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A New α-Iodination of Ketones Using Iodine-Ammonium Cerium(IV) Nitrate in Alcohol or Acetic Acid

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The direct α-iodination of various ketones using iodine-ammonium cerium(IV) nitrate in acetic acid or alcohol gave the corresponding α-iodo ketones in high yields. The effect of cerium salt on the iodination of ketones, and the iodination of 5α-cholestan-3-one using several methods are also discussed. In the reaction of 3,3,5-trimethylcyclohexanone and unsymmetrical ketones, such as 2-hexanone and 2-heptanone, using methanol, ethanol, 1-propanol, and 2-propanol, the regioselective iodination product was obtained. In the case of bromination, the reaction of ketones with bromine and ammonium cerium(IV) nitrate also yielded the corresponding α-bromo ketones.

α-Iodo ketones are important as synthetic intermediates. They are usually prepared by one of the following methods: the halogen interchange[1] of bromo compounds with sodium iodide in acetone; the reaction of *N*-iodosuccinimide[2] or iodine chloride[3] with the enol acetates,[4] and silyl ethers[5] with iodine-metal acetate; or the reaction of an alkene with iodine-silver chromate,[6] iodine-pyridinium dichromate,[7] or bis(2, 4,6-trimethylpyridine)iodine(I) tetrafluoroborate.[8] More recently, it has been reported that the reaction of the carbonyl compounds with iodine-mercury(II) chloride gave α-iodo ketones,[9] although this method was found not to be applicable to cyclic ketones.

There has been only very little information on the direct α-iodination of ketones under acidic conditions. In connection with our studies, we had found that iodine-copper(II) acetate[10] in acetic acid is a useful reagent for the syntheses of some iodo compounds; in a previous paper,[11] we reported on a novel α-iodination of ketones using iodine-copper(II) acetate in acetic acid. The procedure suffers some deficiencies, the most serious being the loss of iodine from the reaction as metallic iodide and the low regioselectivity in unsymmetrical ketones. Still earlier, we described: a new α-iodination of ketones to afford the corresponding iodo ketones;[12] a new alkoxyiodination and nitratoiodination of olefins;[13] new oxidative aromatization of α,β-unsaturated cyclohexenones;[14] and a new α,α′-diiodination of ketones[15] using iodine-ammonium cerium(IV) nitrate(CAN).[16] Through our studies we have found that iodine-CAN is a useful reagent for the syntheses of a large number of iodo compounds. Now, in this paper we report details concerning a new and improved iodination of some ketones using iodine-CAN (Figs. 1 and 2).

Results and Discussion

The reaction of certain ketones with iodine-cerium(IV) salts, iodine-potassium permanganate, iodine-potassium iodate, iodine-potassium bromate, or iodine-potassium chlorate gave the corresponding α-iodo ketones in good yields. These results are summarized in Table 1.

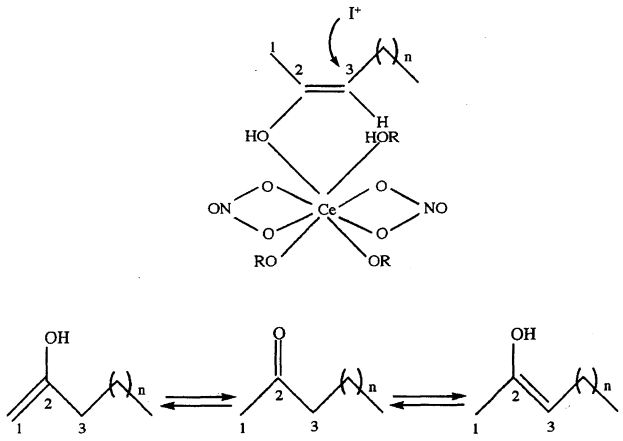
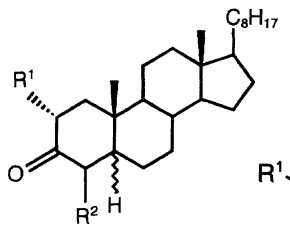


Fig. 1.

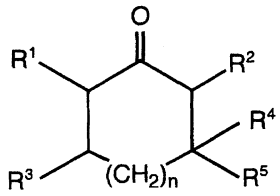
On the basis of these results, it was found that the present iodination using CAN proceeds well under conditions that are milder than those with the method using copper(II) acetate; moreover, CAN is more active than the other cerium(IV) salts. Also, it was found that the added iodine is almost completely consumed, and that two moles of α-iodo ketone are formed from one mole of iodine. It is particularly noteworthy that this reaction may provide a new synthetic method for α-iodo ketone that is more convenient than those which heretofore used iodine-copper(II) acetate (Runs 12, 14, and 22), *N*-iodosuccinimide, iodine-silver chromate, or iodine-thallium(I) acetate. This reagent is also applicable to a reaction under acidic conditions, and also to those cyclic ketones that are unreactive with mercury(I) chloride.

Moreover, it was concluded that iodine-potassium iodate, iodine-potassium bromate, and iodine-potassium chlorate are efficient iodinating agents for 5α-cholestan-3-one (**1**). How-



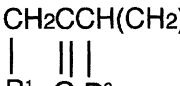
1: 5α, $R^1=R^2=H$
2: 5β, $R^1=R^2=H$

10a: 5α, $R^1=I$, $R^2=H$
10b: 5α, $R^1=Br$, $R^2=H$
11a: 5β, $R^1=H$, $R^2=I$
11b: 5β, $R^1=H$, $R^2=Br$

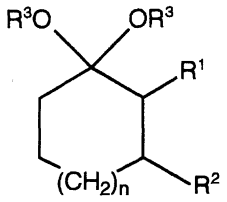


3: n=1, $R^1=R^2=R^3=R^4=R^5=H$
4: n=2, $R^1=R^2=R^3=R^4=R^5=H$
5: n=1, $R^1=R^2=H$, $R^3=R^4=R^5=Me$
6: n=1, $R^1=R^2=R^3=R^5=H$, $R^4=Me$
7: n=1, $R^1=R^3=R^4=R^5=H$, $R^2=Me$

12a: n=1, $R^1=R^3=R^4=R^5=H$, $R^2=I$
12b: n=1, $R^1=R^3=R^4=R^5=H$, $R^2=Br$
13a: n=2, $R^1=R^3=R^4=R^5=H$, $R^2=I$
13b: n=2, $R^1=R^3=R^4=R^5=H$, $R^2=Br$
14: n=1, $R^1=H$, $R^2=I$, $R^3=R^4=R^5=Me$
15: n=1, $R^1=I$, $R^2=H$, $R^3=R^4=R^5=Me$
16: n=1, $R^1=I$, $R^2=R^3=R^4=H$, $R^5=Me$



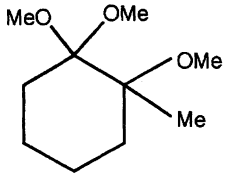
8: n=2, $R^1=R^2=H$
9: n=3, $R^1=R^2=H$



17: n=2, $R^1=I$, $R^2=H$
18: n=2, $R^1=H$, $R^2=I$
19: n=3, $R^1=I$, $R^2=H$
20: n=3, $R^1=H$, $R^2=I$

21a: n=1, $R^1=I$, $R^2=H$, $R^3=Me$
21b: n=1, $R^1=Br$, $R^2=H$, $R^3=Me$
22: n=1, $R^1=OMe$, $R^2=H$, $R^3=Me$
23: n=1, $R^1=I$, $R^2=H$, $R^3=Et$
24: n=1, $R^1=OEt$, $R^2=H$, $R^3=Et$
25: n=1, $R^1=I$, $R^2=R^3=Me$
26: n=1, $R^1=OMe$, $R^2=R^3=Me$

27: n=1, $R^1=I$, $R^2=Me$, $R^3=Et$
28: n=1, $R^1=OEt$, $R^2=Me$, $R^3=Et$
29: n=2, $R^1=I$, $R^2=H$, $R^3=Me$
30a: n=1, $R^1=I$, $R^2=H$, R^3-$R^3=CH_2CH_2$
30b: n=1, $R^1=Br$, $R^2=H$, R^3-$R^3=CH_2CH_2$
31: n=1, $R^1=I$, $R^2=Me$, R^3-$R^3=CH_2CH_2$



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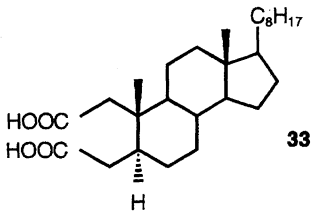

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Fig. 2.

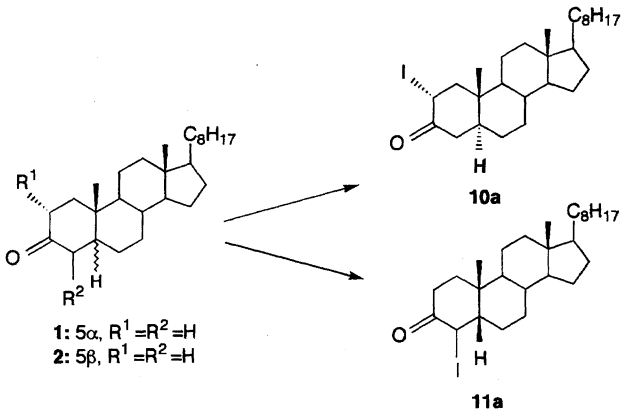
ever, these methods are not applicable to other ketones. Also, the reaction of **1** with iodine-excess CAN for 22 h or with potassium permanganate for 38 h gave the 2,3-seco-5α-cholestane-2,3-dioic acid (**33**). From these results, it can be considered that the 2α-iodo ketone (**10a**) produced would be oxidized to 2,3-seco dioic acid (**33**) (Scheme 1).

It is known that cerium(IV) ion forms a cerim(IV)–alcohol-complex in alcohol solvents.[17,18] In view of this fact, we have attempted regioselective iodination using iodine-CAN in alcohols. As can be seen in Table 2, in the case of unsymmetrical ketones, such as 2-hexanone (**8**) and 2-heptanone (**9**) in alcohols (methanol, ethanol, 1-propanol, and 2-propanol), the more substituted position (C^3-position) is preferentially iodinated at 25 °C. However, in the case of the more bulky alkoxyl group, mixed C^1- and C^3-iodination products were obtained, and the yields were diminished compared with those of the methoxy group. At 50 °C, the cerium(IV)–alcohol complex is formed preferentially faster than in the case of the reaction at 25 °C. Therefore, except for methanol, I^+ ion attacks the less hindered position (C^1-position). Thus, it is assumed that the cerium(IV) ion is coordinated to the oxygen of the carbonyl group, and that the unsymmetrical ketone enolizes predominantly towards the C^3-position. Since the cerium(IV)–alcohol complex is preferentially formed, the I^+ ion attacks the C^3-position. However, due to the bulkiness of the alkoxyl group, it is difficult for the I^+ ion to attacks the C^3-position. Therefore, it would seem that the I^+ ion attacks the C^1-position. Also, in the case of **5**, it seems that the

Table 1. Products and Isolated Yields (%) in the α-Iodination of Ketone in Acetic Acid–Water (9 : 1) at 50 °C

Run	Reagents (molar amount)	Substrate	Time/h	Product	Yield/%	Product Ratio[d]
1	CAN (0.5)[a]	**1**	6	**10a**	80	
2	CAN (0.3)[a]	**1**	6	**10a**	80	
3	CAN (0.1)[a]	**1**	15	**10a**	60	
4	CAN (1.0)[a]	**1**	22	**33**	27	
5	CAS (0.5)[b]	**1**	30	**10a**	68	
6	CS (0.5)[c]	**1**	15	**10a**	39	
7	$KMnO_4$ (0.2)	**1**	9	**10a**	32	
8	$KMnO_4$ (0.2)	**1**	38	**33**	33	
9	$KBrO_3$ (0.083)	**1**	15	**10a**	84	
10	KIO_3 (0.1)	**1**	15	**10a**	82	
11	$KClO_3$ (0.083)	**1**	24	**10a**	78	
12	$Cu(OAc)_2$ (1.0)	**1**	6	**10a**	70[11]	
13	CAN (0.5)[a]	**2**	2.5	**11a**	60	
14	$Cu(OAc)_2$ (1.0)	**2**	6	**11a**	65[11]	
15	CAN (0.5)[a]	**3**	2	**12a**	94	
16	CAS (0.5)[b]	**3**	7	**12a**	74	
17	CS (0.5)[c]	**3**	10	**12a**	40	
18	$KMnO_4$ (0.1)	**3**	16	**12a**	46	
19	$KBrO_3$ (0.083)	**3**	20	**12a**	41	
20	KIO_3 (0.1)	**3**	20	**12a**	53	
21	$KClO_3$ (0.083)	**3**	20	**12a**	47	
22	$Cu(OAc)_2$ (1.0)	**3**	3	**12a**	100[11]	
23	CAN (0.5)[a]	**4**	8	**13a**	95	
24	CAN (0.5)[a]	**9**	14	**19/20**	89	46/54
25	$KMnO_4$ (0.1)	**9**	14	**19/20**	49	58/42
26	$KBrO_3$ (0.083)	**9**	14	**19/20**	48	60/40
27	KIO_3 (0.1)	**9**	14	**19/20**	32	60/40
28	$KClO_3$ (0.083)	**9**	14	**19/20**	51	54/46

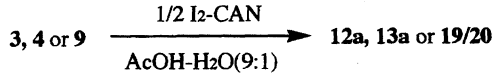
a) Ammonium cerium(IV) nitrate. b) Ammonium cerium(IV) sulfate. c) Cerium(IV) sulfate. d) Removal of solvent from the dried solution gave the iodo ketone as an unstable oil which was examined by NMR spectrum as soon as possible after preparation. The composition of reaction mixtures was determined from the peak area ratio of NMR spectrum.



Scheme 1.

consideration mentioned above is supported as being valid.

The reaction of **3** with iodine (0.5 molar amount)-CAN (0.5 molar amount) in methanol at 25 °C yielded 2-iodocyclohexanone (**12a**) and a pearl-yellow oil (**21a**) in 47% yield (Scheme 2). This compound (**21a**) showed absorptions of 1164, 1100, and 1052 cm^{-1} (C–O) in its IR spectrum. The NMR spectrum showed two singlets at $\delta = 3.19$ (C^1–OMe) and 3.20 (C^1–OMe), and a triplet at $\delta = 4.51$ ($J = 2.5$ Hz). Accordingly, **21a** was presumed to be 2-iodocyclohexanone dimethyl acetal. This presumption was also supported by



Scheme 2.

the ^{13}C NMR spectral data. The reaction of **3** with iodine-CAN containing trimethyl orthoformate in MeOH at 50 °C for 1 h gave **21a** in 66% yield. In the case of the reaction under refluxing, 2-methoxycyclohexanone dimethyl acetal (**22**) was obtained in good yield (80%). These results are summarized in Table 3, and seem to indicate that this reaction provides a new simple method for preparing 2-iodo- and 2-alkoxycycloalkanone dimethyl or diethyl acetal. Also, this reaction may provide a new synthetic method for α-bromocyclohexanone acetal. Then, in order to ascertain the method's applicability to the bromination of ketones, the reaction of a ketone with bromine-CAN in acetic acid–water was carried out. 5α-Cholestan-3-one (**1**) and 5β-isomer (**2**) were each treated with bromine (0.5 molar amount)-CAN (0.5 molar amount) in acetic acid at room temperature for 5—8 h. Both reactions gave 2α-bromo ketone (**10b**) and 4β-bromo ketone (**11b**) in good yields. The results are summarized in Table 4, showing that in bromination with molecular bromine, 0.5 mmol of bromine for 1.0 mmol of substrate is sufficient to complete the reaction in 80% yield based on ketones. 4β-

Table 2. α-Iodination of Ketones with Iodine-Ammonium Cerium(IV) Nitrate in Alcohols

Run	Substrate	Solv.	Temp/°C	Time/h	Product	Yield/%	Product ratio[a)]
1	**5**	MeOH	25	17	**14/15**	90	14/86
2	**5**	MeOH	50	12	**14/15**	55	16/84
3	**5**	EtOH	25	7	**14/15**	66	26/74
4	**5**	EtOH	50	6	**14/15**	70	28/72
5	**5**	*n*-PrOH	25	14	**14/15**	73	37/63
6	**5**	*n*-PrOH	50	15	**14/15**	78	37/63
7	**5**	*i*-PrOH	25	20	**14/15**	91	39/61
8	**5**	*i*-PrOH	50	7	**14/15**	86	39/61
9	**8**	MeOH	25	15	**17/18**	83	4/96
10	**8**	MeOH	50	6	**17/18**	58	9/91
11	**8**	EtOH	25	15	**17/18**	46	30/70
12	**8**	EtOH	50	3	**17/18**	94	70/30
13	**8**	*i*-PrOH	25	15	**17/18**	46	32/68
14	**8**	*i*-PrOH	50	6	**17/18**	91	73/27
15	**9**	MeOH	25	20	**19/20**	62	0/100
16	**9**	MeOH	50	15	**19/20**	73	8/92
17	**9**	EtOH	25	15	**19/20**	51	21/79
18	**9**	EtOH	50	3	**19/20**	88	64/36
19	**9**	*n*-PrOH	25	15	**19/20**	47	8/92
20	**9**	*n*-PrOH	50	3	**19/20**	95	71/29
21	**9**	*i*-PrOH	25	30	**19/20**	49	7/93
22	**9**	*i*-PrOH	50	6	**19/20**	97	72/28

a) Removal of solvent from the dried solution gave the iodo ketone as an unstable oil which was examined by NMR spectrum as soon as possible after preparation. The composition of reaction mixtures was determined from the peak area ratio of NMR spectrum.

Table 3. Reaction of Cyclohexanone Derivatives with Iodine- or Bromine-Ammonium Cerium(IV) Nitrate in Alcohols

Run	Substrate	Alcohol	Temp/°C	Time/h	Product (Yield/%)		
1	**3**	MeOH	25	8	**12a** (8)	**21a** (47)	
2	**3**	MeOH	50	8	**12a** (9)	**21a** (2)	**22** (9)
3	**3**	MeOH[a)]	50	1		**21a** (66)	
4	**3**	MeOH[a)]	Reflux	8			**22** (80)
5	**3**	EtOH[b)]	Reflux	4		**23** (41)	
6	**3**	EtOH[b)]	Reflux	16&		**24** (61)	
7	**6**	MeOH	50	8	**16** (8)	**25** (8)	**26** (13)
8	**6**	MeOH[a)]	Reflux	8		**25** (62)	
9	**6**	MeOH[a)]	Reflux	15			**26** (77)
10	**6**	EtOH[b)]	Reflux	3			**27** (41)
11	**6**	EtOH[b)]	Reflux	16			**28** (61)
12	**7**	MeOH	25	8			**32** (12)
13	**4**	MeOH	50	8			**29** (38)
14	**3**	EG/MeCN	Reflux	5			**30a** (86)
15	**6**	EG/MeCN	Reflux	5			**31** (48)
16	**3**	MeOH[c)]	25	3			**21b** (52)
17	**3**	EG/ MeCN[d)]	Reflux	5			**30b** (86)

a) $CH(OCH_3)_3$ was added. b) $CH(OC_2H_5)_3$ was added. c) Cyclohexanone (**3**) (5.74 mmol), CAN (2.87 mmol), bromine (2.87 mmol), $CH(OCH_3)_3$ (28.73 mmol), and methanol (55 ml) were employed. d) Cyclohexanone (**3**) (5.09 mmol), CAN (2.56 mmol), bromine (2.56 mmol), ethyleneglycol (153 mmol), and acetonitrile (20 ml) were employed.

Bromo ketone (**11b**) produced by this method is more easily crystallized to give the pure product than one prepared by Shoppee's method.[19)]

Experimental

All of the boiling points are uncorrected. The IR spectra were measured using a Hitachi Model 270-30 grating infrared spectrometer. The NMR spectra were measured using either a JEOL FX 200 Model or a GSX 400 Model Spectrometer in deuterio-chloroform with TMS as an internal standard. The high-resolution mass spectra were recorded at 75 eV on a JEOL JMS-O1SG-2 instrument with a direct inlet.

Typical Procedure: A mixture of 5α-cholestan-3-one (**1**) (200 mg, 0.517 mmol), iodine (66 mg, 0.259 mmol), and ammonium cerium(IV) nitrate (142 mg, 0.259 mmol) in acetic acid–water (9 : 1) (20 ml) was stirred at 50 °C for 6 h. The reaction mixture was poured into water and extracted with ether. The ethereal solution

Table 4. Products and Isolated Yields (%) in the α-Bromination of Ketones with Bromine (0.1 molar amount)–Ammonium Cerium(IV) Nitrate (0.1 molar amount) in Acetic Acid–Water (9 : 1)

Run	Substrate	Temp/°C	Time/h	Product	Yield/%
1	**1**	R.T.	5	**10b**	87
2	**2**	R.T.	16	**11b**	85
3	**3**	R.T.	10	**12b**	90
4	**4**	50	7	**13b**	85

was washed with aqueous sodium hydrogencarbonate and water, dried, and concentrated. Crystallization of the residue from ethanol gave needles of 2α-iodo-5α-cholestan-3-one (**10a**) (213 mg), mp 132—133 °C (lit,[17] mp 125—127 °C), IR (KBr) 1713 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.89 (dd, J = 6.0, 13.5 Hz, 1H). These results are summarized in Table 1.

11a: Mp 118—119 °C, IR (KBr) 1724 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 5.03 (d, J = 12 Hz, 1H). Found: *m/z* 512.2516. Calcd for $C_{27}H_{45}IO$: M, 512.2518.

33: Mp 197—200 °C (lit,[20] mp 195—200 °C), IR (KBr) 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 9.50 (brs, 2H); ^{13}C NMR ($CDCl_3$) δ = 178.3 and 180.5. Found: *m/z* 434.3400. Calcd for $C_{27}H_{46}O_4$: M, 434.3398.

12a: Pale yellow oil, IR (NaCl) 1708 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.70 (t, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 22.62, 26.61, 32.52, 36.32, 37.07, and 204.72.

13a: Pale yellow oil, IR (NaCl) 1706 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.57 (q, J = 10.6, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 25.33. 28.27, 29.27, 32.21, 35.53, 38.16, and 207.41.

14: Pale yellow oil, IR (NaCl) 1714 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.17 (d, 1H).

15: Pale yellow oil, IR (NaCl) 1714 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.42 (m, 1H).

16: Pale yellow oil, IR (NaCl) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.57 (d, J = 8.6 Hz, 1H).

19: Pale yellow oil, IR (NaCl) 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.80 (s, 2H); ^{13}C NMR ($CDCl_3$) δ = 203.32, 39.28, 31.14, 23.87, 22.37, 13.90, and 6.28.

20: Pale yellow oil, IR (NaCl) 1714 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.45 (t, 1H); ^{13}C NMR ($CDCl_3$) δ = 202.61, 34.28, 33.43, 31.49, 25.89, 22.00, and 13.81.

Reaction of Ketone (1, 2, 3 or 4) with Bromine (0.5 Molar Amount) and CAN (0.5 Molar Amount) in AcOH (Scheme 5). 5β-Cholestan-3-one (**2**) (200 mg) in acetic acid–water (9 : 1) (20 ml) was treated with bromine (40 mg) and CAN (190 mg) at room temperature for 5 h. After the usual work-up, the resulting oil, upon crystallization from ethanol, gave needles of **11b** (205 mg), mp 113—114 °C (lit,[14] 111—113 °C). These results are summarized in Table 2.

10b: Needle crystals; mp 173—174 °C (lit,[20] mp 174—174.5 °C).

12b: Pale yellow oil, IR (NaCl) 1732 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.48 (t, J = 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 22.28, 26.75, 36.89, 38.05, 53.75, and 203.26.

13b: Pale yellow oil, IR (NaCl) 1714 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.40 (q, J = 9.7, 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ = 24.94, 27.06, 29.51, 35.03, 39.38, 53.92, and 206.00.

Reaction of 2-Hexanone (8), 2-Heptanone (9), or 3,3,5-Trimethylcyclohexanone (5) with Iodine and CAN in Alcohols (Methanol, Ethanol, 1-Propanol, or 2-Propanol). A mixture of 2-hexanone (**8**) (510 mg, 5.095 mmol), iodine (647 mg, 2.547 mmol), and CAN (1.397g, 2.547 mmol) in methanol (50 ml) was stirred at 25 °C for 15 h. After the usual work-up, removal of the solvent from the dried solution gave the iodo ketone as an unstable oil, which was examined by ^1H NMR spectroscopy as soon as possible after preparation. The composition of the reaction mixture was determined from the peak area ratio of the NMR spectrum (Scheme 3). These results are summarized in Table 3.

17: Pale yellow oil, IR (NaCl) 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.81 (s, 2H); ^{13}C NMR ($CDCl_3$) δ = 203.30, 39.03, 26.24, 22.13, 13.78, and 6.28.

18: Pale yellow oil, IR (NaCl) 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.47 (t, 1H); ^{13}C NMR ($CDCl_3$) δ = 202.61, 36.44, 33.19, 25.33, 22.61, and 13.30.

Reaction of Cyclohexanone Derivatives with Iodine (0.5 Molar Amount) and CAN (0.5 Molar Amount) in Alcohols. Cyclohexanone (**3**) (500 mg) in methanol (50 ml) was stirred with iodine (647 mg), CAN (5.407 g), and trimethyl orthoformate (5.407 g) at 50 °C for 1 h. After the usual work-up, the resulting pale-yellow oil, upon reduced pressure distillation, gave 2-iodocyclohexanone dimethyl acetal (**21a**) (902 mg): Bp 85 °C/1 mmHg, (1 mmHg = 133.322 Pa), IR (NaCl): 1164 and 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.19 (s, 3H), and 4.51 (t, 1H) ^{13}C NMR ($CDCl_3$) δ = 99.46, 48.74, 46.79, 36.03, 33.51, 27.79, 22.20, and 21.95. Found: *m/z* 270.0128. Calcd for $C_8H_{15}O_2I$: M, 270.0118.

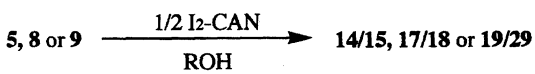
22: Bp 52 °C/1 mmHg; IR (NaCl) 1176 and 1106 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.20 (s, 3H), 3.22 (s, 3H), 3.37 (s, 3H) and 3.37 (m, 1H); ^{13}C NMR ($CDCl_3$) δ = 100.31, 77.14, 56.28, 47.52, 47.46, 28.19, 25.08, 22.07, and 19.61. Found: *m/z* 174.1270. Calcd for $C_9H_{18}O_3$: M, 174.1250.

24: Pale yellow oil; IR (NaCl) 1176 and 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.17 (m, 9H) and 3.39—3.65 (m, 7H); ^{13}C NMR ($CDCl_3$) δ = 100.40, 76.00, 63.93, 54.87, 54.80, 33.85, 26.11, 23.04, 22.32, 15.73, 15.54, and 15.44. Found: *m/z* 216.1731. Calcd for $C_{12}H_{24}O_3$: M, 216.1726.

25: Pale yellow oil; IR (NaCl) 1166 and 1114 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.18 (s, 3H), 3.19 (s, 3H), and 4.50 (t, 1H); ^{13}C NMR ($CDCl_3$) δ = 101.50, 48.68, 46.86, 36.06, 35.36, 33.14, 30.41, 28.82, and 21.83. Found: *m/z* 284.0273. Calcd for $C_9H_{17}O_2I$: M, 284.0274.

26: Pale yellow oil; IR (NaCl) 1170 and 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.16 (s, 3H), 3.21 (s, 3H), 3.35 (s, 3H), and 3.35 (m, 1H); ^{13}C NMR ($CDCl_3$) δ = 100.89, 75.59, 56.19, 47.46, 47.19, 36.12, 28.55, 27.79, 24.48, and 22.01. Found: *m/z* 188.1420. Calcd for $C_{10}H_{20}O_3$: M, 188.1413.

27: Pale yellow oil; IR (NaCl) 1176 and 1120 cm^1; ^1H NMR ($CDCl_3$) δ = 1.17 (t, 3H), 1.20 (t, 3H), 3.47 (dq, 4H), and 4.55 (t, 1H); ^{13}C NMR ($CDCl_3$) δ = 100.40, 76.08, 54.84, 54.81, 29.19, 26.18, 22.35, 19.92, 15.54, and 15.45. Found: *m/z* 298.0423. Calcd



Scheme 3.

for $C_{10}H_{19}O_2I$: M, 298.0431.

28: Pale yellow oil; IR (NaCl) 1170, 1124, and 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.16 (t, 3H), 1.17 (t, 3H), 1.18 (t, 3H), 3.42 (dq, 4H), and 3.52 (dq, 2H); ^{13}C NMR ($CDCl_3$) 100.50, 74.53, 63.74, 54.92, 54.86, 42.36, 33.30, 29.33, 22.60, 22.26, 15.73, 15.52, and 15.49. Found: *m/z* 230.1876. Calcd for $C_{13}H_{26}O_3$: M, 230.1883.

29: Pale yellow oil; IR (NaCl) 1166 and 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.36 (s, 6H) and 4.60 (dd, 1H); ^{13}C NMR ($CDCl_3$) δ = 86.48, 81.24, 57.56, 56.74, 40.80, 31.20, 28.49, 25.60, and 23.29. Found: *m/z* 284.0281. Calcd for $C_9H_{17}O_2I$: M, 284.0274.

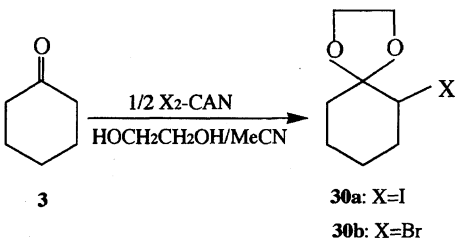
30a: Pale yellow oil (Scheme 4); IR (NaCl) 1126 and 1106 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.31 (dd, 1H); ^{13}C NMR ($CDCl_3$) δ = 107.78, 65.47, 65.29, 38.58, 37.21, 33.66, 26.46, and 23.34. Found: *m/z* 267.9937. Calcd for $C_8H_{13}O_2I$: M, 267.9901.

31: Pale yellow oil; IR (NaCl) 1110 and 1092 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 4.34 (dd, 1H); ^{13}C NMR ($CDCl_3$) δ = 108.44, 65.25, 64.59, 38.80, 36.37, 33.58, 30.04, 29.80, and 21.80. Found: *m/z* 282.0113. Calcd for $C_9H_{15}O_2I$: M, 282.0118.

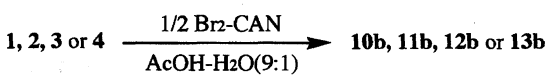
32: Pale yellow oil; IR (NaCl) 1176, 1116, and 1052 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.23 (s, 3H), 3.24 (s, 3H), 3.30 (s, 3H), and 3.33 (s, 3H); ^{13}C NMR ($CDCl_3$) δ = 102.29, 80.00, 50.32, 49.61, 48.63, 32.78, 28.46, 22.33, 21.63, and 18.08. Found: *m/z* 188.1483. Calcd for $C_9H_{17}O_2I$: M, 188.1413.

Reaction of Cyclohexanone (3) with Bromine and CAN in Alcohols. Cyclohexanone (**3**) (564 mg) in methanol (50 ml) was treated with bromine (918 mg), trimethyl orthoformate (3.046 g), and CAN (1.575 g) at room temperature for 3 h. After the usual work-up, the resulting oil (819 mg) was chromatographed on silica gel (25 g). Elution with hexane–ether (5 : 1) (30 ml) gave 2-bromocyclohexanone dimethyl acetal (**21b**) (664 mg), IR (NaCl) 1168 and 1112 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.20 (s, 3H), 3.23 (s, 3H), and 4.35 (m, 1H); ^{13}C NMR ($CDCl_3$) δ = 99.86, 53.60, 48.39, 46.95, 31.91, 27.07, 21.95, and 20.18. Found: *m/z* 222.0258. Calcd for $C_8H_{15}O_2Br$: M, 222.0236.

Reaction of Cyclohexanone (3) with Bromine and CAN in Ethylene Glycol/Acetonitrile. Cyclohexanone (**3**) (500 mg) in ethylene glycol (9.522 g)–acetonitrile (20 ml) was treated with bromine (409 mg) and CAN (1.403 g) under refluxing for 5 h. After the usual work-up, the resulting oil, upon reduced distillation, gave 6-bromo-1,4-dioxaspiro[4.5]decane (**30b**) (1.025 g), bp 96 °C/10 mmHg (lit,[21] 90—92 °C/5 mm Hg); IR (NaCl) 1156, 1134, 1110, and 1088 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 3.97—4.01 (m, 2H) and 4.09—4.17 (m, 3H); ^{13}C NMR ($CDCl_3$) δ = 107.96, 65.69, 65.54, 63.71, 57.18, 34.90, 34.18, and 23.14. Found: *m/z* 222.0077, 222.0080. Calcd for $C_8H_{13}O_2Br$: M, 220.0099, 222.0079.



Scheme 4.



Scheme 5.

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