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The Preparation of (α-Alkylidene)tetrahydrofurans by Tungsten Catalyzed Decarboxylation of Aldol Precursors

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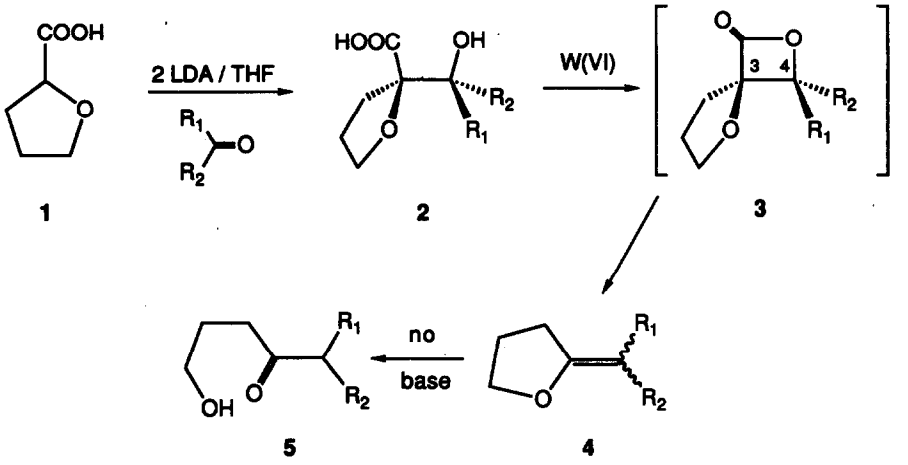
Abstract. A series of substituted (α-alkylidene)tetrahydrofurans was prepared by tungsten catalyzed reaction of substituted hydroxyfuroic acids. These reactions likely involve β-lactone intermediates which decarboxylate under the reaction conditions, and rates for olefin synthesis correlated with donor properties of substituents at C(4).

We recently noted a method for the stereospecific synthesis of olefins from 3-hydroxycarboxylic acids which is based on W(VI) complex catalysis and which involves *in situ* generated β-lactone intermediates.[1] Since these W(VI) complex catalysts are Lewis acidic, we were interested to learn if acid-labile functionality could survive this reagent system.[2] Accordingly, we examined our methodology in the context of (α-alkylidene)tetrahydrofuran synthesis from appropriate hydroxy acid precursors. We find that such sensitive products can indeed be prepared under catalytic conditions, and that qualitative relative rates for product formation are in accord with observations[3] and predictions[4] made for decarboxylation of simple β-lactone analogs. Tetra-, tri-, and dialkyl substituted olefins were all made with comparable ease, including cases in which spirocyclic β-lactone intermediates occurred; in contrast, (α-alkylidene)tetrahydrofurans were formed far more slowly, and only when dialkyl or activated phenyl substitution were present at C(4).

3-Hydroxycarboxylic acid precursors were prepared[5] by aldol condensation between the dianion of tetrahydro-2-furoic acid and an aldehyde or ketone.[6] For example, an approximately 1:1 mixture of *threo*-3-hydroxycarboxylic acid **2a** (R_1 = H; R_2 = Ph) and its *erythro* isomer (R_1 = Ph; R_2 = H) was obtained when the dianion of **1** was treated with benzaldehyde. Only the *threo* isomer could be isolated by column chromatography (the *erythro* isomer apparently decomposed during chromatographic separation on the silica). When **2a** (44 mg, 0.2 mmol) was reacted with a catalytic amount (3.4 mg, 0.01 mmol, 0.05 equiv) of $WOCl_4$ at 150 °C for 15 hrs in acetonitrile, enol ether **4a**[7] (6.4 mg, 0.04 mmol, 20%) and hydrolysis product[8] hydroxyketone **5a**[9] (5.3 mg, 0.8 mmol, 15%) were separated. The yield of **4a** was improved by simply adding Proton Sponge® (0.2 equivalent) to the reaction medium.

Reactivities of *threo* and *erythro* hydroxycarboxylic acids[10] were comparable, and we note facile isomerization between *E* and *Z* isomers of **4**; chloroform solutions of pure isomers equilibrated (*E*: *Z* = 1:5) in several hours (X = OMe) to a few days (X = NO_2) at room temperature. As expected for an asynchronous transition state for β-lactone decarboxylation,[4] qualitative relative rates for olefin synthesis from para-substituted analogs of **2a** varied as CH_3O (**2b**) > H > NO_2 (**2c**).[12] Decarboxylation of independently prepared[12,13] β-lactones proceeded much faster than overall enol ether formation, so decarboxylation can not be rate limiting

for the overall reaction and β-lactone concentration did not build up during this process. Therefore it seems likely that tungsten-catalyzed β-lactone synthesis, too, correlates with donor properties of "R", since these donor properties should affect the nucleophilicity of the hydroxyl group in the context of the lactonization step; apparently, oxygen substitution at C(3) inductively retards both processes.[14]



1 2 3 4 5

Hydroxy Acid 2	Reaction Temp. (°C)	Reaction Time (hr)	Yield (%) 4	*E* : *Z*	Turnovers
R_1 = H; R_2 = Ph, **2a** (*threo*)	150[a]	72	50	1 : 5	10
R_1 = Ph; R_2 = H + **2a** (1:1)	150[a]	72	50	1 : 5	10
R_1 = H; R_2 = $C_6H_4OCH_3$, **2b**	140[a]	24	50	1 : 5	10
R_1 = $C_6H_4OCH_3$; R_2 = H + **2b** (1:1)	140[a]	24	63	1 : 5	13
R_1 = H; R_2 = $C_6H_4NO_2$, **2c**	165[a]	100	15	1 : 5	3.0
R_1 = $C_6H_4NO_2$; R_2 = H + **2c** (1:1)	165[a]	100	12	1 : 5	2.4
R_1 = R_2 = $(CH_2)_6$, **2d**	150[b]	24	50	-	5.0
R_1 = R_2 = CH_3, **2e**	145[b]	24	27	-	2.7
R_1 = R_2 = CH_3CH_2, **2f**	150[b]	20	36	-	3.6

[a] 0.05 equiv. $WOCl_4$, 0.2 equiv. Proton Sponge ; [b] 0.1 equiv. $WOCl_4$, 0.5 equiv. Proton Sponge

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References and Notes

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

2. For reactions of 2,3-dihydroxycarboxylic acids, see Bae Yu, H. K.; Schwartz, J. in the accompanying manuscripts.

3. Imai, T.; Nishida, S. *J. Org. Chem.* **1980**, *45*, 2354; Adam, W.; Fick, H.-H. *J. Org. Chem.* **1979**, *43*, 4574.

4. Minato, T.; Yamabe, S. *J. Org. Chem.* **1983**, *48*, 1479; Moyano, A.; Pericàs, M. A.; Valentí, E. *J. Org. Chem.* **1989**, *54*, 573.

5. A solution of tetrahydro-2-furoic acid (2.32 g, 20 mmol) dissolved in 10 ml of dry THF was added dropwise to a LDA solution (40 mmol in 150 ml of dry THF) at 0 °C and was then stirred at that temperature for 1 hr (a yellow solution formed). A solution of benzaldehyde (2.12 g, 20 mmol) in 10 ml of dry THF was injected to the first solution over 5 min and was then stirred at 0 °C for 30 minutes; it was then allowed to warm to room temperature over 1.5 hrs. After work-up and crystallization from chloroform, a *ca* 1 : 1 mixture of the diastereomers of the 3-hydoxycarboxylic acid was obtained (2.8 g, 63%). The *threo* isomer **2a** was separated by column chromatography and was recrystallized from chloroform as white crystals. ^{1}H NMR ($CDCl_3$): δ1.82 (m, 2H), 2.30 (m, 1H), 2.48 (m, 1H), 3.81 (m, 1H, CHH'O), 4.06 (m, 1H, CHH'O), 5.00 (s, 1H, CHOH) 7.30-7.48 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$): δ26.32 (CH_2), 32.37 (CH_2), 71.48 (CH_2O), 76.07 (CHOH), 89.30 (CCOOH), 128.11 (Ph), 128.73 (Ph), 128.89 (Ph), 138.98 (Ph), 176.81 (COOH). The *erythro* isomer decomposed on the column, so it was separated by fractional recrystallization from chloroform/ether as white needles. ^{1}H NMR ($CDCl_3$): δ1.42 (m, 1H), 1.74 (m, 1H), 2.02 (m, 1H), 2.24 (m, 1H), 3.70 (m, 1H, CHH'O), 3.97 (m, 1H, CHH'O), 4.97 (s, 1H, CHOH) 7.30-7.50 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$): δ25.83 (CH_2), 33.27 (CH_2), 71.18 (CH_2O), 77.39 (CHOH), 89.97 (CCOOH), 128.53 (Ph), 128.85 (Ph), 129.12 (Ph), 138.97 (Ph), 177.22 (COOH). For $C_{12}H_{14}O_4$ calcd: C 64.85%, H 6.35%; found: C, H.

6. We have been unable to synthesize 3-hydroxycarboxylic acids (or their esters) from γ-butyrolactone and an alkylcarboxylate dianion (see Caldwell, C. G.; Rupprecht, K. M.; Bondy, S. S.; Davis, A. A. *J. Org. Chem.* **1990**, *55*, 2355).

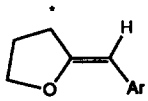
7. For the *E* isomer of **4a**; ^{1}H NMR ($CDCl_3$): δ2.11 (m, 2H, CH_2), 2.85 (m, 2H, CH_2 allyl), 4.14 (m, 2H, CH_2O), 5.93 (s, 1H, C=C(H)Ph), 7.06-7.36 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$): δ25.96 (CH_2), 28.99 (CH_2), 70.11 (CH_2O), 99.67 (=C(H)Ph), 125.20 (Ph), 127.55 (Ph), 128.98 (Ph), 138.40 (Ph), 159.91 (=C(R)O). For the *Z* isomer of **4a**; ^{1}H NMR ($CDCl_3$): δ2.05 (m, 2H, CH_2), 2.75 (m, 2H, CH_2 allyl), 4.36 (m, 2H, CH_2O), 5.28 (s, 1H, C=C(H)Ph), 7.26-7.60 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$): δ24.96 (CH_2), 31.72 (CH_2),

72.36 (CH_2O), 97.44 (=$\underline{C}$(H)Ph), 125.17 (Ph), 127.62 (Ph), 128.82 (Ph), 137.62 (Ph), 158.24 (=C(R)O). For $C_{11}H_{12}O$ calcd: C 82.46%, H 7.55%; found: C 82.69%, H 7.78%.

8. (a) Jones, D. M.; Wood, N. F. *J. Chem. Soc.* **1964**, 5400; (b) Kresge, A. J.; Chiang, Y. *J. Chem. Soc. B*, **1967**, 53.

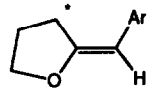
9. ^{1}H NMR (CD_3CN): δ2.02 (m, 2H, CH_2), 2.62 (t, 2H, J = 7.5 Hz, $CH_2\underline{CH_2}C$=O), 3.57 (t, 2H, J = 7.5 Hz; $\underline{CH_2}OH$), 3.70 (s, 2H, $\underline{CH_2}Ph$), 7.02-7.30 (m, 5H, Ph). ^{13}C NMR (CD_3CN): δ29.74 (CH_2), 34.22 ($CH_2\underline{CH_2}C$=O), 64.24 (CH_2OH), 88.76 ($\underline{CH_2}Ph$), 128.43, 128.85, 129.22 and 139.89 (Ph), 201.44 (C=O). HRMS: For $C_{11}H_{14}O_2$ calcd: 178.0994; found: 178.0990.

10. *Threo* acid **2a** was converted to the *Z* olefin[7] using DEAD and triphenylphosphine;[11] it showed NOE for the singlet at δ5.28 on irradiation of the multiplet at δ2.75. The *E* olefin prepared from the *erythro* acid showed no NOE. Similar results were obtained for *threo* acids **2b** and **2c** and their *erythro* counterparts.



4Z

δ2.75; 5.28
δ2.73; 5.23
δ2.80; 5.34



4E

δ2.85; 5.93
δ2.79; 5.89
δ2.89; 5.97

11. Mitsunobu, O.; Eguchi, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3427; Mitsunobu, O.; Kimura, J.; Yanagida, N. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 510.

12. Authentic samples of **3a-c** were prepared from the corresponding 3-hydroxycarboxylic acids using Adam's method.[13] These β-lactones were dissolved in deuterated acetonitrile and then put into NMR tubes. After being sealed, the NMR tubes were heated to 145 °C and the decarboxylation reaction was monitored by NMR. Decarboxylation rates varied as expected:[4] $CH_3O > H > NO_2$:

β-Lactone 3	Temp. (°C)	Time (hr)	Yield (%) 4	*E* : *Z*
3b	145	<0.05	85	1 : 5
3a	145	0.5	80	1 : 5
3c	145	50	75	1 : 5

13. Adam, W.; Baeza, J.; Liu, J.-C. *J. Am. Chem. Soc.* **1972**, *94*, 2000.

14. C(4)-Monoalkyl-substituted lactones did not thermally decarboxylate.

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