3066 *Organometallics* **2002,** *21,* 3066−3068

Organotin Hydride Reduction of Benzyl Bromides

Lawrence W. Menapace,* Matthew B. Loewenthal, Jeremy Koscielecki,
Lucas Tucker, Linda C. Passaro, Rosa Montalbano, Anthony J. Frank,
Joseph Marrantino, and Jeanette Brunner

Marist College, School of Science, Poughkeepsie, New York 12601

Received April 5, 2002

Summary: A Hammett study was carried out on the tributyltin hydride reduction of substituted benzyl bromides. Electron-withdrawing groups facilitate the reaction, whereas electron-releasing groups have little or no impact on the rate. This unusual effect creates a discontinuity in the Hammett plot. Electron-withdrawing groups stabilize both the free radical and polar character of the transition state. Electron-releasing groups, however, stabilize the free radical character but destabilize the polar character of the transition state.

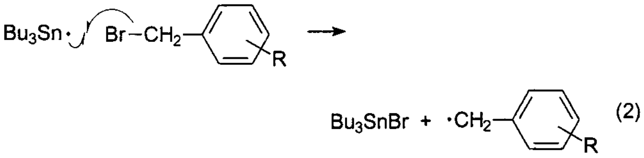
Introduction

In 1957, van der Kerk showed that allyl bromide reacted with tributyltin hydride not by addition to the double bond but by reduction of the C−Br bond to give propene (eq 1).[1] This hydrostannolysis reaction has since

$$\mathrm{RBr + Bu_3SnH \longrightarrow RH + Bu_3SnBr} \qquad (1)$$

been extended to a variety of other functional groups and now provides a widely used procedure in organic synthesis.[2]

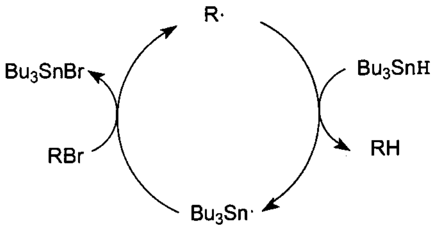
The mechanism is well-established to be a radical chain process (Scheme 1) in which the stannyl radical executes an S_H2 reaction at the bromine center[3] (eq 2)



and the rate of the reaction between $Bu_3Sn^{\bullet}$ radical and benzyl bromide (eq 2, R = H) has been measured to be 1.5×10^9 L mol^{-1} s^{-1} at 298 K.

It has long been recognized that the transition state for reaction 2 has some polar character, as shown in Scheme 2, in which the canonical form **III** makes a significant contribution to the structure of the transition state.[4] The rate of reaction 2 might therefore be expected to be affected by the electronic effect of substituents in the benzene ring: electron-attracting groups accelerating and electron-releasing groups retarding the reaction.

Scheme 1



Scheme 2

$$[\mathrm{M}^{\bullet}\ \ \mathrm{X{-}CH_2Ar}] \longleftrightarrow [\mathrm{M{-}X}\ \ {}^{\bullet}\mathrm{CH_2Ar}] \longleftrightarrow [\mathrm{M}^{+}\ \ \dot{\mathrm{X}}\ \ {}^{-}\mathrm{CH_2Ar}]$$

I **II** **III**

A number of studies of systems of this type involving different ring-substituted benzyl halides and different metal-centered radicals have been carried out with the aim of correlating the rates with Hammett substituent constants, and these studies are summarized in Table 1. Absolute rate constants were determined for entries 2, 6, and 7. All others were carried out by causing a limited amount of the metal radical to compete for a mixture of $YC_6H_4CH_2X$ and $C_6H_5CH_2X$ and determining the relative reactivities by analyzing the products by GLC.

The positive Hammett ρ value that was obtained in all these studies confirms that the metal radical is acting as a nucleophile, and the polar substituents can be envisaged to exert their effect by stabilizing structure II and either stabilizing or destabilizing structure **III**. The question that then arises is what form of substituent constant, or what combination of constants, σ, $\sigma^{\bullet}$, σ^{-}, and σ^{+}, best correlates the relative reactivities.

The most relevant of these studies to the present work is that by Blackburn and Tanner (entries 3−5), in which a variety of ring-substituted benzyl chlorides, bromides, and iodides were reduced by tributyltin hydride in benzene at 363 K, with benzoyl peroxide as initiator.[5] They reported that a Hammett plot of $\log(k/k_0)$ against the substituent constants σ^{-} gave quite a good correlation with ρ values of +0.34 (X = Cl), 0.17 (X = Br), and 0.81 (X = I), while only fair correlations were obtained with σ constants.

On the other hand, Chatgilialoglu, Ingold, and Scaiano (entry 7) found that the absolute rate constants for the reaction of triethylsilyl radicals with ring-substituted benzyl chlorides correlated rather better

---

* To whom correspondence should be addressed. E-mail: Lawrence.Menapace@Marist.edu. Phone: (845) 575-3000, ext. 2235. Fax: (845) 575-3184.

[1] van der Kerk, G. J. M.; Noltes, J. G.; Luijten, J. G. A. *J. Appl. Chem.* **1957**, *7*, 356.

[2] Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, 1987.

[3] Davies, A. G. *Organotin Chemistry*; VCH: Weinheim, Germany, 1997.

[4] Menapace, L. W.; Kuivila, H. G. *J. Am. Chem. Soc.* **1964**, *86*, 3047.

[5] Blackburn, E. V.; Tanner, D. D. *J. Am. Chem. Soc.* **1980**, *102*, 692.

10.1021/om0202726 CCC: $22.00

Table 1. Studies of the Hammett Relationships in the Reaction of Metallic Free Radicals with Substituted Benzyl Halides

	benzyl halide	M$^\bullet$	substituent const	ρ
1	$YC_6H_4CH_2Cl$	$Et_3Ge^\bullet$ [a]	σ	+0.31
2	$YC_6H_4CH_2Br$	$^\bullet Co(DMGH)(PPh_3)_3$[b]	σ	+1.4
3	$YC_6H_4CH_2Cl$	$Bu_3Sn^\bullet$ [c]	σ^-	+0.34
4	$YC_6H_4CH_2Br$	$Bu_3Sn^\bullet$ [c]	σ^-	+0.17
5	$YC_6H_4CH_2I$	$Bu_3Sn^\bullet$ [c]	σ^-	+0.81
6	$YC_6H_4CH_2Br$	$^\bullet Re(CO)_4P(^iPrO)_3$[d]	σ	+0.75
7	$YC_6H_4CH_2Cl$	$Et_3Si^\bullet$ [e]	σ	+0.64
8	$YC_6H_4CH_2Br$	$(Me_3Si)_3Si^\bullet$ [f]	$\sigma + \sigma^\bullet$	+0.31

[a] Reference 11. [b] Reference 12. [c] Reference 5. [d] Reference 13. [e] Reference 6. [f] Reference 7.

with σ than with σ^-, although with a ρ value of +0.64 there was apparently a greater degree of charge separation in the transition state than in the reaction with the tributylstannyl radicals.[6]

Jiang, Ding, and Zhang carried out a thorough study of the reaction of the radical $(Me_3Si)_3Si^\bullet$ with ring-substituted benzyl chlorides and found that the correlation with the single parameters σ or σ^- gave fair results, but the best correlation was against $\sigma + \sigma^\bullet$, which gave a ρ value of 0.31.[7]

Other previous work of importance to this study was conducted by Pratt, Wright, and Ingold.[8] They examined bond dissociation enthalpies for 4-$YC_6H_4CH_2$-X where X = H, Br, Cl, F. Their work suggests that a substituent group can stabilize the benzyl radical while concurrently having a stabilizing or destabilizing effect on the polar benzyl halide. Thus, any given substituent can, in fact, display two distinct effects. These effects can either reinforce or oppose each other.

Results and Discussion

Against this rather confusing background, we have returned to the question of substituent effects on the rate of reaction of ring-substituted benzyl bromides with tributyltin radicals. Mixtures of benzyl bromide and of the substituted benzyl bromide were reduced with a limited amount of tributyltin hydride in toluene at 353 K. The relative yields of toluene and the substituted toluene were analyzed by GLC, and the k/k_0 values of the bromine-abstraction step (reaction 2) were derived.

Table 2 shows values of k/k_0 and of σ,[9] σ^-,[9] and $\sigma^\bullet$[10] for 11 ring-substituted benzyl bromides.

Figure 1 shows a Hammett plot of log k/k_0 against σ, and three points stand out. First, there is a reasonably linear region of *positive* slope ($\rho = 0.29$) relating to the electron-attracting substituents with σ values between zero (X = H) and 0.7 (X = CN). Second, a discontinuity occurs at $\sigma = 0$, log $k/k_0 = 0$, to give a region relating to the electron-releasing substituents, with now a marginally *negative* slope ($\rho = -0.024$). Third, the point for the *p*-nitro substituent lies far off the region of positive slope.

Table 2. Relative Rate Constants for the Organotin Hydride Reduction of Substituted Benzyl Bromides at 353 K[a,b]

group	k/k_0	σ	σ^-	$\sigma^\bullet$
m-methyl	1.01 ± 0.02	−0.06	−0.060	−0.001
p-methoxy	1.04 ± 0.05	−0.270	−0.260	0.034
p-methyl	1.02 ± 0.01	−0.170	−0.170	0.015
p-*tert*-butyl	0.98 ± 0.01	−0.260	−0.130	0.036
toluene (H)	1.00	0.000	0.000	0.000
p-carbomethoxy	1.34 ± 0.01	0.440	0.750	0.043
p-chloro	1.16 ± 0.01	0.280	0.190	0.017
p-cyano	1.64 ± 0.02	0.700	1.000	0.043
p-trifluoromethyl	1.4 ± 0.05	0.540	0.650	0.001
p-bromo	1.22 ± 0.01	0.230	0.230	
p-nitro	4.1 ± 0.03	0.810	1.270	

[a] Average values of four individual reactions. The error values are standard deviations from the mean. [b] Percentages of reaction for all reactions listed in the table lie between 78 and 98%, based on 3.72 mmol of organotin hydride.

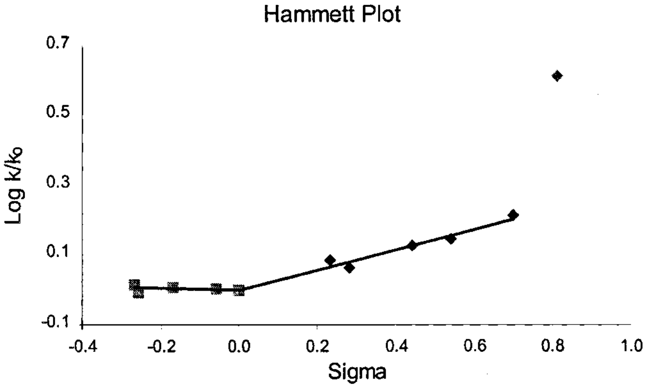


Figure 1. Plot of log k/k_0 versus σ.

The region of positive slope corresponds to a value of $\rho = 0.29$ ($R^2 = 0.967$). We have also carried out plots of our data using the constants σ^-, $\sigma + \sigma^\bullet$, and $\sigma^- + \sigma^\bullet$; a slight improvement is obtained with the combination $\sigma + \sigma^\bullet$ in a 1:1 ratio ($\rho = 0.29$, $R^2 = 0.989$), and further improvement might perhaps be given by combining two constants in a different ratio, but we doubt whether such a refinement is justified.

The change of slope from positive to negative as X changes from electronegative to electropositive has not been noted before, but signs of it are evident in previous work.[11,12] It is not apparent in Blackburn and Tanner's results on benzyl bromides (the same system as that which we have studied), but it is clear in their results on the benzyl chlorides, where they find, as we do, that both *m*- and *p*-methyl groups give positive values of log k/k_0 but the *tert*-butyl group gives a value that is marginally negative. The discontinuity that we observe is consistent with a situation in which electron-withdrawing groups stabilize both structures II and III, leading to an overall increase in the stability of the transition state. Electron-releasing groups stabilize structure II but destabilize structure III. These effects tend to cancel each other and result in little or no change in the stability of the transition state.

The only previous studies that have included nitro substituents appear to be the two involving transition metals (Table 1, entries 2 and 6). Halpern and Phelan[12] found that their point for *p*-NO_2 fitted their σ_p plot (though only four X groups were studied), but Lee and

---

(6) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Org. Chem.* **1987**, *52*, 938.

(7) Jiang, X.-K.; Ding, W. F.-X.; Zhang, Y.-H. *Tetrahedron* **1997**, *53*, 8479.

(8) Pratt, D.; Wright, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1999**, *121*, 4877.

(9) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

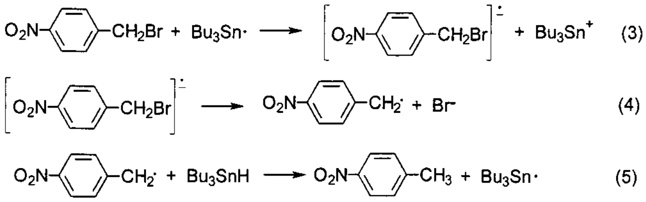
(10) Arnold, D. R. In *Substituent Effects in Radical Chemistry*; Viehe, H. G., Janousek, Z., Merenyi, R., Eds.; NATO ASI Series C; Reidel: Dordrecht, The Netherlands, 1986; Vol. 189, pp 171−188.

(11) Sakurai, H.; Mochida, K. *J. Organomet. Chem.* **1972**, *42*, 339.

(12) Halpern, J.; Phelan, P. F. *J. Am. Chem. Soc.* **1972**, *94*, 1981.

Brown's σ plot shows that the point for *p*-NO_2 is anomalous in the same sense as ours.[13]

The departure of the point from the plot is so extreme that no change in the nature of the σ constant, for example to σ^-, can correct the anomaly, and it may be that it indicates a change in mechanism. Whatever might be proposed, it must accommodate the fact that the GLC shows that the CH_2Br group is cleanly reduced to CH_3. One possibility might be that $Bu_3Sn^\bullet$ adds to the NO_2 group to give a radical that is (catalytically) more reactive in abstracting Br from the benzyl bromide than is $Bu_3Sn^\bullet$ itself. Pedulli and co-workers report that the stannyl radical preferentially adds to the nitro group instead of abstracting the bromine atom in the case of 2-(nitrophenyl)-1-bromoacetylene.[14] It seems unlikely, however, that such an adduct would increase the reactivity. A more reasonable possibility might be that an electron-transfer mechanism, operating through the nitroarene radical anion might be involved (eqs 3−5).



These possibilities are being investigated.

Experimental Section

The benzyl bromides were commercial samples from Aldrich, Lancaster, or Acros Chemical Co., except *p*-methoxybenzyl bromide, which was synthesized.[15] Chromatography was carried out using a Hewlett-Packard Model 5840A gas chromatograph, fitted with a flame ionization detector.

Competitive Reduction of Benzyl Bromides. A glass ampule was flushed with nitrogen and then charged with 3.72 mmol of each of the two benzyl bromides, along with 2.00 mmol of heptane as the internal standad and 0.10 g (0.61 mmol) of the free radical initiator AIBN. The solvent, ethylbenzene (10 mL), was then added, and finally tri-*n*-butyltin hydride (1 mL, 3.72 mmol) was added by pipet. The ampule was quickly flushed with nitrogen, sealed, and placed in an oil bath at 353 K for a minimum of 2 h. A minimum of four reactions were run for each substituted benzyl bromide, and each reaction mixture was analyzed in triplicate by GLC.

The final concentration of each reduction product was determined using an internal standard method.[16] Three mixtures in the ratio of 1:1, 1:2, and 2:1 with the internal standard (heptane) were prepared for each of the reduction products. A computer-generated plot of the ratio of the areas versus the number of moles was subjected to regression analysis, and the equation of the line was used to determine the molar amounts of each reduction product. The ratio of the rate constants was then determined by Ingold's equation:[16]

$$(\log B_0 - \log B)/(\log A_0 - \log A) = k_b/k_a$$

In this expression, B_0 and B are the initial and final concentrations, respectively, of the substituted benzyl bromide and A_0 and A are the initial and final concentrations, respectively, of benzyl bromide. The term k_b/k_a represents the ratio of the two rate constants.

Acknowledgment. We thank Dr. Brian Roberts, University College London, for his comments and suggestions. We are also deeply indebted to Dr. Alwyn G. Davies, University College London, for his encouragement, support, and advice on the preparation of this paper.

OM0202726

---

(13) Lee, K. W.; Brown, T. L. *J. Am. Chem. Soc.* **1987**, *109*, 3269.

(14) Alberti, A.; Pedulli, G. F.; Ciminale, F. *Tetrahedron* **1982**, *38*, 3605.

(15) Kornblum, N.; Smiley, R. A.; Blackwood, R. K.; Iffland, D. C. *J. Am. Chem. Soc.* **1955**, *77*, 6269.

(16) Keulemans, A. I. M. *Gas Chromatography*; Reinhold: New York, 1957.

(17) Ingold, C. K.; Shaw, F. R. *J. Chem. Soc.* **1927**, 2918.