$C_{17}H_{19}NO_2S$: C, 67.74; H, 6.35; N, 4.65; S, 10.64. Found: C, 67.55; H, 6.43; N, 4.50; S, 10.55.

o-Ethenyl-*N*,*N*-dimethylbenzenesulfonamide (8c): yield, 47%. The compound rapidly polymerized upon heating. The oily, crude **8c** was purified by chromatography over silica (60–120 mesh), using first petroleum/ether (bp 40–60 °C) and then dichloromethane as the eluent. ^1H NMR δ 2.70 (s, 6 H), 5.33 (br s, 1 H), 5.58 (br s, 1 H), 7.13–7.97 (m, 5 H); ^{13}C NMR δ 36.9, 117.8, 127.3, 128.0, 129.5, 132.6, 133.9 (q), 134.2, 137.3 (q). No correct elemental analysis could be obrained because of polymerization.

o-3-Penten-2-yl-*N*-methylbenzenesulfonamide (8d,e, mixture of *E*/*Z* isomers; from 1d): yield, 98%. One isomer (**8d**) had mp 88–91 °C (from petroleum ether, bp 60–80 °C). ^1H NMR δ 1.04 (t, 3 H), 1.38 (dd, 3 H), 2.58 (d, 3 H), 4.36 (br t, 1 H), 5.65 (br t, 1 H), 7.05–8.10 (m, 4 H); ^{13}C NMR δ 12.5, 15.0, 29.5, 31.1, 121.2, 126.8, 129.7, 131.5, 132.3, 136.4 (q), 140.6 (q), 143.3 (q). Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85; S, 13.40. Found: C, 60.18; H, 7.20; N, 5.83; S, 13.29. The other isomer is a liquid and showed the following NMR data: ^1H NMR δ 0.94 (t, 3 H), 1.80 (d, 3 H), 2.4 (dq, 2 H), 2.49 (d, 3 H), 4.36 (br q, 1 H), 5.38 (br q, 1 H), 7.05–8.10 (m, 4 H). No definite assignment of the *E* and *Z* isomers could be made on the basis of the available data.

o-2-Propenyl-*N*,*N*-dimethylbenzenesulfonamide (8f): yield, 90%; mp 52–53 °C (from petroleum ether, bp 40–60 °C). ^1H NMR δ 2.12 (s, 3 H), 2.73 (s, 6 H), 4.77 (br s, 1 H), 5.17 (br s, 1 H), 7.00–7.50 (m, 3 H), 7.70–7.90 (m, 1 H); ^{13}C NMR δ 25.3, 36.9, 115.3, 126.9, 129.3, 130.9, 132.2, 135.6 (q), 143.7 (q), 144.9 (q). Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22; S, 14.23. Found: C, 58.80; H, 6.70; N, 6.22; S, 14.34.

Sulfonamide **8f** was also prepared from o-2-propenylbenzenesulfonyl chloride (**17**) and dimethylamine. Sulfonamide **8g** was obtained by a similar procedure.

o-2-Propenylbenzenesulfonyl Chloride (17). Sodium o-2-propenylbenzenesulfonate[1b] (2.0 g, 9.08 mmol) was suspended in thionyl chloride (3 mL), a few drops of DMF were added, and the mixture was kept at 70 °C for 2 h. Then the mixture was poured into water containing sufficient sodium bicarbonate to neutralize the acid. The aqueous mixture was extracted with ether (3 × 25 mL). Separation of the ethereal layer and evaporation of the solvent gave oily **17** (1.65 g, 84%), which was purified by Kugelrohr distillation [bp 100 °C (0.1 mmHg)]. ^1H NMR δ 2.15 (s, 3 H), 5.00 (s, 1 H), 5.32 (s, 1 H), 7.13–7.80 (m, 3 H), 8.00 (br m, 1 H); ^{13}C NMR δ 24.9, 117.4, 127.8, 128.7, 131.4, 134.9, 141.7 (q), 142.1 (q), 143.8 (q). Anal. Calcd for $C_9H_9O_2SCl$: C, 49.89; H, 4.19; S, 14.80; Cl, 16.36. Found: C, 49.72; H, 4.19; S, 14.90; Cl, 16.42.

o-2-Propenyl-*N*,*N*-dimethylbenzenesulfonamide (8f). A mixture of 2 mL of 40% dimethylamine (in water) and **17** (0.5

g, 2.31 mmol) in benzene (10 mL) was refluxed for 2 h. The mixture was poured into cold water, neutralized with a dilute solution of HCl, and extracted with benzene (3 × 25 mL). The benzene layer was dried over $MgSO_4$. Evaporation of benzene gave almost pure **8f** (0.43 g, 82%). Pure **8f** (vide supra) was obtained after one crystallization from petroleum ether (bp 40–60 °C).

o-2-Propenyl-*N*-methyl-*N*-phenylbenzenesulfonamide (8g). A mixture of *N*-methylaniline (0.75 g, 7 mmol) and **17** (1.08 g, 5 mmol) in pyridine (10 mL) was heated overnight at 80 °C. Workup was carried out as described for **8f**. The yield was 67%. Kugelrohr distillation gave pure **8g**, mp 55 °C. ^1H NMR δ 2.03 (s, 3 H), 3.20 (s, 3 H), 4.75 (s, 1 H), 5.05 (s, 1 H), 7.0–7.7 (m, 9 H); ^{13}C NMR δ 25.5, 38.3, 115.2 (t), 126.1, 126.7, 126.8, 128.8, 129.6, 130.9, 132.3, 136.1 (q), 141.3 (q), 143.9 (q), 144.8 (q). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.87; S, 11.16. Found: C, 66.91; H, 5.97; N, 4.86; S, 11.12.

Synthesis of 13a,b (Scheme VI). **o-[1-Methyl-1-(dimethylamino)ethyl]-*N*,*N*-dimethylbenzenesulfonamide (13a).** A solution of **8f** (0.5 g, 2.22 mmol) in 100% CF_3CO_2H (5 mL) was stirred at 25 °C for 4 days. The solvent was distilled off, and the residue was poured into 10 mL of a 40% aqueous solution of dimethylamine. The solid sulfonamide was filtered off, dried, and crystallized from ether–*n*-hexane. The yield of **13a** was 0.4 g (70%), mp 102–103 °C. ^1H NMR δ 1.47 (s, 6 H), 2.12 (s, 6 H), 2.75 (s, 6 H), 7.00–7.67 (m, 4 H); ^{13}C NMR δ 23.9, 37.4, 38.3, 60.6, 126.2, 128.2, 128.3, 131.2, 139.4 (q), 151.9 (q). Anal. Calcd for $C_{13}H_{22}N_2O_2S$: C, 57.75; H, 8.20; N, 10.36; S, 11.86. Found: C, 57.67; H, 8.17; N, 10.35; S, 11.79.

o-[1-Methyl-1-(dimethylamino)ethyl]benzenesulfonic Acid (13b). If the reaction mixture (see **13a**) is poured into water and the solvent is removed, the sulfonic acid **13b** is formed. A pure sample (mp 257 °C dec) is obtained after crystallization from 96% ethanol (yield 82%). ^1H NMR (D_2O) δ 1.87 (s, 6 H), 2.75 (br s, 6 H), 7.5–7.8 (m, 3 H), 8.06–8.23 (m, 1 H); ^{13}C NMR (D_2O) δ 23.2, 38.0, 67.9 (q) 129.8, 130.7, 131.6, 132.9, 135.6 (q), 142.3 (q). Anal. Calcd for $C_{11}H_{17}NO_3S$: C, 54.30; H, 7.04; N, 5.76; S, 13.18. Found: C, 53.91; H, 6.97; N, 5.63; S, 13.31.

Reduction of Benzophenone with Metal Hydrides. A Kinetic Isotope Effect and Substituent Effect Study

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Carbonyl carbon kinetic isotope effects (KIEs) have been determined for the reduction of benzophenone-7-^{14}C with various metal hydrides at 25 °C. The observed KIEs are as follows: BH_3/THF, $^{12}k/^{14}k = 1.035 \pm 0.002$; AlH_3/Et_2O, 1.021 ± 0.004; 9-BBN/THF, 1.027 ± 0.004; DIBAL/hexane, 1.000 ± 0.003; $LiAlH_4$/THF, 1.017 ± 0.007. The relative reactivities of ortho-, meta-, and para-substituted benzophenones with these reagents were also determined by the competition experiments. The absence of ^{14}C KIE, the small ρ value (0.5), and the absence of steric rate retardation due to ortho substituents in the reduction of the ketone with DIBAL suggest that the reaction goes through the rate-determining electron transfer from DIBAL to the ketone. The reactions of other reducing agents showed positive KIE as well as a variable extent of steric effect and are concluded to proceed via a polar mechanism. The difference in the nature of the transition state is discussed on the basis of these results.

The reduction of carbonyl compounds with metal hydrides is one of the elemental processes in organic

syntheses, and recent achievement in developing stereoselective reductions of prochiral carbonyl compounds with

Table I. Carbonyl Carbon-14 Kinetic Isotope Effects in Reduction of Benzophenone at 25.0 ± 0.1 °C[a]

reagent/solvent	R_0, R_r, R_p	f, R_0, R_r	f, R_0, R_p	f, R_r, R_p	$^{12}k/^{14}k$ (av)
BH$_3$/THF	1.035 ± 0.002	1.034 ± 0.003	1.035 ± 0.002	1.035 ± 0.002	1.035 ± 0.002
AlH$_3$/Et$_2$O	1.021 ± 0.005	1.020 ± 0.005	1.019 ± 0.004	1.021 ± 0.004	1.021 ± 0.004
9-BBN/THF	1.029 ± 0.001	1.024 ± 0.005	1.030 ± 0.002	1.027 ± 0.001	1.027 ± 0.004
DIBAL/hexane	1.001 ± 0.001	0.998 ± 0.005	1.001 ● 0.001	1.000 ± 0.002	1.000 ± 0.003
NaBH$_4$/2-PrOH	1.065 ± 0.003	1.071 ± 0.005	1.060 ± 0.013	1.069 ± 0.004	1.066 ± 0.004[b]
LiBH$_4$/Et$_2$O	1.041 ± 0.007	1.047 ± 0.007	1.039 ± 0.008	1.043 ± 0.006	1.043 ± 0.007[b]
LiAlH$_4$/Et$_2$O	1.024 ± 0.003	1.022 ± 0.002	1.027 ± 0.004	1.023 ± 0.002	1.024 ± 0.003[b]
LiAlH$_4$/THF	1.017 ± 0.007	1.014 ± 0.006	1.019 ± 0.007	1.016 ± 0.006	1.017 ± 0.007

[a] Listed KIEs are averages from 5 to 6 runs whose fractions of reaction are in the range of 30–70%. Error limits are the standard deviations. For definition of R_0, R_r, R_p, and f, see the Experimental Section. [b] Reference 6.

chiral reducing agents is impressive.[1,2] There are two classes of metal hydrides, complex metal hydrides (e.g., LiAlH$_4$, NaBH$_4$) and simple metal hydrides (e.g., AlH$_3$, BH$_3$), and since the former is nucleophilic and the latter is electrophilic in nature, the reaction mechanism should be different. Furthermore within the same class of reducing agents, intimate mechanistic details, especially the structure of the transition state (TS), can be different. Understanding of such difference should be important in elaborating a new reducing agent.

Many mechanistic studies for the reductions with LiAlH$_4$ and NaBH$_4$ have been carried out, and the role of solvents and metal ions has been well recognized.[3] The position of the TS along the reaction coordinate has been assumed to be in the range of 0.25–0.4 for LiAlH$_4$ and 0.6–0.7 for NaBH$_4$ on the basis of the Hammett ρ values in the reduction of aromatic ketones.[4,5] Recently we have concluded from the combined experimental–theoretical kinetic isotope effect (KIE) study that these reactions proceed via an acyclic TS in which the extent of H$^-$ transfer is 0.35 for LiAlH$_4$ and 0.75 for NaBH$_4$.[6] On the other hand, mechanistic study of the reduction of ketones with simple metal hydrides is scarce, and little is discussed on the difference in mechanism between, e.g., AlH$_3$ and BH$_3$.
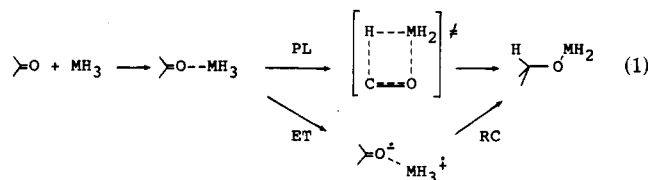
Another point of mechanistic interest is the possibility of single electron transfer (SET) in these reductions. It has been shown that LiAlH$_4$ and AlH$_3$ yield EPR-active species when mixed with aromatic hydrocarbons and N-heterocyclic compounds.[7] Reductions of RX (X = I or Br) with these reagents were also suggested to proceed via SET.[8,9] We have recently shown in the reactions of benzophenone with alkyllithium reagents that measuring carbon KIEs and substituent effects is a useful experimental means of distinguishing SET from the direct polar addition process.[10]

In the present investigation, we carried out a mechanistic

study on the reductions of benzophenones with various reducing agents by means of the KIE and the substituent effect techniques and discussed the differences in the nature of the TS of these reductions.

Results and Discussion

Simple Metal Hydrides. The reduction of benzophenone with four different simple metal hydrides, alane (AlH$_3$), borane (BH$_3$), diisobutylaluminum hydride (DIBAL), and 9-borabicyclo[3.3.1]nonane (9-BBN), were carried out, which allows us to investigate the effect of the central metal (Al vs B) and of the alkyl groups on the central metal. These metal hydrides are Lewis acids, and the first step of the reactions of the hydrides with benzophenone may involve the complex formation as shown in eq 1. The next step is either the polar hydride transfer

$$\begin{array}{c}
\ce{>C=O + MH3 -> >C-O--MH3} \xrightarrow{\text{PL}} \left[\begin{array}{c} \ce{H---MH2} \\ | \quad | \\ \ce{C===O} \end{array}\right]^{\ddagger} \longrightarrow \ce{H-C-O^{MH2}} \quad (1)
\end{array}$$

process (PL), or the electron transfer process (ET) giving the radical ion pair followed by the hydrogen atom transfer (RC, recombination of the radical pair). Ashby et al. reported that when equimolar amounts of dimesityl ketone and AlH$_3$ were mixed in THF the solution showed an EPR signal due to the radical ion pairs. An EPR signal was also observed for the reaction of BH$_3$/THF with dimesityl ketone with much less intensity. These results suggested the possibility that the reduction of the ketone with AlH$_3$ or BH$_3$ goes through a SET mechanism,[11] although such spectroscopic evidence is not conclusive as to the mechanism of the main reaction pathway.[12]

A carbonyl ^{14}C KIE has been shown to be a useful guide to the nature of the rate-determining TS of such reactions of ketones; it is of considerable magnitude when the carbonyl carbon–nucleophile bond formation is rate-determining (PL or RC in eq 1) while the magnitude of the KIE should be smaller and may be near unity when SET is rate-determining. For example, the positive (larger than unity) carbon KIEs were observed for the reactions of benzophenone-*carbonyl*-^{14}C with LiAlH$_4$ ($^{12}k/^{14}k = 1.024$),[6] NaBH$_4$ (1.066),[6] Me$_2$CuLi (1.029),[10] and MeMgI (1.056);[13] in all these reactions the carbon-nucleophile (or Me radical) bond formation was concluded to be rate-determining. On the other hand, the KIE for the reaction with MeLi was unity,[10] which was attributed to the rate-determining ET.

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Table II. Relative Reactivity of Substituted Benzophenones with Various Reducing Agents at 25.0 ± 0.1 °C[a]

| substituent	k_X/k_H					
	BH$_3$/THF	AlH$_3$/Et$_2$O	9-BBN/THF	DIBAL/hexane	LiAlH$_4$/Et$_2$O	NaBH$_4$/2-PrOH
2,4,6-Me$_3$	0.125 ± 0.042	0.108 ± 0.051	0.039 ± 0.017	0.484 ± 0.017	0.105 ± 0.017	0.009 ± 0.002
p-MeO	0.859 ± 0.013	0.288 ± 0.009	2.34 ± 0.07	0.650 ± 0.101	0.620 ± 0.047	0.035 ± 0.006
m-MeO	0.832 ± 0.009	0.994 ± 0.007	0.949 ± 0.029	1.04 ± 0.09	1.01 ± 0.05	0.854 ± 0.086
p-Me	1.04 ± 0.07	0.646 ± 0.049	1.51 ± 0.05	0.862 ± 0.109	0.811 ± 0.015	0.379 ± 0.056
m-Me	1.05 ± 0.15	0.858 ± 0.001	1.04 ± 0.04	1.00 ± 0.01	0.952 ± 0.001	0.700 ± 0.20
o-Me	0.942 ± 0.016	b	0.361 ± 0.011	0.912 ± 0.068	0.608 ± 0.035	0.154 ± 0.015
p-F	1.10 ± 0.07	1.24 ± 0.11	0.827 ± 0.025	0.953 ± 0.127	1.09 ± 0.01	1.44 ± 0.19
p-Cl	0.835 ± 0.057	1.75 ± 0.12	0.729 ± 0.019	1.09 ± 0.05	1.21 ± 0.10	3.74 ± 0.55
m-Cl	0.899 ± 0.093	2.82 ± 0.15	0.478 ± 0.050	1.39 ± 0.16	1.46 ± 0.02	7.03 ± 0.27
o-Cl	0.239 ± 0.018	0.483 ± 0.034	0.219 ± 0.080	1.42 ± 0.16	0.824 ± 0.040	0.638 ± 0.040
m-CF$_3$	0.959 ± 0.181	2.39 ± 0.26	0.518 ± 0.042	1.87 ± 0.17	1.62 ± 0.04	12.4 ± 0.4

[a] Listed values are averages of two to four determinations. Error limits are the standard deviations. [b] Reproducible value could not be obtained.
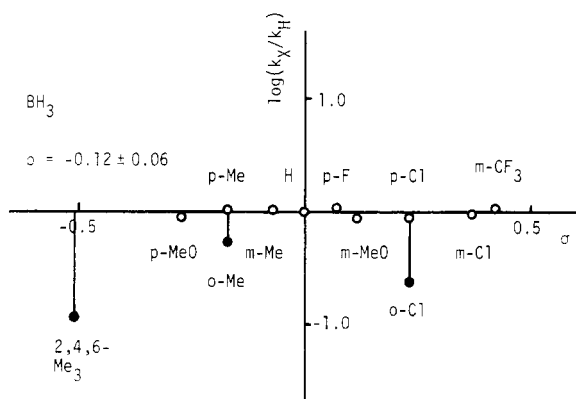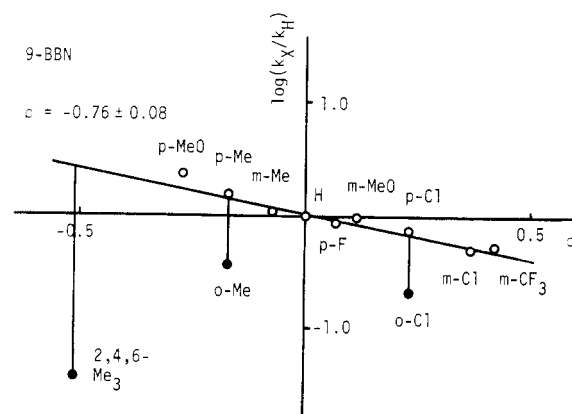

Figure 1. Variations of reactivity with σ values for the reactions of substituted benzophenones with BH$_3$.

Figure 2. Variations of reactivity with σ values for the reactions of substituted benzophenones with AlH$_3$.

Figure 3. Variations of reactivity with σ values for the reactions of substituted benzophenones with 9-BBN.

Figure 4. Variations of reactivity with σ values for the reactions of substituted benzophenones with DIBAL.

As can be seen in Table I, the observed KIE in the present study is positive for the AlH$_3$, BH$_3$, and 9-BBN reductions while it is unity in the reduction with DIBAL. Clearly the reaction mechanism is different between these two cases. The KIE of unity for the DIBAL reduction indicates that there is little change in the bonding of the carbonyl carbon in the TS; this is consistent with the ET mechanism in which the transfer of an electron is the rate-determining step.[10] In contrast, the positive carbon KIEs for the AlH$_3$, BH$_3$, and 9-BBN reductions show a bonding change occurring at the rate-determining TS. These reactions probably proceed via the polar mechanism with a four-centered TS. Slightly different magnitudes of the KIEs for the different reducing agents suggest that the extent of formation of the two new bonds (C–H and O–M) in the TS is variable.

While the magnitude of KIEs depends on the geometrical change at the labeled position on going from the reactant to the TS, substituent effects provide information on the electronic and steric requirement of the reactions, and thus these two are complementary. The relative reactivities of substituted benzophenones with various reducing agents were determined by the competition experiments. Benzophenones used here include ortho derivatives, which, in comparison with the corresponding para derivatives, allow the detection of the steric effect. Figures 1–4 show the Hammett plots for the reactions of four simple metal hydrides. Since the σ constants of the ortho substituents were not available, the log (k_X/k_H) values for the ortho derivatives were plotted against the corresponding σ_p constants and are indicated by closed circles. The deviations observed for p- and m-MeO derivatives may be attributed to the inadequacy of applying the standard σ constants of the hydrogen-bond-accepting substituents for the reactions carried out in the nonpolar
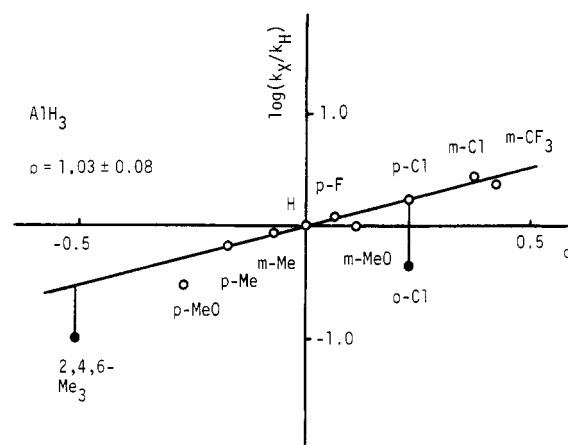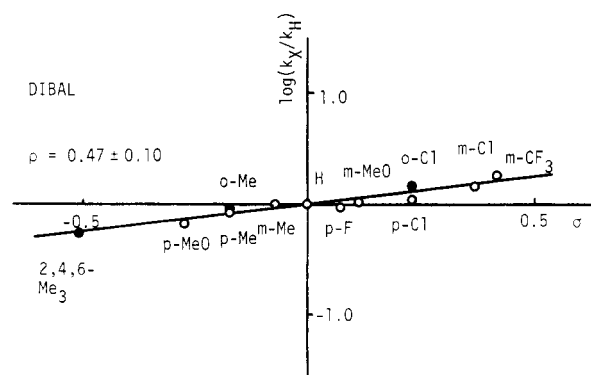
solvent and/or the additional demand of the σ^+-type resonance in the TS of these reactions. Other substituents gave reasonably good straight lines, from which the ρ values were calculated. It is apparent in these figures that the substituent effects show different patterns in these reactions. In the DIBAL reduction, the ρ value is slightly positive and no reactivity difference between the ortho and para substituted derivatives is observed (Figure 4). The absence of steric rate retardation by the ortho substituents in the DIBAL reduction is in sharp contrast to the other three reductions, in which the rate retardations are substantial. The results are consistent with the idea that the DIBAL reduction proceeds via the SET mechanism while the other three reductions go through the polar process.

There are two reasons why only the DIBAL reduction proceeds via SET. First, in comparing the central metal (Al vs B) Al lies in a lower row in the periodic table and is a better electron donor; thus AlH_3 and DIBAL have greater possibility to react via SET compared to their boron counterparts. Second, the two isobutyl groups in DIBAL not only reduce the oxidation potential of the reagent (making the reagent a better electron donor) but also introduce steric hindrance in the alternative polar process. Thus, DIBAL has the greatest possibility to react via SET among the four simple metal hydrides.[14] It is noteworthy, however, that there is a possibility that AlH_3 or other reagents reacts via SET with a ketone (or other electrophiles) of higher (less negative) reduction potential (such as fluorenone) and/or of larger steric bulkiness (such as dimesityl ketone).[11]

Yoon et al. carried out the systematic study of the reactions of DIBAL with various compounds.[15] In toluene at 0 °C, aldehydes and ketones of diverse structures are reduced quantitatively to give the corresponding alcohol; enones are also reduced to allylic alcohols by 1,2-additions. In general, enones are known to give either 1,2- or 1,4-adducts or the mixture of the two depending on the nucleophile. For example, $LiAlH_4$, $LiBH_4$, and $NaBH_4$ have been shown to give the 1,2-adduct predominantly,[16] while Me_2CuLi is known to undergo exclusively 1,4-addition.[17] Since the former reducing agents are believed to react via the polar mechanism whereas the latter react via the SET mechanism, one might consider that 1,2-addition is characteristic to the polar mechanism and 1,4-addition to SET. If so, the exclusive occurrence of the 1,2-addition in the DIBAL reduction suggests that the reduction mechanism is polar. However, although this idea might basically be correct, the relation is not straightforward. For example, t-BuMgCl, which is known to react with ketones via the SET pathway,[18] gives more 1,2-adduct than 1,4-adduct.[19] MeLi, which was recently shown to react with benzophenone via the rate-determining ET mechanism,[10] gives exclusively the 1,2-adduct when mixed with an enone.[17]

It seems that whether a reaction gives a 1,2- or 1,4-adduct depends on the lifetime of the radical-ion pair. If the reaction goes through the SET pathway, only when the radical-ion pair has a sufficiently long lifetime does the reaction give a 1,4-adduct. Therefore it is likely that a reaction which goes through rate-determining ET behaves as if it goes through the polar mechanism because of the limited lifetime of the intermediate.

It is suprising that there are few examples in the literature of the Hammett correlation of the reduction of ketones with simple metal hydrides. It was reported that the reduction of substituted benzophenones with AlH_3 gave the positive ρ value of 0.89 in THF at 0 °C.[20] Brown has recently mentioned that electron-withdrawing substituents decrease the rate of reduction of acetophenone with 9-BBN; the reported data give the negative ρ value of about -1.2 in THF at 25 °C.[21] The Hammett ρ value determined in the present study is positive (1.0) for the AlH_3 reduction in diethyl ether (Figure 2) and negative (-0.8) for the 9-BBN reduction in THF (Figure 3) both at 25 °C; these are similar in magnitude to the reported values. The sign of the ρ values indicated that the reaction is nucleophilic in nature for AlH_3 and electrophilic for 9-BBN. The BH_3 reduction gave the ρ value of nearly 0.0 (Figure 1), implying that the reaction has an intermediate character between the above two cases.

It should be noted, however, that the near zero ρ value does not mean that the H–C and the B–O bond formations progress to exactly the same degree in the TS. It merely reflects that the electron demand of the reaction center is the same both at the initial state and the TS. Although the Hammett ρ value on the equilibrium is not known, it is likely to have some positive value since the hydration equilibrium shown in eq 2 gave ρ^+ of 1.62.[22] Therefore,

$$ArCOCF_3 + H_2O \rightleftharpoons Ar-\underset{\underset{OH}{|}}{\overset{\overset{OH}{|}}{C}}-CF_3 \qquad (2)$$
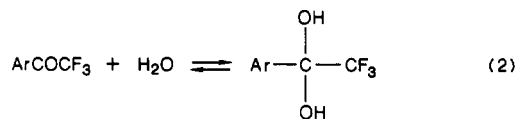
the reaction of the perfectly synchronous TS should give some positive ρ value.

Complex Metal Hydrides. Unlike the simple metal hydrides, there have been considerable mechanistic studies of the complex metal hydride reductions. It is established by now that in the $NaBH_4$ reduction in 2-PrOH the metal ion (Na^+) does not play any significant mechanistic role while in $LiBH_4$ or $LiAlH_4$ reduction in an ethereal solvent the metal ion (Li^+) plays a crucial role in the mechanism.[1] Another interesting difference between $NaBH_4$ and $LiAlH_4$ is that in the $NaBH_4$ reduction transfer of the first hydride is rate-determining (slowest) while in $LiAlH_4$ reduction transfer of the first hydride is fastest; replacement of the hydrogens with alkoxy groups exerts the effect on the reactivity of these reagents in different directions.[1]

Here we summarize our KIE and substituent effect study on the complex metal hydride reductions. As Table I shows, the carbonyl-^{14}C KIE is positive in all complex metal hydride reagents; the KIE for $LiAlH_4$ in THF was found to be of similar magnitude to that for $LiAlH_4$ in diethyl ether reported earlier.[6] We have previously concluded on the basis of the combined experimental–theoretical KIE technique that the $NaBH_4$ reduction in 2-PrOH goes through an acyclic TS in which the bond order

(14) The positive ^{14}C KIE, the positive ρ value, and the steric rate retardation by the ortho substituents observed in the AlH_3 reduction per se do not exclude the possibility that the reaction proceeds via fast SET followed by the rate-determining H⁻ transfer. However, this possibility can be eliminated by comparing the results for AlH_3 with those for DIBAL. If ET is faster than the H⁻ transfer in the AlH_3 reduction, it is highly unlikely that ET becomes slower than the H⁻ transfer in the DIBAL reduction because the two alkyl groups on Al in DIBAL should make ET faster rather than slower relative to H⁻ transfer for both electronic and steric reasons as described in the text.

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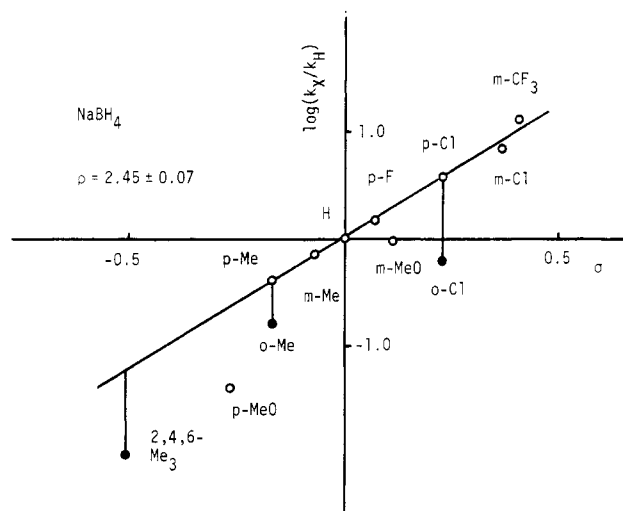(17) (a) House, H. O.; Respess, W. L.; Whitesides, G. M. *J. Org. Chem.* **1966**, *31*, 3128–3141.

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Figure 5. Variations of reactivity with σ values for the reactions of substituted benzophenones with NaBH$_4$.
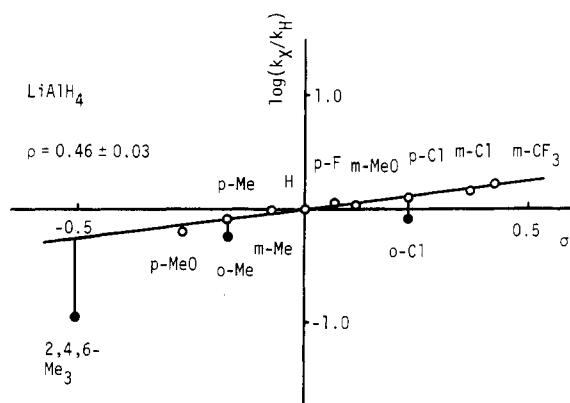
Figure 6. Variations of reactivity with σ values for the reactions of substituted benzophenones with LiAlH$_4$.

of the C–H bond is 0.75 (product-like).[6] Under the assumption that the LiAlH$_4$ reduction also proceeds via an acyclic TS, the reduction in diethyl ether was concluded to have a TS in which the C–H bond order is 0.35 (reactant-like).[6] The KIE for the LiAlH$_4$ reduction in THF suggests that this reaction also has a reactant-like TS as in diethyl ether.

Figure 5 shows the Hammett plots for the NaBH$_4$ reduction, from which a large ρ value (2.5) was obtained. This is similar in magnitude to those reported in the literature; ρ = 2.5 for X-C$_6$H$_4$COCH$_3$ + NaBH$_4$ at 25 °C in H$_2$O,[23] 2.65 for substituted fluorenones + NaBH$_4$ at 25 °C in 2-PrOH,[24] and 3.06 for X-C$_6$H$_4$COCH$_3$ + NaBH$_4$ at 30 °C in 2-PrOH.[25]   The Hammett plots for the LiAlH$_4$ reduction (Figure 6), on the other hand, gave the small ρ value of 0.5, which is smaller than the reported value (1.95) for ArCOMes + LiAlH$_4$ at 25 °C in diethyl ether.[26] The difference may be attributed to the steric effect of the mesityl group; the two o-Me of the mesityl moiety reduce the coplanarity between the carbonyl function and the mesityl moiety, which in turn increases the coplanarity between the carbonyl function and the phenyl ring to

which the substituents are introduced. The two o-Me of the mesityl moiety may also shift the TS to a later position along the reaction coordinate (the Leffler–Hammond principle). In any event, it is apparent in the present study, in which the reactions of the same series of substrates are compared, that the Hammett ρ value is larger for NaBH$_4$ than for LiAlH$_4$. Furthermore, the ortho–para reactivity difference is much larger for NaBH$_4$ as can be seen in Figures 5 and 6, indicating that the NaBH$_4$ reduction is much more susceptible to the steric effect. These substituent effect results are fully consistent with the view that the TS of the NaBH$_4$ reduction lie in the later position along the reaction coordinate compared to that of the LiAlH$_4$ reduction.

Experimental Section

Materials. Diethyl ether and THF were dried over LiAlH$_4$ and distilled before use. Hexane was fractionally distilled and stored over Linde MS 4A. 2-Propanol was dried over and distilled from calcium hydride. NaBH$_4$ was recrystallized from diglyme.[27] LiAlH$_4$ (Merck Sharp & Dohme), DIBAL (1.0 M in hexane, Aldrich), and 9-BBN (0.5 M in THF, Aldrich) was used as received. BH$_3$[28] and AlH$_3$[29] were prepared according to the literature. All glassware was flame-dried, and the solution of the reducing agents was handled under nitrogen by using Schlenk tube techniques.[30] The hydride activities of the reagent solutions were determined before use by the methods described in the literature.[31] Substituted benzophenones and ^{14}C-labeled benzophenone at the carbonyl carbon were prepared as described previously.[10]

Competition Experiments and Determination of KIE. Relative reactivities of substituted benzophenones and ^{14}C KIEs with various reducing agents were determined by the methods described before.[6,10] Four equations of Tong and Yankwich were used; these equations allow KIE calculations in four ways by using any three of the measured parameters, fraction of reaction, f, radioactivity of starting ketone, R_0, activity of the recovered ketone, R_r, and activity of the product alcohol, R_p.[32] Agreement among the KIEs calculated by the four different equations was excellent in all cases and the KIE thus obtained showed no trend with the fraction of reaction. These facts indicate the high reliability of the results.

Registry No. 9-BBN, 280-64-8; DIBAL, 1191-15-7; BH$_3$, 13283-31-3; AlH$_3$, 7784-21-6; LiAlH$_4$, 16853-85-3; carbon-14, 14762-75-5; benzophenone, 119-61-9; 2,4,6-trimethylbenzophenone, 954-16-5; p-methoxybenzophenone, 611-94-9; m-methoxybenzophenone, 6136-67-0; p-methylbenzophenone, 134-84-9; m-methylbenzophenone, 643-65-2; o-methylbenzophenone, 131-58-8; p-fluorobenzophenone, 345-83-5; p-chlorobenzophenone, 134-85-0; m-chlorobenzophenone, 1016-78-0; o-chlorobenzophenone, 5162-03-8; m-(trifluoromethyl)benzophenone, 728-81-4.

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