A New α,α'-Diiodination of Ketones Using Iodine–Cerium(IV) Ammonium Nitrate

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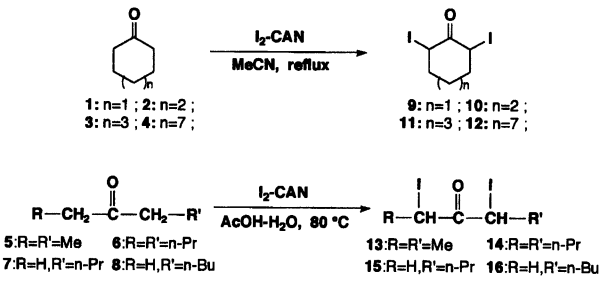
Synopsis. The direct iodination of some ketones using iodine–cerium(IV) ammonium nitrate in acetic acid or acetonitrile gave the corresponding α,α'-diiodoketones in good yield. In the case of cyclododecanone (**4**), 3-pentanone (**5**), and 5-nonanone (**6**), *cis*- (*meso*-) compounds [2,12-diiodocyclododecanone (**12**), 2,4-diiodo-3-pentanone (**13**), and 4,6-diiodo-5-nonanone (**14**)] were obtained preferentially.

α,α'-Dihalogenoketones are highly reactive and are used as important intermediates in organic synthesis.[1—3]

Much work has been reported concerning the α,α'-dibromination and α,α'-dichlorination of ketones.[4] To our knowledge, no study concerning the α,α'-diiodination of ketones has been described in the literature. Recently, Fierz and co-workers reported that simple α,α'-diiodoketones, such as 1,3-diiodo-2-butanone and 2,4-diiodo-3-pentanone, were prepared by a halogen interchange of α,α'-dibromoketones with sodium iodide. However, the physical data for these compounds were not described.[5] In addition, this method is not applicable to cyclic ketones.

We have been investigating a novel iodination method using iodine–copper(II) acetate.[6] The procedure suffers some deficiencies. In a previous paper we reported on a novel α-iodination of ketones in acetic acid or methanol; a new alkoxyiodination and nitratoiodination of olefins using iodine–cerium(IV) ammonium nitrate (CAN) was also described.[7] The added iodine was almost completely consumed. Two moles of α-iodoketone were formed from one mole of iodine. In this paper we report that the reaction of some ketones [cyclohexanone (**1**), cyclohetanone (**2**), cyclooctanone (**3**), cyclododecanone (**4**), 3-pentanone (**5**), 5-nonanone (**6**), 2-hexanone (**7**), and 2-heptanone (**8**)] with iodine–CAN in acetic acid or acetonitrile gave the corresponding α,α'-diiodoketones in good yield (Scheme 1). These results are summarized in Table 1.

The ^{1}H NMR spectra of compounds **10a** and **10b** showed a double-doublet (J=4.4 and 11.1 Hz) at δ=4.90 and a double-doublet (J=4.4 and 8.8 Hz) at δ=4.84, due to the CHI, respectively. The C=O stretching band appeared at 1704 cm^{-1} for **10a** and at 1720 cm^{-1} for **10b**, respectively, in the IR spectrum. From these results, the structures of the diiodoketones were assigned to be a *trans*-compound (**10a**) and a *cis*-compound (**10b**), respectively. Moreover, it is known that cycloheptanone prefers the C_2 comformation, which allows the halogens of the observed *trans* isomer to occupy quasiequatorial positions at the periphery.[4] It can therefore be seen that *trans*-diiodocycloheptanone is produced more preferentially than is the *cis*-derivative. Assignments of the configuration for other α,α'-diiodoketones were tentatively made based on data concerning the corresponding α,α'-dibromoketones.[4]



Scheme 1.

As can be seen in Table 1, the present α,α'-diiodination appears to be more efficient than the method described heretofore; the reaction provides a new simple method for the preparation of α,α'-diiodoketones. In the case of **4**, **5**, and **6**, the *cis*-(*meso*-) compounds (**12**, **13**, and **14**) were obtained preferentially. Acyclic α,α'-diiodoketones such as **13**, **14**, **15**, and **16** are sensitive to light. These crude mixtures cannot be allowed to stand for a long time, since these compounds decompose slowly.

In order to clarify the effects of other cerium salts, reactions of **2** with cerium(IV) ammonium sulfate dihydrate [$(NH_4)_4Ce(SO_4)_4\cdot 2H_2O$], cerium(IV) sulfate tetrahydrate [$Ce(SO_4)_2\cdot 4H_2O$], and cerium(III) ammonium nitrate tetrahydrate [$(NH_4)_2Ce(NO_3)_5\cdot 4H_2O$] were carried out according to a procedure similar to that mentioned above; the results are presented in Table 2. From these results, it was found that the observed reactivity order for the cerium salts, [$(NH_4)_2Ce(NO_3)_6$ > $(NH_4)_4Ce(SO_4)_4\cdot 2H_2O$ > $Ce(SO_4)_2\cdot 4H_2O$ > $(NH_4)_2Ce(NO_3)_5\cdot 4H_2O$], indicated that they are less oxidizing reagents than CAN for iodination. These cerium salts give 2-iodocycloheptanone (**17**) as the major products.

Experimental

All of the melting points are uncorrected. The IR spectra were measured using a Hitachi model 215 grating infrared spectrometer. The NMR spectra were measured on a JOEL GSX 400 spectrometer in deuteriochloroform with TMS as the internal standard.

Reaction of Cycloheptanone (2) with Iodine and Cerium(IV) Ammonium Nitrate in Acetonitrile. A mixture of cycloheptanone (**2**) (0.740 g, 6.60 mmol), iodine (6.60 mmol), and cerium(IV) ammonium nitrate (6.60 mmol) in acetonitrile (50 ml) was stirred under reflux for

Table 1. α,α'-Diiodination of Ketones with Iodine–Cerium(IV) Ammonium Nitrate[a)]

Substrate	Solvent	Temp/°C	Time/h	Product	Yield/%[b)]	*trans/cis* (*dl/meso*)
1	MeCN	Reflux	5	2,6-Diiodocyclohexanone (**9**)	55	67/33
2	MeCN	Reflux	6	2,7-Diiodocycloheptanone (**10**)	85	92/8
3	MeCN	Reflux	24	2,8-Diiodocyclooctanone (**11**)	50	100/0
4	MeCN	Reflux	50	2,12-Diiodocyclododecanone (**12**)	75	0/100
5	AcOH–H_2O	80	30	2,4-Diiodo-3-pentanone (**13**)[c)]	62	0/100
6	AcOH–H_2O	80	15	4,6-Diiodo-5-nonanone (**14**)[c)]	86[d)]	25/75
7	AcOH–H_2O	80	4	1,3-Diiodo-2-hexanone (**15**)[c)]	61	—
8	AcOH–H_2O	80	4	1,3-Diiodo-2-heptanone (**16**)[c)]	82	—

a) Substrate (6.60 mmol), I_2 (6.60 mmol), CAN (6.60 mmol), and AcOH–H_2O (9:1) (50 ml); or Acetonitrile (50 ml). b) Isolated yield. c) I_2 (7.92 mmol) and CAN (7.92 mmol). d) Ratio was based on isolated products.

Table 2. Reaction of Cycloheptanone (**2**) with I_2–Cerium Salt in Acetonitrile[a)]

Run	Cerium salt	Product (Yield/%)
1	$(NH_4)_2Ce(NO_3)_6$	**10**(72)
2	$(NH_4)_4Ce(SO_4)_4\cdot 2H_2O$	**10**(14) + **17**(26)
3	$Ce(SO_4)_2\cdot 4H_2O$	**10**(9) + **17**(28)
4	$(NH_4)_2Ce(NO_3)_5\cdot 4H_2O$	**10**(8) + **17**(12)

a) A mixture of cycloheptanone (**2**) (6.60 mmol), iodine (6.60 mmol), cerium salt (6.60 mmol), and acetonitrile (30 ml) was stirred under reflux for 4 h affording 2,7-diiodocycloheptanone (**10**) and 2-iodocycloheptanone (**17**).

6 h. The reaction mixture was poured into water and extracted with ether. The ethereal solution was washed with aqueous sodium hydrogencarbonate and water, dried, and evaporated, to yield a mixture of *trans*- (**10a**) and *cis*-2,7-diiodocycloheptanone (**10b**) as yellow solids (2.042 g, 85%, mp 88—90 °C, *trans/cis*=92/8). The composition of the mixture was determined from the peak-area ratio of the ^{1}H NMR spectrum. Recrystallization of the mixture from hexane–ether (20:1) gave *trans*-2,7-diiodocycloheptanone (**10a**) as plates (1.632 g, 68%), mp 91—93 °C; IR (KBr) 1704 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.90 (dd, 2H, J=4.4 and 11.1 Hz, C_2- and C_7-H), 2.42—2.50 (m, 2H), 1.96—2.07 (m, 2H), 1.87—1.95 (m, 2H), and 1.36—1.47 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=200.9, 36.1, 29.1, and 26.6. Found: *m/z* 363.8818. Calcd for $C_7H_{10}OI_2$: M, 363.8819. The filtrate was then evaporated under reduced pressure. The residue was chromatographed on silica gel (25 g). Elution with hexane–ether (5:1) (90 ml) gave plates of *trans*-isomer (**10a**) (0.075 g, 3%, mp 91—93 °C) from hexane–ether (20:1). The next fraction eluted by the same solvent (45 ml) gave *cis*-isomer (**10b**) as plates (0.041 g, 2%) from hexane, mp 70—72 °C; IR (KBr) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.84 (dd, 2H, J=4.0 and 9.1 Hz, C_2- and C_7-H), 2.43—2.47 (m, 2H), 2.07—2.27 (m, 2H), 1.83—1.87 (m, 2H), and 1.56—1.63 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=202.1, 34.8, 28.9, and 27.7. Found: *m/z* 363.8858. Calcd for $C_7H_{10}OI_2$: M, 363.8819.

***trans*- and *cis*-2,6-Diiodocyclohexanone (9):** **9a**(*trans*): Mp 58—60 °C; IR (KBr) 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=5.38 (dd, 2H, J=5.3 and 8.0 Hz, C_2- and C_6-H), 2.20—2.44 (m, 4H), and 1.91—1.98 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=197.0, 39.0, 28.7, and 24.5. Found: *m/z* 349.8711. Calcd for $C_6H_8OI_2$: M, 349.8662.

9b(*cis*): Mp 101—103 °C; IR (KBr) 1728 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.93 (dd, 2H, J=5.9 and 10.3 Hz, C_2- and C_6-H), 2.58—2.66 (m, 2H), 2.26—2.35 (m, 2H), and 1.80—1.88 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=195.8, 40.1, 27.2, and 27.2.

***trans*-2,8-Diiodocyclooctanone (11a):** Mp 96—98 °C; IR (KBr) 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.79 (dd, 2H, J=5.3 and 10.7 Hz, C_2- and C_8-H), 2.35—2.42 (m, 4H), and 1.34—1.64 (m, 6H); ^{13}C NMR ($CDCl_3$) δ=206.0, 37.7, 28.0, 24.0, and 22.0. Found: *m/z* 377.8951. Calcd for $C_8H_{12}OI_2$: M, 377.8975.

***cis*(*meso*)-2,12-Diiodocyclododecanone (12b):** Mp 115—117 °C; IR (KBr) 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=5.16 (dd, 2H, J=3.4 and 9.3 Hz, C_2- and C_{12}-H), 2.29—2.39 (m, 2H), 1.96—2.06 (m, 2H), and 1.08—1.50 (m, 14H); ^{13}C NMR ($CDCl_3$) δ=198.9, 35.1, 25.8, 25.2, 24.8, 24.7, and 21.8. Found: *m/z* 434.9695. Calcd for $C_{12}H_{20}OI_2$: M, 433.9603.

Reaction of 3-Pentanone (5) with Iodine Cerium-(IV) Ammonium Nitrate in Acetic Acid–Water. A mixture of 3-pentanone (**5**) (0.567 g, 6.60 mmol), iodine (7.92 mmol), and CAN (7.92 mmol) in acetic acid–water (9:1) (50 ml) was stirred at 80 °C for 30 h. The reaction solvent was removed under reduced pressure. The residue was poured into water and extracted with ether. The ethereal solution was washed successively with aqueous sodium hydrogencarbonate and water, dried, and concentrated. The resulting oil was chromatographed on silica gel (25 g). In the case of ioslation from the reaction mixture, decomposition occurs during column chromatography on silica gel. A column covered with Aluminum-foil was thus used, and carried out quickly (within 30 min). Elution with hexane–benzene (1:1) (90 ml) gave *meso*-2,4-diiodo-3-pentanone (**13b**) as oil (1.363 g, 62%), IR (neat) 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=5.21 (q, 2H, J=6.6 Hz, C_2- and C_4-H) and 1.96 (d, 6H, J=6.6 Hz); ^{13}C NMR ($CDCl_3$) δ=198.1, 21.8, and 20.9.

***dl*- and *meso*-4,6-Diiodo-5-nonanone (14):** **14a**(*dl*): IR (neat) 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.71 (dd, 2H, J=6.2 and 8.4 Hz C_4- and C_6-H), 1.88—2.05 (m, 4H), 1.32—1.63 (m, 4H), and 0.97 (t, 6H, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ=199.5, 38.3, 29.3, 22.9, and 13.2;

14b(*meso*): IR (neat) 1708 cm^{-1}; ^{1}H NMR($CDCl_3$) δ=5.00 (t, 2H, J=7.3 Hz, C_4- and C_6-H), 1.94—2.11 (m, 4H), 1.29—1.52 (m, 4H), and 0.99 (t, 6H, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ=196.3, 36.2, 29.8, 22.4, and 13.4.

1,3-Diiodo-2-hexanone (15): IR (neat) 1706 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.96 (t, 1H, J=7.3 Hz, C_3-H), 4.36 (d, 1H, J=9.9 Hz, C_1-H), 3.86 (d, 1H, J=9.9 Hz, C_1-H), 1.90—2.05 (m, 2H), 1.28—1.52 (m, 2H), and 0.97 (t, 3H, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ=196.3, 36.4, 28.1, 22.4, 13.3, and 2.6.

1,3-Diiodo-2-heptanone (16): IR (neat) 1704 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.93 (t, 1H, J=7.3 Hz, C_3-H), 4.34 (d, 1H, J=9.9 Hz, C_1-H), 3.84 (d, 1H, J=9.9 Hz, C_1-H), 1.95—2.04 (m, 2H), 1.28—1.40 (m, 4H), and 0.91 (t, 3H, J=7.3 Hz); ^{13}C NMR ($CDCl_3$) δ=196.3, 34.1, 31.2, 28.7, 21.9, 13.8, and 2.7.

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