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Tungsten Complex Catalyzed Dehydrative Decarboxylation of 2,3-Dihydroxycarboxylic Acids

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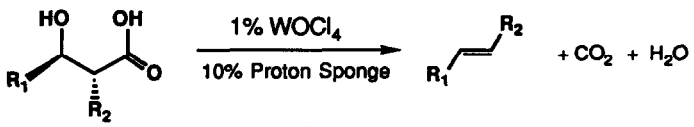
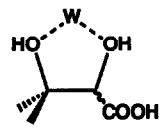
Abstract: $WOCl_4$ catalyzes dehydrative decarboxylation of 2,3-dihydroxycarboxylic acids to enols, likely via β-lactone intermediates. Classical reagents for conversion of 3-hydroxycarboxylic acids to β-lactones fail with these substrates.

We recently reported[1] that $WOCl_4$ catalyzes the dehydrative decarboxylation of 3-hydroxycarboxylic acids to olefins. We found this reaction proceeds via a β-lactone intermediate; the W(VI) reagent presumably serves as an acyl transfer reagent by activating the carboxylate as a mixed organic-inorganic "anhydride" species, RC(O)-W(O). To examine the reactivity of this reagent in cases where additional W-coordinating functionality was present, we studied the reaction between $WOCl_4$ and 2,3-dihydroxycarboxylic acids. In this way, we could compare the chemistry of these sensitive substrates and $WOCl_4$ with that of other well-known reagents[2] which also effect β–lactonization from simple 3-hydroxycarboxylic acids.

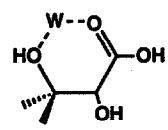


$WOCl_4$ chelates simple 3-hydroxy acids via both the hydroxy and carboxy groups,[1] but this chelate may not be on the reaction coordinate to product; strong chelation could even impede β-lactone formation. β–Lactone formation from a polyhydroxylated precursor could be complicated by multiple possibilities for chelation. The size of the metal ion has been found[3] to be important in determining preferred chelation modes offered by the polyfunctional substrate, as are the chemical natures of the substituent groups, conformational factors,[4] and solvation. For example, 2,3-dihydroxy-2-methylbutanoic acid forms 5-membered ring chelates with several metal ions using its *2*-OH substituent.[4] For a similar system with additional alkyl substituents at the 3- position, the mode of coordination to a given metal ion is changed to involve the *3*-OH group.[4] We found that when *erythro-* or *threo*-2,3-dihydroxyhexanoic acids were separately treated with $WOCl_4$ in acetonitrile, a family of chelates for each diastereomer was formed: [2-OH, 3-OH]; [3-OH, CO_2H]; and [2-OH, CO_2H]. For the *erythro-* diastereomer, chelation using the 2- and 3-OH groups was the main species;[5] for the *threo-* isomer, chelation using the 3-OH and the carboxylate group predominated.[6] These complexes can be easily discerned by

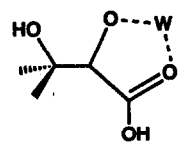
^{1}H NMR: coordination of W to an hydroxy group shifts the proton on that same carbon downfield by at least 1.7 ppm, and the proton on that carbon whose hydroxy group is not coordinated to W moves downfield by 0.7 ppm, at most. Two species were observed with chemical shifts denoting a [2-OH, 3-OH] chelate of *erythro*-2,3-dihydroxyhexanoic acid; based on coupling constant data (Table 2), these are assigned as rotamers, but their thermal lability precluded definitive NMR coalescence studies.[7]



[2-OH, 3-OH]



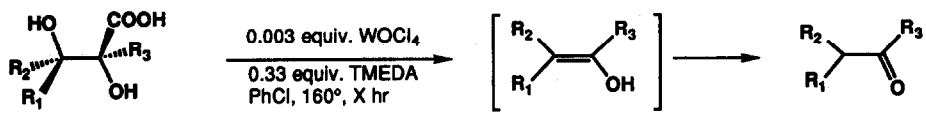
[3-OH, CO_2H]



[2-OH, CO_2H]

3-Hydroxycarboxylic acids are susceptible to acid catalyzed dehydration.[8] In fact, reacting $WOCl_4$ in acetonitrile with either *erythro*- or *threo*-2,3-dihydroxyhexanoic acids, in the absence of base, rapidly gave only dehydration to the α-ketoacid, even at room temperature. Interestingly, we note that warming a solution of *threo*-2,3-dihydroxy-2-methylbutanoic acid and TMEDA in chlorobenzene with a catalytic amount of $WOCl_4$ gave the desired product (the enol; the carbonyl compound is isolated) in high yield. In a typical procedure, 0.10 mmol of the 2,3-dihydroxycarboxylic acid, was treated in 0.50 mL of chlorobenzene with 10 μl of a stock catalyst solution, prepared from 0.009 g of $WOCl_4$ and 1.00 mL of CD_3CN (giving 0.003 equiv. of the catalyst), and 0.33 equiv. TMEDA. For NMR experiments, the mixture was cooled in liquid nitrogen, evacuated, and sealed. The reaction mixture was then immersed in an oil bath at 160°. Reaction products were obtained by distillation and comparison with authentic samples.

Table 1. Aldehydes or Ketones from 2,3-Dihydroxy Acids (*via* the Enols).



2,3-Dihydroxy Acid	Products	Time (hr)	Yield (%)[a]	Byproduct;Yield (%)[b]
$R_1 = R_2 = R_3 = CH_3$[11a]	3-methyl-2-butanone	11	quant.	-
$R_1 = R_2 = CH_3$; $R_3 = H$[11b]	2-methylpropanal	15	84	-
$R_1 = R_3 = CH_3$; $R_2 = H$[11c]	2-butanone	37	57	-
$R_1 = H$; $R_2 = R_3 = CH_3$[11c]	2-butanone	46	51	-
$R_1 = R_3 = H$; $R_2 = n$-propyl[11d]	*n*-pentanal	17	43	2-propyl-2-heptenal; 24
$R_1 = n$-propyl; $R_2 = R_3 = H$[11e]	*n*-pentanal	15	58	2-propyl-2-heptenal; 20
$R_1 = i$-propyl; $R_2 = R_3 = H$[11f]	3-methylbutanal	13	78	-

[a]by gc; [b]byproduct formed by aldol condensation of the desired product, followed by dehydration.

For all substrates examined, there was no correlation between relative amounts of chelates observed by NMR and yields of decarboxylation; therefore we conclude that chelation is labile, as was found[1] for monosubstituted carboxylic acids. Significantly, conventional methods[2] for β-lactone formation failed for 2,3-dihydroxy acids,[9] and these substrates were more labile toward dehydration than were simple 3-hydroxy acids in the presence of W(VI). Perhaps W not only activates the carboxylate group, but also participates in dehydration by -OH group coordination;[10] this latter process can be suppressed by appropriate addition of base.

The authors acknowledge support for this work given by the National Institutes of Health. They also thank Mr. Tomoya Tanzawa for helpful comments.

Notes and References

1. Tanzawa, T.; Schwartz, J. *Organometallics* **1990**, *9*, 3026.

2. 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) Schöllkopf, U.; Hoppe, I. *Angew. Chem., Int. 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.

3. For example, see (a) Taga, T.; Kuroda, Y.; Ohashi, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2278; (b) Nieuwenhuis, J. J.; Jordaan, J. H. *Carbohydrate Res.* **1976**, *51*, 207.

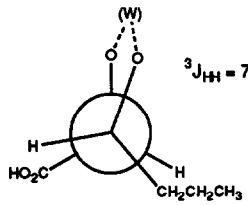
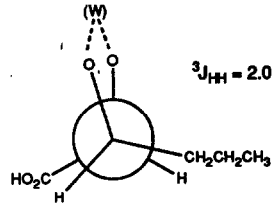
4. Powell, J. E.; Porter, M. W.; Burkholder, H. R. *J. Inorg. Nucl. Chem.* **1979**, *41*, 1771.

5. *erythro*-2,3-Dihydroxyhexanoic acid was prepared by reaction between *trans*-2-hexenoic acid and H_2O_2 in formic acid (Armstrong, F. B.; Lipscomb, E. L.; Crout, D. H. G.; Morgan, P. J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 691) and was treated with 1 equiv. of $WOCl_4$ in CH_3CN. ^1H NMR showed the major components to be [2-OH, 3-OH] chelates; the [2-OH, CO_2H] chelate was observed as a minor constituent (Table 2).

6. *threo*-2,3-Dihydroxyhexanoic acid was prepared from *trans*-2-hexenoic acid by osmolysis. As for the *erythro*-2,3-dihydroxybutanoic acid, three kinds of chelates were found (Table 2). For this diastereomer, [3-OH, CO_2H] was the largest component (50%), [2-OH, 3-OH] was the next most abundant (30%), and [2-OH, CO_2H] was the smallest (20%).

7. For *threo*-2,3-dihydroxy-4-methylpentanoic acid, only [3-OH, CO_2H] and [2-OH, CO_2H] chelates were observed; no [2-OH, 3-OH] chelate was detected. Five rotameric isomers are suggested for these chelates based on chemical shift correlations.

Table 2. ^{1}H NMR data for tungsten chelates

Acid[a]	Chelate	δH_2(ppm)	shift (ppm)[b]	δH_3(ppm)	shift (ppm)[b]	$J_{2,3}$ (Hz)
EH	[2-OH, 3-OH], A	6.27 (d)	2.2	5.63 (ddd)	1.9	7.2
	B	6.06 (d)	2.0	5.86 (dt)	2.1	2.0
		 $^3J_{HH}$ = 7.2 Hz, A		 $^3J_{HH}$ = 2.0 Hz, B		
	[2-OH, CO_2H]	6.32 (d)	2.3	4.23 (dt)	0.5	3.0
TH	[2-OH, 3-OH]	6.71 (d)	2.7	5.98 (ddd)	2.2	5.9
	[3-OH, CO_2H]	4.75 (d)	0.7	5.75 (dt)	1.9	8.9
	[2-OH, CO_2H]	6.25 (d)	2.2	4.34 (ddd)	0.5	2.3
TMP	[3-OH, CO_2H]	4.85 (d)	0.6	5.66 (dd)	2.3	
		4.54 (d)	0.3	5.22 or 5.20 (dd)	1.8	
		4.60 (d)	0.4	5.20 or 5.22 (dd)	1.8	
	[2-OH, CO_2H]	6.11 (d)	1.9	3.81 (dd)	0.4	
		5.90 (d)	1.7	3.79 (dd)	0.4	

[a] EH = *erythro*-2,3-Dihydroxyhexanoic acid; TH = *threo*-2,3-Dihydroxyhexanoic acid; TMP = *threo*-2,3-Dihydroxy-4-methylpentanoic acid; [b] from free acid.

8. Dehydration is the final step in the Knoevenagel reaction. See Jones, G. *Org. Reactions* **1967**, *15*, 204.

9. Attempts to prepare β-lactones of *threo*-2,3-dihydroxyhexanoic, *threo*-2,3-dihydroxy-4-methylpentanoic, or *threo*-2,3-dihydroxy-4,4-dimethylpentanoic acids by treating[2f] a pyridine solution of the acid with benzenesulfonyl chloride at 0° for ca. 3 hours failed. Reaction mixtures showed only broad NMR spectra, perhaps due to polymerization. Heating the mixture to 50° for several hours still gave no aldehyde.

10. Bae Yu, H. K.; Schwartz, J. see the accompanying manuscript.

11. (a) Powell, J. E.; Osuch, C.; Burkholder, H. R.; Kulprathipanja, S.; Miller, J. H.; Stadtherr, L. G.; Baughman, R. G. *J. Org. Chem.* **1978**, *43*, 3166; (b) Hill, R. K.; Yan, S-J. *Bioinorg. Chem.* **1971**, *1*, 446; (c) Closs, G. L.; Miller, R. J. *J. Am. Chem. Soc.* **1978**, *100*, 3483; (d) For $C_6H_{12}O_4$, calcd: C 48.68; H 8.16; C, H; (e) C, H; (f) C, H.

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