Ready Conversion of Sugar Derived 5,6-Dihydro-2-pyrones into 3-Acyloxy- and 3-Acylamido-2-Pyrones

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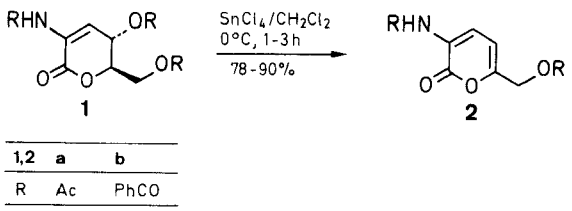
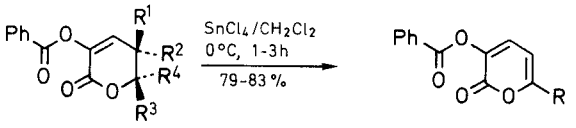
5-Acyloxy-6-acyloxymethyl-5,6-dihydro-2-pyrone derivatives (**1a, b** and **3b** and 5-acyloxy-6-methyl-5,6-dihydro-2-pyrone (**3a**), obtained by acylation of 2-amino-2-deoxy-D-gluconic acid or L-rhamono- and D-glucono-1,5-lactones, react with tin(IV) chloride to give 3-acylamido- and 3-acyloxy-6-acyloxymethyl-2-pyrones (**2a,b** and **4b**, respectively) and 3-benzoyloxy-6-methyl-2-pyrone (**4a**), in excellent yield. On prolonged reaction time (5h), the pyrone **4b** underwent substitution of the allylic benzoate by chlorine to afford the corresponding 6-chloromethyl derivative **4c**.

Unsaturated derivatives of 1,4- and 1,5-lactones have been used as key intermediates in the synthesis of natural products.[1-3] We have previously reported the synthesis of unsaturated derivatives by acylation of lactones. Multiple elimination was observed for 1,4-lactones,[4,5] whereas 1,5-lactones, under similar conditions, afforded 5,6-dihydro-2-pyrones in excellent yield.[3,6] However, the second elimination of acetic or benzoic acid from 5,6-dihydro-2-pyrones to give 6-substituted 3-acyloxy-2-pyrones required more vigorous conditions, and in the case of benzoylated derivatives only moderate yields of products were obtained.[7,8] The mechanism of this second elimination of acetic or benzoic acid was rationalized as a process which would involve the acid-catalyzed cleavage of the RCO_2—C-5 bond, with formation of an incipient carbocation stabilized by allylic resonance. Hence, we considered that a Lewis acid could promote the elimination, and therefore we studied the reaction of unsaturated sugar-lactone derivatives (**1a,b, 3a,b**) with tin(IV) chloride.



1,2	a	b
R	Ac	PhCO



3a $R^1 = PhCO_2$, $R^2 = R^3 = H$, $R^4 = CH_3$
b $R^1 = R^4 = H$, $R^2 = PhCO_2$, $R^3 = PhCO_2CH_2$

4a $R = CH_3$
b $R = PhCO_2CH_2$
c $R = ClCH_2$

5,6-Dihydro-2-pyrone derivatives **1a,b** were obtained on acylation of 2-amino-2-deoxy-D-gluconic acid,[9] **3a** was prepared by benzoylation of L-rhamnono-1,5-lactone,[3] and **3b** was synthesized from commercially available D-glucono-1,5-lactone.[6] The crude products of the reaction of **1a,b** and **3a,b** with tin(IV) chloride were isolated with a high degree of purity, as shown by TLC and ^{1}H-NMR spectroscopy.

On prolonged reaction time, 5,6-dihydro-2-pyrone **3b** underwent elimination followed by substitution of the allylic benzoyloxy group by chlorine, to afford almost quantitatively the halogenated pyrone **4c**. Under the same conditions compounds **2a** and **2b** were recovered unaltered.

The procedure here described constitutes a facile, two step synthesis of substituted 2-pyrones from 5-hydroxy-6-hydroxymethyl-5,6-dihydro-2-pyrones via their acyl derivatives. The pyrone derivatives are easily purified by recrystallization, avoiding the chromatographic isolation required in previously reported syntheses.[7,8] In particular, benzoylated pyrone derivatives, otherwise prepared under harsh conditions and with only moderate yields,[7] can be readily synthesized by the tin(IV) chloride promo-

Table. 2-Pyrones **2a**, **b**, **4a–c** Prepared

Starting Lactone	Reaction Time (h)	Product	Yield[a] (%)	mp[b] (°C)	Molecular Formula[c] or Lit. Data	^{1}H-NMR ($CDCl_3$/TMS)[d,e] δ, J(Hz)	^{13}C-NMR ($CDCl_3$/TMS)[d,e] δ
1a	3	**2a**	90	116–117	117–118[9]	8.22 (d, 1H, $J_{4,5}$ = 7.2, H-4), 8.00 (br s, 1H, NH), 6.33 (d, 1H, H-5), 4.84 (s, 2H, CH_2OAc)	159.0 (C-2), 150.4 (C-6), 125.1 (C-3), 122.5 (C-4), 106.4 (C-5), 61.5 (CH_2OAc)
1b	3	**2b**	78	144–145	$C_{20}H_{15}NO_5$ (349.3)	8.7 (br s, 1H, NH), 8.42 (d, 1H, $J_{4,5}$ = 7.5, H-4), 6.49 (d, 1H, H-5), 5.15 (s, 2H, CH_2OCOPh)	159.2 (C-2), 150.6 (C-6), 125.2 (C-3), 122.4 (C-4), 106.4 (C-5), 61.8 (CH_2OCOPh)
3a	1	**4a**	79	113–115	113–115[7]	7.15 (d, 1H, $J_{4,5}$ = 7.4, H-4), 6.02 (dd, 1H, H-5), 2.28 (d, 3H, J_{5,CH_3} = 0.8, CH_3	159.7 (C-6), 158.1 (C-2), 134.9 (C-3), 131.7 (C-4), 102.1 (C-5), 19.5 (CH_3)
3b	1	**4b**	83	152	$C_{20}H_{14}O_6$ (350.3)	7.25 (d, 1H, $J_{4,5}$ = 7.2, H-4), 6.41 (d, 1H, H-5), 5.15 (s, 2H, CH_2OCOPh)	158.9 (C-2), 155.5 (C-6), 136.9 (C-3), 130.7 (C-4), 103.8 (C-5), 61.6 (CH_2OCOPh)
3b	5	**4c**	83	130	$C_{13}H_9ClO_4$ (264.7)	7.24 (d, 1H, $J_{4,5}$ = 7.3, H-4), 6.35 (d, 1H, H-5), 4.34 (s, 2H, CH_2Cl)	156.7 (C-2), 155.8 (C-6), 137.0 (C-3), 130.6 (C-4), 104.0 (C-5), 40.7 (CH_2Cl)

[a] Yields after recrystallization from EtOH.
[b] Uncorrected, determined in a Thomas-Hoover apparatus.
[c] Satisfactory microanalyses obtained C ±0.27, H ±0.23, N ±0.10, Cl ±0.26.
[d] ^{1}H- and ^{13}C-NMR Spectra recorded on a Varian XL-100 spectrometer at 100.1 and 25.2 MHz, respectively.
[e] Selected NMR Data only.

ted reaction. Furthermore, this reaction leads to halogenated pyrones, such as **4c**, which are potentially key precursors of a variety of 6-substituted 2-pyrones.

$SnCl_4$ was distilled under reduced pressure over granullar tin, in an all-glass system. CH_2Cl_2 was refluxed over P_2O_5, distilled and stored over 4 Å molecular sieves. TLC was performed on precoated aluminum plates (0.2 mm) of silica gel 60F-254 (Merck) with toluene/EtOAc (9:1) as solvent.

6-Substituted 3-Acyloxy- and 3-Acylamido-2-pyrones; General Procedure:

A solution of the 1,5-lactone derivative **1a,b**, **3a,b**, (1 mmol) in anhydrous CH_2Cl_2 (4 mL) is cooled to 0 °C, and $SnCl_4$ (1.5 mmol) is added. The reaction is monitored by TLC, and when the starting material is completely consumed (1–3 h for preparing **2a,b** and **4a,b**, and 5 h for **4c**) the mixture is diluted with CH_2Cl_2 (100 mL) and slowly added to sat. aq $NaHCO_3$ (50 mL). The phases are separated and the aqueous layer is extracted with CH_2Cl_2 (2 × 50 mL). The organic extracts are pooled, dried ($MgSO_4$) and evaporated. The product usually crystallizes upon evaporation of the solvent, and it is recrystallized from EtOH (Table).

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