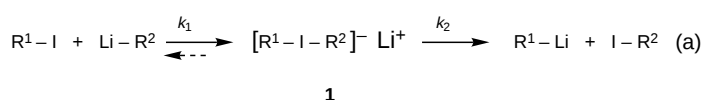


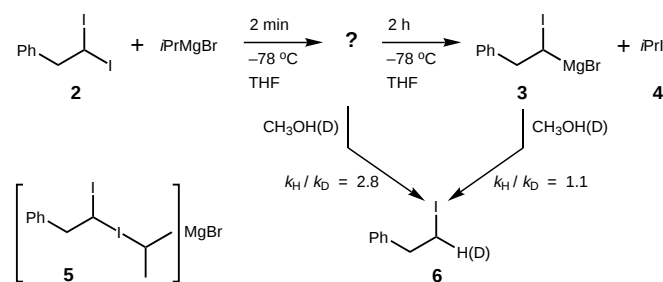
α -Iodoalkyl–Iodine–Ate Complexes as Observable Intermediates in the Iodine–Magnesium Exchange Reaction**

Volker Schulze, Mark Brönstrup, Volker P. W. Böhm, Peter Schwerdtfeger, Michael Schimeczek, and Reinhard W. Hoffmann*

Since its discovery by Wittig^[1] and Gilman,^[2] the halogen–metal exchange reaction has been the focus of mechanistic speculations:^[3] Four-center transition states,^[4] free radical chain reactions,^[5] or reaction via a halogen–ate complex^[6] have been discussed. Kinetic evidence for the formation of an intermediate—possibly the iodine–ate complex **1**—in the iodine–lithium exchange reaction [Eq. (a)] was reported by



Reich.^[7] He was subsequently able to observe spectroscopically the iodine–ate complex **1** ($\text{R}^1 = \text{R}^2 = \text{Ph}$).^[8] In parallel, Calabrese successfully crystallized an ate complex (**1**, $\text{R}^1 = \text{R}^2 = \text{C}_6\text{F}_5$) in which the lithium cation is shielded by two TMEDA ligands.^[9] We report here the direct observation of an iodine–ate complex (**5**) in the iodine–magnesium exchange reaction^[10] of 1,1-diiodoalkanes **2** (Scheme 1).



Scheme 1. Formation of the iodine–ate complex in the iodine–magnesium exchange reaction of 1,1-diiodoalkane **2**.

Treatment of **2** with isopropylmagnesium bromide for two hours at -78°C in THF provided the carbenoid **3** quantitatively, as evidenced by the formation of the iodoalkane **6** upon quenching with CH_3OH . When isopropylmagnesium bromide or diisopropylmagnesium was mixed with **2**, an intense yellow color formed immediately^[11] and faded over about two hours. We surmised that the color could be caused by the ate complex **5**. Hints as to the nature of the species responsible for the color can be attained by comparing the kinetics of the

decay in color with the time dependence of other observables of the system: Low-temperature UV/Vis spectroscopy of a 0.007 M solution of **2** showed an absorption at $\lambda_{\text{max}} = 409 \text{ nm}$ after addition of one equivalent of diisopropylmagnesium. The absorption disappeared at -78°C with a pseudo-first-order rate constant of $1.2 \times 10^{-4} \text{ s}^{-1}$ (Figure 1); when two equivalents of diisopropylmagnesium were added the rate constant increased to $3.8 \times 10^{-4} \text{ s}^{-1}$.

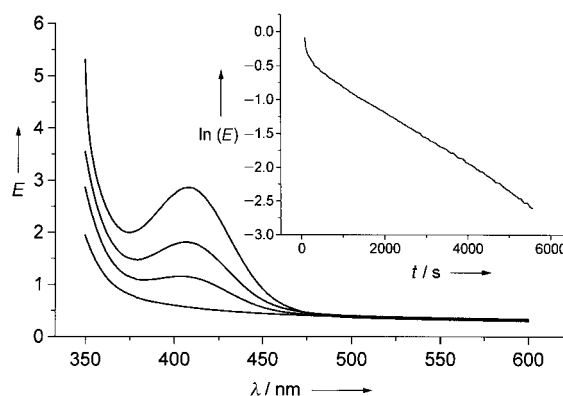


Figure 1. Time dependence of the UV/Vis spectra of the α -iodoalkyl–iodine–ate complex **5**.

Since the chromophore is the “fingerprint” of the species formed, we carried out calculations on the UV absorption expected for a model compound, the α -iodomethyl–iodine–ate anion **8**. CAS/MP2 calculations^[12] reproduced the absorption characteristics of diiodomethane reasonably well. When applied to **8**, the same calculations resulted in a predicted absorption maximum at 431 nm, which is in qualitative agreement with our findings.

Still, the question remains whether the colored species is formed stoichiometrically as an intermediate en route from **2** to **3**, or whether it is formed in substoichiometric amounts in an unrelated side reaction. No clue was obtained by quenching the yellow solution after two minutes with methanol, which resulted again in the formation of the iodoalkane **6** (97%).

A short-lived intermediate may be characterized by a competition constant by which it selects between two reaction pathways.^[13] We therefore quenched the reaction mixture with a 1:1 mixture of CH_3OH and CH_3OD . Quenching of the colorless solution after two hours showed that **3** is “protonated” with an apparent isotope effect of $k_{\text{H}}/k_{\text{D}} = 1.1$. However, quenching of the yellow solution two minutes after mixing of **2** with isopropylmagnesium bromide resulted in an apparent isotope effect of $k_{\text{H}}/k_{\text{D}} = 2.6$. This suggests that substantial amounts of a species different from **3** must be present in the yellow solution. Data for quenching at various time intervals (Figure 2) indicate that a species is initially formed which protonates with an isotope effect of about 2.8. The change in the isotope effect with time shows that this species decays with a rate constant of $4.8 \times 10^{-4} \text{ s}^{-1}$, which matches the rate of decrease in the intensity of the yellow color.

At this point we tried to characterize the intermediate by low-temperature rapid-injection ^1H NMR spectroscopy. To

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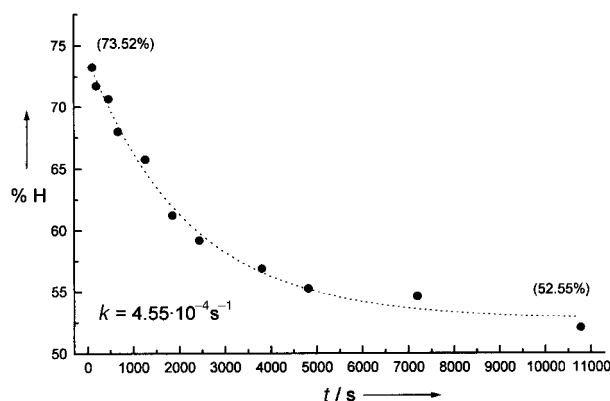


Figure 2. Proton content (%) in product **6** as a function of the time upon quenching with $\text{CH}_3\text{OH}/\text{CH}_3\text{OD}$. Conditions: 1.0 equiv of **2**, 0.8 equiv of $i\text{PrMgBr}$, THF, -78°C , $c = 0.4\text{M}$.

this end, a solution of the diiodoalkane **2** in $[\text{D}_8]\text{THF}$ was injected into a solution of diisopropylmagnesium in $[\text{D}_8]\text{THF}$ at -75°C . The ^1H NMR signals of the starting material **2** disappeared with a rate constant of $5 \times 10^{-2} \text{L mol}^{-1} \text{s}^{-1}$, whereas the signals of the (easier to observe) product **4** increased in intensity with a rate constant of $5 \times 10^{-4} \text{s}^{-1}$. This roughly 100-fold difference in rate requires the formation of an intermediate. The following ^1H NMR signals could be assigned to the intermediate: $\delta = 2.98$ (dd, $J = 12.7, 7.9 \text{ Hz}$, 1H), 3.24 (t, $J = 11.9 \text{ Hz}$, 1H), 3.45 (dd, $J = 10.4$ and 8.0 Hz , 1H).

The intensity of the signal at $\delta = 2.98$ decreased with a rate constant of $4 \times 10^{-4} \text{s}^{-1}$, which is again in line with the time dependence of the isotope effect upon quenching with methanol and with the time dependence of the decoloration. In view of the precedent set by Calabrese^[9] and Reich^[8] we feel confident that the intermediate observed is the iodine–ate complex **5**.

What is so special about the ate complex **5** that its lifetime becomes long enough to be observed under the ordinary conditions of the halogen–metal exchange reaction? The substantial stabilization has to be associated with the second iodine atom present, which helps to delocalize the negative charge. This is suggested by the results of ab initio calculations (Figure 3).^[14, 15] They indicate that the negative charge in the ate complex **7** does not reside on the hypervalent iodine atom. Instead, it is evenly distributed to the carbon atoms in **7** and unevenly distributed to the two sides in the ate complex **8**. Preliminary information on the reactivity of such ate complexes shows that electrophiles (MgX^+ , H^+) attack the ate complex **5** at the side carrying the larger part of the negative charge or, in other words, at the weaker and longer carbon–iodine bond.

The finding that iodine–ate complexes are readily protonated led us to the following experiment: When isopropylmagnesium chloride was added at -78°C to a solution containing **2** and 20 equivalents of $\text{CH}_3\text{OH}/\text{CH}_3\text{OD}$, the iodoalkane **6** was again obtained in 15% yield. Its isotope content revealed that protonation had occurred at the stage of the ate complex **5** and not at that of the carbenoid **3**. This result challenges the notion^[20] that halogen–metal exchange reactions can be carried out to completion in the presence of

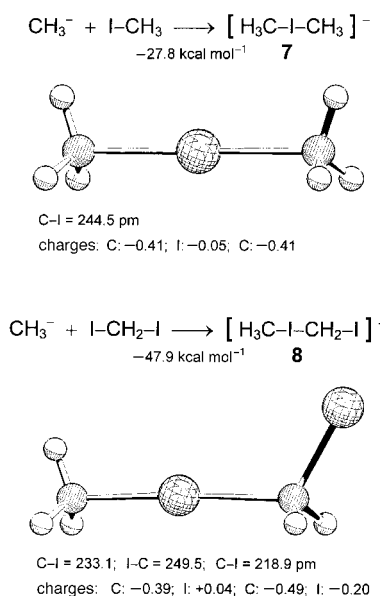


Figure 3. Calculated structures of iodine–ate complexes.

proton donors. Our findings rather suggest that completion of the halogen–metal exchange reaction is foiled under these conditions, since protonation takes place at the stage of the intermediate ate complexes.^[21] It may therefore be prudent to check which of the in situ trapping reactions or intramolecular reactions hitherto ascribed to organolithium compounds generated by halogen–metal exchange reactions are actually reactions of organolithium compounds and which are rather caused by halogen–ate complexes.^[22]

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- [1] G. Wittig, U. Pockels, H. Dröge, *Ber. Dtsch. Chem. Ges.* **1938**, *71*, 1903–1912.
- [2] H. Gilman, W. Langham, A. L. Jacoby, *J. Am. Chem. Soc.* **1939**, *61*, 106–109.
- [3] W. F. Bailey, J. J. Patricia, *J. Organomet. Chem.* **1988**, *352*, 1–46.
- [4] J. Villiéras, *Bull. Soc. Chim. Fr.* **1967**, 1520–1532.
- [5] a) H. R. Ward, R. G. Lawler, R. A. Cooper, *J. Am. Chem. Soc.* **1969**, *91*, 746–748; b) A. R. Lepley, R. L. Landau, *ibid.* **1969**, *91*, 748–749; c) E. C. Ashby, T. N. Pham, *J. Org. Chem.* **1987**, *52*, 1291–1300.
- [6] G. Wittig, U. Schöllkopf, *Tetrahedron* **1958**, *3*, 91–93.
- [7] H. J. Reich, N. H. Phillips, I. L. Reich, *J. Am. Chem. Soc.* **1985**, *107*, 4101–4103.
- [8] a) H. J. Reich, D. P. Green, N. H. Phillips, *J. Am. Chem. Soc.* **1989**, *111*, 3444–3445; b) H. J. Reich, D. P. Green, N. H. Phillips, *ibid.* **1991**, *113*, 1414–1416.
- [9] W. B. Farnham, J. C. Calabrese, *J. Am. Chem. Soc.* **1986**, *108*, 2449–2451.
- [10] J. Villiéras, *Organomet. Chem. Rev. A* **1971**, *7*, 81–94.
- [11] This observation was made first by P. Meister in our Laboratory in 1992.
- [12] The CAS/MP2 calculation^[16] was performed with a relativistic effective core potential for iodine, which replaces the 46 core electrons.^[17] The valence basis set for iodine is (8s,8p,1d)/[6s,6p,1d]. For carbon and hydrogen we used 6-311++G(d,p) basis sets.^[18] The geometry of the model compound **8** was optimized at the MP2 level of theory with the same basis set. This was followed by a CAS/MP2

- calculation with an active space of 45 configurations. All calculations were carried out with Gaussian 94.^[19]
- [13] R. Huisgen, *Angew. Chem.* **1970**, 82, 783–820; *Angew. Chem. Int. Ed. Engl.* **1970**, 9, 751–762.
- [14] a) J. Cioslowski, P. Piskorz, M. Schimeczek, G. Boche, *J. Am. Chem. Soc.*, submitted; b) G. Boche, M. Schimeczek, J. Cioslowski, P. Piskorz, *J. Org. Chem.*, submitted.
- [15] MP2(full) with 6-31++G(d)^[18] for C and H; ECP and (4s,4p,1d)/[3s,3p,1d] for iodine. Charges quoted are AIM charges, cf. R. W. F. Bader, *Atoms in Molecules: A Quantum Theory*, Clarendon Press, Oxford **1994**.
- [16] J. J. McDouall, K. Peasley, M. A. Robb, *Chem. Phys. Lett.* **1988**, 148, 183–196.
- [17] P. Schwerdtfeger, M. Dolg, W. H. E. Schwarz, G. A. Bowmaker, P. D. W. Boyd, *J. Chem. Phys.* **1989**, 91, 1762–1774.
- [18] a) R. Krishnan, J. S. Binkley, R. Seeger, J. A. Pople, *J. Chem. Phys.* **1980**, 72, 650–654; b) T. Clark, J. Chandrasekhar, G. W. Spitznagel, P. von R. Schleyer, *J. Comp. Chem.* **1983**, 4, 294–301.
- [19] Gaussian 94 from Gaussian Inc., Pittsburgh, PA, **1995**.
- [20] a) W. F. Bailey, J. J. Patricia, T. T. Nurmi, W. Wang, *Tetrahedron Lett.* **1986**, 27, 1861–1864; b) A. Schmidt, G. Köbrich, R. W. Hoffmann, *Chem. Ber.* **1991**, 124, 1253–1258; c) P. Beak, T. J. Musick, C. Liu, T. Cooper, D. J. Gallagher, *J. Org. Chem.* **1993**, 58, 7330–7335, and references quoted.
- [21] Such a possibility was explicitly discussed for the sulfoxide–lithium exchange reaction: G. Theobald, W. H. Okamura, *Tetrahedron Lett.* **1987**, 28, 6565–6568.
- [22] This may also apply to reactions ascribed to a 1,1-dilithioalkene,^[23] as suggested by A. Maercker.^[24]
- [23] J. Barluenga, M. A. Rodriguez, P. J. Campos, *J. Am. Chem. Soc.* **1988**, 110, 5567–5568.
- [24] A. Maercker, B. Bös, *Main Group Metal Chem.* **1991**, 14, 67–71.

Stabilities of Hydrogen-Bonded Supramolecular Complexes with Various Numbers of Single Bonds: Attempts To Quantify a Dogma in Host–Guest Chemistry**

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It is generally accepted that optimal preorganization for molecular recognition requires an optimal geometric fit between convergent binding sites A(H), A'(G), B(G), B'(G), etc. of host and guest molecules H and G.^[1] If binding sites within host and/or guest are connected by single bonds, this can give rise to enthalpy or strain penalties if a transoid fragment must convert into a *gauche* conformation for an optimal orientation of binding sites. At the same time the presence of freely rotatable single bonds can lead to a loss of rotational freedom on complexation, which is generally regarded as a major drawback of, for instance, open-chain versus macrocyclic receptors. However, systematic analyses of complexes with crown and open-chain poly(ethylene glycol)

ethers show that the formation of macrocyclic hosts is based to a large degree on enthalpy advantages (macrocyclic effect).^[2]

Entropic contributions to the formation of noncovalent bonds are one of the most often invoked problems in molecular recognition, and until now they were among the least predictable factors. Systematic analyses of free energies of association ΔG_{cplx} of many supramolecular associations show little dependence of ΔG_{cplx} on the presence of single bonds in either host or guest molecule, and $\Delta\Delta G_{\text{cplx}}$ contributions from the different binding sites are generally additive.^[3] However, most of the investigated complexes were constructed so as to avoid the presence of many freely rotatable bonds. This also holds for the few studies of noncovalent intramolecular interactions, which also show little strengthening upon rigidification of the underlying frameworks.^[4] In the gas phase one expects rotational entropy contributions ΔS_{rot} of 13–21 J mol^{−1} K^{−1} per single bond.^[5, 6] If the rotations were completely frozen upon complex formation, which is expected only if rigid covalent bonds are formed,^[6] the corresponding loss of free energy $\Delta\Delta G_{\text{rot}}$ would be 3.9–6.4 kJ mol^{−1} at room temperature. For noncovalent interactions Williams et al. assume a value between 2 and 6 kJ mol^{−1} per restricted bond.^[7]

Unfortunately these numbers translate into a large uncertainty of prediction. The presence of only two nonrestricted bonds^[8] in host and guest would correspond to differences in the association constant K of between 2 and 11 M^{−1}. Therefore, it seems to be essential to obtain experimental values for the change of free energy ΔG_{cplx} associated with the presence of single bonds in host–guest complexes. Surprisingly, there were no studies till now in which the number of single bonds in supramolecular complexes was systematically varied. We chose a series of α,ω -diamides as hydrogen-bond donors^[9] and α,ω -dicarboxylates as acceptors.^[10] The tetrabutylammonium salts of the latter are soluble in chloroform. The functional groups were connected by spacers of different length and flexibility (Scheme 1). The advantage of these chloroform-soluble compounds is that interactions other than hydrogen bonds are suppressed, and problems in the measurements, such as self-association and salt effects, are minimized.

The initially prepared amides of long-chain fatty acids were only sparingly soluble in chloroform, probably owing to strong dispersive interactions between the alkyl chains in the solid state. Therefore, derivatives with the bulky and more spherical adamantyl group were prepared from the corresponding adamantyl acid chloride and, as expected, were sufficiently soluble in chloroform. Dilution experiments with these amides in CDCl₃ in which the chemical shift of the NH protons was monitored gave dimerization constants $K < 30 \text{ M}^{-1}$, so that at least 85 % of the monomer was present in the observed concentration range ($\leq 5 \times 10^{-3} \text{ M}$). Equilibrium constants were determined according to ref. [11] and gave a satisfactory fit to a 1:1 model for the association between host and guest monomers (e.g., Figure 1). The spacers were chosen to allow contact between the corresponding binding sites without buildup of substantial strain; this was checked by computer-aided molecular modeling (Figure 2). All amide groups and the alkyl chains can retain their transoid

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