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Oxidation of 2-Alkylcycloalkanones with Iodine–Cerium(IV) Salts in Alcohols†

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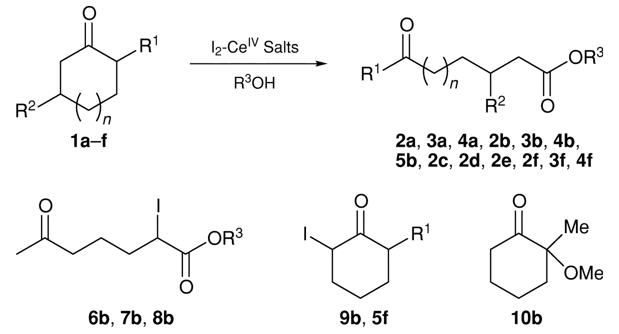
The reaction of 2-alkylcycloalkanones with iodine–cerium(IV) salts in alcohols (methanol, ethanol, propan-1-ol or propan-2-ol) gave the respective oxo ester in 28–98% yields.

Oxocarboxylic acids and esters are important as intermediates in organic synthesis. There are many syntheses of oxo esters, involving regiospecific oxidative ring-opening of cycloalkanones with ferric salts by oxygen,[1] ring opening oxygenation on treatment with $VO(OEt)Cl_2$ in alcohols under oxygen,[2] electrochemical oxidation of enol ethers of cyclohexanone,[3] specific cleavage of silyl enol ethers by $MoO_2(acac)_2$ (Hacac = pentane-2,4-dione) and *tert*-butyl peroxide,[4] and Mo-catalyzed oxygenation of cyclic ketones by molecular oxygen.[5] It is known that many of these reactions proceed by a Baeyer–Villiger type process. Atlamsani *et al.* have recently reported that the oxidation of 2-methylcyclohexanone by oxygen in the presence of vanadium-containing heteropolyanions in $AcOH–H_2O$ gives 6-oxoheptanoic acid.[6]

We have investigated novel iodination methods using iodine–copper(II) acetate.[7] These methods, however, have disadvantages in that the iodide ions produced are consumed as copper(I) iodide. During the course of our studies we found new reactions when using iodine–ammonium cerium(IV) nitrate (CAN).[8]

We have also described the reaction of 5α-cholestan-3-one with iodine and CAN in acetic acid–water (9:1) at 50 °C for 22 h to give 2,3-seco-5α-cholestane-2,3-dioic acid.[9] Through our studies we have found that iodine–CAN and iodine–cerium(IV) sulfate tetrahydrate (CST)[10] are useful reagents for the syntheses of a large number of iodo compounds. Here we report that the reaction of 2-alkylcycloalkanones **1a**–**1f** with iodine–cerium(IV) salts in alcohols (methanol, ethanol, propan-1-ol, or propan-2-ol) yields the corresponding oxo ester (Scheme 1). The reaction of 2-methylcyclohexanone **1b** with iodine (0.1 mol. equiv.)–CST (1.5 mol. equiv.) in methanol at 50 °C for 15 h gave methyl 6-oxoheptanoate **2b** (82%). With iodine (0.6 mol. equiv.)–CST (1.0 mol. equiv.), **2b** (29%) and 2-methoxy-2-methylcyclohexanone **10b** (59%) were obtained. The results are summarized in Table 1.



1a: $n = 0$, $R^1 = CH_3$, $R^2 = H$
1b: $n = 1$, $R^1 = CH_3$, $R^2 = H$
1c: $n = 1$, $R^1 = CH_3$, $R^2 = CH_3$
1d: $n = 1$, $R^1 = Pr^n$, $R^2 = H$
1e: $n = 1$, $R^1 = Pr^i$, $R^2 = CH_3$
1f: $n = 1$, $R^1 = Ph$, $R^2 = H$
2a: $n = 0$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OMe$
2b: $n = 1$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OMe$
2c: $n = 1$, $R^1 = CH_3$, $R^2 = CH_3$, $R^3 = OMe$
2d: $n = 1$, $R^1 = Pr^n$, $R^2 = H$, $R^3 = OMe$
2e: $n = 1$, $R^1 = Pr^i$, $R^2 = CH_3$, $R^3 = OMe$
2f: $n = 1$, $R^1 = Ph$, $R^2 = H$, $R^3 = OMe$
3a: $n = 0$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OEt$
4a: $n = 0$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OPr^n$
3b: $n = 1$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OEt$
4b: $n = 1$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OPr^n$
5b: $n = 1$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OPr^i$
6b: $n = 1$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OMe$
7b: $n = 1$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OEt$
8b: $n = 1$, $R^1 = CH_3$, $R^2 = H$, $R^3 = OPr^n$
9b: $n = 1$, $R^1 = CH_3$
3f: $n = 1$, $R^1 = Ph$, $R^2 = H$, $R^3 = OEt$
4f: $n = 1$, $R^1 = Ph$, $R^2 = H$, $R^3 = OPr^n$
5f: $n = 1$, $R^1 = Ph$

Scheme 1

As can be seen from Table 1, the reaction provided a general synthesis of oxo ester derivatives. Moreover, it is particularly noteworthy that in contrast to the case of 2-alkylcycloalkanones, the reaction of 2-phenylcyclohexanone yielded oxo esters in high yield. It was found that with 0.6 mol. equiv. of iodine, the 2-methoxy compound was obtained as the major product. In order to clarify the reaction pathway, the reaction of **10b** with iodine–CST was attempted. The reaction of **10b** under the conditions for C–C bond cleavage described above resulted in the recovery of the starting material. This result eliminates **10b** as an intermediate.

Table 1 Reactions of 2-alkylcycloalkanones with $I_2–Ce^{IV}$ salts in MeOH[a]

Reagent (mol. equiv.)	Substrate	$T/°C$	t/h	Products and yields (%) by NMR[b] (isolated)		
CST (1.5)–I_2(0.1)	**1a**	50	7	**2a**[11a]	79 (66)	
CAN (1)–I_2(0.5)	**1b**	Room temp.	3.5	**2b**[11a]	(28)	**9b** (54)
CAN (1)–I_2(0.1)	**1b**	50	25	**2b**	(46)	**10b** (20)
CAS (1)–I_2(0.2)	**1b**	Reflux	10	**2b**	(63)	**6b** (11)
CST (1)–I_2(0.2)	**1b**	Room temp.	4d	**2b**	65 (52)	
CST (1)–I_2(0.6)	**1b**	50	9	**2b**	(29)	**10b** (59)
CST (1.5)–I_2(0.1)	**1b**	50	15	**2b**	82 (71)	
CST (1.5)–I_2(0.1)	**1c**	50	10	**2c**[11c]	80 (67)	
CST (1.5)–I_2(0.1)	**1d**	50	10	**2d**[11e]	80 (68)	
CST (1.5)–I_2(0.1)	**1e**	Reflux	11	**2e**[11f]	72 (60)	
CST (1.5)–I_2(0.1)	**1f**	Reflux	10	**2f**[11g]	95 (89)	
CAS (1)–I_2(0.2)	**1f**	Reflux	10	**2f**	81 (67)	

[a] Substrate (2.72 mmol) in MeOH (20 ml). [b] Yields determined by ^1H NMR with added internal standard methyl benzoate.

Moreover, we tried the reaction in other alcohols (ethanol, propan-1-ol and propan-2-ol). The results are

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Table 2 Reactions of 2-alkylcycloalkanones with I_2–CST in R^3OH[a]

Substrate	Solvent	T/°C	t/h	Products (%)[b]	
1a	EtOH	65	20	**3a**[11b] (61)	
1a	Pr^nOH	65	21	**4a** (63)	
1b	EtOH	Room temp.	4d	**3b**[11d] (66)	**7b** (16)
1b	EtOH	65	20	**3b** (57)	
1b	Pr^nOH	Room temp.	6d	**4b** (36)	**8b** (27)
1b	Pr^nOH	65	20	**4b** (51)	
1b	Pr^iOH	Room temp.	6d	**5b** (43)	
1b	Pr^iOH	65	20	**5b** (44)	
1f	EtOH	65	18	**3f**[11h] (90)	
1f	Pr^nOH	65	7	**4f** (98)	

[a]Substrate (2.72 mmol) with I_2 (0.54 mmol)–CST (2.72 mmol) in alcohol (20 ml). [b]Isolated yield.

summarized in Table 2. For the more bulky alkoxy groups, the yields of the oxo esters are diminished compared with those for the methoxy reactions. However, in the case of 2-phenylcyclohexanone, the yields were not affected.

In conclusion, the present method provides a new alternative to others previously reported for the preparation of oxo esters from cyclic ketones by using I_2–cerium(IV) salts in alcohol.

Experimental

IR spectra were measured using a Jasco FT-IR 230. NMR spectra were measured on a JEOL GSX 400 spectrometer with the samples dissolved in deuteriochloroform with Me_4Si as the internal standard. High-resolution mass spectra were recorded at 75 eV on a JEOL JMS-O1 SG-2 instrument with a direct inlet.

General Procedure. Reaction of 2-Methylcyclohexanone with CST–I_2 in MeOH.—A mixture of 2-methylcyclohexanone **1b** (0.305 g, 2.72 mmol), iodine (0.138 g, 0.54 mmol) and cerium(IV) sulfate tetrahydrate (1.099 g, 2.72 mmol) in MeOH (20 ml) was stirred at room temperature for 4 days. The white precipitate of Ce^{III} salt was filtered off and the solvent was evaporated under reduced pressure. The residue was poured into water (20 ml) and extracted with dimethyl ether (50 ml). The ethereal solution was washed successively with aq. sodium thiosulfate (10 ml), saturated aq. NaCl (10 ml) and water (10 ml) and dried (Na_2SO_4). Evaporation of the solvent gave a pale yellow oil. Methyl benzoate was added as an internal standard if the yield was to be estimated by ^1H NMR spectroscopy. The oil was chromatographed on silica gel with hexane–ether (4:1) as the eluent to give the corresponding compound **2b** as a pale yellow oil (0.225 g, 52%).

Spectroscopic and Analytical Data.—**4a**: Pale yellow oil, ν_{max}/cm^{-1} (NaCl) 1718 and 1172; δ_H ($CDCl_3$) 4.01–4.06 (t, 2 H), 2.50–2.54 (t, 2 H), 2.32–2.36 (t, 2 H), 2.15 (s, 3 H), 1.87–1.91 (m, 2 H), 1.62–1.68 (m, 2 H) and 0.92–0.96 (t, 3 H); δ_C ($CDCl_3$) 208.0, 173.3, 66.0, 42.5, 33.3, 29.9, 22.0, 19.0 and 10.4 (Found: M^+, 172.1086. $C_9H_{16}O_3$ requires M_r, 172.1100).

4b: Pale yellow oil, ν_{max}/cm^{-1} (NaCl) 1735 and 1716; δ_H ($CDCl_3$) 4.01–4.04 (t, 2 H), 2.45–2.48 (t, 2 H), 2.30–2.34 (t, 2 H), 2.14 (s, 3 H), 1.60–1.68 (m, 6 H), and 0.92–0.96 (t, 3 H); δ_C ($CDCl_3$) 208.5, 173.5, 65.9, 43.3, 34.1, 29.9, 24.5, 23.2, 22.0 and 10.4 (Found: M^+, 186.1227. $C_{10}H_{18}O_3$ requires M_r, 186.1256).

5b: Pale yellow oil, ν_{max}/cm^{-1} (NaCl) 1727 and 1719; δ_H ($CDCl_3$) 4.97–5.02 (m, 1 H), 2.45–2.48 (t, 2 H), 2.26–2.29 (t, 2 H), 2.14 (s, 3 H), 1.60–1.61 (m, 4 H) and 1.21–1.27 (d, 6 H); δ_C ($CDCl_3$) 208.4, 172.8 67.5, 43.2, 34.4, 29.8, 24.5, 23.2, 21.8 and 21.8; MS (EI): m/z 186 [M^+], 127, 58, 43; MS (CI): m/z 187 $[M + 1]^+$.

6b: ν_{max}/cm^{-1} (NaCl) 1740 and 1156; δ_H ($CDCl_3$) 4.48 (t, 1 H), 3.68 (s, 3 H), 2.43 (s, 3 H), 2.36 (t, 2 H), 1.88–2.02 (m, 2 H), 1.72–1.84 (m, 1 H) and 1.54–1.68 (m, 1 H); δ_C ($CDCl_3$) 202.2, 173.3, 51.6, 33.7, 33.0, 32.2, 26.1 and 24.6 (Found: M^+, 283.9939. $C_8H_{13}O_3I$ requires M_r, 283.9909).

7b: ν_{max}/cm^{-1} (NaCl) 1732; δ_H ($CDCl_3$) 4.48 (t, 1 H), 4.13 (q, 1 H), 2.43 (s, 3 H), 2.35 (dt, 2 H), 1.88–2.02 (m, 2 H), 1.72–1.84 (m, 1 H), 1.55–1.68 (m, 1 H) and 1.26 (t, 3 H); δ_C ($CDCl_3$) 202.2, 172.9, 60.5, 33.8, 33.3, 32.4, 26.1, 24.6 and 14.2 (Found: M^+, 298.0038. $C_9H_{15}O_3I$ requires M_r, 298.0066).

8b: ν_{max}/cm^{-1} (NaCl) 1732; δ_H ($CDCl_3$) 4.50 (t, 1 H), 4.04 (t, 2 H), 2.43 (s, 3 H), 2.36 (dt, 2 H), 1.91–2.03 (m, 2 H), 1.71–1.84 (m, 1 H), 1.55–1.71 (m, 1 H) and 0.94 (t, 3 H); δ_C ($CDCl_3$) 202.2, 172.9, 66.1, 33.7, 33.2, 32.3, 26.1, 24.6, 21.9 and 10.4 (Found: M^+, 312.0209. $C_{10}H_{17}O_3I$ requires M_r, 312.0222).

9b: Colorless plates; mp 63–64 °C; ν_{max}/cm^{-1} (KBr) 1716; δ_H ($CDCl_3$) 4.88 (d, 1 H), 2.74 (m, 1 H), 2.60 (m, 1 H), 2.11–2.31 (m, 2 H), 1.74–1.83 (m, 2 H), 1.40–1.54 (m, 1 H) and 1.13 (d, 3 H); δ_C ($CDCl_3$) 203.9, 44.5, 42.3, 37.5, 36.1, 27.9 and 15.9 (Found: M^+, 237.9831. $C_7H_{11}OI$ requires M_r, 237.9855).

4f: Pale yellow oil; ν_{max}/cm^{-1} (NaCl) 1731 and 1685; δ_H ($CDCl_3$) 7.93–7.96 (2 H), 7.52–7.55 (1 H), 7.42–7.47 (2 H), 4.00–4.04 (t, 2 H), 2.97–3.00 (t, 2 H), 2.35–2.38 (t, 2 H), 1.71–1.80 (m, 4 H), 1.61–1.67 (m, 2 H) and 0.91–0.95 (t, 3 H); δ_C ($CDCl_3$) 199.7, 173.5, 136.9, 133.0, 128.6, 128.6, 128.0, 128.0, 65.9, 38.1, 34.1, 24.7, 23.7, 22.0 and 10.4; MS (EI): m/z 248 [M^+], 189($M^+ - 59$), 105 and 77; MS (CI): m/z 249 $[M + 1]^+$.

5f: Colorless plates; mp 73–76 °C; ν_{max}/cm^{-1} (KBr): 1712; δ_H ($CDCl_3$) 7.33–7.39 (m, 2 H), 7.25–7.31 (m, 1 H), 7.11–7.17 (m, 2 H), 4.78–4.82 (m, 1 H), 4.75 (dd, 1 H) and 1.89–2.32 (m, 6 H); δ_C ($CDCl_3$) 204.6, 137.8, 128.7, 128.4, 127.2, 50.4, 37.0, 34.8, 31.4 and 22.0 (Found: M^+, 299.9985. $C_{12}H_{13}OI$ requires M_r, 300.0011).

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References

1 S. Ito and M. Matsumoto, *J. Org. Chem.*, 1983, **48**, 1133.

2 T. Hirao, M. Mori and Y. Oshiro, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2399.

3 T. Shono, Y. Matsumura, T. Imanishi and K. Yoshida, *Bull. Chem. Soc. Jpn.*, 1979, **51**, 2179.

4 K. Kaneda, N. Kii, K. Jitsukawa and S. Teranishi, *Tetrahedron Lett.*, 1981, **22**, 2595.

5 B. El Ali, J-M. Bregeault, J. Mercier, J. Martin, C. Martin and O. J. Convert, *J. Chem. Soc., Chem. Commun.*, 1989, **825**.

6 A. Atlamsani and J.-M. Bregeault, *J. Org. Chem.*, 1993, **58**, 5663.

7 (*a*) C. A. Horiuchi, Y. Suzuki, M. Takahashi and J. Y. Satoh, *Chem. Lett.*, 1987, 393; (*b*) C. A. Horiuchi and Y. Suzuki, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2919; (*c*) C. A. Horiuchi, H. Kiyomiya, M. Takahashi and Y. Suzuki, *Synthesis*, 1989, 785.

8 (*a*) C. A. Horiuchi and S. Kiji, *Chem. Lett.*, 1988, 31; (*b*) C. A. Horiuchi, Y. Nishio, D. Gong, T. Fujisaki and S. Kiji, *Chem. Lett.*, 1991, 607; (*c*) C. A. Horiuchi, K. Ochiai and H. Fukunishi, *Chem. Lett.*, 1994, 185; (*d*) C. A. Horiuchi, H. Fukunishi, M. Kajita, A. Yamaguchi, H. Kiyomiya and S. Kiji, *Chem. Lett.*, 1991, 1921; (*e*) C. A. Horiuchi and E. Takahashi, *Bull. Chem. Soc. Jpn.*, 1994, **67**, 271.

9 C. A. Horiuchi and S. Kiji, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 421.

10 C. A. Horiuchi, A. Ikeda, M. Kanamori, H. Hosokawa, T. Sugiyama and T. Takahashi, *J. Chem. Res.* (*S*), 1997, 60.

11 (*a*) W. G. Daub, R. N. Zuckermann and W. S. Johnson, *J. Org. Chem.*, 1985, **50**, 1599; (*b*) T. Ishida and K. Wado, *J. Chem. Soc., Perkin Trans. 1*, 1979, 323; (*c*) R. S. Randad, N. G. Bhat and G. H. Kulkarni, *Indian J. Chem., Sect. B*, 1984, **22**, 947; (*d*) K. I. Kohdair, A. A. Magd, K-K. S. Hussain, H. M. Khairy and E-K. M. Ahmed, *Rev. Roumaine Chim.*, 1983, **28**, 921; (*e*) A. E. Berhanu and G. Sendaba, *J. Chromatogr.*, 1985, **3**, 440; (*f*) S. Takano, K. Masuda and K. Ogasawara, *Heterocycles*, 1981, **16**, 1509; (*g*) B. M. Vivekananda, M. Ravindranathan, S. Viswanatha and R. G. Venkoba, *J. Org. Chem.*, 1984, **49**, 3170; (*h*) T. Mukaiyama, M. Araki and H. Takei, *U.S. Nat.* 3,867,453, (Cl. 260-570AB; C07c), 18 Feb. 1975.