

Comparative Mechanistic Study of the Reactions of Benzophenone with *n*-BuMgBr and *n*-BuLi

Hiroshi Yamataka,* Nobutaka Miyano, and Terukiyo Hanafusa

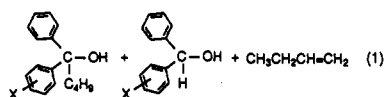
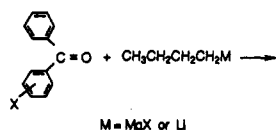
The Institute of Scientific and Industrial Research, Osaka University, Ibaraki, Osaka 567, Japan

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Substituent effects on reactivity and product distribution (addition vs reduction) were determined for the reactions of benzophenones with *n*-BuMgBr and *n*-BuLi at 0 °C. In case of the reaction with *n*-BuMgBr, meta- and para-substituted benzophenones gave a reasonably linear Hammett plot, from which the ρ value of 1.45 was calculated, while ortho-substituted derivatives deviated downward from the correlation line. In contrast, the reaction with *n*-BuLi exhibited very small substituent effects on reactivity. The product distribution is highly dependent on substituents in the *n*-BuMgBr reaction, whereas it is essentially independent of substituents in the *n*-BuLi reaction. Mechanistic differences between the reactions of these two reagents are discussed on the basis of these experimental results.

The mechanism of additions of organomagnesium and organolithium reagents to ketones has been extensively studied, and the reactions are now considered to go through a single electron transfer (SET) mechanism.¹⁻³ However, there appears to be distinct mechanistic differences between the two kinds of reagents, as shown by the magnitude of the carbonyl carbon kinetic isotope effect (KIE) and the substituent effect on reactivity; the addition of MeMgI to benzophenone gave a large ¹⁴C KIE, a medium-sized ρ value, and large steric rate retardation; the addition of MeLi to benzophenone showed no KIE, a very small ρ value, and little steric effect on reactivity.^{2,3} The former reaction was then concluded to proceed via initial SET followed by the slow rate-determining C-C bond formation.² On the other hand, the rate-determining step of the latter reaction was assigned SET.³

Reactions of ketones with the organometallic reagents bearing β hydrogens are known to give reduction products together with normal addition products. However, in contrast to the large number of investigations on the additions of the organometallic reagents to ketones, mechanistic studies on the reductions of ketones by these reagents are limited.^{1b,4} In the present paper, we report the results of substituent effects on reactivity and product distribution for the reactions of substituted benzophenones with *n*-BuMgBr and *n*-BuLi, in which both addition and reduction occur competitively (eq 1). The mechanistic difference for *n*-BuMgBr and *n*-BuLi will be discussed on the basis of the results.



The reactions with *n*-BuMgBr in diethyl ether and *n*-BuLi in hexane were carried out at 0.0 ± 0.1 °C. The

Table I. Product Ratios in the Reactions of Substituted Benzophenones with *n*-BuMgBr and *n*-BuLi^a

substituent	addition/reduction	
	<i>n</i> -BuMgBr	<i>n</i> -BuLi
<i>o,p</i> -Me ₂	2/98	65/35
<i>p</i> -MeO	62/38	77/23
<i>p</i> -Me	40/60	73/27
<i>m</i> -Me	39/61	72/28
<i>o</i> -Me	6/94	71/29
H	33/67	73/27
<i>p</i> -F	32/68	71/29
<i>p</i> -Cl	10/90	73/27
<i>o</i> -Cl	4/96	67/33
<i>m</i> -CF ₃	13/87	72/28
<i>o</i> -CF ₃	3/97	77/23

^a Reactions were carried out at 0.0 ± 0.1 °C with 0.067 M ketone and 0.14 M *n*-BuMgBr, or 0.08 M ketone and 0.12 M *n*-BuLi. Listed values are in percent and are averages of two runs. Errors are less than 3%.

Table II. Effect of Concentration on Product Ratio^a

X	addition/reduction ^b			
	0.170, 0.083	0.140, 0.067	0.095, 0.047	0.058, 0.031
H	37/63	26/74	24/76	18/82
<i>o</i> -Me	8/92	6/94	5/95	5/95
<i>m</i> -Me	37/63	32/68	30/70	26/74
<i>p</i> -Me	40/60	38/62	32/68	29/71

X	addition/reduction ^c				
	0.19, 0.095	0.17, 0.086	0.14, 0.071	0.10, 0.052	0.062, 0.034
H	67/33	65/35	65/35	69/31	65/35
<i>o</i> -Me	68/32	65/35	68/32	70/30	72/28
<i>m</i> -Me	68/32	68/32	65/35	66/34	63/37
<i>p</i> -Me	68/32	67/33	67/33	68/32	67/33

^a Reactions were carried out at 0.0 ± 0.1 °C. ^b *n*-BuMgBr (M), X-C₆H₄COC₆H₅ (M). ^c *n*-BuLi (M), X-C₆H₄COC₆H₅ (M).

relative reactivities of substituted benzophenones with these reagents were determined by the competition experiments as described previously.^{3a} In Figures 1 and 2 are shown the Hammett plots of these reactions. Both reactions gave reasonably good straight lines for meta- and para-substituted derivatives.⁵ The two sets of plots in

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(5) 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 point for the *p*-CH₃O substituent in Figure 1 deviates downward, but this is a rather general phenomenon for reactions of benzophenones with RMgX and other organometallic reagents in diethyl ether or THF.^{3,3b} This is probably due to inadequacy of using the standard σ constant for the hydrogen-bond accepting substituent in ethereal solvent.⁵

mechanism of the competitive formations of *n*-Bu and H radicals as noted above. In the *n*-BuMgBr reaction, on the other hand, reduction is more favored under more dilute conditions. The results suggest that the reduction takes place as a unimolecular decomposition of the ketone-Grignard reagent complex, while the addition occurs in higher order molecularity, as proposed by earlier studies.⁷

In conclusion, both organomagnesium and organolithium reagents react with benzophenone via an ET mechanism, but these reactions are different in the rate-determining steps and in the fates of the radical-ion pair formed via initial ET.

Experimental Section

Materials. Diethyl ether was dried over LiAlH₄ and distilled before use. Hexane was dried over CaH₂ and distilled. All glassware was flame-dried, and anhydrous solutions were handled under dry nitrogen by using Schlenk tube techniques.⁸ Substituted benzophenones were prepared as described previously.^{3a} *n*-BuLi was purchased from Merck (1.6 M, hexane soln). *n*-BuMgBr was prepared from *n*-BuBr (bp 101 °C) and doubly

sublimed Mg (Ventron). These organometallic reagents were standardized by a method described in the literature.⁹

Reactions. All reactions were carried out at 0.0 ± 0.1 °C. The relative reactivities of the substituted benzophenones were determined as described before.^{3a} The concentrations of the ketone and the reagent in this experiment were 0.07 M and 0.03 M, respectively. Reactions to determine the product ratio were carried out under various concentrations as noted in footnotes to Tables I and II. All substituted tertiary alcohols (1-aryl-1-phenyl-pentanol) were isolated from the reaction solution by using silica gel column chromatography. Substituted benzhydrols were obtained by the reactions of substituted benzophenones with LiAlH₄. The identity of these compounds was confirmed by ¹H NMR (Bruker-AM360) and IR (HITACHI 260-10) spectroscopy as well as melting points (where the literature values were available), and the purity was judged to be >98% by GLC (dibenzyl ether, internal standard). Product ratios were determined by GLC (PEG HT, 2 m) by calibrating detector response factors of these products. Material balance was confirmed for the parent benzophenone and found to be excellent (>98% for both reagents).

Acknowledgment. We are indebted to the Material Analysis Center of ISIR for the NMR measurements.

Supplementary Material Available: Relative reactivity data of benzophenones with *n*-BuMgBr and *n*-BuLi and the NMR and IR data and spectra of the products (15 pages). Ordering information is given on any current masthead page.

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Phenylazophenol-Quinone Phenylhydrazone Tautomerism in Chromogenic Cryptands and Corands with Inward-Facing Phenolic Units and Their Acyclic Analogues

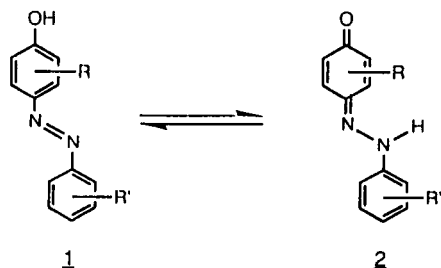
Eddy Chapoteau,¹ Bronislaw P. Czech,¹ Carl R. Gebauer,¹ Anand Kumar,*¹ Koonwah Leong,¹ Daniel T. Mytych,¹ Wolodymyr Zazulak,¹ Dhimant H. Desai,² Elzbieta Luboch,² Jan Krzykawski,² and Richard A. Bartsch*²

Technicon Instruments Corporation, Tarrytown, New York 10591-5097, and Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409-1061

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A series of 4-(4'-nitrophenol)azophenol compounds is prepared in which ether oxygen-containing substituents are attached at the 2- and 6-positions or connect the 2- and 6-positions to incorporate the chromophoric unit into corand or cryptand structures with inward-facing phenolic groups. The phenylazophenol-quinone phenylhydrazone tautomerism of these compounds, as probed by ultraviolet-visible spectroscopy, reveals a pronounced effect of the structure of the ether oxygen-containing substituents or bridging unit upon the tautomeric equilibrium. Chromogenic responses of five cryptands with inward-facing phenolic groups to sodium and potassium ions are determined and compared.

The tautomerism between *p*-arylazophenols **1** and *p*-quinone arylhydrazones **2** has been investigated extensively on compounds derived from phenols, anthranols, and particularly naphthols and summarized in several reviews.³⁻¹⁰ On the basis of the results of early investiga-



(1) Technicon Instruments Corporation.
(2) Texas Tech University.

tions, compounds from the phenol series were long assumed to exist in the azo form only. Later studies by ¹H NMR¹¹⁻¹³ and IR¹⁴ spectroscopy revealed that introduction

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