On the Mechanism of the Reduction of α-Halo Ketones by 1,3-Dimethyl-2-phenylbenzimidazoline. Reduction by a SET–Hydrogen Atom Abstraction Chain Mechanism

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Received December 19, 1988

A series of α-halocarbonyl compounds are dehalogenated by 1,3-dimethyl-2-phenylbenzimidazoline (DMBI) to give their corresponding carbonyl compounds. Contrary to the original proposal, the mechanism for these reductions was shown to proceed via a free-radical chain process whose mechanism contains a SET–hydrogen atom abstraction propagation sequence. The reduction by DMBI of a representative number of substrates is initiated by AIBN (3–5%) and inhibited by dinitrobenzene (3–5%). Competitive kinetics show that the relative rate constants for primary halides (α-haloacetophenones) and tertiary halides differ by less than 5 to 1. Although the tertiary halides do not undergo chain reduction, the presence of radical intermediates was indirectly confirmed by the observation of an inhibitory effect by the α-haloisobutyrophenones on the rate of reduction of the α-haloacetophenones. The enolyl radicals from primary and secondary halides could be trapped by 1-hexene. These results are interpreted as being in agreement with the SET–hydrogen atom abstraction radical chain mechanism.

Introduction

The reduction of carbonyl compounds is one of the basic reactions in organic syntheses. However, the mechanistic details of most of these reductions are still not clearly delineated. The reduction mechanism may conceivably proceed by either a homolytic or heterolytic pathway. In recent years considerable attention has been given to the proposal that a single-electron-transfer (SET) step is involved in a number of organic reactions that were previously considered to proceed by polar mechanisms.[2] A variety of chemically based probes have been used to differentiate polar and ET pathways. α-Haloacetophenones have been used successfully as probes to differentiate the two possible pathways in the reductions by organotin hydrides,[3,4] organosilanes,[5] 1,4-dihydropyridines,[6] and the enzyme (HLADH) mediated reductions of NADH[7] (Scheme I). It is of some importance to extend this probe to other reduction systems in order to gather more information about the elementary steps involved, see Scheme I.

It was reported recently that 1,3-dimethyl-2-phenylbenzimidazoline (DMBI) could selectively reduce a series of α-halocarbonyl compounds to their corresponding aldehydes or ketones without affecting the carbonyl group.[8] The authors proposed a direct S_N2 hydride transfer mechanism based on both steric and electronic arguments. The order of reactivities was found to be Br > Cl > F, and qualitatively the rates of reduction were found to be primary > secondary > tertiary (for substitution at the halogenated carbon). Since the reagent, DMBI, is structurally analogous to a 1,4-dihydropyridine (DHP) and its reactions with α-halo ketones were identical with those of DHP, the previously proposed mechanism for the DMBI reductions was reexamined in more detail. Moreover, the structure–reactivity relationships reported[8] were equally well consistent with the alternative SET–H atom transfer process proposed for the DHP reductions (Scheme I).

Scheme I

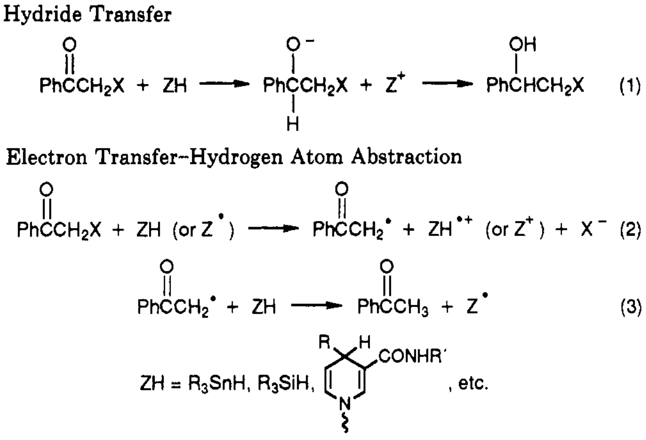

Table I. Reduction of α-Haloacetophenone (Ia–c) by DMBI ($C_6H_5COCH_2X$)

X	reaction	conditions[a]	additive	yield, % ($PhCOCH_3$)
Br (Ia)	1	C_6H_6, 61 °C, 0.4 h	-	29.1
	2		*m*-DNB (2%)	0.8
	3	C_6H_6, 23 °C, 2 h	-	33.6
	4		*m*-DNB (2%)	1.4
	5		DBPO (5%)[b]	99.5
	6	C_6H_6, 61 °C, 4 h[c]	-	1.1
	7		AIBN (6%)	78.9
Cl (Ib)	8	C_6H_6, 61 °C, 20 h	-	29
	9		AIBN (5%)	99
	10		*m*-DNB (4%)	0
	11	THF, 61 °C, 5 h	-	55
	12		AIBN (4%)	78
	13		*m*-DNB (5%)	0
F (Ic)	14	THF, 61 °C, 53 h	-	1.9
	15		AIBN (5%)	77.9
	16	MeOH, 61 °C, 64 h	-	15.2
	17		AIBN (5%)	89.1
	18		*p*-DNB (5%)	10.1[d]

[a] A mole ratio of 1/1 of ketone/DMBI was used, 0.1 M/0.1 M. [b] Rapid reaction took place when the reagents were mixed. [c] DMBI (0.01 M) and $PhCOCH_2Br$ (0.01 M). [d] 1.8% of $PhCHOHCH_2F$ was also observed. In all other cases no $PhCHOHCH_2X$ was detected by GC.

Results

Several α-halocarbonyl compounds (I–V) were chosen as model compounds to study the mechanism of the re-

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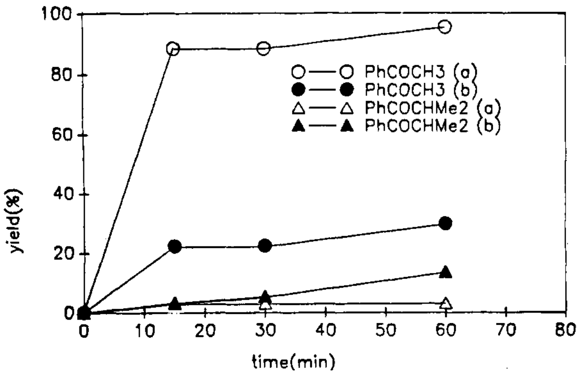


Figure 1. The reduction of $PhCOCH_2Br$ and $PhCOCMe_2Br$ by DMBI (yield vs reaction time): (a) reactions of a single substrate; (b) competitive reactions.

Table II. Reduction of $C_6H_5COCHCH_3X$ (IIa–c) by DMBI[a]

X	reaction	time, h	additive	yield, % ($PhCOC_2H_5$)
Br (IIa)	19	48	-	45.2
	20		AIBN (4%)	101
	21		*p*-DNB (5%)	8.8
Cl (IIb)	22	73	-	46.3
	24		AIBN (6%)	85.6
	24		*p*-DNB (6%)	1.4
F (IIc)	25	51	-	3.0
	26		AIBN (8%)	29.1

[a] All reactions were run in THF at 61 °C.

action. The reductions were carried out in several solvents (C_6H_6, THF, MeOH). Radical initiation (AIBN; di-*tert*-butylperoxyoxalate, DBPO) and inhibition (dinitrobenzene, *p*-DNB or *m*-DNB) were used to establish whether a free radical chain reduction sequence was followed. The reaction yields were purposely not optimized since conditions were chosen so that initiation and/or inhibition could be observed easily. The results of these studies are listed in Tables I–IV.

$C_6H_5COCH_2X$

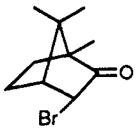
Ia: X = Br
b: X = Cl
c: X = F

$C_6H_5COCHMeX$

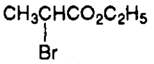
IIa–c

$C_6H_5COCMe_2X$

IIIa,b



IV



$$\underset{\displaystyle Br}{CH_3\overset{|}{C}HCO_2C_2H_5}$$

V

Since both steric and electronic factors have been proposed to effect the kinetics of these reductions, and since these effects have been used to argue for the S_N2 hydride transfer mechanism,[8] a series of relative rate constants were measured for substrates (I–III) by competitive kinetic experiments. The results are listed in Table V. Competitive rates of reduction between the series of different halogens could not be carried out directly, since with the primary and secondary halo ketones nucleophilic halogen substitution resulted in halogen exchange in the reactants (see Table VI).

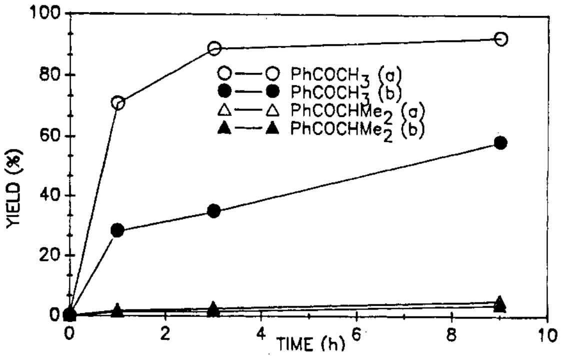


Figure 2. The reduction of $PhCOCH_2Cl$ and $PhCOCMe_2Cl$ by DMBI: (a) individual reactions; (b) competitive reactions.

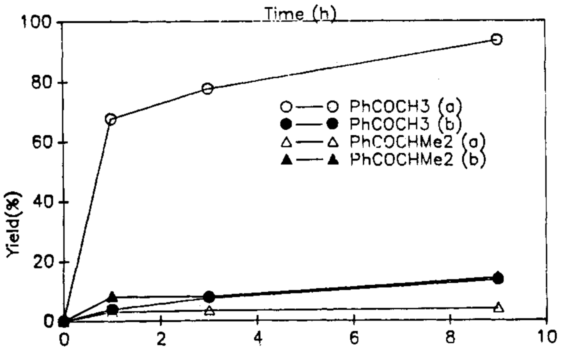


Figure 3. The reduction of $PhCOCH_2Cl$ and $PhCOCMe_2Br$ by DMBI: (a) individual reactions; (b) competitive reactions.

Scheme II. Trapping of the Intermediate Radicals ($\dot{C}_6H_5COCR^1R^2$)

$$C_6H_5COCH_2Cl + DMBI + n\text{-}C_4H_9CH{=}CH_2 \xrightarrow[\text{AIBN}]{61\ ^\circ C} \underset{\text{4 days}}{} \underset{27\%}{C_6H_5COCH_3} + \underset{7.6\%}{C_6H_5COCH_2C_6H_{13}\text{-}n} \quad (4)$$

$$C_6H_5COCH(CH_3)Cl \rightarrow \underset{5.6\%}{C_6H_5COC_2H_5} + \underset{16.6\%}{C_6H_5COCH(CH_3)C_6H_{13}\text{-}n} \quad (5)$$

$$C_6H_5COC(CH_3)_2Cl \rightarrow \underset{1.4\%}{C_6H_5COCH(CH_3)_2} + \underset{0.0\%}{C_6H_5COC(CH_3)_2C_6H_{13}\text{-}n} \quad (6)$$

In the competitive experiments the reduction of α-bromoacetophenone or α-chloroacetophenone appeared to be inhibited when it was carried out in the presence of α-chloro- or α-bromoisobutyrophenone. The reductions of several pairs of α-halo ketones were examined as a function of time. The results are graphically displayed in Figures 1–3.

More direct evidence for the free-radical mechanism was obtained by trapping the intermediate enolyl radical with use of 1-hexene as solvent. Scheme II lists the results of these trapping experiments.

Discussion

Free-Radical Chain Reduction. Examination of the results obtained from the reduction of α-bromoacetophenone by DMBI in benzene (Table I, entries 1 and 2)

Table III. Reduction of $PhCOC(CH_3)_2X$ (IIIa–b) by DMBI[a]

X	reaction	time, h	additive	yield, % ($PhCOCH(CH_3)_2$)	yield, % (starting material)
Br (IIIa)	27	96	-	5.4	89.6
	28		AIBN (4%)	11.4	79.7
Cl (IIIb)	29	77	-	4.7	84.8
	30		AIBN (3%)	14.8	81.7

[a] All reactions were run in THF at 61 °C.

Table IV. Reduction of Substrates IV and V by DMBI

substrate	reaction	conditions	additive	yield, %
IV	31	THF, 61 °C, 48 h	-	1.4
	32		AIBN (7%)	47.6
	33	THF, 90 °C, 72 h	-	26.8
	34		*p*-DNB (4%)	2.2
V	35	THF, 21 °C, 9 h	-	73.3
	36		*m*-DNB (5%)	0.0

Table V. Relative Rate Constants for $C_6H_5COR^1R^2X$

	Ia–c	IIa–c	IIIa–b
	$C_6H_5COCH_2X$	$C_6H_5COCHCH_3X$	$C_6H_5COC(CH_3)_2X$
X = Br	1	0.78	0.40
X = Cl	1	0.78	0.20
X = F	1	0.40	

at 61 °C clearly establishes that the reduction proceeds via a free-radical chain mechanism. Very small amounts of dinitrobenzene could inhibit the chain reaction. In order to observe radical chain initiation the reduction was also carried out at room temperature for a longer time with a low-temperature radical initiator, DBPO.[9] A reaction that could be initiated or inhibited took place upon mixing the reagents and solid $DMBI^+Br^-$ precipitated from solution (Table I, entries 3–5). At lower concentrations the induced initiation was not effective (1.1%) and the reaction had to be initiated with AIBN (Table I, entries 6 and 7). Similar results were obtained for the reduction of α-chloro- and α-fluoroacetophenone, which suggested that all of the α-haloacetophenones were reduced via the same mechanism (see Table I). Qualitatively, the reactivity followed the order $PhCOCH_2Br > PhCOCH_2Cl > PhCOCH_2F$, obtained previously for the reductions by organotin hydrides and DHP compounds.[4,6]

The effect of solvent polarity was studied for the reduction of α-fluoroacetophenone. In the more polar protic solvent methanol, the thermal reaction becomes more facile, but more importantly, the heterolytic product ($PhCHOHCH_2F$) was detected for the reactions run with added *p*-DNB (Table I, entry 18). Similar results were also obtained for the reductions of the halo ketones by Ph_3SnH[4] and the DHP reducing agents.[6] In the polar solvents, when the rapid radical chain is inhibited, the slower heterolytic reaction can compete.

The reduction of the α-halopropiophenones (Table II), α-bromocamphor and ethyl 2-bromopropionate (Table IV) appears to proceed by the same free-radical chain mechanism since initiation by AIBN and/or inhibition by DNB was also observed. However, the reduction of α-haloisobutyrophenones (Table III) showed only a slight initiation by AIBN and no inhibition was observed. Nevertheless, it is difficult to rationalize that the reduction of the tertiary halides would proceed via a S_N2 direct hydride transfer mechanism while primary and secondary halides are reduced by a free-radical chain mechanism.

Competitive Reactivity Study. The relative reactivities for the α-haloacetophenones could not be measured directly; however, qualitatively the same order reported previously (Br > Cl > F)[8] can be recognized for the rates of reaction of the series of primary, secondary, and tertiary halo ketones (see Tables I–III). This order, which is attributed to the leaving ability of the halogen, can also be correlated to the ability of the substrate to accept an electron (i.e., its electron affinity).[4] Since electron transfer to the halo ketones is thought to be dissociative,[7] the ability of the halo ketone to undergo reduction should reflect the leaving ability of the halide. This trend has been established previously for a number of reductions that proceed via SET mechanisms.[4,6]

The primary–secondary–tertiary reactivities of the halo ketones appear to be the same within a factor of 2 for each series of halogens. Within a series, the largest difference between a primary and a tertiary halide is 5:1. This value is rather small for an S_N2 displacement by hydride, for which the differences are expected to be from 60 to 300.[10] The magnitude of the difference is, however, that which would be expected for a chain reaction involving dissociative electron transfer and hydrogen atom abstraction (e.g., Scheme III). The same insensitivity to structure was observed when the α-deuterio-α-haloacetophenones are reduced: no secondary deuterium isotope effect was detected.[4]

More revealing, however, was the observation that the reduction of α-bromoacetophenone (Ia) by DMBI could be inhibited by the addition of 1 equiv of α-bromoisobutyrophenone (IIIa). The tertiary halo ketone was not appreciably reduced during these competitive reductions (see Figure 1). The same behavior was observed when α-chloroacetophenone was reduced in the presence of α-chloroisobutyrophenone (see Figure 2). These observations are not in agreement with the one-step direct hydride transfer mechanism as previously proposed.[8] Since the reduction of primary and secondary halides are shown to proceed via a free-radical chain mechanism (vide supra), the reduction of the tertiary halide (IIIa) must proceed via the same mechanism in order to explain the inhibition. Inhibition could be rationalized by a comparison of the expected differences in the rates of the propagating steps proposed for the chain mechanism (eq 7 and 8). Electron

$$C_6H_5CO\dot{C}R^1R^2 + ZH \xrightarrow{k_{Ht}} C_6H_5COCHR^1R^2 + Z^\bullet \qquad (7)$$

$$C_6H_5COR^1R^2X + Z^\bullet \xrightarrow{k_{ET}} C_6H_5CO\dot{C}R^1R^2 + Z^+X^- \qquad (8)$$

transfer from the DMBI radical ($Z^\bullet$) to Ia or IIIa would not be expected to differ greatly, although a dissociative electron transfer would no doubt favor the tertiary halide ($k_{ET}^{IIIa} > k_{ET}^{Ia}$). On the other hand, hydrogen atom transfer would be much more favorable for the primary enolyl radical than for the analogous tertiary radical ($k_{Ht}^{1°} > k_{Ht}^{3°}$). Such inequalities in rates can result in the apparent inhibition since the tertiary substrate (IIIa) reacts rapidly but does not carry the chain. The primary substrate (Ia) would then appear to be unreactive. The effect would be even greater when the tertiary substrate (IIIa) is competitively reduced along with the less reactive primary halide (Ib). The same inequalities will exist, but the differences in electron transfer rates would be amplified even further ($k_{ET}^{IIIa} > k_{ET}^{Ia} > k_{ET}^{Ib}$), see Figure 3. The amount of inhibited reduction of Ib exhibited during the competitive reductions of Ib and IIIa (Figure 3) must be taken as an upper limit since halogen exchange, bromide for chloride, produces α-bromoacetophenone (Ia), which is reduced to acetophenone ~50 times faster rate than Ib. Consistent with the observation that no α-bromoacetophenone was detected in the unreacted reduction mixture, it can be suggested that the small amount of acetophenone produced (<10%) would be even smaller if no Ia had been formed by the exchange pathway.

Enolyl Radical Addition to 1-Hexene. By carrying out the reductions in 1-hexene, the intermediate enolyl radicals could be trapped for both the primary and sec-

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Table VI. Halogen Exchange in the PhCOCH$_2$Cl/PhCOCHCH$_3$Br, 1/1, Mixtures

			products (mol % of starting material)			
reaction	conditions[a]	additive	PhCOCH$_2$Cl	PhCOCHCH$_3$Cl[b]	PhCOCH$_2$Br[c]	PhCOCHCH$_3$Br
37	56 h	-	98.2	-	-	101.7
38	56 h	AIBN (12%)	90.3	6.5	10.8	97.0
39	56 h	Et$_4$N$^+$Br$^-$ (10%) Me$_4$N$^+$Cl$^-$ (20%)	50.0	58.6	45.8	49.8
40	8 h	DMBI (9%)	44.9	50.6	31.8	31.2
41	8 h	DMBI$^+$Br$^-$ (10%)	49.7	55.5	35.7	40.1

[a] All the reactions were carried out in THF at 61 °C in the dark. [b] The yield was calculated based on PhCOCHCH$_3$Br used. [c] The yield was calculated based on PhCOCH$_2$Cl used.

ondary radicals, i and ii, produced during the reduction of Ia or IIb. As expected, the trapping reaction of the

$$\text{DMBI} + \text{PhCOCH}_2\text{Cl} \rightarrow \underset{\text{i}}{\text{PhCOCH}_2{}^{\bullet}} \xrightarrow{\text{1-hexene}} \rightarrow \text{PhCOCH}_2\text{CH}_2\text{CH}_2\text{C}_4\text{H}_9\text{-}n \quad (9)$$

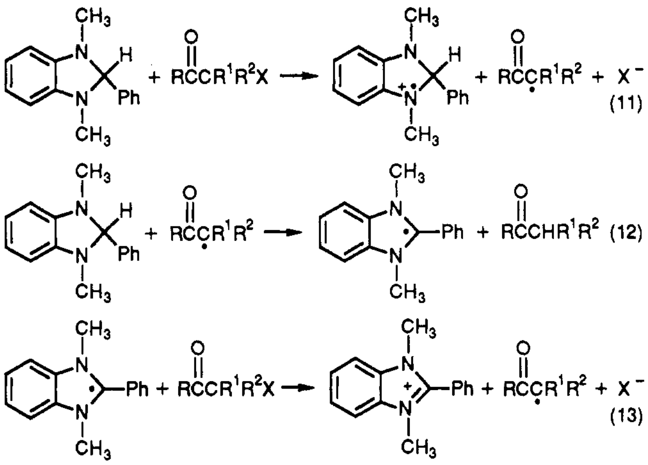
$$\text{DMBI} + \text{PhCOCH(CH}_3\text{)Cl} \rightarrow \underset{\text{ii}}{\text{PhCOCH(CH}_3\text{)}^{\bullet}} \xrightarrow{\text{1-hexene}} \rightarrow \text{PhCOCH(CH}_3\text{)CH}_2\text{CH}_2\text{C}_4\text{H}_9\text{-}n \quad (10)$$

tertiary radical produced from IIIb was unsuccessful since addition of the stabilized tertiary enolyl radical is expected to be unfavorable.

Mechanism. The reduction by DMBI of the 10 α-halo ketones studied proceeds via a free-radical chain mechanism. A detailed mechanism analogous to the general SET mechanism (Scheme I) previously established[3-7] is shown in Scheme III. The initiation involves electron transfer between halo ketones and DMBI to give a radical ion pair (eq 11). The ease of this ET step depends upon the electron affinity of the halide. For example, α-bromoacetophenone undergoes facile, uninitiated reduction while α-fluoroacetophenone requires initiation by AIBN in order to achieve a reasonable yield of reduction product. In accord with our proposed initiation reaction, the facility of electron transfer from DMBI has been established with several acceptors, 2,4,6-triphenylpyrylium perchlorate and triphenylmethyl chloride.[11] When DMBI was allowed to react in acetonitrile with either of these substrates, the corresponding EPR spectra from the 2,4,6-triphenylpyranyl radical or the triphenylmethyl radical were observed.[11] Other examples of the SET reduction of a variety of acceptors with substituted benzimidazolines have been reported to give EPR spectra.[12]

Since the reduction is established to proceed by a radical chain process, the propagation sequence that we have proposed appears to be an acceptable rationalization for the mechanistic pathway of the reductions.

Scheme III



Experimental Section

Materials. The preparation or purification of α-fluoroacetophenone, α-chloroacetophenone, α-bromoacetophenone, *p*-di-*tert*-butylbenzene, α,α-azoisobutyronitrile, dinitrobenzene, and acetophenone has been described previously.[6] The purification of solvents was also described.[4]

(1*R*)-(+)-3-Bromocamphor (General Intermediate of Canada) was recrystallized from 95% ethanol and dried under vacuum over P$_2$O$_5$, mp 75–77 °C (lit.[13] mp 75–78 °C).

(±)-Camphor (Eastman) was purified by sublimation, mp 174–175 °C (lit.[13] mp 175–177 °C).

Ethyl 2-bromopropionate (Fluka) was redistilled, bp 155–157 °C (lit.[13] bp 156–160 °C).

Ethyl propionate (Aldrich, 97%) was used as received.

α-Bromopropiophenone was prepared from propiophenone by bromination with copper bromide,[14] bp 140–143 °C (20 mmg) (lit.[13] bp 245–250 °C): ^{1}H NMR (80 MHz, CDCl$_3$) δ 8.0 (m, 2 H), 7.5 (m, 3 H), 5.25 (q, 1 H), 1.95 (d, 3 H).

α-Bromoisobutyrophenone (Aldrich, 98%), propiophenone (Aldrich, 99%), and isobutyrophenone (Aldrich, 97%) were redistilled, and their purity was checked by GC and found to be >99.5%.

α-Chloropropiophenone was prepared by literature procedure,[15] bp 105–108 °C (6 mmHg) (lit.[14] bp 78 °C (1.5 mmHg)): ^{1}H NMR (80 MHz, CDCl$_3$) δ 8.0 (m, 2 H), 7.5 (m, 3 H), 5.2 (q, 1 H), 1.25 (d, 3 H).

α-Chloroisobutyrophenone was prepared from isobutyrophenone by the literature method,[16] bp 100–102 °C (2.2 mmHg) (lit.[16] bp 69–70 °C (0.4 mmHg)): ^{1}H NMR (80 MHz, CDCl$_3$) δ 8.15 (m, 2 H), 7.5 (m, 3 H), 1.85 (s, 6 H).

α-Fluoropropiophenone was prepared from α-bromopropiophenone and potassium fluoride,[17] bp 85–90 °C (4.5 mmHg) (lit.[17] bp 105–107 °C (15 mmHg)): ^{1}H NMR (200 MHz, CDCl$_3$) δ 7.5 (m, 5 H), 5.65–5.70 (2 q, 1 H), 1.65 (2 d, 3 H). Anal. Calcd for C$_9$H$_9$OF: C, 71.04; H, 5.96. Found: C, 70.77; H, 5.99.

1-Phenyl-1-octanone was prepared from octanoyl chloride by a Friedel–Crafts reaction,[18] bp 145–150 °C (2 mmHg) (lit.[19] bp 164 °C (15 mmHg)): ^{1}H NMR (80 MHz, CDCl$_3$) δ 8.0 (m, 2 H), 7.5 (m, 3 H), 3.0 (t, 2 H), 1.4 (m, 10 H), 0.9 (skewed t, 3 H).

1-Phenyl-2-methyl-1-octanone was prepared similarly from 2-methyloctanoyl chloride, bp 158–160 °C (3 mmHg) (lit.[20] bp 130–131 °C (2 mmHg)): ^{1}H NMR (80 MHz, CDCl$_3$) δ 7.5–7.9 (m, 5 H), 3.5 (m, 1 H), 1.2–1.35 (m, 13 H), 0.8 (skewed t, 3 H). Anal. Calcd for C$_{15}$H$_{22}$O: C, 82.52; H, 10.16. Found: C, 82.31; H, 10.03.

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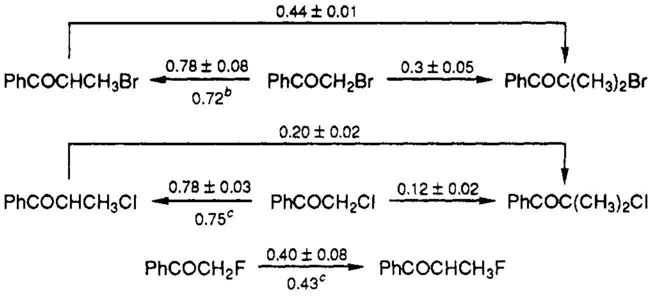
Scheme IV. Summary of the Competitive Reductions of the α-Halo Ketones (I–III)[a]



[a] The reactions were carried out at 61 °C in THF. Arrows indicate direct competitions; numbers are relative reactivities for molecule at the head of the arrow to that at the tail. Values reported are averages of two or more experiments. Unless otherwise stated the rates were determined from the disappearance of the starting substrates. [b] Analyzed by ^{1}H NMR spectroscopy. [c] Measured from the appearance of the products.

1-Phenyl-2-methyl-1-octanone was prepared by literature the procedure[21] and purified by preparative gas chromatograph (Aerograph 1520) on a glass column (10 ft × $^1/_4$ in.) packed with 20% FFAP on Chromosorb PAW, 60–80 mesh. Its structure was confirmed by analysis of its GC–MS spectra (75-ft DB-1 glass capillary column): m/z 232 (M^+), 207, 148, 126, 127, 105, 85, 71, 57, 43.

DMBI and DBPO were prepared as described previously.[22]

General Procedure for the Reduction of α-Halo Ketones. An aliquot of a solution of ketone (0.10 M), 1,4-di-*tert*-butylbenzene (0.025 M), DMBI (0.10 M), and the additive in the desired solvent was placed in a reaction ampoule, degassed, sealed under vacuum, and thermostated at the specified temperature for the specified time. The ampoule was opened, and the mixture was analyzed by GC using an HP 5840A gas chromatograph interfaced to a HP 5840A integrator. Two glass columns (20 ft × $^1/_4$ in.) were used: 10% FFAP on Chromosorb WAW DMCS, 60–80 mesh and 5% OV-101 on Chromosorb WAW DMCS, 100–200 mesh. The area ratios were converted to mole ratios for quantitative determinations by using standard calibration curves constructed from known mixtures. Products were identified by a comparison of their retention times, GC–MS and GC–IR spectra with those of authentic samples. All the reactions were carried out in duplicate.

The reaction carried out with added DBPO were run in H-shaped ampoules. The two solutions were mixed after they were degassed, sealed, and thermostated at 23 °C.

General Procedure for the Competitive Kinetic Studies. An aliquot solution of the two α-halo ketones (0.1 M in each of the ketones), DMBI (0.1 M), and internal standard (0.05 M) was analyzed by GC to obtain initial values of the relative areas of each ketone to the internal standard ($(A_{RX}/A_S)^\circ$). The solution was quickly added to 0.10 mmol of DMBI and then placed in a Pyrex ampoule, degassed, sealed under vacuum, and thermostated at 61 °C in the absence of light for 24–120 h, depending upon the reactivity of the ketones. The ampoule was then opened, and the mixture was analyzed by GC using the same conditions that were used before the reaction. The relative rate constant ($k_{RX}/k_{RX'}$) was calculated according to the following equation, where $(A_{RX}/A_S)^f$ was the area ratio of halo ketone (RX) to the internal standard(s) after the reaction was completed. The results of the

$$k_{RX}/k_{RX'} = \log [(A_{RX}/A_S)^\circ/(A_{RX}/A_S)^f]/\log [(A_{RX'}/A_S)^\circ/(A_{RX'}/A_S)^f]$$

relative reactivities actually measured were schematically drawn on Scheme IV. The results shown in Table V were calculated from this scheme. For the reduction involving α-fluoro ketones 3–5% of AIBN was used to initiate the reductions. Control experiments showed that the presence of AIBN did not significantly change the relative rates of reduction of the α-bromo ketones.

The competitive relative rate constants of several halo ketones were also measured by ^{1}H NMR (200 MHz). A 1-mL solution of the halo ketones (0.1 M) and di-*tert*-butylbenzene (0.03 M) in THF-d_8 and a 1-mL solution of DMBI (0.1 M) in THF-d_8 were placed in the separate arms of a H-shaped Pyrex ampoule. The ampoule was degassed, sealed, and thermostated at 61 °C. The solutions were mixed and allowed to react for 48 h. The ampoule was opened, the contents were filtered, and the filtrate was analyzed by GC (OV-101 column) and by ^{1}H NMR, see Scheme IV. In several cases the relative rates were determined from the appearance of the reaction products. In this case, a THF solution of 0.1 M of the two substrates (RX, RX′) and a THF solution of 0.01 M of DMBI with the internal standard (0.02 M) were allowed to react at 61 °C in the dark for 2–5 days.

General Procedure for Kinetic Studies. A 1-mL THF solution of α-halo ketones (0.10 M) and the internal standard (0.05 M) and a 1-mL THF solution of DMBI (0.10 M) were each placed in the separate arms of the H-shaped Pyrex ampoule. The ampoule was degassed, sealed under vacuum, and thermostated at 61 °C; the contents were mixed and allowed to react for the specified time. The ampoule was then cooled with liquid nitrogen, thawed, and opened, and the mixture was analyzed by GC on the OV-101 column. Three series of reactions (R_X + DMBI, R_X + $R_{X'}$ + DMBI, $R_{X'}$ + DMBI) were run in one batch. The results are presented in Figures 1–3.

General Procedure for Trapping Experiments. An aliquot solution of halo ketones (0.01 M), internal standard (0.005 M), and DMBI (0.01 M) in 1-hexene was used. The same procedure was followed that was used in the reductions carried out in the other solvents. After reaction the solutions were analyzed by GC using the OV-101 column. The products were identified by a comparison of their retention time, GC–MS, and GC–IR spectra with those of authentic samples. In case of the α-chloroisobutyrophenone, the trapping product (1-phenyl-2,2-dimethyl-1-octanone) was not detected. Its absence was confirmed by the comparison of the GC retention time of an authentic sample with the retention times of the products formed in the reaction mixture.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada and the University of Alberta for their generous support of this work. J.J.C. thanks the Killam Committee of the University of Alberta for providing a predoctoral fellowship.

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