rotation $[\alpha]^{25}{}_D$ -8.79° (c 3.73, benzene).

Normal- and Inverse-Addition Reactions of (+)-(*S*)-2-Octyl Bromide with (Triphenylstannyl)lithium (Prepared from Triphenyltin Chloride) were carried out as previously described.[2a]

Normal-Addition Reaction of (+)-(*S*)-2-Octyl Chloride with (Triphenylmethyl)lithium (Prepared from Triphenylmethyl Chloride) (Typical Procedure). After several rinses with dry pentane in a glovebox to remove its mineral oil coatings, lithium (0.140 g, 20.2 mmol) was placed in a flame-dried, 40-mL centrifuge tube containing a Teflon-coated magnetic stirrer bar and capped with a rubber septum. THF (5 mL) was added by syringe. The centrifuge tube was placed in a water bath (25 °C) and a solution of triphenylmethyl chloride (1.210 g, 4.34 mmol) in THF (10 mL) was added through a cannula. The resulting dark red solution was allowed to stir for 2 h and then passed through a 70–100-μm fritted glass filter into a 100-mL, three-necked, flame-dried flask equipped with a Teflon-coated magnetic stirrer bar and a 30-mL Kontes slow-addition funnel stoppered with a rubber septum and charged with a solution of (+)-(*S*)-2-octyl chloride ($[\alpha]^{25}{}_D$ +31.6°, optical purity 85%; 0.595 g, 4.00 mmol) in THF (10 mL). Addition was accompanied by efficient mixing and was completed in 2 h; the resulting reaction mixture was allowed to stir for an additional 3 h before quenching with water (10–20 mL). After being extracted with pentane, the organic layer was dried ($MgSO_4$). 2-Octyltriphenylmethane was isolated from GC by injection of the crude product which had been previously collected from HPLC. This material exhibited the following: $[\alpha]^{25}{}_D$ -35.20° (c 3.17, benzene); ^1H NMR (CCl_4) δ 0.6–1.7 (m, 16 H), 3.3 (m, 1 H), 7.0–7.5 (m, 15 H); mass spectrum *m/e* (relative intensity) 357 (0.1), 356 (0.2), 244 (21.7), 243 (100.0), 166 (3.5), 165 (19.5).

Inverse-Addition Reaction of (+)-(*S*)-2-Octyl Bromide with (Triphenylmethyl)lithium (Prepared from Triphenylmethane) (Typical Procedure). Into a flame-dried, nitrogen-flushed 40-mL centrifuge tube equipped with a Teflon-coated magnetic stirrer bar were added *n*-butyllithium (1.6 M in pentane, 2.5 mL, 4.0 mmol) and THF (5 mL) by syringe, and the solution was chilled to -78 °C. Triphenylmethane (1.231 g, 5.04 mmol) in THF (10 mL) was slowly added by syringe. The temperature was slowly increased to 25 °C. A solution of (+)-(*S*)-2-octyl bromide ($[\alpha]^{25}{}_D$ + 30.3°, optical purity 70%; 0.773 g, 4.00 mmol) was placed in a 100-mL, three-necked, flame-dried, nitrogen-flushed flask equipped with a Teflon-coated magnetic stirrer bar and a 30-mL Kontes slow-addition funnel. The solution of (triphenylmethyl)lithium was filtered through 70–100-μm fritted-glass filter into a Kontes slow-addition funnel. Addition was carried out over a 2-h period; this mixture was then stirred an additional 0.5 h at 25 °C and finally quenched with water. The resulting mixture was extracted with pentane and the organic layer dried ($MgSO_4$) and filtered. The optical rotation of (-)-(*R*)-2-octyltriphenylmethane was $[\alpha]^{25}{}_D$ -28.80° (c 3.41, benzene).

Normal-Addition Reaction of (+)-(*S*)-2-Octyl Chloride with Triphenylsilyllithium (Prepared from Triphenylsilyl Chloride) (Typical Procedure). After several rinses with dry pentane in a glovebox to remove its mineral oil coatings, lithium (0.140 g, 20.2 mmol) was placed in a flame-dried, 40-mL centrifuge tube equipped with a Teflon-coated magnetic stirrer bar and capped with a rubber septum. THF (5 mL) was added by syringe. The centrifuge tube was placed in a water bath (25 °C), and a solution of triphenylsilyl chloride (1.240 g, 4.20 mmol) in THF (10 mL) was added through a cannula. The resulting dark brown solution was allowed to stir for 2 h and then transferred by cannula into a 70–100-μm fritted-glass filter and whence into a 100-mL, three-necked, flame-dried, nitrogen-flushed flask equipped with a Teflon-coated magnetic stirrer bar and a 30-mL Kontes slow-addition funnel stoppered with a rubber septum containing a solution of (+)-(*S*)-2-octyl chloride ($[\alpha]^{25}{}_D$ +31.6°, optical purity 85%; 0.595 g, 4.00 mmol) in THF (10 mL). Addition was carried out over a 2-h period, and the resulting mixture was allowed to stir for an additional 3 h before quenching with water (10 mL). After being extracted with pentane, the organic layer was dried ($MgSO_4$). Analyses by HPLC showed 70% 2-octyltriphenylsilane ($[\alpha]^{25}{}_D$ -6.47° (c 4.39, benzene).

Reaction of the Tosylate of (-)-(*R*)-2-Octanol with Ph_3MLi (M = C, Si, Ge, Sn) (Typical Procedure). The solution Ph_3MLi in THF (15 mL) (prepared as described above) was filtered through a 70-100-μm fritted-glass filter into a 30-mL Kontes slow-addition funnel equipped with a 100-mL, three-necked, flame-dried flask containing a solution of the tosylate of (-)-(*R*)-2-octanol ($[\alpha]^{25}{}_D$ -9.61°, optical purity 97%; 1.074 g, 4.00 mmol) in THF (10 mL). Addition was complete after 2 h and the resulting reaction mixture allowed to stir at 25 °C for additional 3 h before quenching with water (10–20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Pure 2-$C_8H_{17}MPh_3$ was collected from GC by injection of the concentrated crude 2-$C_8H_{17}MPh_3$ collected from HPLC.

Relative Reactivity Profile. The relative reactivity of Ph_3MLi was determined by injecting a solution of the appropriate reagent into a 40-mL centrifuge tube equipped with a Teflon-coated stirrer bar, capped with a rubber septum and containing a solution of 2-octyl chloride or bromide in THF. After a predetermined period of time, the mixture was quenched with water and the yield of unreacted 2-octyl chloride or bromide determined.

Registry No. (-)-(*R*)-1, 82838-62-8; (+)-(*S*)-1, 82823-90-3; (-)-(*R*)-2, 82823-87-8; (+)-(*S*)-2, 82823-91-4; (-)-(*R*)-3, 82823-88-9; (+)-(*S*)-3, 82823-92-5; (+)-(*S*)-2-$C_8H_{17}Br$, 1191-24-8; (+)-(*S*)-2-$C_8H_{17}Cl$, 16844-08-9; (-)-(*R*)-2-$C_8H_{17}OTs$, 27770-99-6; (-)-(*R*)-2-$C_8H_{17}SnPh_3$, 82823-89-0; (+)-(*S*)-2-$C_8H_{17}SnPh_3$, 79055-00-8; Ph_3CH, 519-73-3; (-)-(*R*)-2-$C_8H_{17}OH$, 5978-70-1; Ph_3SiLi, 791-30-0; Ph_3GeLi, 3839-32-5; Ph_3SnLi, 4167-90-2; Ph_3CLi, 733-90-4; Ph_3CCl, 76-83-5; Ph_3SiCl, 76-86-8; TsCl, 98-59-9; hexaphenyldisilane, 1450-23-3; hexaphenyldigermane, 2816-39-9.

Secondary α-Deuterium Isotope Effects on Reactions of the Grignard Reagent from 1-Bromopentane-*1,1*-d_2

E. Alexander Hill* and Daniel C. Link

Department of Chemistry, University of Wisconsin—Milwaukee, Milwaukee, Wisconsin 53201

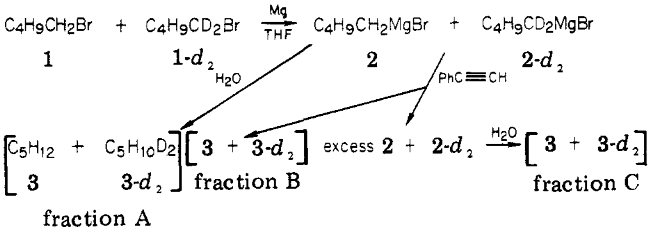
Received March 25, 1982

Secondary α-deuterium isotope effects have been determined for reactions of the Grignard reagent from 1-bromopentane-*1,1*-d_2 with phenylacetylene and with benzonitrile. Isotope effects were found to be $0.99_8 \pm 0.03$ and $1.00_3 \pm 0.02_2$, respectively. The small isotope effects may be consistent with a variety of mechanisms, including electron transfer and cyclic or open polar electrophilic attacks on the carbon–magnesium bond.

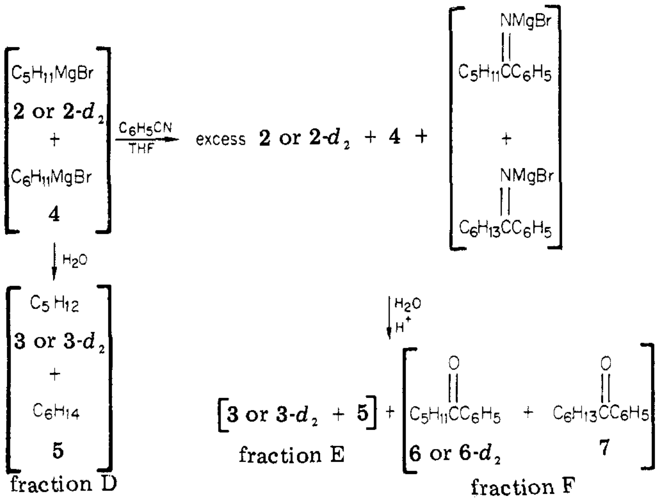
Secondary deuterium isotope effects have assumed a very significant role in identifying mechanisms of nucleophilic substitution at saturated carbon and in refining our understanding of the details of these mechanisms.[1]

0276-7333/82/2301-1501$01.25/0 © 1982 American Chemical Society

Scheme I



Scheme II



For this reason, we have explored α-deuterium isotope effects on electrophilic substitution at the saturated carbon of a Grignard reagent. This paper reports results for two such reactions: protolysis of the Grignard reagent by an alkyne and addition of the Grignard reagent to a nitrile.

Results

1-Bromopentane-*1,1*-d_2 (1-d_2) was prepared by reduction of pentanoyl chloride with lithium aluminum deuteride, followed by reaction of the alcohol with phosphorus tribromide.

A Grignard reagent prepared from an equimolar mixture of undeuterated and deuterated 1-brompentanes was allowed to react with a deficiency of phenylacetylene. Volatile constituents were pumped to a cold trap, and the residual Grignard reagent was hydrolyzed. A sample of the original Grignard reagent mixture was also hydrolyzed. The experiment is outlined in Scheme I. The isotopic compositions of the pentane in the three fractions A–C (Scheme I) were compared mass spectrometrically with isotopically normal and dideuterated *n*-pentane. Within experimental error, the three fractions had essentially identical composition, leading to an isotope effect $k_{H_2}/k_{D_2} = 0.99_8 \pm 0.03$ (see Experimental Section for details).

The isotope effect in the reaction of Grignard reagents 2 and 2-d_2 with benzonitrile was determined in a "third-party" competition experiment (see Scheme II). A Grignard reagent from a mixture of 1-bromopentane and 1-bromohexane (reagents 2 and 4) was allowed to compete for a deficiency of benzonitrile. After hydrolysis, the hydrocarbon fraction E (representing unreacted Grignard reagent) and the ketone fraction F (representing reacted Grignard reagent) were analyzed by GC. A sample of Grignard reagent removed and hydrolyzed before addition of the nitrile yielded a hydrocarbon fraction D representing the initial reactant composition. A parallel reaction was performed in which Grignard reagents 2-d_2 and 4 competed. From the competition experiments, the relative rate constants for reaction of pentyl and hexyl Grignard reagents with benzonitrile were evaluated. The ratio of these for the undeuterated and deuterated reactions gives the isotope effect k_{H_2}/k_{D_2}.

Table I. Relative Rates and Isotope Effects for Reaction of Pentyl and Hexyl Grignard Reagents with Benzonitrile in Tetrahydrofuran[a, b]

basis for calculatn[c]	$k_{\text{pentyl}}/k_{\text{hexyl}}$	$k_{\text{pentyl-}d_2}/k_{\text{hexyl}}$	$(k_{H_2}/k_{D_2})_{\text{pentyl}}$[d]
G_0, G_t	0.96 ± 0.03	0.98 ± 0.02	0.98
G_0, K_t[e]	1.02 ± 0.01	0.98 ± 0.03	1.03
G_t, K_t[e]	0.98 ± 0.02	0.98 ± 0.02	1.00
average	0.984 ± 0.023	0.980 ± 0.003	1.003 ± 0.022

[a] Approximately 0.40 M in each Grignard reagent and 0.46 M in benzonitrile; temperature about 27 °C. [b] Uncertainties listed in columns 2 and 3 are average deviations among sample tubes; replicate analyses for a single tube generally showed less scatter. Uncertainties for the last line are average deviations from the mean for the three calculation bases. [c] G_0 = initial Grignard reagent concentration; G_t = final Grignard reagent concentration; K_t = final ketimine salt concentration. [d] Ratio of column 2 to column 3. [e] Assuming $G_t + K_t = G_0$.

In order to calculate relative rates for a competition experiment, it is necessary to know initial and final concentrations of each of the competing reactants.[2] Since the addition appears to be quite clean and free of major side reactions, the three concentrations determined in the experiment provide redundant information which allows the relative rates to be calculated on three different bases (see Experimental Section and Table I). Though there was some scatter both between methods and in the workup of data from different reaction samples, all of the data are in agreement that the isotope effect is close to unity. An average $k_{H_2}/k_{D_2} = 1.00_3 \pm 0.02_2$ is obtained. There did not appear to be any significant trends with the time the reaction was allowed to run before workup, and a repeated analysis after storage of samples for an additional period of time led to similar results.

Discussion

The origin of secondary α-deuterium isotope effects is reasonably well understood.[1] As with most hydrogen isotope effects, the principal contributor to the effect is a change in zero-point energy between reactant and transition states, which reflects an increase or decrease in the constraint of the isotopic atom in the transition state. A decrease in constraint results in a "normal" effect ($k_H/k_D > 1$). Most typically for an α-deuterium isotope effect, the change in constraint resides largely in an altered bending frequency, commonly associated with a change in hybridization. For example, in S_N1 ionization of an alkyl halide, an sp^3 spending frequency of the halide is replaced in the carbonium ion-like transition state by a lower frequency sp^2 out-of-plane bending mode, leading to an isotope effect $k_H/k_D \approx 1.1$–1.2 per deuterium. Changes in steric congestion also influence the relative degree of constraint. Although hybridization in an S_N2 transition state also approaches sp^2, the out-of-plane bending frequency is increased by the presence of (and bonding to) both entering and leaving groups. Hence, isotope effects on the order of unity $k_H/k_D = 0.96$–1.06 per deuterium) are typical. A further contribution to the α-deuterium isotope effect

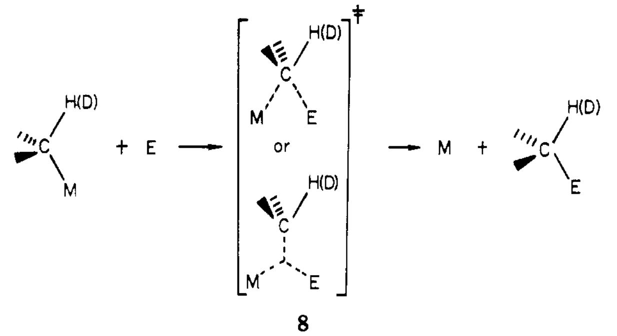
---

(1) (a) Shiner, V. J. In "Isotopes and Chemical Principles"; Rock, P. A., Ed.; Washington: D.C. 1978; *ACS Symp. Ser. No. 11*, pp 172–182. (b) Melander, L.; Saunders, W. H., Jr. "Reaction Rates of Isotopic Molecules"; Wiley-Interscience: New York, 1980; pp 171–180.

(2) Reference 1b, p 95.

arises because deuterium is effectively more electron releasing than protium (ultimately a consequence of anharmonicity, which results in a shorter average C–D distance).

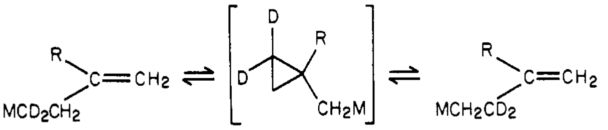
At the inception of this work, it appeared possible that quite sizeable inverse α-deuterium isotope effects might be found in reactions in which an electrophile replaces a carbon–metal bond. Although there is no formal change in hybridization, a transition state for electrophilic attack on the carbon–metal bond resembling 8 has a carbon which is effectively pentacoordinate.



8

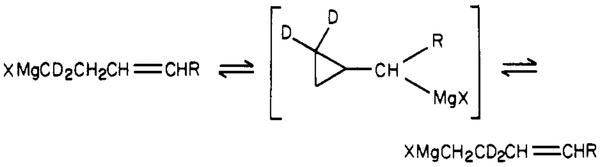
An *increase* in constraint might reasonably accompany this increase in coordination, producing an inverse isotope effect ($k_H/k_D < 1$).

In addition, there is some evidence that the α-hydrogens of a Grignard reagent may be "less constrained" than the "typical" sp^3-CH, adding to the magnitude of the inverse effect. Equilibrium constants reported[3-6] for eq 1–3 imply



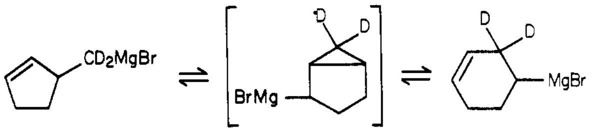
(1)

$R = C_6H_5, CH_3$; $M = MgBr, MgR, Li$



(2)

a, $R = CH_3$, $X = Br$; b, $R = C_6H_5$, $X = Cl$



(3)

a preference of the magnesium for an undeuterated carbon. This preference corresponds to an equilibrium constant greater than unity for the scrambling process in eq 4 or

$$\mathrm{R{-}CH_2{-}CD_2MgX \rightleftharpoons R{-}CD_2{-}CH_2MgX} \qquad (4)$$

alternatively to an isotope effect $K_H/K_D > 1$ for the hypothetical equilibrium of eq 5.[7] The origin of this isotope

$$\mathrm{R{-}CH_2{-}\underset{\cdot\cdot}{\overset{\cdot\cdot}{C}}{-}MgX \rightleftharpoons R{-}\underset{\cdot\cdot}{\overset{\cdot\cdot}{C}}{-}CH_2MgX} \qquad (5)$$

effect, and particularly its magnitude, is not entirely clear. It is in the direction expected for the electron-releasing inductive effect of deuterium relative to hydrogen.[8] Lowered bending or stretching frequencies of the α-hydrogens could also be associated with characteristics of a carbon–magnesium bond other than its polarity—its length or strength or perhaps a more nearly planar hybridization at the carbon. Whatever the source of the "looseness" of the hydrogens α to magnesium, it is reasonable that their environment should become more "normally constrained" as electrophilic attack converts them to "normal" sp^3-CH bonds.

Two reactions were chosen for initial study. Protolysis of an organometallic is a fundamental process involving electrophilic attack on the carbon–metal bond.[17] Reaction with hydroxylic proton is very fast and exothermic, with undesirable consequences both in principle and in practice. The expected early transition state (consistent with reported primary isotope effects near unity[18,19]) should reflect little electronic and structural modification by the electrophile, and the rapidity introduces experimental problems of mixing.[20] However, protolysis by alkynes is a well studied[17] and much slower reaction. The rate is first order each in organomagnesium and alkyne, and primary deuterium isotope effects of 2.8–6.2[19,21] indicate a transition state in which the electrophilic attack has progressed to a significant degree.

Reaction of the Grignard reagent with benzonitrile was also studied to provide an example of an addition process (also formally an electrophilic substitution at C–Mg). It also is slow enough that possible mixing control is not a concern.[22,23]

---

(3) Maercker, A.; Weber, K. *Justus Liebigs Ann. Chem.* **1972**, *756*, 43.

(4) Maercker, A.; Streit, W. *Chem. Ber.* **1976**, *109*, 2064.

(5) Richey, H. G., Jr.; Veale, H. S. *Tetrahedron. Lett.* **1975**, *615*.

(6) Maercker, A.; Geuss, R. *Chem. Ber.* **1973**, *106*, 773.

(7) Equilibrium Constants for eq 1 are tabulated in a different form and are recalculated here. A substantial range of equilibrium constants is reported: 1.08–1.96 for eq 1,[3] 0.98–1.21 for eq 2a,[4] 1.39 for eq 2b,[5] and 1.22 for eq 3.[6] It is not apparent whether the range of values reported reflects real systematic variations, the difficulty of making accurate measurements, or both.

(8) It is uncertain whether the magnitude is appropriate for a purely inductive isotope effect. Relevant comparisons are complicated by uncertainties in the extrapolation of more remote substituent effects to α substitution and in the extent of charge development. Exchange of the benzylic hydrogens of toluene with lithium cyclohexylamide occurs with a secondary isotope effect $k_H/k_D = 1.31$ for two α-deuteriums.[9] It was estimated that about two-thirds of that effect (about 1.1/D) might correspond to the inductive effect and the remainder to hybridization change. It might be noted for comparison that only a fractional anionic charge is involved in each case: the carbon–magnesium bond may be estimated from Pauling electronegativities[10] as about 35% ionic, and a Brøsted α value of about 0.4 is found to relate kinetic and equilibrium hydrocarbon acidities.[11] Another approach to the α-deuterium inductive effect would utilize a σ^* value of −0.0027 for CH_2D vs. CH_3,[12] a fall-off factor of about 3[13] (giving $\sigma^*_D - \sigma^*_H = -0.008$) and a ρ value of about 4 (representative for equilibria $RY \rightleftharpoons RZ^\pm$).[14] On this basis, an effect of 1.08/D is predicted for generation of a *carbanion*. A larger effect might be predicted based on the isotope effect in ionization of formic-*d* acid[15] and a smaller one based on a nonhyperconjugating β-effect on solvolysis.[16]

(9) Streitwieser, A., Jr.; Van Sickle, D. E. *J. Am. Chem. Soc.* **1962**, *84*, 254.

(10) Pauling, L. "The Nature of the Chemical Bond", 3rd ed.; Cornell University Press: Ithaca, N.Y., 1960; pp 93, 98.

(11) Streitwiser, A., Jr.; Brauman, J. I.; Hammons, J. H.; Pudjaatmaka, A. H. *J. Am. Chem. Soc.* **1965**, *87*, 384.

(12) Streitwieser, A., Jr.; Klein, H. S. *J. Am. Chem. Soc.* **1963**, *85*, 2759.

(13) Taft, R. W., Jr. In "Steric Effects in Organic Chemistry"; Newman, M. S., Ed.; Wiley: New York, 1956; p 592.

(14) Wells, P. R. "Linear Free Energy Relationships"; Academic Press: London, 1968; pp 37, 38.

(15) Bell, R. P.; Miller, W. B. T. *Trans. Faraday Soc.* **1963**, *59*, 1147.

(16) Shiner, V. J., Jr.; Humphrey, J. S. *J. Am. Chem. Soc.* **1963**, *85*, 2416.

(17) Abraham, M. H. In "Comprehensive Chemical Kinetics"; Bamford, C. H.; Tipper, C. F. H., Eds.; Elsevier: Amsterdam, 1973; Vol. 12, Chapter 7, p 107.

(18) Orchin, M.; Wender, I.; Friedel, R. A. *Anal. Chem.* **1949**, *21*, 1073. Wiberg, K. *J. Am. Chem. Soc.* **1955**, *77*, 5987. Assarsson, L. O. *Acta. Chem. Scand.* **1958**, *12*, 1545.

(19) Pocker, Y.; Exner, J. H. *J. Am. Chem. Soc.* **1968**, *90*, 6764.

(20) Eaborn, C.; Walton, D. R. M.; Seconi, G. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1857.

(21) Dessy, R. E.; Wotiz, J. H.; Hollingsworth, C. A. *J. Am. Chem. Soc.* **1957**, *79*, 358.

(22) Ashby, E. C.; Chao, L.-C.; Neumann, H. M. *J. Am. Chem. Soc.* **1973**, *95*, 4896 and references therein.

(23) Gilman, H.; St. John, E. L.; St. John, N. B.; Lichtenwalter, M. *Recl. Trav. Chem. Pays-Bas* **1936**, *55*, 577.

In both reactions, we find that the deuterated and undeuterated Grignard reagents react with very similar rates. Within error limits of about 3% both isotope effects appear to be unity. Thus, our hopes of finding large secondary isotope effects, which might exhibit mechanistically meaningful differences between reactions, were not fulfilled. It is, nevertheless, useful to examine briefly some possible explainations for the absence of a sizeable isotope effect.

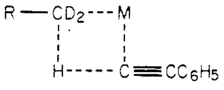
One basic reason for a small secondary isotope effect might be a very early transition state. In that case, the electrophile would still be remote from the carbon–magnesium bond, so that it would not appreciably influence the electronic or steric environment of the α-hydrogens. Substituent and primary isotope effects seem to argue against this explanation. In Grignard addition to nitriles, Hammett equation reaction parameters imply a reasonably advanced transition state ($\rho = -2.85$ for arylmagnesium bromides[24] and +1.6 for substituted benzonitriles[25]). An early report[23] that tertiary and branched Grignard reagents react more slowly than primary ones may suggest a considerable steric effect, which would also be inconsistent with a very early transition state. In the protolysis of Grignard reagents, substitution in the alkyne has a substantial influence on the rate,[26] and the Grignard reagent reactivity sequence[27] (CH_3 < primary < secondary) is consistent in direction and magnitude with other reactions (e.g., reaction with benzophenone[28] or *tert*-butyl peroxide[29]). Sizeable primary isotope effects[19,21] on this reaction also imply that the transition state lies well along the reaction coordinate, at least with respect to the proton transfer. On the other hand, the transition state for the protolysis of dialkylmercury compounds by acetic acid[30] probably lies later along the reaction coordinate. The reactivity sequence for cleavage of alkyl groups in that reaction is CH_3 > primary < secondary < tertiary (interpreted as resulting from opposing electronic and steric effects), and the primary isotope effect is larger (k_H/k_D = 9–11).

Alternatively, the zero-point energy of the α-hydrogens may be only slightly affected in the transition state, despite substantial progress along the reaction coordinate. One possibility of this sort might be an electron-transfer mechanism:

$$RCD_2M + E \rightarrow [RCD_2M^{+}\cdot\ E^{-}\cdot] \rightarrow [RCD_2\cdot\ M^{+}\ E^{-}\cdot] \rightarrow \text{products}$$

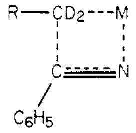
If the electron transfer is a vertical, outer-sphere process, the hybridization at the α-carbon and the steric environment of the α-hydrogens are not changed. It is not clear whether an inductive isotope effect should be present;[31] if so, it should be inverse ($k_H/k_D < 1$). If the electron transfer is not vertical, stretching of the C–M bond and rehybridization toward planar geometry could produce a "normal" ($k_H/k_D > 1$) contribution, countering any inductive component. Steric congestion in an inner-sphere electron transfer could make a further inverse contribution. Effects of impurities on the reaction of methylmagnesium bromide with benzonitrile[33] suggest the involvement of an electron-transfer pathway, and a reported lack of correlation of reaction rates of alkynes with their relative acidities[34] might possibly be consistent with such a process. However, reduction potentials[35] indicate that electron transfer to either benzonitrile or phenylacetylene should be much more endothermic than transfer to benzophenone (the latter more so). Although this step should be still more endothermic for aliphatic nitriles or alkynes, they are comparable to their aromatic analogues in reactivity.

A cyclic four-center transition state might also have a balance of electronic and steric influences which would result in a cancellation of contributions to the secondary isotope effect:



9a

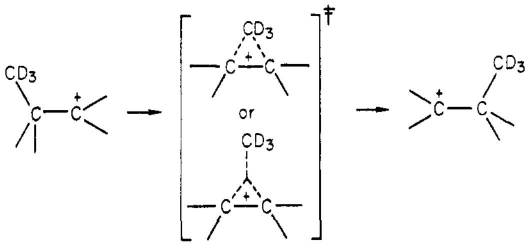
or



9b

Such mechanisms have been prominently considered for both reactions.[22,24,34,36] However, it would seem a surprising coincidence that special features arising from the cyclic transition-state structure should lead to exactly the same cancellation in two rather dissimilar reactions.

We should like to suggest that recent reports of isotope effects on carbonium ion rearrangements[37–39] may help to explain the small effects found in the present study. Migration of a methyl group occurs more readily than a methyl-d_3 group by 10–20% or more. It is possible to look upon such migrations as intramolecular electrophilic substitution reactions at the *C*-methyl bond, the original cationic carbon being the electrophile:



10

(Transition states **10** for rearrangement and **8** for substitution are drawn in analogous fashion.) There may then

---

(24) Edlestein, H.; Becker, E. I. *J. Org. Chem.* **1966**, *31*, 3375.

(25) Citron, J. D.; Becker, E. I. *Can. J. Chem.* **1963**, *41*, 1260.

(26) Wotiz, J. H.; Hollingsworth, C. A.; Dessy, R. A. *J. Org. Chem.* **1955**, *20*, 1545.

(27) Dessy, R. E.; Hollingsworth, C. A.; Wotiz, J. H. *J. Am. Chem. Soc.* **1955**, *77*, 4410.

(28) Holm, T. *Acta Chem. Scand., Ser. B* **1974**, *B28*, 809.

(29) Nugent, W. A.; Bertini, F.; Kochi, J. K. *J. Am. Chem. Soc.* **1974**, *96*, 4945.

(30) Nugent, W. A.; Kochi, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 5979.

(31) We find no good precedent for α-deuterium isotope effects (see: Klingler, R. J.; Mochida, K.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 6626), although some β effects on electron-transfer and charge-transfer complexes have been reported.[32]

(32) Pryor, W. A.; Hendrickson, W. H., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 1582. Martens, F. M.; Verhoeven, J. W.; de Boer, Th. J. *Tetrahedron Lett.* **1979**, 2919. Burns, J. M.; Wharry, D. L.; Koch, T. H. *J. Am. Chem. Soc.* **1979**, *101*, 2750. Okamoto, T.; Ohno, A.; Oka, S. *J. Chem. Soc., Chem. Commun.* **1977**, 181. Baciocchi, E.; Rol, C.; Mandolini, L. *J. Am. Chem. Soc.* **1980**, *102*, 7597. Holm, T.; Crossland, I. *Acta Chem. Scand., Ser. B.* **1979.**, *B33*, 421.

(33) Wawzonek, S.; Wearring, D. *J. Am. Chem Soc.* **1959**, *81*, 2067. Sioda, R. E.; Cowan, D. O.; Koski, W. S. *Ibid.* **1967**, *89*, 230. Bartak, D. E.; Houser, K. J.; Rudy, B. C.; Hawley, M. D. *Ibid.* **1972**, *94*, 7526. Kojima, J.; Bard, A. J. *Ibid.* **1975**, *97*, 6317. Mann, C. K.; Barnes, K. K. "Electrochemical Reactions in Non-Aqueous Systems"; Marcel Dekker: New York, 1970.

(34) Ashby, E. C.; Neumann, H. M.; Walker, F. W.; Laemmle, J.; Chao, L.-C. *J. Am. Chem. Soc.* **1973**, *95*, 3330.

(35) Dessy, R. E.; Okuzumi, Y.; Chen, A. *J. Am. Chem. Soc.* **1962**, *84*, 2899.

(36) Swain, C. G. *J. Am. Chem. Soc.* **1947**, *69*, 2306. Scala, A. A.; Becker, E. I. *J. Org. Chem.* **1965**, *30*, 3491.

(37) Schubert, W. M.; Le Fevre, P. H. *J. Am. Chem. Soc.* **1972**, *94*, 1639.

(38) Shiner, V. J., Jr.; Tai, J. J. *J. Am. Chem. Soc.* **1981**, *103*, 436.

(39) Ando, T.; Hiroshi, Y.; Hisao, M.; Junko, Y.; Junjiro, K.; Yasuhide, Y. *J. Am. Chem. Soc.* **1981**, *103*, 430.

be an inherent preference for electrophilic attack at a protium-substituted carbon relative to a deuterium-substituted one, despite a possible increase in positive charge density and congestion, which should generate the opposite effect. The source of this preference in the carbonium ion rearrangement was discussed briefly in terms of lengthening of the β–γ bond.[39] Since the electrons of the cleaving bond must be used also to interact with the incoming electrophile, a lengthening and weakening of the bond (possibly with concurrent rehybridization toward planarity) are entirely reasonable. Small secondary isotope effects, resulting from a cancellation between "normal" contributions from this source and "inverse" inductive contributions, may perhaps be characteristic of *any* electrophilic substitution at saturated carbon. A cyclic transition-state structure (**9**) should modify the situation only slightly; departure of the metal is assisted, but the environment at the carbon is not greatly changed.

Conclusion

The small secondary α-deuterium isotope effects observed for reactions of the Grignard reagent $C_4H_9CD_2MgBr$ with phenylacetylene and benzonitrile may be consistent with a variety of mechanisms, including open or cyclic electrophilic attack or single electron transfer. At this point, the magnitude of the secondary isotope effect does not appear particularly promising as a criterion for distinction among potential mechanisms for electrophilic substitution at the saturated carbon. We intend to look for other examples that may provide a significantly different effect.

Experimental Section

1-Bromopentane, 1-bromohexane, phenylacetylene, and benzonitrile were redistilled commercial samples. Tetrahydrofuran (THF) for Grignard reactions was freshly distilled under a slow flow of nitrogen from lithium aluminum hydride. Reactions were carried out under a nitrogen or argon atmosphere, in a reaction flask sealed to a condenser, with a side arm above the condenser for connection with an inert gas or vacuum line. Transfers to or from the flask or to other containers were made by syringe, maintaining the inert atmosphere with a brisk flow of nitrogen or argon through the top of the apparatus.

Gas chromatography was on Varian A90-P3 chromatographs with the following colums: A, 10 ft × $^1/_4$ in., 20% Carbowax 20M on 60–80 mesh Chromosorb W; B, 5 ft × $^1/_4$ in., 5% Carbowax 20M on Chromosorb W; C, 10 ft × $^1/_4$ in., 15% tricresyl phosphate on 60–80 mesh firebrick. NMR spectra were run on a Varian T-60 spectrometer. Mass spectra were obtained on a Hewlett-Packard 5985 gas chromatograph/mass spectrometer.

1-Bromopentane-*1,1*-d_2 (1-d_2). Pentanoyl chloride (26.4 g, 0.219 mol) in 50 mL of ether was added over about 40 min to lithium aluminum deuteride (5.0 g, 0.119 mol) in 250 mL of ether. After an additional hour of reflux, the reaction mixture was hydrolyzed by gradual addition of 9 mL of saturated aqueous sodium chloride and worked up by dissolving salts in dilute HCl, extracting with ether, and distilling. To the deuterated 1-pentanol (16.7 g, 0.185 mol), maintained at −15 to 0 °C, phosphorus tribromide (18.4 g, 0.068 mol) was added dropwise. The reaction mixture was allowed to stir at room temperature for 5 h and heated under the vacuum of a water aspirator to distill the crude product. The distillate was washed with concentrated H_2SO_4 and then with water and dried (K_2CO_3). Distillation yielded 14 g (52%) of 1-d_2, bp 129 °C. Approximately 2% of an impurity of longer retention time was detected by GC (column A). NMR spectra of both alcohol and bromide indicated less than 1% protium in the α-position.

Isotope Effect in Reaction of 2 and 2-d_2 with Phenylacetylene. A Grignard reagent was prepared by reaction of 0.996 g (6.59 mmol) of 1 and 1.043 g (6.81 mmol) of 1-d_2 with magnesium (0.492 g, 20.2 mmol) in 15 mL of THF. Titration of a 2-mL aliquot with *sec*-butyl alcohol, using 1,10-phenanthroline as indicator,[40] gave a concentration of 0.65–0.70 M. Three milliliters of this reagent was removed and hydrolyzed, and the volatile products and solvent were vacuum transferred to a cold trap (fraction A, Scheme I). To the remaining Grignard reagent was added phenylacetylene (0.518 g, 5.07 mmol). The solution was heated to reflux for 0.5 h, and the volatile constituents were vacuum transferred to a cold trap (fraction B). Fresh THF (5 mL) was added, the mixture was hydrolyzed by addition of water, and the volatiles were again transferred to a cold trap (fraction C). The isotopic compositions of the pentane in fractions A–C should correspond to those of the original Grignard reagent and to the portions of it that reacted with the phenylacetylene and that did not react, respectively.

Isotopic analyses were carried out by gas chromatography/mass spectrometry (GC/MS), utilizing electron-impact ionization at 15 V to reduce the extent of fragment. The abundances of ions in the spectra of the pentane peak in each fraction were summed over the MS scans of that peak and, after elimination of atmospheric constituents, were expressed as a fraction of the total pentane ion current. Spectra of pentane and pentane-d_2 showed that peaks at *m/e* 41, 42, 55, 56, 57, and 72 are 2 or more times as abundant in the spectrum of the undeuterated compound as in the deuterated; *m/e* 43 was 1.7 times as abundant. The peaks at *m/e* 44, 45, 46, 58, 59, and 74 were more abundant in the spectrum of pentane-d_2 by factors of 4–1000. It was then possible to compare the isotopic compositions of fractions A–C by comparison of the abundances of those peaks that discriminate between pentane and pentane-d_2. For convenience, the comparisons were made by grouping abundances in masses *m/e* 41–43, 44–46, 55–57, 58–59, and 72–74. In averaging results, double weight was given to the more abundant *m/e* 41–43 and 44–46 groupings. No significant difference was noted in a comparison of fractions A and B when consideration was restricted to scans of the central part of the pentane peak (total ion current geater than half of maximum), and there was no indication of partial isotopic fractionation on the chromatograph column. Absolute analysis of the isotopic content was rendered inaccurate by apparently insufficient control of the ionizing voltage. However, relative isotopic compositions could be compared more accurately. Assigning the composition of fraction A as exactly 50.00% d_0, we calculated fractions B and C to be within 0.15% of the same composition, with an average deviation among peak group analyses of 0.6%. This result translates to an isotope effect $k_{H_2}/k_{D_2} = 0.99_8 \pm 0.03$.

Isotope Effect in the Reactions of 2 and 2-d_2 with Benzonitrile. A Grignard reagent was prepared by reaction of a mixture of 1-bromopentane (1.905 g, 12.61 mmol) and 1-bromohexane (2.070 g, 12.54 mmol) with sublimed magnesium (0.699 g, 28.7 mmol) in 20 mL of tetrahydrofuran under argon. Solvent and any volatile materials produced during Grignard reagent formation were vacuum transferred to a cold trap. Subsequent GC analysis (column C) showed that monomeric hydrocarbon in the transferred volatiles corresponded to about 1.5% of the total and consisted of alkane and alkene in a ration of about 5:1. Fresh solvent (20 mL) was added, along with 250 μL of 2,3-dimethylbutane (as a GC internal standard). A 5-mL sample of the Grignard reagent was removed, cooled on an ice bath, hydrolyzed with 1 mL of water, and stored in a freezer until analyzed by GC. Benzonitrile (0.91 mL, 8.9 mmol) was added to about 20 mL of the remaining solution. Three 5-mL aliquots were tranferred by syringe to glass tubes and sealed under a reduced pressure of argon.

After various periods of standing at room temperature, the tubes were opened under a stream of argon and the contents removed by syringe, hydrolyzed by addition of 1 mL of water, and placed in a freezer until GC analysis for hydrocarbon was completed. Then, 3 mL of 3 N HCl was added, followed by 200 μL (1.33 mmol) of butyrophenone as an internal reference. After 0.5 h, 3 mL of isooctane was added, and the organic phase was separated and analyzed for the ketones by GC.

A parallel experiment was carried out by using 1-d_2 (1.910 g, 12.5 mmol) and 1-bromohexane (2.064 g, 12.5 mmol).

Samples were analyzed for pentane and hexane by GC on column C, using 2,3-dimethylbutane as the internal reference.

---

[40] Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

Ketones were analyzed on column B, with butyrophenone as standard. Relative detector responses were determined for undeuterated samples; the responses of deuterated and undeuterated samples were assumed equal on a weight basis. In both cases, the yield of Grignard reagent, taken as equivalent to hydrocarbon produced by hydrolysis after replacement of the solvent, was about 90%. In all samples, reaction of the nitrile was complete before hydrolysis of the reaction mixture. The material balance after reaction with benzonitrile was approximately quantitative (100 ± 10%); uncertainties in the total solution volumes made a more accurate determination difficult. Three tubes were analyzed for each reaction, and three or more replicate GC analyses were made for each tube. Areas were calculated as peak height times width at half-height; relative areas agreed within ±1% with those from cutting and weighing peaks.

In each of the experiments, relative rate constants were determined by substitution into the integrated form of the equation for competition between two reactants for a single reagent[2] [$k_A/k_B = \ln (A_t/A_0)/\ln (B_t/B_0)$, where A_0 and B_0 are initial reactant concentrations and A_t and B_t are final concentrations]. If the yield is taken as quantitative, then the three pieces of data—initial concentration of Grignard reagent, final concentration of Grignard reagent, and concentration of product—provide a redundancy that allows three different combinations to be used in the calculation. Results are summarized in Table I.

Acknowledgment. We thank Mr. Frank Laib for assistance with mass spectrometric analyses and Jeffrey R. Schneider for help in the gas chromatographic measurements.

Registry No. 1, 110-53-2; 1-d_2, 77734-75-9; 1-bromohexane, 111-25-1; phenylacetylene, 536-74-3; benzonitrile, 100-47-0; deuterium, 7782-39-0; pentanoyl chloride, 638-29-9; 1-pentanol-*1,1*-d_2, 35658-10-7.

Preparation and Properties of Paramagnetic Bis(η-butadiene)(Lewis base)manganese Complexes[†]

R. L. Harlow, P. J. Krusic, R. J. McKinney, and S. S. Wreford*

Central Research and Development Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898

Received April 12, 1982

$MnCl_2$ reacts with $Mg(C_4H_6)\cdot 2THF$ in the presence of Lewis bases and butadiene to form stable, monomeric Mn(0) complexes, $Mn(\eta\text{-}C_4H_6)_2L$ (L = PMe_3, PEt_3, $P(OMe)_3$ and CO). The related derivatives $Mn(\eta\text{-}2,3\text{-}Me_2C_4H_4)_2P(OMe)_3$ and $Mn(\eta\text{-}2\text{-}MeC_4H_5)_2PMe_3$ were prepared by cocondensation of substituted butadienes, $P(OMe)_3$ or PMe_3, and Mn atoms. The trimethyl phosphite and carbonyl adducts are rapidly reduced by Na/Hg, forming salts of the closed-shell anions $Mn(\eta\text{-}C_4H_6)_2L^-$; NBu_4^+ and $Na(18\text{-crown-}6)^+$ salts of $Mn(\eta\text{-}C_4H_6)_2P(OMe)_3^-$ were isolated. The Mn(0) compounds are 17-electron, fully paramagnetic complexes and show no propensity for dimerization. Crystals of $Mn(\eta\text{-}C_6H_6)_2P(OMe)_3$ are monoclinic, space group $P2_1/c$, with unit-cell dimensions at −100 °C of a = 14.137 (2), b = 7.841 (1), c = 12.017 (2) Å, and β = 97.73 (1)°. The refinement of 229 variables (all atomic coordinates, isotropic thermal parameters for H, anisotropic for Mn, P, O, and C) using 2245 reflections converged at $R = 0.037$ and $R_w = 0.032$. The Mn coordination can be described as a square pyramid with axial η^4-butadiene ligands and an apical $(CH_3O)_3P$ group. The butadiene ligands have Mn–C(internal) bond lengths that average 2.070 Å, Mn–C(terminal)'s that average 2.137 Å, and C–C bond lengths that are nearly equivalent and average 1.408 Å within a range of ±0.005 Å. ESR spectra with resolvable ^{55}Mn and ^{31}P hyperfine are observable in solution and frozen solution. Frozen solution spectra have highly anisotropic ^{55}Mn hyperfine components, one component being much larger than the other two. This observation is consistent with EHMO calculations that place the unpaired electron in an orbital oriented perpendicular to the C_2 axis and directed toward the butadiene ligands. These compounds do not undergo associative substitution reactions with facility. The EHMO calculations suggest that the deformations necessary to approach the transition state for such a displacement reaction are energetically unfavorable.

Recently, we reported that $Mg(C_4H_6)\cdot 2THF$ is a conveniently prepared, useful reagent for the preparation of transition-metal butadiene complexes.[1] The compound was found to react with a wide variety of transition-metal halides, affording the corresponding butadiene complexes with, generally, superior yields in comparison to more conventional procedures. While surveying the reactions of $Mg(C_4H_6)\cdot 2THF$, we found that it reacted with manganese chloride in the presence of lewis bases and excess butadiene to yield compounds with the stoichiometry $Mn(C_4H_6)_2$(Lewis base). These derivatives are formally analogous to $Mn(CO)_5$, a short-lived, 17-electron, organometallic radical with a controversial chemistry,[2] which has only very recently been definitively characterized by low-temperature matrix-isolation ESR[3] and IR[4] techniques. The determination of the chemical and physical properties of these manganese butadiene complexes appeared to be of value in order to assess the similarities and differences between these stable paramagnetic species and the $Mn(CO)_5$ radical, whose lifetime is essentially controlled by diffusion kinetics.[5] $Mn(\eta\text{-}C_4H_6)_2(CO)$ has been previously

---

[†] Contribution No. 3031.

(1) Wreford, S. S.; Whitney, J. F. *Inorg. Chem.* **1981,** *20,* 3918.

(2) (a) Byers, B. H.; Brown, T. L. *J. Am. Chem. Soc.* **1977,** *99,* 2527. (b) Kidd, D. R.; Brown, T. L. *Ibid.* **1978,** *100,* 4095. (c) Brown, T. L. *Ann. N.Y. Acad. Sci.* **1980,** *333,* 80. (d) Wrighton, M. S.; Ginley, D. S. *J. Am. Chem. Soc.* **1975,** *97,* 2065. (e) Poë, A. *Inorg. Chem.* **1981,** *20,* 4029 and 4032. (f) Atwood, J. D. *Ibid.* **1981,** *20,* 4031. (g) Fawcett, J. P.; Poë, A.; Sharma, K. R. *J. Chem. Soc., Dalton Trans.* **1979,** 1886. (h) Sweany, R. L.; Halpern, J. *J. Am. Chem. Soc.* **1977,** *99,* 8335. (i) Fox, A.; Malito, J.; Poë, A. *J. Chem. Soc., Chem. Commun.* **1981,** 1053.

(3) Howard, J. A.; Morton, J. R.; Preston, K. F. *Chem. Phys. Lett.* **1981,** *83,* 226.

(4) Church, S. P.; Poliakoff, M.; Timney, J. A.; Turner, J. J. *J. Am. Chem. Soc.* **1981,** *103,* 7515.