

Evidence for an Iodine Ate Complex as an Observable Intermediate in the Iodine/Magnesium Exchange on a 1,1-Diiodoalkane

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On reaction of the 1,1-diiodoalkane **1** with isopropyl Grignard reagents at $-78\text{ }^{\circ}\text{C}$ a long-lived intermediate is generated, which was characterized by its UV-vis spectrum, ^1H and ^{13}C NMR data, and the apparent isotope effect $k_{\text{H}}/k_{\text{D}} = 2.8$ on protonation with $\text{CH}_3\text{OH}/\text{CH}_3\text{OD}$. Arguments are presented that led us to assign the structure of the α -iodoalkyl iodine ate complex **4** to this intermediate.

Introduction

The halogen/metal exchange reaction has been, ever since its discovery by Wittig¹ and Gilman,² a standard reaction in organometallic chemistry. When we applied it to the generation of α -iodoalkyl Grignard reagents from 1,1-diiodoalkanes, e.g. **1** \rightarrow **2**^{3,4} (Scheme 1), we noted the formation of an intense pumpkin yellow coloration of the reaction mixture upon addition of isopropylmagnesium bromide to **1**, a color that slowly faded to give eventually a clear, almost colorless solution of **2**.^{5,6}

We were able to show that this color signals the presence of the iodine ate complex **4**, which is a long-lived intermediate in the iodine/magnesium exchange reaction from **1** to **2**.^{5,7} We wish to report here the experiments in detail that lead us to propose **4** to be the observable intermediate in this iodine/magnesium exchange reaction. While it was initially by no means clear that the observed color is directly connected with the halogen/magnesium exchange reaction or which kinds of alternatives had to be considered, we will present our results—for the sake of clarity—in a manner that assumes the intermediacy of **4** as established.

General Observations on the Iodine/Magnesium Exchange on **1**

Qualitative observations mark the beginning of the study of a reaction: the rate of decolorization of the

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(3) (a) Hoffmann, R. W.; Kusche, A. *Chem. Ber.* **1994**, *127*, 1311–1316. (b) Schulze, V.; Hoffmann, R. W. *Chem. Eur. J.* **1999**, *5*, 337–344.

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(5) When we speak of **2**, we refer to the Grignard solution obtained by iodine/magnesium exchange of the diiodoalkane **1**. For most cases in the present study we have not ascertained whether the major species in solution is **2** or—more likely—the bis(α -iodoalkyl)magnesium species **6** resulting from a Schlenk equilibrium.

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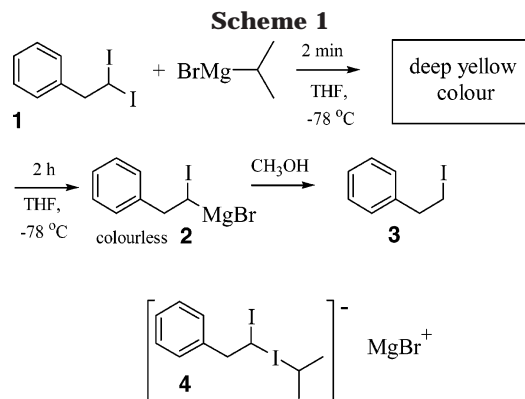


Table 1

Equiv. of $i\text{PrMgBr}$ rel. to 1	1.0	1.5	2.0	3.0
Time for decolorisation (min) at $-78\text{ }^{\circ}\text{C}$	70	30	20	3
Temperature ($^{\circ}\text{C}$) (1 Equiv. of $i\text{PrMgBr}$ rel. to 1)	-100	-80	-70	-60
Time for decolorisation (min)	300	70	40	15

solution depends on the amount of isopropyl Grignard reagent added and on the temperature (Table 1). These observations define the time and temperature limits under which “colored” solutions may be handled.

Giving the impression that the color of the solution is concentration dependent, concentrated solutions are almost orange, while dilute solutions have a yellowish green tint. Low-temperature UV-vis spectroscopy showed a strong absorption of the “intermediate” at 409 nm. Assuming an almost quantitative formation of the intermediate, the extinction coefficient ϵ would be ca. 450. When one considers the 409 nm absorption band to be superimposed on the weak edge absorption of either the diiodo compound **1** or the α -iodoalkyl Grignard reagent **2**,⁵ one can rationalize the concentration-dependent changes of the apparent color of the “intermediate”: cf. Figure 1.

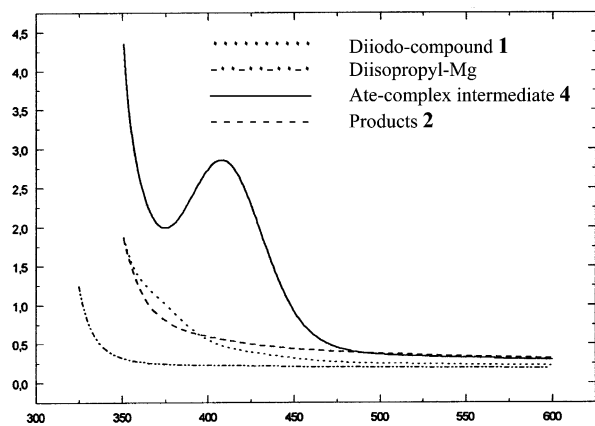


Figure 1. UV-vis absorption spectra of the educts, intermediate, and product in the reaction of the diiodoalkane **1** with diisopropylmagnesium.

Table 2. Quenching of the Reaction Mixture with CH₃OH

time, s ^a	1:3	time, s ^a	1:3
in situ ^b	84:16	60	10:90
20	72:28	120	0:100

^a Time span between addition of *i*PrMgBr to **1** and the addition of CH₃OH at $-78\text{ }^{\circ}\text{C}$ in THF. ^b *i*PrMgBr was added at $-78\text{ }^{\circ}\text{C}$ to a THF solution of **1** containing 2 equiv of CH₃OH.

When methanol is added to the solution, the color is quenched instantaneously. Workup provided the monoiodo compound **3** in high yield (>90%). With the aid of such a methanol quench one can estimate how quickly the starting material (**1**) is consumed (Table 2). It thus became clear that the starting material **1** is consumed within 2 min, whereas the yellow color persisted for 1 h or more. Given these data, the intriguing question is whether the yellow color is in any direct way related to the formation of the α -iodoalkyl Grignard **2** or is completely unrelated. The question may be rephrased: is 2 min after mixing the reactants, i.e., when the starting material **1** has disappeared, the product **2** already present to a stoichiometric extent in the yellow solution, or is a different (yellow) species present in high concentration, which slowly transforms into **2**? The nature of that species must be such that it is also protonated to give **3**.

Isotope Effects

One way to characterize and identify a reacting species is by a competition constant:⁸ i.e., the ratio in which a species chooses to react via two parallel reaction pathways. An established reaction of **2** is its protonation by methanol to give **3** (Scheme 2). To offer a second reaction path, which will be used with a similar rate, we considered deuteration by CH₃OD to give **3-D**. In practice we determined the extent of deuterium incorporation into **3**, when the colorless solution of **2**⁵ 3 h after mixing **1** with isopropylmagnesium bromide in THF at $-78\text{ }^{\circ}\text{C}$ is reacted with 44 equiv of a 1:1 mixture of CH₃OH/CH₃OD. The percentage of deuterium incorporation can be expressed as an apparent H/D isotope effect, a number which is characteristic for the reacting

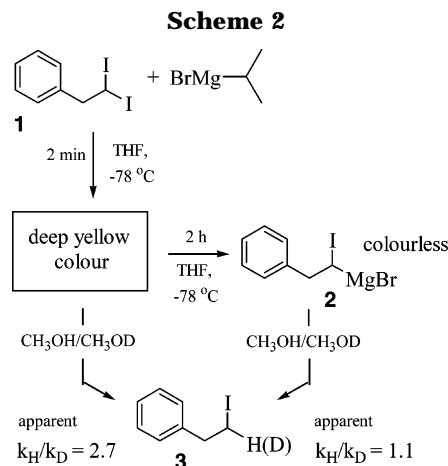
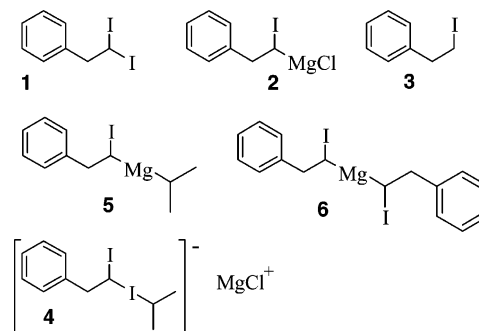


Chart 1



species **2**⁵ under defined reaction conditions. The competition constant determined for **2** is $k_{\text{H}}/k_{\text{D}} = 1.1$, a number which falls into the range of isotope effects reported previously for the protonation of Grignard reagents.⁹ When the (deep yellow) reaction mixture was quenched 2 min after mixing the reactants, the deuterium incorporation into the product **3** corresponded to the apparent isotope effect $k_{\text{H}}/k_{\text{D}} = 2.7$. Thus, when the solution is yellow, substantial amounts of a species different from **2**⁵ must be present, a species that is more selective than **2** in its differentiation between CH₃OH and CH₃OD. This species is initially formed on reaction of the diiodo compound **1** with isopropylmagnesium bromide, because after addition of isopropylmagnesium bromide to a solution of **1** containing 10 equiv of a 1:1 mixture of CH₃OH/CH₃OD (in situ trapping), the monoiodo compound **3** could be isolated (15%) with a deuterium incorporation corresponding to the apparent isotope effect $k_{\text{H}}/k_{\text{D}} = 3.5$.

NMR Spectroscopy

These conclusions invited low-temperature NMR studies to give direct spectroscopic information on "the intermediate". Initial results were obtained by mixing a solution of 1-¹³C-labeled **1** with a solution of ¹PrMgCl at $-90\text{ }^{\circ}\text{C}$ in an NMR tube and rapidly transferring the tube into the NMR spectrometer, which was precooled to $-75\text{ }^{\circ}\text{C}$. In the ¹³C NMR spectrum of the yellow solution signals of the compounds shown in Chart 1 could be detected. Assignments of the signals to these compounds are based on the data shown in Table 3.

After 2 h, when decolorization of the solution had occurred, the signal at 33 ppm assigned to **4** had

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Table 3. Characteristic NMR Spectroscopic Data of the Compounds Involved in the Iodine/Magnesium Exchange on Compound 1^a

Compound Nr.	Chemical Structure	Characteristic NMR-Data
1		$\delta_C = -23^b$ H-1, 5.39 t, $J = 7.7$ Hz, 1H H-2, 3.67 d, $J = 7.7$ Hz, 2H
3		$\delta_C = +8^b$ H-1, 3.39 d, $J = 8.1$ Hz, 2H H-2, 3.13 d, $J = 8.1$ Hz, 2H
7		H-1, 1.79, d, $J = 6.6$ Hz, 6H H-2, -0.44 sept, $J = 6.6$ Hz, 1H
8		H-1, 1.2, d, $J = 6$ Hz, 6H H-2, -0.44 sept, $J = 6$ Hz, 1H
9		$\delta_C = +9.6, 26.3$ H-1, 1.13 d, $J = 8.0$ Hz, 12H H-2, -0.57 sept, $J = 7.8$, Hz, 2H
5		$\delta_C = +41.4$ (d, $J_{C-H} = 115$ Hz); 9.0 (d, $J_{C-H} = 106$ Hz), 26.55, 26.59, 48.3 (t, $J_{C-H} = 128$ Hz), 125.8, 128.5, 128.8, 146.3. H-1, 3.03 dd, $J = 7.8$ and 12.6 Hz, 1H H-2a, 3.30 dd, $J = 7.8$ and 12.0 Hz, 1H H-2b, 3.48 dd, $J = 7.8$ and 12.0 Hz, 1H 1.29, d, $J = 7.3$ Hz, 3H 1.30, d, $J = 7.3$ Hz, 3H -0.32, sept, $J = 7.7$ Hz, 1H
6		<i>meso</i> and <i>d,l</i> : $\delta_C = +44.1$ (d, $J_{C-H} = 114$ Hz); + 46.7 (d, $J_{C-H} = 112$ Hz); 46.9 (t, $J_{C-H} = 126$ Hz); 47.3 (t, $J_{C-H} = 127$ Hz), 125.4, 125.6, 128.1, 128.2, 128.6, 128.9, 146.5, 146.7. H-1, 3.13, dd, $J = 9.4$ Hz, 1H H-2, 3.25 - 3.37 m; 3.43, 2d, $J \approx 14$ Hz, 2H
2		$\delta_C = +49?$ tentative?
4		$\delta_C = +33$ H-1, 2.95 dd, $J = 7.8$ and 12.7 Hz, 1H H-2a, 3.22 t, $J = 12.7$ Hz, 1H H-2b, 3.45 dd, $J = 8.0$ and 10.4 Hz, 1H

^a All values are given for THF or THF-*d*₈ as solvent. Legend: (*) for further data see ref 3b.

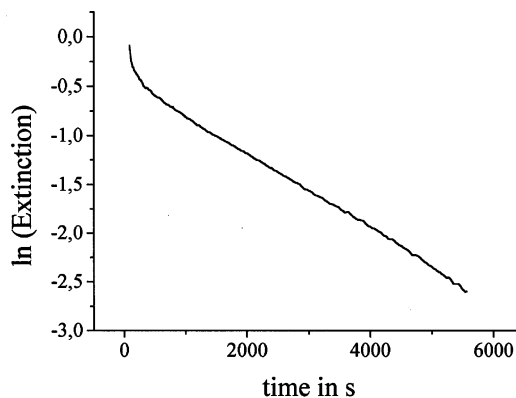
disappeared. Moreover, the 49 ppm signal, tentatively assigned to **2**, had decreased in intensity, while that of **6** had increased. This suggests the establishment of a Schlenk equilibrium between **2** and **6** (that between **5** and **6** is established only very slowly).¹⁰

Similar measurements of the ¹H NMR spectrum using unlabeled **1** and diisopropylmagnesium in THF-*d*₈ were less conclusive, due to considerable signal overlap. Nevertheless a doublet of doublets at 2.95 ppm assigned to **4** disappeared on decolorization of the solution.

Kinetic Studies

We now have the following hints regarding the occurrence of a long-lived intermediate in the iodine/magnesium exchange reaction on **1**: the yellow color, the change in the isotope effect on protonation with CH₃-OH/CH₃OD, and the ¹³C NMR signal at 33 ppm, which belongs to neither starting material nor final products. A correlation of these phenomena should be possible by comparing their time dependence. To this end we initiated a kinetic study.

First we followed the decline of the UV-vis absorption at 409 nm. To this end a precooled solution of diisopropylmagnesium was injected into a solution of **1** contained in a UV cell at -85 °C. The time-dependent absorption changes are documented in the Supporting Information. The data correspond to a (pseudo-) first-

**Figure 2.** Pseudo-first-order decrease of the extinction at 409 nm.**Table 4**

concn of 1 , 10 ⁻³ mol L ⁻¹	diisopropylmagnesium		rate constant, 10 ⁻⁴ s ⁻¹
	amt, equiv	concn, 10 ⁻³ mol L ⁻¹	
8.5	1	8.5	1.2
7	2	14	3.8
28	1	28	9.5
19	2	38	15

order reaction (cf. Figure 2) with the rate constants given in Table 4. When these rate data are plotted against the total concentration of Mg²⁺—a number that remains constant throughout the reaction—a linear plot results.¹¹ This indicates that the conversion of **4** into **2**⁵ is first order, in both the ate complex and magnesium cations. This makes sense, when the intermediate **4** is an ionic species that is present in solution as dissociated ions.

We next looked at the time dependence of the apparent isotope effect on quenching of the mixture with CH₃-OH/CH₃OD. The reaction was initiated by addition of 0.9 equiv of isopropylmagnesium bromide into a solution of **1** in THF at -78 °C. The mixture was then quenched after a given reaction time into an excess (44 equiv) of a 1:1 mixture of CH₃OH/CH₃OD. The resulting 2-phenyl-1-iodoethane was isolated and the degree of protonation at C-1 was determined by integration of the ¹H NMR signal for the protons at C-1 versus that at C-2. The time dependence of the percentage of protons introduced at C-1 by quenching with this CH₃OH/CH₃OD mixture is depicted in Figure 3. When the curve is extrapolated to time 0, the apparent isotope effect $k_H/k_D = 2.8$ results.¹² The time-dependent changes observed correspond to a first-order rate law with a rate constant of $(4.8 \pm 0.5) \times 10^{-4} \text{ s}^{-1}$.

We also wanted to follow the course of the reaction by ¹H NMR. To have a definite starting point for the reaction, we resorted to rapid-injection NMR.¹³ ¹H NMR spectra were recorded after injecting a precooled (-78 °C) solution of 0.9 equiv of **1** into a cooled (-75 °C)

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(12) This apparent isotope effect, $k_H/k_D = 2.8$, is smaller than that recorded on in situ trapping: $k_H/k_D = 3.5$. The latter value may be too high, given the alteration in the methanol-*OH*/methanol-*OD* composition due to the concurrent protonation of isopropylmagnesium bromide, which occurs with an inverse isotope effect.⁹ Hence, we favor the isotope effect value of 2.8 for the protonation/deuteration of the intermediate **4**.

(13) McGarrity, J. F.; Prodoliet, J.; Smyth, T. *Org. Magn. Reson.* **1981**, *17*, 59–64.

(10) Schulze, V.; Löwe, R.; Fau, S.; Hoffmann, R. W. *J. Chem. Soc., Perkin Trans. 2* **1998**, 463–465.

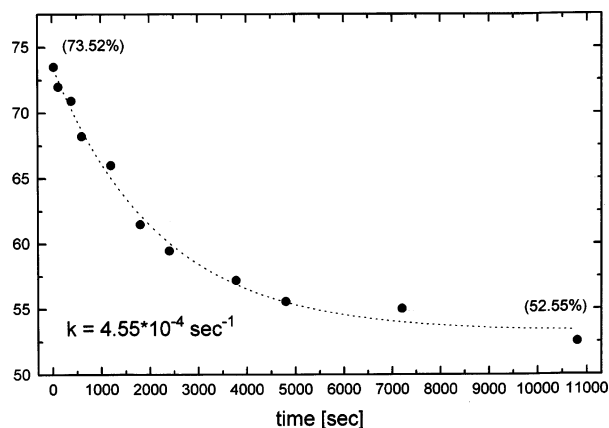


Figure 3. Time dependence of the apparent H/D isotope effect on quenching of the reaction mixture with $\text{CH}_3\text{OH}/\text{CH}_3\text{OD} = 1:1$.

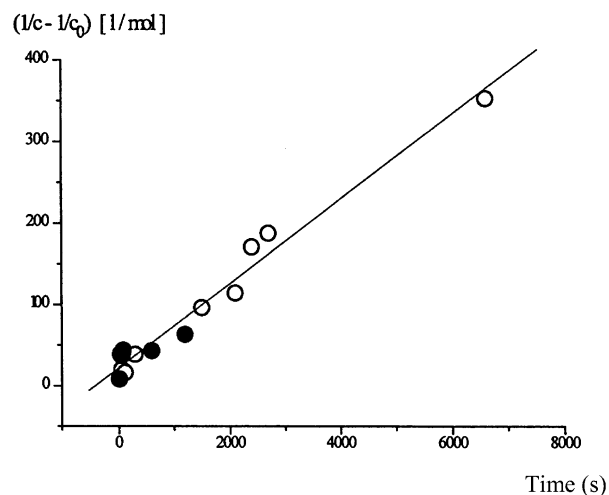


Figure 4. Second-order plot for the decrease of the ^1H NMR signals of **1** from two rapid-injection runs at $-75\text{ }^\circ\text{C}$.

solution of diisopropylmagnesium in $\text{THF-}d_8$. Even though the lines were rather broad, the time dependence of the concentration of **1** (signal at δ 5.39 ppm), **4** (δ 2.98 ppm), and 2-iodopropane (δ 4.34 ppm) could be monitored.

The starting material **1** disappeared in a second-order reaction with diisopropylmagnesium. The rate constant was found to be $(5.4 \pm 0.4) \times 10^{-2} \text{ L mol}^{-1} \text{ s}^{-1}$ (cf. Figure 4).

The signals of the intermediate **4** disappeared in a first-order reaction with a rate law of $k = (3.6 \pm 0.8) \times 10^{-4} \text{ s}^{-1}$ (cf. Figure 5)

Finally, the appearance of 2-iodopropane (**7**) occurred in a first-order reaction (Scheme 3) which may be approximated by a rate constant of $(4.7 \pm 0.6) \times 10^{-4} \text{ s}^{-1}$ (cf. the data in the Supporting Information).

These data allow the conclusion that the species that causes the yellow color, the species that is protonated with a high apparent H/D isotope effect, and the species with the ^1H NMR signal at δ 2.98 are identical (or in rapid equilibrium), because they decay at the same rate. Moreover, this decay leads to 2-iodopropane, as the latter appears with the same rate.

The kinetic findings can best be summarized as a sequence of two irreversible reactions. The first is a

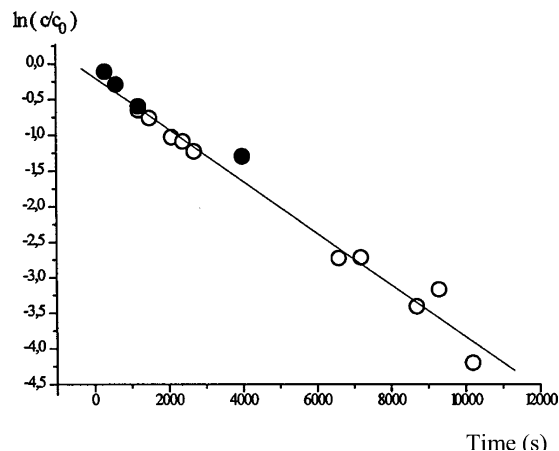


Figure 5. (Pseudo-) first-order plot for the decrease of the ^1H NMR signals of **4** from two rapid-injection runs at $-75\text{ }^\circ\text{C}$.

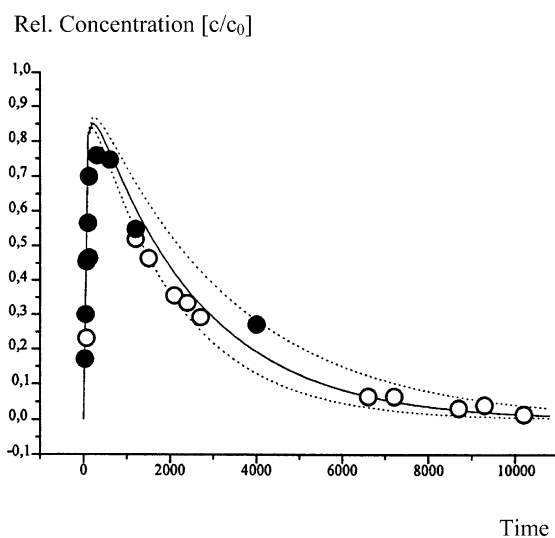
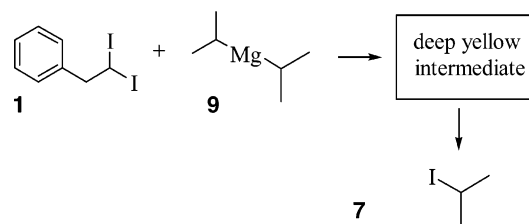


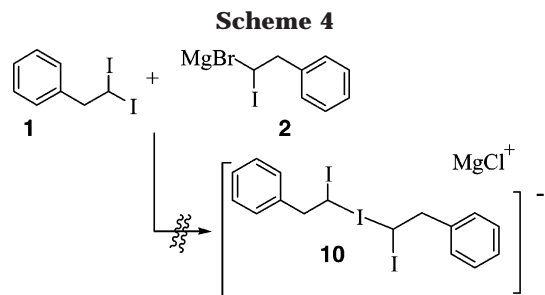
Figure 6. Time dependence of the relative concentration of **4** from two rapid-injection runs at $-75\text{ }^\circ\text{C}$: comparison between experimental results and calculated behavior using the rate constants given in the text. Dotted lines correspond to the error limits given in the equations.

Scheme 3



second-order reaction between **1** and diisopropylmagnesium to give an intermediate with the rate constant $(5.4 \pm 0.4) \times 10^{-2} \text{ L mol}^{-1} \text{ s}^{-1}$. This intermediate is then transformed into 2-iodopropane in a pseudo-first-order reaction with a rate constant of $(4.2 \pm 0.8) \times 10^{-4} \text{ s}^{-1}$ for a total concentration of $[\text{Mg}^{2+}]$ of 0.225 mol L^{-1} .

The time dependence of the relative concentration of the intermediate may be calculated with these rate constants (cf. the solid line in Figure 6). A comparison with the relative concentrations of the intermediate as determined by the rapid injection NMR study shows a reasonably good fit.



Nature of the Intermediate

Ate complexes have been suggested by Wittig and Schöllkopf¹⁴ as intermediates in the halogen/metal exchange reaction, and iodine ate complexes have been shown to be intermediates in certain iodine/lithium exchange reactions.^{15,16} Moreover, certain iodine ate complexes have been isolated¹⁷ or shown to enjoy considerable stability.^{18,19} It is therefore not far-fetched to think of the α -iodoalkyl iodine ate complex **4** to be the intermediate in the reaction studied here. One then has to check whether the spectroscopic data obtained for the intermediate would be consistent with such a proposal.

As the deep yellow color of **4** is notprecedented, Professor Schwerdtfeger (Auckland, New Zealand) kindly carried out CAS/MP2 calculations on the chromophore of $\text{I}-\text{CH}_2-\text{I}-\text{CH}_3$.⁷ The absorption maximum at long-est wavelengths was calculated to occur at 431 nm with an oscillator strength of 0.26. The agreement with the values found for **4** is better than could be expected.

What of the NMR chemical shifts, especially the value δ_{C} 33 ppm? Reich observed¹⁶ the chemical shift of the ipso-C signal of the diphenyliodinate anion to be intermediate between that of phenyllithium and that of iodobenzene and closer to the former. The signal of **4** (δ 33 ppm) is also between those of **2**, **5**, and **6** (δ 42–49) and that of **1** (δ –23 ppm): i.e., closer to the former. The spectroscopic data of the intermediate are therefore not counter to the proposal of structure **4** for the intermediate. However, would structure **4** be the only one to agree with the data? The symmetrical ate complex **10**¹⁹ (Scheme 4) should be equally compatible with the spectroscopic data for the intermediate. While there should be stereoisomers (*meso*, *dl*) of **10**, it is questionable whether the stereoinformation is sufficiently felt across the central iodine atom to render the ¹³C NMR signals of *meso*- and *dl*-**10** anisochronous.

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If **10** were the intermediate, the maximum intensity of the color should be reached with a **1**:Grignard ratio of 2. Qualitatively this was not found to be the case; the maximum intensity was reached when 1 equiv of isopropylmagnesium bromide was added to **1**. Moreover, when **1** was added to a colorless solution of **2**⁵ at –78 °C, conditions that should favor the formation of **10**, no yellow color indicative of an iodine ate complex developed. Likewise, when **1** was added to a solution of **6**, no NMR signals (other than those of **1** and **6**) could be recorded that could be ascribed to **10**. For these reasons we exclude **10** as being the long-lived intermediate in the iodine/magnesium exchange reaction on **1** and maintain that **4** is the most probable structure of the intermediate, pending evidence to the contrary.

What could be the reason that iodine ate complexes had not been detected in iodine/magnesium exchange reactions before Meister's observation?⁶ Why had they not been conspicuous in many subsequent studies on the iodine/magnesium exchange reaction?²⁰ The only feature that is special about the ate complexes **4** is the additional iodine atom in the α -position. This iodine atom is instrumental in stabilizing the negative charge in the ate complex **4** and in stabilizing the ate complex as a whole, as the calculations by Boche and Schimeczek²¹ showed. This stabilization may amount to as much as 20 kcal mol⁻¹ and is the key to rendering species such as **4** as long-lived observable intermediates.

Experimental Section

General Remarks. All temperatures quoted are uncorrected. All reactions with organometallic reagents were carried out in flame-dried glassware under an argon atmosphere. The concentration of Grignard solutions was determined by titration with menthol against 1,10-phenanthroline as indicator,²² or after hydrolysis with 1 M hydrochloric acid by back-titration with 0.1 M NaOH.²³ Boiling range of petroleum ether: 40–60 °C. ¹H NMR, ¹³C NMR: Bruker ARX-200, AC-300, WH-400, DRX-400, AM-400, AMX-500. UV–vis spectroscopy: Perkin-Elmer Lambda 9 with a shop-made low-temperature inert-atmosphere sample-holder system. Analytical gas chromatography: Siemens Sichromat 3, 30 m \times 0.3 mm quartz capillary column with DB 5, 1 bar He. Flash chromatography: silica gel SI 60, E. Merck KGaA, Darmstadt, Germany, 40–63 μm .

Materials and Reagents. Isopropylmagnesium bromide was produced from magnesium turnings (4.4 g, 0.18 mol) in THF (50 mL) and isopropyl bromide (12.3 g, 0.1 mol) in THF (30 mL). The supernatant solution was transferred via cannula into a storage vessel. For diisopropylmagnesium, 1,4-dioxane (2.60 g, 29.5 mmol) was added at 0 °C over 30 min into a solution of isopropylmagnesium bromide (1.34 M in diethyl ether, 20 mL, 26.8 mmol). The resulting suspension was stirred for 2 h and filtered after 12 h at –10 °C. The filtrate was concentrated, and the residue was heated to 60 °C in vacuo for 6 h. One milliliter of THF was added, and vacuum-drying was repeated to remove any residual solvent. The diisopropylmagnesium was then dissolved in THF or THF-*d*₆. Isopropylmagnesium chloride was used as obtained from Aldrich.

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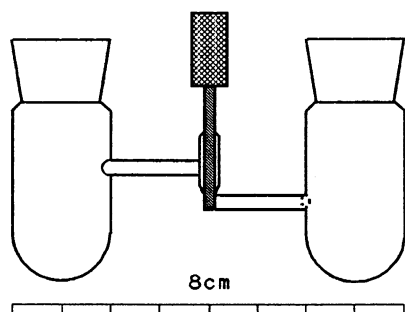


Figure 7. Two-compartment reactor used for the isotope effect studies.

Reaction of 1,1-Diiodo-2-phenylethane (1) with Isopropyl Grignard Reagent. A 10 mL flask with a 10 cm high neck, carrying a sidearm for argon blanketing, was immersed in a cooling bath. A solution of **1**^{3b} (100 mg, 0.3 mmol) in THF (2 mL) was cooled to -78°C . A solution of isopropylmagnesium bromide (0.60 M in THF, 0.42 mL, 0.25 mmol) was added via cannula so that the solution was cooled while flowing down the wall of the flask. Methanol-OD (0.5 mL) was added to the yellow (or to the decolorized) solution. The mixture was allowed to reach room temperature. *tert*-Butyl methyl ether (20 mL) was added, and the solution was extracted with water (20 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3×20 mL). The combined organic layers were dried (MgSO_4) and concentrated. The crude product was purified by flash chromatography with petroleum ether to furnish the iodoalkane **3** (63 mg, 97%).

^1H NMR (300 MHz, CDCl_3): δ 3.10 (t, $J = 7.7$ Hz, 2H), 3.27 (tt, $J = 7.7$ Hz, $^2J_{\text{H,D}} = 1.1$ Hz, 1H), 7.11–7.70 (m, 5H). ^{13}C NMR (75 MHz, CDCl_3): δ 5.3 (t, $^1J_{\text{C,D}} = 22.7$ Hz), 40.3, 126.8, 128.3, 128.6, 140.6.^{3b} Anal. Calcd for $\text{C}_8\text{H}_8\text{DI}$ (233.07): C, 41.23; H, 3.89. Found: C, 41.52; H, 4.19.

Isotope-Effect Studies. A solution of the diiodoalkane **1** (100 mg, 0.28 mmol) in THF (2 mL) was charged into one vessel of the reaction system shown in Figure 7. A 1:1 mixture of methanol-*OH* and methanol-*OD* (0.5 mL, 12.3 mmol) was charged into the other compartment. The top openings were sealed with septum caps. The apparatus was immersed into a cooling bath at -78°C . Both compartments were magnetically stirred. After 30 min, the solution of isopropylmagnesium bromide (0.60 M in THF, 0.4 mL, 0.24) was injected with a syringe along the wall of the vessel. After the indicated period, the stopcock was opened and the contents of the two compartments were mixed. Workup was as described above using diethyl ether for extraction.

In situ quenching with methanol-*OH*/methanol-*OD* was carried out as described above for the standard reaction of **1**: a solution of isopropylmagnesium bromide (1.34 M, 0.336 mL, 0.45 mmol) was added to a solution of **1** (160 mg, 0.45 mmol) in THF containing 2.2 mmol of CH_3OH and 2.2 mmol of CH_3OD . Workup as above afforded the monoiodo compound **3** (33%) with a proton content corresponding to an apparent isotope effect of 3.5.

NMR Measurements. Into a dried NMR tube was added under argon a solution of 0.06–0.14 mmol of the Grignard reagent dissolved in THF- d_8 (0.5 mL). The tube was sealed with a septum cap. Argon pressure was maintained via a needle. The tube was cooled to -105°C in a copper block. The solution of the diiodoalkane in THF- d_8 (0.1 mL) was added via syringe, and the total assembly was shaken to ensure thorough mixing. Removal of the tube from the copper block,

application of a spinner, and insertion into the precooled spectrometer were then effected in less than 30 s.

For rapid injection NMR²⁴ the tube was prepared as above but opened before insertion into the precooled spectrometer. The solution of the diiodoalkane was also precooled in the injection syringe of the apparatus.

Preparation of Labeled Starting Materials. (a) 1-Deuterio-1,1-diiodo-2-phenylethane (1-1D). A solution of hexamethyldisilazane (4.20 mL, 20.0 mmol) in THF (7 mL) was cooled to -78°C . *n*-Butyllithium (1.57 M in hexane, 12.7 mL, 20.0 mmol) was added, and the mixture was allowed to reach room temperature. A solution of dideuteriodiodomethane²⁵ (1.1 g, 4.0 mmol) in THF (3 mL) was cooled to -105°C . One equivalent of the lithium hexamethyldisilazide solution was added dropwise over 20 min. After the mixture was stirred for 2.5 h at -105°C , benzyl bromide (1.0 g, 6.0 mmol) was added dropwise at -100°C . The mixture was allowed to reach room temperature over 12 h. Saturated aqueous NH_4Cl solution (25 mL) was added, the layers were separated, and the aqueous layer was extracted with *tert*-butyl methyl ether (3×40 mL). The combined organic layers were dried (MgSO_4) and concentrated. The crude product was purified by flash chromatography to give 422 mg (30%) of the product. ^1H NMR (300 MHz, CDCl_3): δ 3.65 (s, 2H), 7.12 (m, 2H), 7.25 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = -25.6$ (t), 54.1, 127.6, 128.7, 128.8, 139.7.

(b) 2,2-Dideuterio-1,1-diiodo-2-phenylethane (1-2D₂). This compound was prepared in a similar manner from α,α -dideuteriobenzyl bromide²⁶ in 64% yield. ^1H NMR (300 MHz, CDCl_3): δ 5.03 (s, 1H), 7.16–7.20 (m, 2H), 7.26–7.35 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = -25.5$, 53.5 (quint), 127.6, 128.6, 128.8, 139.6.

(c) 1- ^{13}C -1,1-diiodo-2-phenylethane (1-1- ^{13}C). A solution of *n*-butyllithium (1.38 M in hexane, 1.84 mL, 2.53 mmol) was added dropwise at -105°C into a solution of ^{13}C -triodomethane¹⁹ (1.00 g, 2.53 mmol) in THF (10 mL). After the mixture was stirred for 30 min at -105°C , benzyl bromide (0.30 mL, 2.53 mmol) was added dropwise. Workup as above provided the product (0.58 g, 32%) as a colorless oil which solidified on storage at -5°C . Mp: 36°C . ^1H NMR (300 MHz, CDCl_3): δ 3.66 (dd, $^3J_{\text{H,H}} = ^2J_{\text{H,C}} = 6.8$ Hz, 2H), 5.00 (dd, $^1J_{\text{H,C}} = 171$ Hz, $^3J_{\text{H,H}} = 7.4$ Hz, 1H), 7.20–7.36 (m, 5H). ^{13}C NMR (75 MHz, CDCl_3): $\delta = -25.6$ (labeled), 54.3 (d, $^1J_{\text{C,C}} = 33.9$ Hz), 127.6, 128.7, 128.9, 139.8.

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Supporting Information Available: NMR and UV-vis spectra for the various compounds in this paper. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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