A Highly Effective Ligand-Bound Ruthenium Catalyst for Chemoselective Degradation of Aromatic Rings to Carboxylic Acids

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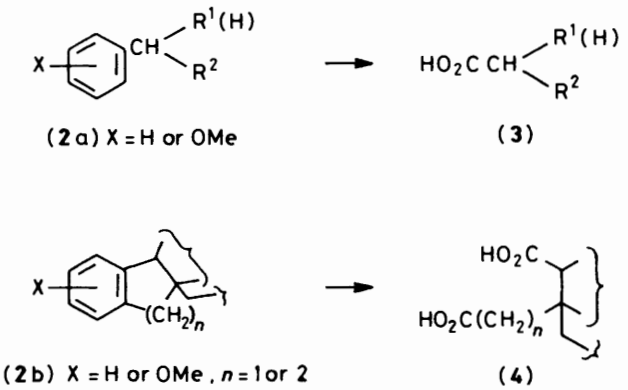
A highly effective oxidation catalyst, generated *in situ* by reaction of *cis*-(2,2'-bipyridine)$_2$RuCl$_2$·2H$_2$O with sodium metaperiodate mimics ruthenium tetraoxide in the chemoselective degradation of aromatic rings in the 2-aryltricyclo[3.2.1.0^{2,7}]octan-6-ones (**5a,b**) and (**6a,b**) and the aryl substituted bicyclo[3.2.1]octanones (**9a,b**), (**10a,b**), (**11**), and (**12**) to the keto monocarboxylic acids (**7a**), (**8a**), (**13a**), (**14a**), (**15a**), and (**16a**) respectively. Similar oxidation reaction of the 2β-benzyl- and 2β-phenethyl-cyclohexane-1,3-carbolactones (**17**)—(**20**) affords the corresponding γ-lactone acids (**20a**)—(**23a**), whilst the fused tetracyclic hydroaromatic ketones (**29a,b**), (**30a,b**), (**31a—c**), and (**35a,b**) provide their respective keto dicarboxylic acids (**32a**)—(**36a**) in excellent yields. The incorporation of a methoxy substitution in the aromatic ring considerably facilitates the oxidation reaction.

An aromatic ring can be used as a latent carboxylic acid functionality in organic synthesis.[1] The oxidative transformation of the aromatic group is usually carried out by exhaustive ozonolysis[1,2] but yields in this step, in most cases, are not satisfactory.[3] The periodate-based ruthenium tetraoxide-catalysed oxidative degradation[4] of aromatic rings to carboxylic acids is an attractive alternative to the ozonolysis method. In many cases, however, the catalytic activity of ruthenium is drastically reduced during the course of such an oxidation,[5] possibly owing to the formation of the carboxylate complexes of lower valent ruthenium formed during the reaction.[6] To obviate this drawback, MeCN was introduced[6] as a co-solvent in the traditional biphase CCl_4–H_2O system in the ruthenium-catalysed periodate oxidation, leading to highly improved conditions for conversions of alkenes and aromatic compounds into carboxylic acids in excellent yields.[6–8] More recently, we have shown[7] that dimethylformamide (DMF) is also equally effective in place of MeCN. Though earlier attempts to find a suitable strongly ligand-bound ruthenium catalyst in the periodate oxidation have been unsuccessful,[6,9] we were particularly attracted by the recent reports[10] that in certain polypyridine complexes of ruthenium, the oxidation state is easily accessible electrochemically, at relatively low redox potentials, by oxidation and loss of protons to give ruthenium-(IV)-oxo-complexes having the metal-ligand bonds intact, which are capable of sustaining catalytic effects in some oxidation reactions. In a preliminary communication we have reported[11] a highly effective catalytic system generated *in situ* by reaction of *cis*-[Ru(bpy)$_2$Cl$_2$]·2H$_2$O (**1**)[12] (bpy = 2,2'-bipyridine) with $NaIO_4$ which mimics RuO_4 in chemoselective degradation of aromatic rings to monocarboxylic acids in a few phenyl substituted bridged-ring ketones and γ-lactones. We now describe in detail the scope of this ligand-bound reagent (**1**) in catalysed periodate induced chemoselective degradation of a variety of phenyl and fused hydroaromatic substrates (**2a**) and (**2b**) incorporating ketonic and γ-lactone functionalities to the corresponding monocarboxylic and dicarboxylic acids (**3**) and (**4**) respectively (Scheme).

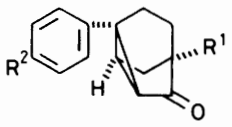


Scheme.

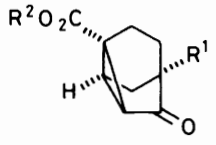
Results and Discussion

In a typical oxidation experiment, an aqueous solution of an excess of the secondary oxidant, $NaIO_4$, was added to a stirred solution of the aromatic substrate and a catalytic amount of the Ru-complex (**1**) in MeCN at 35—40 °C, whereupon the violet colour of the reaction mixture turned to dark orange-red† within a few minutes. When the oxidations were conducted at room temperature (method A), similar to that with uncomplexed ruthenium salts,[7] longer reaction times (16—20 h) were necessary in the case of unsubstituted aromatic compounds. However, the oxidation reactions were complete in a considerably shorter time (1—5 h) at reflux temperature (*ca.* 80 °C) (method B). Under these conditions the easily accessible arylcyclopropyl ketones (**5a,b**)[14] and (**6a,b**)[14] led to the respective acids (**7a**)[15] and (**8a**) in excellent yields. These were further characterised through the respective methyl esters (**7b**) and (**8b**). Similarly, the bridged-cyclopentanones (**9a,b**)[14], (**10a,b**)[14], (**11**),[16a] and (**12**)[16a] were transformed into the corresponding methyl esters (**13b**),[7] (**14b**),[7] (**15b**), and (**16b**) by oxidation followed by esterification of the crude acids with CH_2N_2. The phenyl group in the γ-lactones (**17**),[16b] (**18**),[16b] (**19**),[17] and (**20**)[17] underwent smooth oxidation to afford the respective acids which were characterised as such or as the corresponding methyl esters (**20b**),[7] (**21b**),[7] (**22**),[7] and (**23**).[7] The

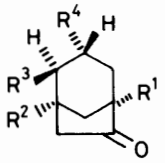
† The dark tan solid, presumably the 'active oxidation catalyst' which could be recovered from the oxidation reactions with the Ru-complex (**1**) or by treatment of this in MeCN or CH_2Cl_2 with aqueous $NaIO_4$, exhibited in the i.r. spectrum (KBr) characteristic bands at 1 600, 1 290, and 1 018 cm^{-1} for the metal-bound (bpy)-ligand.[12] This was further supported[12] by the u.v. spectrum [$\lambda_{max.}$ (CH_2Cl_2) 380, 310sh, 300, and 280sh nm]. In addition, a strong i.r. band at 845 cm^{-1} in this material could be attributed[13] to ν_{as} Ru–O_2.



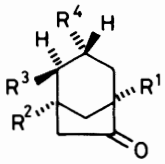
(5) a; $R^1 = R^2 = H$
b; $R^1 = H$; $R^2 = OMe$
(6) a; $R^1 = Me$; $R^2 = H$
b; $R^1 = Me$; $R^2 = OMe$



(7) a; $R^1 = R^2 = H$
b; $R^1 = H$; $R^2 = Me$
(8) a; $R^1 = Me$; $R^2 = H$
b; $R^1 = R^2 = Me$



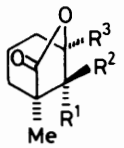
(9) a; $R^1 = R^2 = R^4 = H$; $R^3 = Ph$
b; $R^1 = R^2 = R^4 = H$; $R^3 = C_6H_4OMe$-*p*
(10) a; $R^1 = Me$; $R^2 = R^4 = H$; $R^3 = Ph$
b; $R^1 = Me$; $R^2 = R^4 = H$; $R^3 = C_6H_4OMe$-*p*
(11) $R^1 = Me$; $R^2 = Ph$; $R^3 = R^4 = H$
(12) $R^1 = R^2 = Me$; $R^3 = H$; $R^4 = Ph$



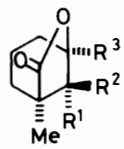
(13) a; $R^1 = R^2 = R^4 = H$; $R^3 = CO_2H$
b; $R^1 = R^2 = R^4 = H$; $R^3 = CO_2Me$
(14) a; $R^1 = Me$; $R^2 = R^4 = H$; $R^3 = CO_2H$
b; $R^1 = Me$; $R^2 = R^4 = H$; $R^3 = CO_2Me$
(15) a; $R^1 = Me$; $R^2 = CO_2H$; $R^3 = R^4 = H$
b; $R^1 = Me$; $R^2 = CO_2Me$; $R^3 = R^4 = H$
(16) a; $R^1 = R^2 = Me$; $R^3 = H$; $R^4 = CO_2H$
b; $R^1 = R^2 = Me$; $R^3 = H$; $R^4 = CO_2Me$

oxidation of the phenyl moiety in the hydroxy acid (**24a**)[16b] and the corresponding methyl ester (**24b**)[16b] gave the γ-lactones (**25a**) and (**25b**) respectively. The results are presented in Table 1. In each of these cases the yield of the oxidation product is similar to or even better than that obtained[7] by using $RuCl_3 \cdot xH_2O$ and $NaIO_4$ in MeCN–CCl_4–H_2O[6] or DMF–CCl_4–H_2O.[7] The fused hydroaromatic ketones (**29a,b**),[18,19] (**30a,b**),[18] (**31a—c**),[18,20] and (**35a,b**)[21] on oxidation using Ru-complex (**1**) (Methods A and B) gave the respective keto dicarboxylic acids (**32a**)—(**36a**) in excellent yields. These acids were further characterised through their respective methyl esters (**32b**)—(**36b**). In parallel with our earlier observations[7] with (**30a**) and (**31a**), $RuCl_3 \cdot xH_2O$–$NaIO_4$ oxidation of (**29a,b**), (**30b**), (**31b,c**), and (**35a,b**) gave their respective keto dicarboxylic acids (**32a**)—(**36a**) in similar or lower yields.

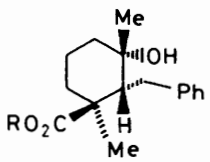
In contrast to the uncomplexed ruthenium-catalysed oxidations, which are highly sensitive towards solvent composition[6] with the Ru-complex (**1**), the reactions in all the substrates (Tables 1 and 2) proceeded equally well when MeCN was replaced by CH_2Cl_2, CH_2Cl_2–CCl_4 (1:1), or DMF. The examination of the present results (Table 1 entries 2, 4, 6, 8, and



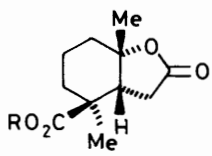
(17) $R^1 = H$; $R^2 = CH_2Ph$; $R^3 = Me$
(18) $R^1 = CH_2Ph$; $R^2 = H$; $R^3 = Me$
(19) $R^1 = R^3 = H$; $R^2 = (CH_2)_2Ph$
(20) $R^1 = H$; $R^2 = (CH_2)_2Ph$; $R^3 = Me$



(20) a; $R^1 = H$; $R^2 = CH_2CO_2H$; $R^3 = Me$
b; $R^1 = H$; $R^2 = CH_2CO_2Me$; $R^3 = Me$
(21) a; $R^1 = CH_2CO_2H$; $R^2 = H$; $R^3 = Me$
b; $R^1 = CH_2CO_2Me$; $R^2 = H$; $R^3 = Me$
(22) a; $R^1 = R^3 = H$; $R^2 = (CH_2)_2CO_2H$
b; $R^1 = R^3 = H$; $R^2 = (CH_2)_2CO_2Me$
(23) a; $R^1 = H$; $R^2 = (CH_2)_2CO_2H$; $R^3 = Me$
b; $R^1 = H$; $R^2 = (CH_2)_2CO_2Me$; $R^3 = Me$



(24) a; R = H
b; R = Me

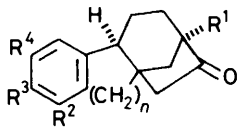


(25) a; R = H
b; R = Me

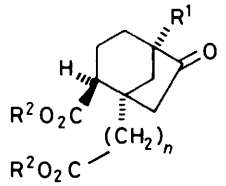
Table 2 entries 2, 4, 6, 7, and 9) clearly indicates that the substrates incorporating aromatic methoxy groups undergo oxidative degradation considerably faster than those having an unsubstituted aromatic ring. The ruthenium catalysed periodate oxidation of aromatic rings possibly proceeds through a similar mechanism as that suggested[4a] for the cleavage of alkenic bonds with RuO_4.

In addition to the stability and non-hygroscopic nature of the bipyridine-complexed ruthenium, a major advantage of this catalyst in the periodate-induced oxidation reactions is that a higher temperature (80 °C) may be used with substantial lowering of the reaction time (see Tables 1 and 2). However, owing to the volatility of the effective oxidation agent RuO_4 with the usual uncomplexed ruthenium catalysts (such as $RuCl_3 \cdot xH_2O$ or RuO_2) the oxidation can only be conducted at room temperature, requiring much longer time. The present work has definitely established that the improved ruthenium-catalysed periodate-induced degradation of aromatic rings constitutes an ideal and reliable procedure for the synthesis of highly functionalised bridged-ring and carbocyclic intermediates. The new and easily accessible Ru-complex oxidation catalyst* could provide the basis of other oxidation reactions of organic compounds where RuO_4 is used.

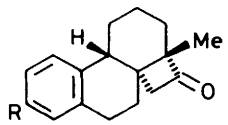
* Very recently, $RuCl_3 \cdot xH_2O$ associated with bipyridine as a catalyst in the stereospecific epoxidation of alkenes by $NaIO_4$ has been reported.[22] Oxidation of alcohols with a stoichiometric amount of $[RuO_2(bpy)_2Cl_2]$ has also been recorded.[23]



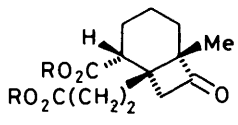
(29) a ; $R^1 = R^2 = R^3 = R^4 = H$; $n = 1$
b ; $R^1 = R^3 = R^4 = H$; $R^2 = OMe$; $n = 1$
(30) a ; $R^1 = R^2 = R^3 = R^4 = H$; $n = 2$
b ; $R^1 = R^2 = R^4 = H$; $R^3 = OMe$; $n = 2$
(31) a ; $R^1 = Me$; $R^2 = R^3 = R^4 = H$; $n = 2$
b ; $R^1 = Me$; $R^2 = R^4 = H$; $R^3 = OMe$; $n = 2$
c ; $R^1 = Me$; $R^2 = R^3 = H$; $R^4 = OMe$; $n = 2$



(32) a ; $R^1 = R^2 = H$; $n = 1$
b ; $R^1 = H$; $R^2 = Me$; $n = 1$
(33) a ; $R^1 = R^2 = H$; $n = 2$
b ; $R^1 = H$; $R^2 = Me$; $n = 2$
(34) a ; $R^1 = Me$; $R^2 = H$; $n = 2$
b ; $R^1 = R^2 = Me$; $n = 2$



(35) a ; R = H
b ; R = OMe



(36) a ; R = H
b ; R = Me

Table 1. Oxidative degradation of aromatic rings to monocarboxylic acid derivatives with the Ru-complex (1) as the catalyst and $NaIO_4$ in acetonitrile and water.

Entry	Starting material	Product	Method[a]	Reaction[b] time (h)	Yield[c] (%)
1	(5a)	(7a)	A	20	84
			B	2.5	86
2	(5b)	(7a)	A	8	84
			B	1	86
3	(6a)	(8a)	A	20	84
			B	2.5	86
4	(6b)	(8a)	A	8	86
			B	1	86
5	(9a)	(13b)[d,e]	A	24	88
			B	2.5	90
6	(9b)	(13b)[d,e]	A	8	92
			B	1	92
7	(10a)	(14a)[f]	A	22	92
			B	2.5	92
8	(10b)	(14a)[f]	A	8	92
			B	1	94
9	(11)	(15b)[d]	A	20	92
			B	2.5	96
10	(12)	(16b)[d]	A	20	96
			B	2.5	96
11	(17)	(20a)[f]	A	20	85
			B	3	85
12	(18)	(21a)[f]	A	24	88
			B	3	88
13	(19)	(22b)[d,e]	A	20	90
			B	3	92
14	(20)	(23b)[d,e]	A	20	90
			B	3	90
15	(24a)	(25a)	A	24	80
			B	2.5	80
16	(24b)	(25b)	A	24	80
			B	2.5	80

[a] At room temperature (25—35 °C) (A) and under reflux (*ca.* 80 °C) (B). [b] Monitored by t.l.c. [c] Yield of purified product. [d] Prepared by direct esterification of the acid with CH_2N_2–Et_2O. Identical (i.r., ^1H n.m.r., and g.l.c.) with the authentic sample.[7] [f] The corresponding methyl ester is identical (i.r., ^1H n.m.r., and g.l.c.) with the authentic sample.[7]

Experimental

M.p.s were measured in open capillary tubes and are uncorrected. I.r. spectra of solids (KBr) and liquids (film) were recorded on a Perkin-Elmer model 298 spectrometer. ^1H N.m.r. spectra were recorded at 60 or 200 MHz (as specified) on Varian Associates T-60A and XL-200 spectrometers, respectively for solutions in CCl_4 or $CDCl_3$ (if specified), with $SiMe_4$ as an internal standard. Analytical g.l.c. was performed on a Hewlett-Packard model 5730A chromatograph equipped with a flame-ionization detector employing a 10% UCW-982 (20 ft × 0.5 in) column at 160 °C with N_2 as the carrier gas. Elemental analyses were performed by P. P. Bhattacharyya of this laboratory. Petroleum and light petroleum refer to the fractions of b.p. 60—80 and 40—60 °C, respectively.

6-Oxotricyclo[3.2.1.$0^{2,7}$]*octane-2-carboxylic Acid* (**7a**).—(*a*) *Oxidation of the phenylcyclopropyl ketone* (**5a**). *Method A.* To a deep violet magnetically stirred solution of *cis*-[$Ru(bpy)_2Cl_2$]·$2H_2O$ (**1**) (5.2 mg, 0.01 mmol, 2 mol %) and the cyclopropyl ketone (**5a**) (99 mg, 0.5 mmol) in acetonitrile (10 ml) at 35—40 °C, a solution of sodium metaperiodate (1.92 g, 9 mmol, 18 equiv.) in water (10 ml) was added. After *ca.* 10—20 min the colour of the reaction mixture turned to dark orange-red. The stirring at room temperature (*ca.* 25—35 °C) was continued for 20 h, by which time the starting material had disappeared (t.l.c.). The mixture was diluted with water (10 ml) and extracted with Et_2O (4 × 20 ml). The combined organic extracts were extracted with 2% aqueous potassium hydroxide (4 × 10 ml) and water. The combined basic aqueous extracts were acidified with 6M-hydrochloric acid, and the acidic material was isolated by extraction with Et_2O (20 ml × 4). The combined ethereal extracts were washed with saturated aqueous sodium chloride (10 ml), 2% aqueous sodium thiosulphate (2 × 5 ml), saturated aqueous sodium chloride (10 ml) and dried (Na_2SO_4). Removal of the solvent under reduced pressure afforded the cyclopropyl keto acid (**7a**) as a colourless solid (68 mg, 82%), m.p. 134 °C [light petroleum–Et_2O, (1:1)] (lit.,[15] m.p. 120—132 °C). The acid (**7a**) (46.5 mg, 0.025 mmol) was esterified with an excess of diazomethane in Et_2O to afford the methyl ester (**7b**) (49.8 mg, 99%) and the product was purified by bulb-to-bulb distillation, b.p. 110 °C at 0.2 mmHg (bath temperature), homogeneous by g.l.c. (R_t 2.6 min); $\nu_{max.}$ 1 735 and 1 725 cm^{-1}; δ ($CDCl_3$; 200 MHz) 1.96 (m, 3 H), 2.13 (m, 1 H), 2.26—2.34 (m, 4 H), 2.68 (m, 1 H), and 3.69 (s, 3 H, CO_2Me) [lit.,[15] 2.2 (m, 8 H), 2.7 (d, 1 H), and 3.72 (s, 3 H)].

Method B. The dark orange mixture of the Ru-complex (**1**) (5.2 mg, 0.01 mmol), and the ketone (**5a**) (99 mg, 0.5 mmol) in acetonitrile (10 ml), were gently refluxed (*ca.* 80 °C) for 2.5 h with sodium metaperiodate (1.92 g, 9 mmol) in water (10 ml) and was worked-up as described above to afford the acid (**7a**)

Table 2. Oxidative degradation of fused aromatic rings to dicarboxylic acid derivatives with Ru-complex (**1**) catalyst and $NaIO_4$ in acetonitrile and water.

Entry	Starting material	Product	Method[a]	Reaction[b] time (h)	Yield[c] (%)
1	(**29a**)	(**32a**)	A	24	72
			B	5	75
2	(**29b**)	(**32a**)	A	10	76
			B	2.5	80
3	(**30a**)	(**33b**)[d,e]	A	24	85
			B	5	85
4	(**30b**)	(**33b**)[d,e]	A	12	86
			B	2	86
5	(**31a**)	(**34a**)[f]	A	24	82
			B	5	82
6	(**31b**)	(**34a**)[f]	A	12	84
			B	2	84
7	(**31c**)	(**34a**)[f]	A	12	85
			B	2	85
8	(**35a**)	(**36a**)	A	24	70
			B	5	72
9	(**35b**)	(**36a**)	A	10	72
			B	2	75

[a] At room temperature (25—30 °C) (A) and under reflux (*ca.* 80 °C) (B). [b] Monitored by t.l.c. [c] Yield of purified product. [d] Prepared by esterification of the acid with CH_2N_2–Et_2O. [e] Identical (i.r., ^1H n.m.r., and g.l.c.) with an authentic sample.[7] [f] The corresponding methyl ester was identical (i.r., ^1H n.m.r., and g.l.c.) with the authentic sample.[7]

(70 mg, 84%) m.p. and mixed m.p. 134 °C with the sample described above.

(*b*) *Oxidation of the* p-*methoxyphenylcyclopropyl ketone* (**5b**). *Method A*. The oxidation of (**5b**) (114 mg, 0.5 mmol) in the presence of the Ru-complex (**1**) (5.2 mg, 0.01 mmol) in acetonitrile (10 ml) with sodium metaperiodate (1.28 g, 6 mmol, 12 equiv.) in water (10 ml) was completed in 8 h at room temperature to afford the acid (**7a**) (70 mg, 84%), m.p. and mixed m.p. 134 °C with the sample described above.

Method B. The oxidation of (**5b**) (114 mg, 0.5 mmol) in the presence of the Ru-complex (**1**) (5.2 mg, 0.01 mmol) in acetonitrile (10 ml) with sodium metaperiodate (1.28 g, 6 mmol) in water (10 ml) under reflux (*ca.* 80 °C) was completed in 1 h to afford the acid (**7a**) (71 mg, 86%), m.p. and mixed m.p. 134 °C with the sample described above.

The following phenyl and methoxyphenyl derivatives were oxidised by similar methods as described for (**5a**) and (**5b**) respectively, using the aromatic substrates and the reagents in identical ratios.

5-*Methyl*-6-*oxotricyclo*[3.2.1.$0^{2,7}$]*octane*-2-*carboxylic Acid* (**8a**): *Oxidation of the Phenylcyclopropyl Ketone* (**6a**).—The oxidation of compound (**6a**) (106 mg, 0.5 mmol) following the Methods A and B as described for (**5a**) afforded the cyclopropyl keto acid (**8a**), m.p. 128 °C [light petroleum–Et_2O, (1:1)] in 84 and 86% yields respectively. (Found: C, 66.4; H, 7.0. $C_{10}H_{12}O_3$ requires C, 66.65; H, 6.7%). Esterification of a portion of the acid (**8a**) with ethereal diazomethane gave the corresponding methyl ester (**8b**), b.p. 115 °C at 0.2 mmHg (bath temperature); $\nu_{max.}$ 1 735 and 1 725 cm^{-1}; δ ($CDCl_3$; 200 MHz) 0.96 (s, 3 H, Me), 1.68 (m, 2 H), and 2.02 (m, 2 H), 2.28—2.41 (m, 3 H), 2.61 (m, 1 H), and 3.68 (s, 3 H, CO_2Me); homogeneous by g.l.c. (R_t 2.7 min).

5-*Methyl*-6-*oxobicyclo*[3.2.1]*octane*-endo-2-*carboxylic Acid* (**14a**): *Oxidation of the Phenyl Ketone* (**10a**).—The oxidation of (**10a**) (107 mg, 0.5 mmol) by Methods A and B as described for (**5a**) afforded the keto acid (**14a**) (85 mg, 92%) m.p. 98 °C [light petroleum–Et_2O, (1:1)]. (Found: C, 65.85; H, 7.75. $C_{10}H_{14}O_3$ requires C, 65.9; H, 7.7%). A portion of this acid on esterification with ethereal diazomethane gave the corresponding methyl ester (**14b**), identical (i.r., ^1H n.m.r., and g.l.c.) with an authentic sample.[7]

Oxidation of the Phenyl Ketone (**11**): *Methyl* 5-*Methyl*-6-*oxobicyclo*[3.2.1]*octane*-1-*carboxylate* (**15b**).—The oxidation of (**11**) (107 mg, 0.5 mmol) by Methods A and B as described for (**5a**) followed by esterification of the resulting gummy acid (**15a**) with ethereal diazomethane afforded the methyl ester (**15b**) in 92 and 96% yields respectively, b.p. 90 °C at 0.5 mmHg (bath temperature); $\nu_{max.}$ 1 735 and 1 725 cm^{-1}; δ 1.03 (s, 3 H, Me), 1.45—2.46 (m, 10 H), and 3.73 (s, 3 H, CO_2Me); homogeneous by g.l.c. (R_t 0.9 min) (Found: C, 78.9; H, 10.6. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%).

Oxidation of the Phenyl Ketone (**12**): *Methyl* 1,5-*Dimethyl*-6-*oxobicyclo*[3.2.1]*octane*-exo-3-*carboxylate* (**16b**).—Oxidation of (**12**) (114 mg, 0.5 mmol) by Methods A and B followed by esterification of the resulting gummy acid (**16a**) with ethereal diazomethane gave the methyl ester (**16b**) in 96% yield, b.p. 90 °C at 0.5 mmHg (bath temperature); $\nu_{max.}$ 1 730 and 1 725 cm^{-1}; δ 1.03 (s, 3 H, Me), 1.21 (s, 3 H, Me), 1.43—1.70 (m, 6 H, methylene), 2.0 (br s, 2 H, $COCH_2$), 2.5 (m, 1 H, methine), and 3.60 (s, 3 H, CO_2Me); homogeneous by g.l.c. (R_t 1.99 min). (Found: C, 68.7; H, 8.9. $C_{12}H_{18}O_3$ requires C, 68.5; H, 8.6%).

Oxidation of the Benzyl Lactone (**17**): endo(1,5-*Dimethyl*-7-*oxo*-6-*oxabicyclo*[3.2.1]*octan*-8-*yl*)*acetic Acid* (**20a**).—The oxidation of (**13**) (122 mg, 0.5 mmol) by Methods A and B as described for (**5a**) afforded the lacto acid (**20a**), m.p. 190 °C [light petroleum–Et_2O, (1:1)] in 80% and 85% yields respectively. A portion of this acid on esterification with ethereal diazomethane gave the corresponding methyl ester (**20b**), identical (i.r., ^1H n.m.r. and g.l.c.) with an authentic sample.[7]

Oxidation of the Benzyl Lactone (**18**): exo-(1,5-*Dimethyl*-7-*oxo*-6-*oxabicyclo*[3.2.1]*octan*-8-*yl*)*acetic Acid* (**21a**).—The oxidation of (**18**) (122 mg, 0.5 mmol) by Methods A and B afforded the lacto acid (**21a**), m.p. 130 °C [light petroleum–Et_2O (1:1)] in 88% yield (Found: C, 62.4; H, 7.35. $C_{11}H_{16}O_4$ requires C, 62.25; H, 7.6%). A portion of this acid on esterification with ethereal diazomethane gave the respective methyl ester (**21b**) identical (i.r., ^1H n.m.r., and g.l.c.) with an authentic sample.[7]

Oxidation of Compound (**24a**): c-2,t-6-*Dimethyl*-8-*oxo*-7-*oxabicyclo*[4.3.0]*nonane*-t-2-*carboxylic Acid* (**25a**).—The oxidation of (**24a**) (131 mg, 0.5 mmol) by Methods A and B as described for (**5a**) afforded the lacto acid (**25a**), m.p. 136 °C [(light petroleum–Et_2O (1:1)] in 80% yield; $\nu_{max.}$ 1 755 and 1 725 cm^{-1} (Found: C, 62.3; H, 7.85. $C_{11}H_{16}O_4$ requires C, 62.25; H, 7.6%). A portion of this acid on esterification with ethereal diazomethane gave the corresponding lacto ester (**25b**), b.p. 140 °C at 0.2 mmHg (bath temperature); $\nu_{max.}$ 1 770 and 1 730 cm^{-1}; δ($CDCl_3$) 1.16 (s, 3 H, Me), 1.36 (s, 3 H, Me), 1.40—1.70 (m, 6 H, methylene), 2.30—2.37 (m, 3 H, $COCH_2$ and methine), and 3.38 (s, 3 H, CO_2Me); homogeneous by g.l.c. (R_t 6.2 min) (Found: C, 63.7; H, 8.1. $C_{12}H_{18}O_4$ requires C, 63.7; H, 8.0%).

Oxidation of the Alcohol (**24b**) *to the Lactone* (**25b**).—The oxidation of (**24b**) (138 mg, 0.5 mmol) by Methods A and B afforded the lacto ester (**25b**) in 80% yield, identical (i.r., ^1H n.m.r., and g.l.c.) with the sample described above.

Oxidation of the Fused Hydroaromatic Ketones (**29a,b**), (**30a,b**), (**31a—c**), *and* (**35a,b**).—1α-*Carboxymethyl*-6-*oxobicy-*

clo[3.2.1]*octane*-2β-*carboxylic acid* (**32a**): *oxidation of* (**29a**). The oxidation of (**29a**) (106 mg, 0.5 mmol) by Methods A and B as described for (**5a**) afforded the diacid (**32a**), m.p. 185 °C [petroleum–ethyl acetate (1:1)] in 72 and 75% yields respectively (Found: C, 55.9; H, 6.8. $C_{10}H_{14}O_5$ requires C, 56.0; H, 6.6%). A portion of this acid on esterification with ethereal diazomethane gave the corresponding dimethyl ester (**32b**), b.p. 150 °C at 0.2 mmHg (bath temperature), $\nu_{max.}$ 2 950 and 1 730 cm^{-1}; δ 1.6—2.8 (m, 12 H) and 3.60 and 3.63 (2 s, 6 H, CO_2Me) (Found: C, 59.45; H, 7.6. $C_{12}H_{18}O_5$ requires C, 59.5; H, 7.5%).

1α-*Carboxyethyl*-5-*methyl*-6-*oxobicyclo*[3.2.1]*octane*-2β-*carboxylic Acid* (**34a**): *oxidation of the ketone* (**31a**). The oxidation of (**31a**) (120 mg, 0.5 mmol) by Methods A and B as described for (**5a**) afforded the diacid (**34a**), m.p. 214 °C (decomp) [Et_2O–MeOH, (9:1)] in 82% yield (Found: C, 61.4; H, 7.3. $C_{13}H_{18}O_5$ requires C, 61.4; H, 7.1%). A portion of this acid on esterification with ethereal diazomethane afforded the respective dimethyl ester (**34b**), identical (i.r., ^1H n.m.r., and g.l.c.) with an authentic sample.[7]

1β-*Carboxyethyl*-6-*methyl*-7-*oxobicyclo*[4.2.0]*octane*-2α-*carboxylic acid* (**36a**): *oxidation of the ketone* (**35a**). The oxidation of compound (**35a**) (120 mg, 0.5 mmol) by Methods A and B as described for (**5a**) afforded the diacid (**36a**), m.p. 223 °C [petroleum–Et_2O (1:1)] in 70 and 72% yields respectively (Found: C, 61.15; H, 7.1. $C_{13}H_{18}O_5$ requires C, 61.4; H, 7.1%). A portion of this acid on esterification with ethereal diazomethane gave the corresponding dimethyl ester (**36b**), b.p. 170 °C at 0.2 mmHg (bath temperature); $\nu_{max.}$ 1 770 and 1 730 cm^{-1}; δ 1.1 (s, 3 H, Me), 1.23—2.56 (m, 13 H), 3.60 and 3.63 (2 s, 6 H, CO_2Me); homogeneous by g.l.c. (R_t 16.3 min) (Found: C, 63.75; H, 7.9. $C_{15}H_{22}O_5$ requires C, 63.8; H, 7.85%).

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References

1 (*a*) M. E. Jung and J. P. Hudspeth, *J. Am. Chem. Soc.*, 1980, **102**, 2463; (*b*) P. Yates and K. E. Stevens, *Can. J. Chem.*, 1982, **60**, 825.
2 (*a*) K. Nakajaki and H. Arakawa, *Bull. Chem. Soc. Jpn.*, 1964, **37**, 464; (*b*) O. Cervinka and O. Belovsky, *Z. Chem.*, 1967, **7**, 226; (*c*) Y. Hayashi and W. B. Wawson, *J. Biol. Chem.*, 1969, **244**, 4158; (*d*) J. J. Pappas, W. P. Keaveney, M. Berger, and R. V. Rush, *J. Org. Chem.*, 1968, **33**, 787.
3 For an exception, see H. Klein and A. Steinmetz, *Tetrahedron Lett.*, 1975, 4249.
4 (*a*) D. G. Lee and M. van den Engh, in 'Oxidation in Organic Chemistry,' W. S. Trahanovsky, ed. Academic Press, New York, 1973, Part B, Chapter 4; (*b*) P. N. Rylander, 'Organic Synthesis with Noble Metal Catalysts,' Academic Press, New York, 1973, p. 133.
5 (*a*) J. A. Caputo and R. Fuchs, *Tetrahedron Lett.*, 1967, 4729; (*b*) J. A. Caputo and R. Fuchs, *J. Org. Chem.*, 1968, **33**, 1959; (*c*) D. M. Piatak, G. Herbst, J. Wicha, and E. Caspi, *J. Org. Chem.*, 1969, **34**, 116; (*d*) V. A. Spitzer and D. G. Lee, *J. Org. Chem.*, 1974, **39**, 2468; (*e*) D. C. Ayres and A. M. M. Hossain, *J. Chem. Soc., Chem. Commun.*, 1972, 428; (*f*) D. C. Ayres and A. M. M. Hossain, *J. Chem. Soc., Perkin Trans. 1*, 1975, 707; (*g*) D. C. Ayres and R. Gopalan, *J. Chem. Soc., Perkin Trans. 1*, 1978, 588; (*h*) S. Imajo, H. Kuritani, K. Shingu, and M. Nakagawa, *J. Org. Chem.*, 1979, **44**, 3587; (*i*) T. K. Sarkar, *J. Chem. Soc., Perkin Trans. 1*, 1973, 2454; (*j*) A. S. Sarma and P. Chattopadhyay, *J. Org. Chem.*, 1982, **47**, 1727.
6 P. H. J. Carlsen, T. Katsuki, V. S. Martin, and K. B. Sharpless, *J. Org. Chem.*, 1981, **46**, 3936.
7 A. K. Chakraborti and U. R. Ghatak, *Synthesis*, 1983, 746.
8 M. Kasai and H. Ziffer, *J. Org. Chem.*, 1983, **48**, 2346.
9 K. B. Sharpless, K. Akashi, and K. Oshima, *Tetrahedron Lett.*, 1976, 2503.
10 (*a*) M. S. Thompson and T. J. Meyer, *J. Am. Chem. Soc.*, 1982, **104**, 4106; (*b*) B. A. Moyer and T. J. Meyer, *J. Am. Chem. Soc.*, 1978, **100**, 3601; (*c*) F. R. Keene, D. J. Salmon, and T. J. Meyer, *J. Am. Chem. Soc.*, 1977, **99**, 4821.
11 A. K. Chakraborti, B. K. Banik, and U. R. Ghatak, *Indian J. Chem.*, 1984, **23B**, 291.
12 B. P. Sullivan, D. J. Salmon, and T. J. Meyer, *Inorg. Chem.*, 1978, **17**, 3334.
13 W. P. Griffith and D. Pawson, *J. Chem. Soc., Dalton Trans.*, 1973, 1315.
14 U. R. Ghatak, S. K. Alam, P. C. Chakraborti, and B. C. Ranu, *J. Chem. Soc. Perkin Trans. 1*, 1976, 1669.
15 D. Becker and H. J. E. Loewenthal, *Isr. J. Chem.*, 1972, **10**, 375.
16 (*a*) A. K. Chakraborti, J. K. Ray, K. K. Kundu, S. Chakrabarty, D. Mukherjee, and U. R. Ghatak, *J. Chem. Soc., Perkin Trans. 1*, 1984, 261; (*b*) U. R. Ghatak, J. Chakravarty, and A. K. Banerjee, *Tetrahedron*, 1968, **24**, 1577.
17 U. R. Ghatak, N. R. Chatterjee, and B. Sanyal, *J. Org. Chem.*, 1979, **44**, 1992.
18 P. N. Chakrabortty, R. Dasgupta, S. K. Dasgupta, S. R. Ghosh, and U. R. Ghatak, *Tetrahedron*, 1972, **28**, 4653.
19 B. C. Ranu, M. Sarkar, P. C. Chakraborti, and U. R. Ghatak, *J. Chem. Soc., Perkin Trans. 1*, 1982, 865.
20 U. R. Ghatak and S. C. Roy, *J. Chem. Res.*, 1981, (*S*) 5; (*M*) 0159—0166.
21 (*a*) U. R. Ghatak, B. Sanyal, G. O. S. V. Satyanarayana, and S. Ghosh, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1203; (*b*) U. R. Ghatak, B. Sanyal, and S. Ghosh, *J. Am. Chem. Soc.*, 1976, **98**, 3721.
22 G. Balavoine, C. Eskenazi, F. Meunier, and H. Riviere, *Tetrahedron Lett.*, 1984, **25**, 3187.
23 G. Green, W. P. Griffith, D. M. Hollinshead, S. V. Ley, and M. Schröder, *J. Chem. Soc., Perkin Trans. 1*, 1984, 681.

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