SHORT PAPER

J. Chem. Research (S),
2002, 631–633

A simple oxidation of γ- and δ-lactones to oxocarboxylic acids by buffered sodium hypochlorite†

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An efficient synthetic procedure is described for the preparation of 4- and 5-oxocarboxylic acids by reaction of the corresponding lactones with commercial bleach

Keywords: oxidation, lactone, oxocarboxylic acid, bleach

Most γ- and δ-hydroxyacids, in acidic or neutral solution, tend to form γ- and δ-lactones respectively. The majority of agents for the oxidation of alcohols work in acidic or neutral conditions. Consequently lactone formation constitutes a protection for the hydroxyl group and prevents its oxidation to a ketone. Sometimes the Jones reagent[1] has been used but, in order to successfully perform such a transformation, it is necessary to use an oxidising agent which can be applied in basic solution.

Previous examples in the literature report that potassium permanganate[2] furnishes poor to fair yields of 4-oxocarboxylic acids, whilst moderate to good yields are obtained with RuO_2–$NaIO_4$[3] and electrochemical oxidation[4] at a nickel hydroxide electrode gives excellent yields. A basic medium is a feature shared by all three procedures. Some drawbacks are that RuO_4 is toxic and in our hands failed to give the desired oxidation, moreover electrochemical techniques are not readily accessible.

Hypochlorous acid[5] is a cheap oxidant particularly used for the conversion of secondary alcohols to ketones, for the nucleophilic epoxidation of unsaturated carbonyls and for the degradation of methyl ketones to carboxylic acids. Hypochlorous acid is a weak acid ($K_a = 3\times10^{-8}$); its salts give rise to hydrolysis and form strongly basic solutions.

A basic medium converts the lactone into its open form, but it weakens the oxidation power of hypochlorous acid; in fact it possesses a standard redox potential roughly twice the value of hypochlorites. However, it is possible to find a pH value where the hypochlorous acid and a hydroxy-carboxylate salt coexist in solution because of their different acidity constants.

Parallel reactions carried out at pH = 4.0, 5.0 and 7.8 (room temperature, ~20 hours) showed that both the lower pHs led to recovery of the lactone substrate whereas the highest value gave a mixture lactone/oxoacid approximatively in the ratio 1.0 : 1.6. Working at decidedly basic conditions, *e.g.* simply stirring the lactone with a commercial solution of NaOCl, the hydroxyl function proved to have been oxidised in a low or zero percentage after the same reaction time.

This is in agreement with the chemical literature reporting that the oxidation of alcohols by hypochlorites has been obtained in acetic acid as solvent.[6] Besides they demonstrated the importance to establish the best pH value and the need to use a buffer for a successful reaction. Three parallel reactions were carried out at pH = 6.2, 7.2 and 7.8: the best result was obtained in the first case. Finally we worked at pH = 6.6 by using a buffer solution of sodium dihydrogen phosphate/disodium hydrogen phosphate.

Unfortunately unsaturated lactones (entries 6 and 7 in Table 1) added HOCl to the double bond. The relatively more abundant derivative of γ-jasmolactone was a 1,6-dioxaspiro[4,5]-decane compound. This ring system has been found in a few secondary metabolites.[9] These results match the findings of Wolinsky and coworkers[10] who treated various olefins with NaOCl in an acidic, two phase-system and obtained chlorohydrins or allylic chlorides after elimination of H_2O. Unsaturated substrates have been neglected in the prior reports on phase-transfer oxidation of alcohols.[11]

Bearing in mind that the methodologies employing $KMnO_4$ and RuO_4 do not allow the use of olefinic substrates, the lack of chemical oxidants to convert functionalised lactones into oxoacids should be noted. However the good yields obtained by our procedure make it, albeit limited to saturated compounds, a practical and valid alternative to the electrochemical method.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Varian XL-300 instrument (^1H at 299.94 MHz, ^{13}C at 75.4 MHz), δ in ppm using residual solvent signals as internal standard ($CDCl_3$ = 77.0 ppm, $CHCl_3$ = 7.25 ppm, CD_3OD = 49.0 ppm, CHD_2OD = 3.31 ppm), multiplicities and peak assignments from DEPT, $^1J_{CH}$- and $^nJ_{CH}$-HETCOR; mass spectra were measured on Kratos MS80 with home-built acquisition system.

A typical procedure is given for entry **2**: 0.5 mMol (78 mg) was hydrolysed overnight in EtOH/NaOH 0.5M (1:1, 2 ml) and the solvent evaporated. The residue was dissolved in 10 ml buffer solution (1.38 g $NaH_2PO_4 \cdot 2H_2O$ and 0.40 g $Na_2HPO_4 \cdot 12H_2O$), commercial NaOCl (2 ml) (~ 1,2 mmol = 2.4 equiv.) was added and stirred for about 20 hours at room temperature. The reaction mixture was then acidified with 260 µl H_3PO_4 85% and silica gel (6 g) was added. The slurry was dried under reduced pressure and then washed with ethyl ether furnishing 92 mg of crude product. The crude product was further purified using a silica gel column and eluted with petroleum / ethyl ether / acetic acid 49:49:2 affording 74 mg of pure compound.

4-oxohexanoic acid: NMR ($CDCl_3$): δ_C 210.1 (s, C-4), 178.1 (s, C-1), 36.7 (t, C-3), 35.8 (t, C-5), 28.3 (t, C-2), 7.7 (q, C-6).

4-oxononanoic acid: NMR ($CDCl_3$): δ_C 209.2 (s, C-4), 178.6 (s, C-1), 42.7 (t, C-5), 36.7 (t, C-3), 31.3 (t, C-7), 27.7 (t, C-2), 23.5 (t, C-6), 22.4 (t, C-8), 13.9 (q, C-9).

4-oxodecanoic acid: NMR ($CDCl_3$): δ_H 2.70 (m, 2H, H-3), 2.62 (m, 2H, H-2), 2.42 (t, 2H, J = 7.5 Hz, H-5), 1.58 (m, 2H, H-6), 1.21–1.27 (m, 6H, H-7, H-8 and H-9), 0.85 (t, 3H, J = 6.8 Hz, H-10); δ_C 209.2 (s, C-4), 178.3 (s, C-1), 42.7 (t, C-5), 36.7 (t, C-3), 31.5 (t, C-8), 28.8 (t, C-7), 27.7 (t, C-2), 23.5 (t, C-6), 22.5 (t, C-9), 14.0 (q, C-10); EIMS *m/z* (intensity %): 169 (M^+-17, 10), 147 (16), 130 (71), 115 (79), 98 (90), 43 (100); HREI-MS *m/z* 169.12278 ± 0.05 $[C_{10}H_{17}O_2]^+$, calc. 169.12286.

4-oxoundecanoic acid: NMR ($CDCl_3$): δ_C 209.2 (s, C-4), 178.3 (s, C-1), 42.7 (t, C-5), 36.7 (t, C-3), 31.6 (t, C-9), 29.1 and 29.0 (2t, C-7 and C-8), 27.7 (t, C-2), 23.8 (t, C-6), 22.6 (t, C-10), 14.1 (q, C-11).

4-phenyl-4-oxobutanoic acid: NMR ($CDCl_3$): δ_H 7.98 (m, 2H, H-2'), 7.55 (m, 1H, H-4′), 7.45 (m, 2H, H-3′), 3.30 (br.t, 2H, J = 6.0 Hz, H-3), 2.80 (br.t, 2H, J = 6.0 Hz, H-2); δ_C 197.9 (s, C-4), 178.8 (s, C-1), 136.3 (s, C-1'), 133.3 (d, C-4′), 128.6 (d, C-2′), 128.0 (d, C-3′), 33.1 (t, C-3), 28.0 (t, C-2); EIMS *m/z* (intensity %): 178 (M^+, 4), 161 (M^+-17, 2), 105 (100); HREI-MS *m/z* 178.06298 ± 0.05 $[C_{10}H_{10}O_3]^+$, calc. 178.06300, *m/z* 161.06013 ± 0.05 $[C_{10}H_9O_2]^+$, calc. 169.06026.

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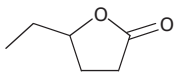
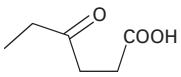
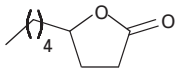
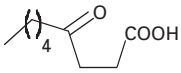
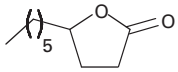
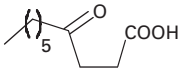
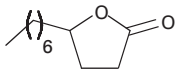
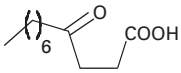
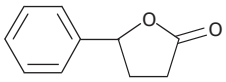
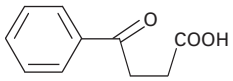
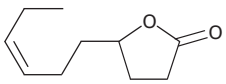
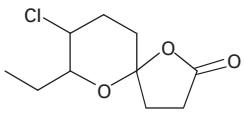
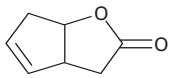
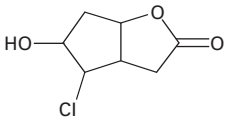
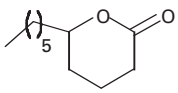
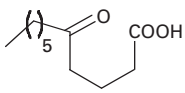
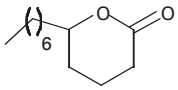
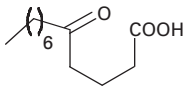
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Oxidation of lactones to oxocarboxilic acids

Entry	Substrate	Product	Yield %	Ref.
1			80	7
2			86	7
3			77	4
4			70	7
5			84	4
6			40	–
7			52	8
8			78	–
9			72	–

Yields refer to isolated products. Products were characterised by NMR and MS spectra.

8-chloro-7-ethyl-2-oxo-1,6-dioxaspiro[4,5]decane: NMR ($CDCl_3$): δ_H 4.15 (m, 1H, *J* = 3.0, 3.0, 1.5, small Hz, H-8), 3.90 (td, 1H, *J* = 7.0, 7.0, 1.5 Hz, H-7), 2.79 (ddd, 1H, *J* = 18.0, 11.0, 9.5 Hz, H_a-2), 2.51 (ddd, 1H, *J* = 18.0, 9.5, 2.2 Hz, H_b-2), 2.37 (tdd, 1H, *J* = 13.0, 13.0, 4.0, 3.0 Hz, H_a-9), 2.32 (ddd, 1H, *J* = 13.5, 9.0, 2.2 Hz, H_a-4), 2.24 (td, 1H, *J* = 13.0, 13.0, 4.0 Hz, H_a-10), 2.10 (m, 1H, H_b-9), 2.08 (ddd, 1H, *J* = 13.5, 11.0, 9.5 Hz, H_b-4), 1.75 (dddd, 1H, *J* = 13.0, 4.0, 1.5, small Hz, H_b-10), 1.64 and 1.54 (m, 2H, H-7′), 0.88 (t, 3H, *J* = 7.0 Hz, H-7″); δ_C 176.4 (s, C-2), 107.3 (s, C-5), 74.8 (d, C-7), 57.5 (d, C-8), 34.2 (t, C-4), 28.6 (t, C-9), 28.1 (t, C-3), 27.7 (t, C-10), 25.8 (t, C-7′), 9.2 (q, C-7″). EI-MS *m/z* (intensity %): 218 (M^+, 1), 189 (2), 176 (2), 174 (7), 162 (8), 160 (26), 98 (100); HREI-MS *m/z* 218.07061 ± 0.05 $[C_{10}H_{15}ClO_3]^+$, calc. 218.07097, *m/z* 189.03207 ± 0.05 $[C_8H_{10}ClO_3]^+$, calc. 189.03185, *m/z* 174.08116 ± 0.05 $[C_9H_{15}ClO]^+$, calc. 174.08114, *m/z* 160.02938 ± 0.05 $[C_7H_9ClO_2]^+$, calc. 160.02911.

6-chloro-7-hydroxy-2-oxabicyclo[3.3.0]octan-3-one: NMR ($CDCl_3$): δ_H 5.06 (ddd, 1H, *J* = 7.0, 7.0, 2.0 Hz, H-1), 4.37 (q, 1H, *J* = 5.8, 5.8, 5.8 Hz, H-7), 4.15 (br.dd, 1H, *J* = 7.0, 5.8, small Hz, H-6), 3.37 (tdd, 1H, *J* = 10.5, 7.0, 7.0, 3.5 Hz, H-5), 2.89 (dd, 1H, *J* = 19.0, 3.5 Hz, H_a-4), 2.72 (dd, 1H, *J* = 19.0, 10.5 Hz, H_b-4), 2.44 (ddd, 1H, *J* = 15.0, 5.8, 2.0 Hz, H_a-8), 2.11 (br.dt, 1H, *J* = 15.0, 7.0, 5.8, small Hz, H_b-8); δ_C 176.3 (s, C-3), 81.9 (d, C-1), 77.3 (d, C-7), 65.8 (d, C-6), 41.0 (d, C-5), 38.2 (t, C-8), 31.0 (t, C-4); EIMS *m/z* (intensity %): 176 (M^+, 11), 160 (5), 158 (15), 141 (31), 112 (38), 97 (92), 42 (100); HREI-MS *m/z* 176.02369 ± 0.05 $[C_7H_9ClO_3]^+$, calc. 176.02402, *m/z* 158.01350 ± 0.05 $[C_7H_7ClO_2]^+$, calc. 158.01346, *m/z* 141.05476 ± 0.05 $[C_7H_9O_3]^+$, calc. 141.05517.

5-oxoundecanoic acid: NMR (CD_3OD): δ_H 2.52 (t, 2H, *J* = 7.5 Hz, H-4), 2.44 (t, 2H, *J* = 7.5 Hz, H-6), 2.30 (t, 2H, *J* = 7.5 Hz, H-2), 1.82 (m, 2H, H-3), 1.55 (m, 2H, H-7), 1.25-1.35 (m, 8H, H-8, H-9 and H-10), 0.90 (t, 3H, *J* = 6.8 Hz, H-11); δ_C 209.6 (s, C-5), 178.8 (s, C-1), 42.9 (t, C-6), 41.2 (t, C-4), 32.9 (t, C-2), 31.5 (t, C-9), 28.8 (t, C-8), 23.8 (t, C-7), 22.4 (t, C-10), 18.5 (t, C-3), 14.0 (q, C-11); EIMS *m/z* (intensity %): 200 (M^+, 1), 183 (M^+-17, 7), 155 (14), 143 (11), 113 (41), 85 (54), 43 (100); HREI-MS *m/z* 200.14085 ± 0.05 $[C_{11}H_{20}O_3]^+$, calc. 200.14124, *m/z* 183.13822 ± 0.05 $[C_{11}H_{19}O_2]^+$, calc. 183.13851, *m/z* 155.14342 ± 0.05 $[C_{10}H_{19}O]^+$, calc. 155.14359.

5-oxododecanoic acid: NMR (CD_3OD): δ_H 2.52 (t, 2H, *J* = 7.5 Hz, H-4), 2.44 (t, 2H, *J* = 7.5 Hz, H-6), 2.28 (t, 2H, *J* = 7.5 Hz, H-2), 1.82 (m, 2H, H-3), 1.53 (m, 2H, H-7), 1.25-1.35 (m, 8H, H-8, H-9, H-10 and H-11), 0.90 (t, 3H, *J* = 6.8 Hz, H-12); δ_C 210.6 (s, C-5), 178.7 (s, C-1), 42.9 (t, C-6), 41.2 (t, C-4), 32.9 (t, C-2), 3.16 (t, C-10), 29.2 and 29.0 (2t, C-8 and C-9), 23.8 (t, C-7), 22.6 (t, C-11), 18.5 (t, C-3), 14.0 (q, C-12); EIMS *m/z* (intensity %): 214 (M^+, 1), 197 (M^+-17, 2), 169 (1), 130 (28), 127 (42), 99 (16), 57 (100); HREI-MS *m/z* 214.15640 ± 0.05 $[C_{12}H_{22}O_3]^+$, calc. 214.15689, *m/z* 197.15348 ± 0.05 $[C_{12}H_{21}O_2]^+$, calc. 197.15416.

This work was supported by the Provincia Autonoma di Trento (Project on insect pest control) and by M.U.R.S.T. (Cofin2000).

Received 19 February 2002; accepted 25 June 2002
Paper 02/1248

References

1 D. Appleton, A.B. Duguid, S. Lee, Y. Ha, H. Ha, and F.J. Leeper, *J. Chem. Soc. Perkin Trans I* 1998, 89.
2 S. Beckmann and H. Geiger, *Chem. Ber.* 1961, **94**, 48.
3 R.M. Moriarty, C.C. Chien and T.B. Adams, *J. Org. Chem.* 1979, **44**, 2210.
4 H. Ruholl and H. Schäfer, *Synthesis* 1987, 408.
5 M. Hudlicky, *Oxidations in Organic Chemistry*, American Chemical Society, Washington DC, 1990.
6 S.O. Nwaukwa, and P.M. Keehn, *Tetrahedron Lett.*, 1982, **23**, 35; R.V. Stevens, K.T. Chapman, C.A. Stubbs, W.W. Tam and K.F. Albizati, *Tetrahedron Lett.*, 1982, **23**, 4647.
7 H. Schick and R. Ludvig, *Synthesis* 1992, 369.
8 T. Inokuchi, H. Kawafuchi and S. Torii, *Synlett* 1992, 510.
9 G. Chen, Z. Li, D. Pan, C. Tang, X. He, G. Xu, K. Chen and K.H. Lee, *J. Nat. Prod.* 1993, **56**, 1114.
10 S.G. Hedge, M.K. Vogel, J. Saddler, T. Hrinyo, N. Rockwell, R. Haynes, M. Oliver and J. Wolinsky, *Tetrahedron Lett.*, 1980, **21**, 441.
11 G.A. Lee and H.H. Freedman, *Tetrahedron Lett.*, 1976, **20**, 1641; M. Schneider, J. Weber and P. Faller, *J. Org. Chem.* 1982, **47**, 364; G.A. Mirafzal and A.M. Lozeva, *Tetrahedron Lett.*, 1998, **39**, 7263.