VI) derivatives are given in Table I. Control experiments were performed to determine background, simple acid-catalyzed olefin formation. Di- or trisubstituted acids gave no olefin (or lactone) in the absence of catalyst, but tetrasubstituted precursors underwent slow conversion to the olefin, likely by lactonization–decarboxylation.[5] For example, heating **1a** for 72 h with no base added gave 13% **2a**. Therefore, by subtraction, the catalyzed reaction had 3000 turnovers under these conditions, and it proceeded, per mole of catalyst,

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(1) Meier, I. K.; Schwartz, J. *J. Am. Chem. Soc.* **1989**, *111*, 3069.

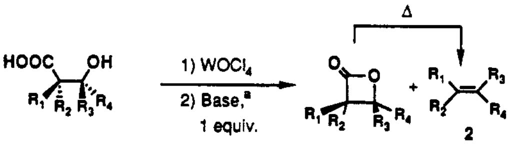
(2) (a) Sultanbawa, M. U. S. *Tetrahedron Lett.* **1968**, 4569. (b) Zaugg, H. E. *Org. React.* **1955**, *8*, 305.

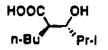
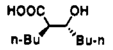
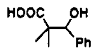
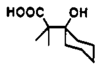
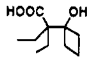
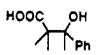
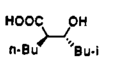
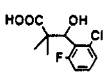
(3) For olefin synthesis via β-lactones, see: (a) Noyce, D. S.; Banitt, E. H. *J. Org. Chem.* **1966**, *31*, 4043. (b) Krapcho, A. P.; Jahngen, E. G. E., Jr. *J. Org. Chem.* **1974**, *39*, 1650. (c) Schollkopf, U.; Hoppe, I. *Angew. Chem., Intl. Ed. Engl.* **1975**, *14*, 765. (d) Mageswaran, S.; Sultanbawa, M. U. S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 884. (e) Imai, T.; Nishida, S. *J. Org. Chem.* **1980**, *45*, 2354. (f) Adam, W.; Baeza, J.; Liu, J.-C. *J. Am. Chem. Soc.* **1972**, *94*, 2000 and references cited therein.

(4) A catalytic synthesis of medium ring lactones using $(Bu_2Sn)_2O$ has been reported (Steliou, K.; Poupart, M.-A. *J. Am. Chem. Soc.* **1983**, *105*, 7130. Steliou, K.; Szczygielska-Nowosielska, A.; Favre, A.; Poupart, M.-A.; Hanessian, S. *J. Am. Chem. Soc.* **1980**, *102*, 7578). This species failed to yield significant quantities of either the β-lactone or the olefin when treated with **1b** under literature conditions. Olefin was formed (≤20%), but nonstereospecifically.

(5) This is a classical manifestation of the "Thorpe–Ingold effect". See: Ingold, C. K. *J. Chem. Soc.* **1921**, *119*, 305.

Table II. Yields of β-Lactones and Olefins Prepared from 3-Hydroxy Acids and $WOCl_4$ (1:1)



			yield, %[b]		
		°C, time	β-lactone	olefin	combined
1b		170/5 min	80[c]	4 (*E*:*Z* = 35:1)	84
1c		170/5 min	74[c]	trace (*E*:*Z* = 10:1)	74
1e		130/5 min 130/20 h	48	39 93*	87 93
1f[a]		130/20 h 130/60 h		44* 64*	44 64
1g[a]		60/15 min 130/20 h	26	37 71*	63 71
1h[a]		130/5 min	41	44	85
1i		170/15 h		71 (*E*:*Z* = 13:1)	71
1j		160/5 min	25	56	81

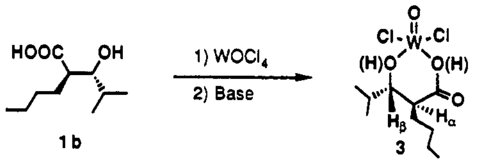
[a] In all cases, TMEDA was used as the base except where indicated, where Proton Sponge was used. [b] Yields given for each product component determined for both lactone and olefin by NMR, unless determined by GC for the olefin indicated by *; the lactone is converted to the olefin on further heating.[2,3] Thus, overall olefin yield (%) following thermolysis is the summation of the values given above. [c] By ^1H NMR, it was determined that only a trace of the erythro compound was present.

ca. 10^4 faster than the control.

Aspects of catalytic olefin formation were elucidated in stoichiometric studies. Oxotungsten tetrachloride (68.4 mg; 0.2 mmol) was suspended in 1 mL of chlorobenzene to which was added 37.6 mg (0.2 mmol) of acid, **1b**. All material immediately dissolved to give a pale-yellow solution. TMEDA (23.2 mg, 1 equiv) was added to this reaction mixture, which was then sealed and warmed to 160 °C for 20 h. Workup gave 2-methyl-3-octene, 80%, *E*:*Z* = 36:1. When this procedure was followed by ^1H and ^{183}W NMR, it was found that a complex was prepared on mixing (^1H NMR for H_β = δ 5.28 [dd; J = 12 and 2 Hz], suggesting a rigid cyclic structure, **3**; ^{183}W NMR δ 581.8). Addition of 1 equiv of TMEDA showed a change for H_β to δ 5.58 (br) and a shift in the ^{183}W spectrum to δ 544.2. Warming this latter reaction mixture for 5 min to 130 °C gave a blue precipitate.[6] Centrifugation followed by analysis of the colorless supernatant by ^{183}W NMR showed that all of the metal was present in the precipitate; ^1H NMR analysis of the supernatant showed that the β-lactone had been formed and in high yield. Under thermally more vigorous reaction conditions, the β-lactone is converted to the olefin.[2] Stoichiometric conversion results for **1b** and for other subtrates are given in Table II.

Catalytic or stoichiometric procedure were performed with a variety of bases, and the latter were followed by ^1H and ^{183}W NMR (Table III). One equivalent of Proton Sponge or 2 equiv of either *N*,*N*-dimethylaniline or 2,6-di-*tert*-butyl-4-methylpyridine could be used in place of TMEDA; ^{183}W NMR spectral analysis showed similar values for δ_W when either the bulky di-*tert*-butylpyridine or the unhindered bases were used. Thus, the amine reacts to deprotonate the chelated ligand, not to coordinate to W.[7,8]

Table III. ^{183}W NMR[a] Analysis of the Reaction between 3 and Various Bases



base	equiv per W	δ_W
no base added		581.77
Proton Sponge	1	543.68
TMEDA	1	544.15
N,*N*-dimethylaniline	1	552.65
	2	542.29
2,6-di-*tert*-butyl-4-methylpyridine	2	547.57

[a] ^{183}W shifts relative to (external) Na_2WO_4.

Chelate isolated from the reaction of $WOCl_4$, **1c**, and base gave no olefin on heating. Apparently, labilization of intermediate chelates by species present in the mother liquors, perhaps the ammonium chloride, is required for lactone formation.[9] The fact that diastereomerically pure acids can yield the corresponding olefin with retention of configuration suggests that lactone formation occurs by metal complex activation of the carboxylate group toward attack by the hydroxyl group terminus; this was proven by ^{18}O labeling.[10] (In this process, alkoxide might be freed from chelation by attack of chloride at tungsten.[9]) Further catalytic implementation of tungsten-catalyzed lactonization is now being pursued as is analysis of the catalytic cycle itself.

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(6) Under catalytic conditions, the reaction mixture remains yellow and no precipitation occurs. Reduction of W(VI) to blue W(V) has been observed only in "stoichiometric" studies and, therefore, is likely unrelated to β-lactone formation.

(7) The chemical shift range for ^{183}W is on the order of 6000 ppm and is strongly dependent on ligation type and coordination number at W. See, for example: (a) Gansow, O. A.; Ho, R. K. C.; Klemperer, W. G. *J. Organomet. Chem.* **1980**, *187*, C27. (b) Acerete, R.; Hammer, C. F.; Baker, L. C. W. *J. Am. Chem. Soc.* **1979**, *101*, 267. (c) Acrete, R.; Harmalker, S.; Hammer, C. F.; Pope, M. T.; Baker, L. C. W. *J. Chem. Soc., Chem. Commun.* **1979**, 777. (d) Brevard, C.; Granger, P. *Handbook of High Resolution Multinuclear NMR*; Wiley-Interscience: New York, 1981; p 192.

(8) In the absence of added base, little lactone or olefin was formed. However, warming $WOCl_4$ and acid **1d** to reflux in chlorobenzene in the presence of even 0.25 equiv of *N*,*N*-dimethylaniline gave the expected olefin in 80% yield after 23 h. When only 0.01 equiv of the base was used, olefin was still formed (21%). It may be that under these conditions, HCl is continuously driven from the reaction mixture; however, when no base was added, the yield of olefin fell to <7%. If base was added to the $WOCl_4$ prior to addition of the acid, or if the dianion of the acid was used without additional base, reduction of the W was the primary reaction outcome. Diethylamine failed to foster lactone formation; only reduced tungsten species were produced.

(9) Because of solubility problems, the effect of exogenous chloride on lactonization has not yet been determined.

(10) Carboxylate ^{18}O-labeled **1b** was assayed by GC/MS of its bis(*tert*-butyldimethylsilyl) derivative and was shown to be 74% ^{18}O. Treatment of free **1b** with either benzenesulfonyl chloride/pyridine or $WOCl_4$/TMEDA gave the β-lactone, and GC/MS analysis of the methanolysis product showed 30–35% ^{18}O incorporation in both cases, consistent with the proposed scheme (lactone formation is known to occur in this way when benzenesulfonyl chloride/pyridine[3f] is used).