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[19] Crystal structure data for **4**: $C_{17}H_{23}NO_6S$, orthorhombic, space group $P2_12_12_1$, $a = 8.107(2)$, $b = 12.627(4)$, $c = 17.653(4)$ Å, $\alpha = \beta = \gamma = 90°$, $Z = 4$, R_1 $[I > 2\sigma(I)] = 0.0310$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-101170. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[21] Crystal structure data for **11**: $C_{18}H_{23}NO_5$, monoclinic, space group $P2_1$, $a = 8.0927(4)$, $b = 13.4179(3)$, $c = 8.1986(4)$ Å, $\alpha = 90$, $\beta = 94.850$ (2), $\gamma = 90°$, $Z = 2$, $R_1[I > 2\sigma(I)] = 0.0505$.

Structure – Reactivity Relationship in the Reaction of Highly Reactive Zinc with Alkyl Bromides**

Albert Guijarro and Reuben D. Rieke*

The reaction of organic halides with magnesium or lithium in the zerovalent state is the most direct and commonly used method to prepare organometallic compounds containing these metals. However, these reactions do not show much structure selectivity. As has been stated, "the reaction of organic bromides with magnesium is among the least selective of organic reactions".[1] The formation of organolithium compounds shows great similarities to that of organomagnesium compounds.[2] In addition to these metals, zinc has become more important in recent years.[3] It tolerates a broad range of functionalities, and, since the introduction of highly reactive zinc, virtually any organozinc reagent can be prepared from the corresponding organic bromide.[4] It is generally accepted that the mechanism of these reactions is similar to those of analogous reactions of magnesium and lithium.[5] However, few mechanistic studies regarding the formation of organozinc halides are available to date.

To study the rates of reaction of alkyl bromides with highly reactive zinc, we used competitive kinetic methods.[1] The rate of reaction of organic bromides depends, in principle, on the concentration of the organic halide $[R^1Br]$ or $[R^2Br]$ and on some undefined physical characteristics of the metal surface $f(Zn)$ [Eqs. (a) and (b)]. The simultaneous determination of the concentration of two different alkyl bromides in solution that react with the same metallic surface permits a simplification to Equation (c).

$$-\,d[R^1Br]/dt = k_1[R^1Br]^x f(Zn) \qquad (a)$$

$$-\,d[R^2Br]/dt = k_2[R^2Br]^x f(Zn) \qquad (b)$$

$$d[R^1Br]/d[R^2Br] = k_1/k_2([R^1Br]/[R^2Br])^x \qquad (c)$$

$$\ln([R^1Br]_t/[R^1Br]_0) = k_1/k_2\ln([R^2Br]_t/[R^2Br]_0) \qquad (d)$$

Assuming that $x = 1$ (that is, the reactions are first order with respect to the alkyl bromide; this is confirmed below) and integrating Equation (c) leads to Equation (d). The experimental kinetic data fit Equation (d) extremely well (Figure 1). Plots of $\ln([R^1Br]_t/[R^1Br]_0)$ versus $\ln([R^2Br]_t/[R^2Br]_0)$ are linear to greater than 95% comsumption of the most reactive halide. Evaluation of the slope by a linear regression analysis yielded k_1/k_2 directly. Every line contains between 8 and 11 points, and the linear regression coefficients are greater than 0.99 in all cases. This confirmed our hypothesis that the reaction was first order with respect to the alkyl bromide, in agreement with kinetic data reported for magnesium and lithium. Table 1 summarizes the ratio of rate constants (k_1/k_2) determined for all pairs of substrates assayed. Since the yields of organozinc bromides obtained with this procedure are very high,[4] side reactions perturb the final results only slightly.

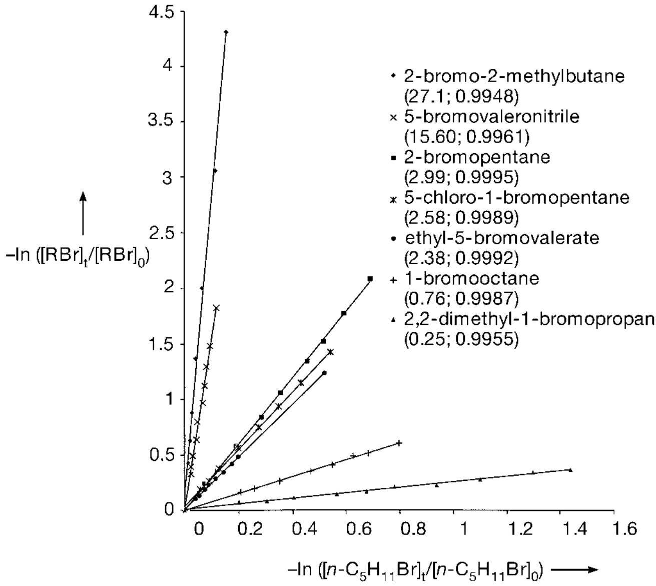

Figure 1. Experimental conformation for the validity of Equation (d) with competition reactions of 1-bromopentane and another bromoalkane with activated zinc. The ratios of the reaction rates, k_1/k_2, and the regression coefficients are given in parentheses.

The reaction shows selectivity with respect to the nature of the organic moiety (Table 1). The effect of the alkyl halide on the rate of the electron transfer decreases in the order tertiary > secondary > primary; the ratio of the rates is

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[*] Prof. Dr. R. D. Rieke, Dr. A. Guijarro
Department of Chemistry
University of Nebraska-Lincoln
Lincoln, Nebraska 68508-0304 (USA)
Fax: (+1)402-472-9402.
E-mail: rrieke@unlinfo.unl.edu

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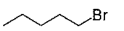
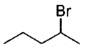
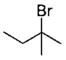
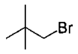
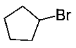
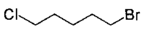
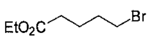
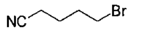
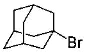
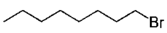
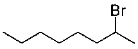
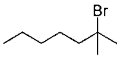
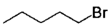
Supporting information for this contribution is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

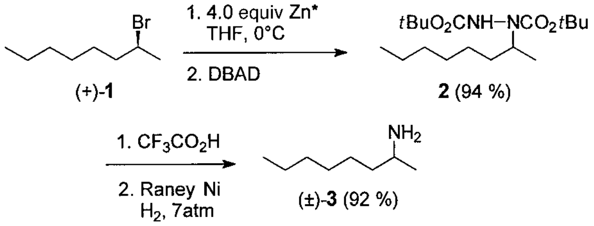
Table 1. Relative reaction rates k_1/k_2.[a]

Entry	R^1Br	k_1/k_2[b] primary R^2Br[c]	secondary
1		*1*	*0.33*
2		2.99	*1*
3		27.1, *28.6*	9.58
4		0.25	*0.084*
5		*10.5*	3.51
6		2.58	*0.86*
7		2.38	*0.80*
8		15.6	*5.22*
9		*0.42*	0.17
10		*1*	*0.39*
11		2.52	*1*
12		31.8, *32.8*	13.0
13		1.32	*0.52*

[a] Corresponding to the reaction of two alkyl bromides (R^1Br, R^2Br) with highly reactive zinc (in THF at 0 °C). The relative rates were determined by the competitive kinetics technique. [b] Estimated error 5%. The k_1/k_2 values for pairs that were not measured directly are given in italics. [c] R^2Br is 1- or 2-bromopentane for entries 1–8, and 1- or 2-bromooctane for entries 9–13.

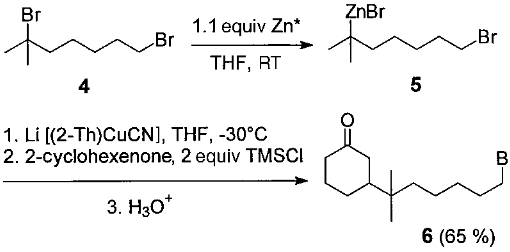
roughly 30:3:1. Cyclopentyl bromide reacts 3.51 times faster than 2-bromopentane, and 1-adamantyl bromide reacts 5.96 times slower than 2-bromooctane (and 77 times slower than 2-bromo-2-methylheptane). These are consistent with the geometric requirements of radical intermediates. To a certain extent, the reaction also seems to be sensitive to steric factors; neopentyl bromide reacts 4.00 times slower than 1-bromopentane. The effect of a polar group in the chain is to increase the rate of the reaction. In the case of 5-bromovaleronitrile, this change is notable and may be governed by binding interactions of the nitrile group to the metal surface prior to electron transfer.

To further explore the existence of radical intermediates, the reaction of highly reactive zinc, Zn*, with an optically active alkyl bromide was studied. (+)-*R*-2-Bromooctane (**1**;[6] $[\alpha]_D^{25} = +39.7°$, >95% *ee*) was prepared and allowed to react with 4.0 equivalents of Zn* at 0 °C. The 2-octylzinc bromide generated was then treated with 1.0 equivalent of di-*tert*-butyl azodicarboxylate (DBAD) at 0 °C.[7] Deprotection and reduction afforded (±)-2-aminooctane (**3**), as shown by NMR spectroscopy using *S*-(+)-*O*-acetylmandelic acid as a chiral solvating agent.[8] The configurational stability of the carbon–zinc bond is well established.[9] Accordingly, racemization most likely occurred during the formation of the organozinc reagent (Scheme 1).[10]



Scheme 1. Synthesis of 2-aminooctane (**3**) from optically active 2-bromooctane (**1**). Racemization most likely takes place in the first step upon reaction with active zinc.

These results suggest that by using highly reactive zinc one can take advantage of not only the structure selectivity exhibited but also the high tolerance with respect to functional groups. To test this theory, 1,6-dibromo-6-methylheptane (**4**)[11] was treated with 1.1 equivalents of Zn* in THF at room temperature to afford the functionalized organozinc bromide **5**, which shows remarkable stability.[12] Transmetalation with lithium 2-thienylcyanocuprate at −30 °C and reaction with the electrophilic mixture of 2-cyclohexenone and two equivalents of Me_3SiCl (TMSCl) yielded, after quenching, the conjugate addition product **6** (65% yield based on **4**, Scheme 2).[13] This reaction demonstrates that a tertiary bromide functionality can be elaborated in the presence of primary bromides. The resulting substituted primary bromide is then available for further elaboration.



Scheme 2. Selective formation of a carbon–zinc bond by reaction at the tertiary bromide functionality of **4**, and synthesis of **6**.2-Th = 2-thienyl.

In conclusion, the oxidative addition of active zinc to alkyl bromides is highly sensitive to structure. Attempts to measure the competitive kinetics of benzylic, allylic, aryl, and vinylic bromides, whose rates of reaction differ largely from those of alkylic bromides, are underway. Additional studies to provide more information on the mechanistic details of the oxidative addition are also in progress.

Experimental Section

6: To a 50-mL centrifuge tube equipped with stirring bar and septum was added under argon active zinc[6] (2.2 mmol) in dry THF (10 mL) and 1,6-dibromo-6-methylheptane[11] (544.1 mg, 2.0 mmol). The reaction was stirred at room temperature for about 10 h. Meanwhile, to a two-necked 100-mL flask containing dry THF (10 mL) and copper(I) cyanide (179.2 mg, 2.0 mmol) was added 2-thienyllithium (2 mL, 1.0 M in THF) at −30 °C, and the mixture was stirred for 30 min. The organozinc reagent was centrifuged for 2 min (2500 rpm), and the content of the tube was transferred by cannula to the flask containing Li(2-Th)CuCN at −30 °C. A solution of 2-cyclohexenone (202.4 mg, 2.0 mmol) and TMSCl (439 mg, 4.0 mmol) was then added to the flask. The reaction was allowed to warm slowly to room temperature for one day. An additional aliquot of the electrophilic mixture (0.5 equiv) was added, and the reaction was allowed to stir for two more days. The mixture was then hydrolyzed (2 M HCl) and extracted with diethyl ether (2 × 100 mL), the organic phases were dried ($MgSO_4$), and the solvents were removed (15 torr, 30 °C). Impure **6** was isolated by column chromatography (Florisil, hexanes/ethyl acetate). By-products were removed by shaking a solution of the impure compound in hexane (50 mL) with a methanolic solution of mercurium(II) acetate (≈0.25 M, 25 mL) for 5 min. Addition of water (50 mL) and extraction with diethyl ether (2 × 100 mL) afforded, after drying ($MgSO_4$) and elimination of solvents, pure **6** (375 mg, 65 %).

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The Crystal Structures of Peroxonium Hexafluoroantimonate $H_3O_2SbF_6$ and Bis(dihydrogenperoxo)hydrogen Hexafluoroantimonate $H_5O_4SbF_6$

Rolf Minkwitz,* Claudia Hirsch, and Hans Hartl

The preparation of peroxonium salts by direct protonation of hydrogen peroxide was accomplished by Christe et al.[1] in 1979 [Eq. (a)]. These salts were characterized by IR, Raman and NMR spectroscopy. Two O–O stretching vibrations at 876 and 915 cm^{-1} were observed in the IR spectrum of peroxonium hexafluoroantimonate and one vibration at 879 cm^{-1} in the Raman spectrum, although the less intensive vibration at 915 cm^{-1} could not be assigned (Table 1). Therefore we decided to examine this salt more closely.

$$H_2O_2 + HF/MF_5 \xrightarrow{HF} H_3O_2^+MF_6^- \qquad \text{(a)}$$
$M = As, Sb$

To avoid the danger of explosion that can arise from the use of highly concentrated hydrogen peroxide, and to ensure that there is no production of $H_3O^+SbF_6^-$ due to traces of water, we decided to use bis(trimethylsilyl)peroxide as the substrate [Eq. (b)]. The crystalline reaction product shows vibrations at 875 and 914 cm^{-1} in the IR spectrum and at 877 and 911 cm^{-1} in the Raman spectrum (Table 1).

$$Me_3SiOOSiMe_3 + 3\,HF + SbF_5 \xrightarrow{HF/-70\,^\circ C} \underset{\mathbf{1}}{H_3O_2^+SbF_6^-} + 2\,Me_3SiF \qquad \text{(b)}$$

Careful examination of the product under a microscope in a stream of cold nitrogen indicated that there were, in addition to crystals[2] of the expected product **1,** some other crystals with a slightly different habit. The composition of these crystals was determined to be $H_5O_4^+SbF_6^-$ (**2**) by structure elucidation,[3] and subsequently **2** was prepared in the pure form by the reaction described in Equation (c), in which double the amount of bis(trimethylsilyl)peroxide was used relative to SbF_5 (cf. [Eq. (b)].

$$2\,Me_3SiOOSiMe_3 + 5\,HF + SbF_5 \xrightarrow{HF/-70\,^\circ C} \underset{\mathbf{2}}{H_5O_4^+SbF_6^-} + 4\,Me_3SiF \qquad \text{(c)}$$

The Raman spectrum of **2** shows no vibration at 879 cm^{-1} but instead one at 908 cm^{-1}. In contrast, the vibration at 874 cm^{-1} in the IR spectrum is retained and no further vibrations were detected in this area (Table 1).

The $H_3O_2^+$ ion and the SbF_6^- ion in the crystal structure of **1** are donor and acceptor for two short hydrogen bonds (O1–H ··· F2 252.1(8) pm and O1–H ··· F4 252.3(8) pm), and for one longer hydrogen bond (O2–H ··· F3 270.8(8) pm). The

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[*] Prof. R. Minkwitz, Dipl.-Chem. Claudia Hirsch
Institut für Anorganische Chemie der Universität
Otto-Hahn-Strasse 6, D-44221 Dortmund (Germany)
Fax: (+49) 231-755-3797

Prof. H. Hartl
Institut für Anorganische und Analytische Chemie
der Freie Universität Berlin (Germany)

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