Reactions of Unsaturated Compounds with Iodine and Bromine on γ Alumina

Richard M. Pagni,* George W. Kabalka,* Richard Boothe, Kevan Gaetano, Lyman J. Stewart, Richard Conaway, Christopher Dial, Donna Gray, Steven Larson, and Teresa Luidhardt

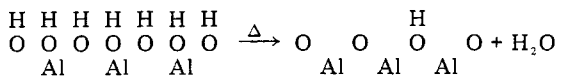
Department of Chemistry, University of Tennessee, Knoxville, Tennessee 37996-1600

Received March 8, 1988

Iodine reacts with a diverse group of unsaturated substrates in the presence of dehydrated alumina. Aromatic substrates, for example, are iodinated at room temperature by electrophilic aromatic substitution. The yields of the iodinated products can be improved dramatically by running the reaction at 110 °C. Aniline, even at 100 °C, is unreactive, presumably because its nitrogen lone pair is complexed to surface aluminum cations or protons. Alkenes react readily with HI, formed in the reaction of surface hydroxyls with I_2, to form alkyl iodides by an ionic mechanism involving carbocations. This is an excellent method for the synthesis of alkyl iodides from alkenes. Alkynes, on the other hand, add I_2 (stereospecific, anti) under very mild conditions to form vinyl diiodides in excellent yield. The behavior of Br_2 with cyclohexene on alumina is considerably different than that of I_2 with cyclohexene. Two products are formed: *trans*-1,2-dibromocyclohexane (1), which is formed in solution during workup, and *trans*-1-bromo-2-chlorocyclohexane (2), which is formed on the surface. The chlorine in 2 arises from intrinsic chloride already on the alumina and CCl_4, the solvent used to adsorb Br_2 onto alumina. Further experiments demonstrate that cyclohexene undergoes intergranular hopping, but that Br_2 does not.

Synthetic chemists continue to explore new methods to carry out chemical transformations. One of these new methods is to run reactions on the surfaces of solids. As the surfaces have properties that are not duplicated in the solution or gas phase, entirely new chemistry may occur. Even in the absence of new chemistry, a surface reaction may be more desirable than a solution counterpart because the reaction is more convenient to run or a higher yield of product is attained. For these reasons, synthetic surface organic chemistry is today a rapidly growing field of study.

Several classes of solids have commonly been used for surface organic chemistry including aluminas, silica gels, zeolites, and clays.[1] γ alumina (γ-Al_2O_3), the material used commonly for column chromatography, is certainly one of the most interesting of these solids because it has surface properties that suggest that a very rich organic chemistry may occur there. According to the widely discussed theories of Peri[2] and Knözinger and Ratmasamy,[3] dehydrated alumina, which is generated by heating the solid, will have on its surface partially exposed oxide anions, which may function as bases or nucleophiles in organic reactions, partially exposed aluminum cations, which may function as Lewis acids, and hydroxyl groups of varying Brønsted activity, the number of which depends on the temperature of the dehydration.



We report that all these properties—and others—manifest themselves in the chemistry of iodine and bromine with unsaturated organic substrates on alumina and that many of the resulting transformations are not only synthetically useful but have distinct advantages over solution counterparts.

Results and Discussion

Chemistry of Aromatic Substrates with Iodine on Alumina.[4] If the hypothesis is correct concerning the chemical behavior of the surface components, the partially exposed aluminum cations will catalyze electrophilic substitution reactions. Indeed benzene reacts with bromine on alumina to form bromobenzene.[5] There are many ways to brominate benzene but very few to iodinate benzene, especially using molecular iodine, because iodine is a weak electrophile and the desired reaction is reversible. Dehydrated alumina should facilitate this reaction because the aluminum ions will polarize and activate the electrophilic iodine, and the basic oxide anions will react irreversibly with the liberated hydrogen iodide, thus driving the desired reaction toward the product side (eq 1 and 2). Furthermore, another electrophile may be present which will also iodinate the benzene ring, and that is OI^-, which may be generated in the reactions: $O^{2-} + I_2 \rightarrow OI^- + I^-$ or OH^- (surface hydroxyl) + $I_2 \rightarrow OI^-$ + HI. This latter reaction is reasonable because experiments to be described later clearly show that HI is liberated when the alumina surface is contacted with I_2. Thus, the iodination of aromatic substrates using I_2 on alumina was attempted.

$$C_6H_6 + I_2 \rightleftharpoons C_6H_5I + HI \quad (1)$$

$$O^{2-} + HI \rightarrow OH^- + I^- \quad (2)$$

The iodination reactions, the results of which are summarized in Table I, were run in two ways: (1) the solid or dry method in which I_2 on one batch of alumina is mixed with a second batch of alumina containing the aromatic substrate and (2) the solution method in which I_2 and excess liquid aromatic substrate are slurried with alumina. To make comparisons easy, most reactions were run at room temperature for 20 h.

The results in general are those expected for the reactions proceeding by electrophilic aromatic substitution, with activated benzenes yielding largely *o*- and *p*-iodobenzenes, naphthalene giving 1-iodonaphthalene, exclusively, and, depending on reaction conditions, azulene

(1) For reviews on surface organic chemistry, see: (a) Posner, G. H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 487. (b) McKillop, A.; Young, D. W. *Synthesis* **1979**, 401 and 481. (c) Cornelis, A.; Laszlo, P. *Synthesis* **1985**, 909. (d) Laszlo, P. *Acc. Chem. Res.* **1986**, *19*, 121. (e) Cornelis, A.; Laszlo, P. In *Chemical Reactions in Organic and Inorganic Constrained Systems*; Setton, R., Ed.; Reidel: Dordrecht, 1986; p 212. (f) Laszlo, P. *Science (Washington, D.C.)* **1987**, *235*, 1473.

(2) Peri, J. B. *J. Phys. Chem.* **1965**, *69*, 220.

(3) Knözinger, H.; Ratmasamy, P. *Catal. Rev. Sci. Eng.* **1978**, *17*, 31.

(4) Some of this work has appeared in preliminary form: Boothe, R.; Dial, C.; Conaway, R.; Pagni, R. M.; Kabalka, G. W. *Tetrahedron Lett.* **1986**, *27*, 2207. See also ref 8.

(5) Gaetano, K., unpublished results.

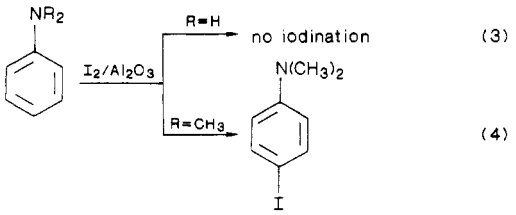
0022-3263/88/1953-4477$01.50/0

Table I. Iodination of Aromatic Substrates Using I_2/Al_2O_3[a]

substrate	relative product distribution	% yield[b] solid method	% yield[b] solution method
benzene	iodobenzene	4.6 (26)	7.7 (8.4)
toluene	o-, m-, p-iodotoluene (32:4:64)	7.2 (8)	36 (37)
phenol	o-, p-iodophenol (50:50)	8	
anisole	o-, m-, p-iodoanisole (41:14:45) + iodophenols[c]	5	50
aniline	no iodoanilines[d]		
acetanilide	cleaved to aniline		
N,N-dimethylaniline	p-iodo-N,N-dimethylaniline	45	
bromobenzene	no reaction		
iodobenzene	no reaction		
naphthalene	1-iodonaphthalene	10	
azulene	1-iodoazulene[e]	7	
azulene	1,3-diiodoazulene[f]	100	
azulene	1-iodo-, 1,3-diiodoazulene[g] (91:9)	80	

[a] Reactions were run at room temperature for 20 h unless otherwise indicated. Al_2O_3 was heated at 400 °C for 20 h under vacuum before use. [b] The numbers in parentheses are yields corrected for unreacted I_2. [c] The distribution of iodophenols was not determined. [d] At 100 °C nitrobenzene and azobenzene are produced in a 3 to 1 ratio. [e] Excess azulene was used. [f] Excess iodine was used. [g] The reaction was run at 100 °C with excess azulene.

affording 1-iodoazulene or 1,3-diiodoazulene. There were, however, several complications and anomalies. For example, anisole not only underwent electrophilic iodination but also ether cleavage to form phenol.[6] The amide bond in acetanilide was also cleaved. Most surprisingly, aniline was unreactive with I_2 (eq 3), even at 100 °C where only oxidation to nitrobenzene and azobenzene was observed. Apparently, aniline is deactivated toward electrophilic aromatic substitution by reaction of its basic nitrogen with surface aluminum cations or HI generated in the reaction of surface hydroxyls with I_2. By way of contrast, N,N-dimethylaniline, whose nitrogen is sterically inhibited in its reaction with Al^{3+} or HI, reacted smoothly with I_2 to form 4-iodo-N,N-dimethylaniline (eq 4).



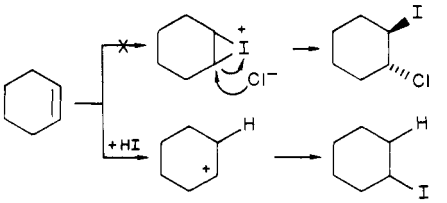
(3)

(4)

Several of the reactions, especially those involving aromatic hydrocarbons, appear to be viable, synthetically useful procedures for making iodoarenes. In order to see if the yields of products could be improved, the effect of Al_2O_3 dehydration time and reaction temperature on the standard benzene-plus-iodine reaction was explored. Not surprisingly, no reaction occurs in the absence of Al_2O_3 activation but, even after extensive dehydration at 400 °C, no iodination is observed. Only after at least 28% of the total water has been driven from the surface are catalytic sites exposed and the reaction commences. Apparently there is considerable physisorbed water on the alumina which must be driven from the surface before adjacent hydroxyls on the top layer of the surface react to form water, which, when driven from the surface, expose the catalytic sites. Above the 28% level, the yield of product goes up as the amount of water driven from the surface goes up.

As expected, temperature has a large effect on the yield of product in the benzene/I_2 reaction. For reactions run identically except for temperature, the yield of iodobenzene varied from 0% for a reaction run at 0 °C to 26% for a reaction run at 110 °C. Clearly the best results, at least for arenes, will occur when the iodination reaction is run using highly activated alumina at temperatures in excess of 100 °C. For highly reactive substrates such as azulene, however, much less stringent reaction conditions are required.

Chemistry of Alkenes with I_2 on Alumina.[7] On the basis of the chemistry of bromine with alkenes on alumina to be described later, a mixture of cyclohexene in petroleum ether (bp 35–36 °C) and iodine was refluxed with dehydrated alumina containing adsorbed sodium chloride. The reaction was expected to yield *trans*-1-chloro-2-iodocyclohexane via backside attack of chloride anion on the intermediate cyclic iodonium ion (eq 5). This did not occur; iodocyclohexane was formed instead (eq 6). It appears that cyclohexene reacts with HI, which is generated in the reaction of surface hydroxyls with I_2.



(5)

(6)

As shown in Table II, the addition of HI to alkenes with I_2 on alumina (I_2/Al_2O_3) is quite general and does not require NaCl. A variety of acyclic and cyclic alkenes affords the corresponding alkyl iodides in moderate to good yield. The yields undoubtedly can be improved. Norbornene, even in refluxing cyclohexane (bp 81 °C), and *trans*-stilbene do not add HI, however, apparently for steric reasons. Styrene does not add HI but instead polymerizes.

The surface of alumina is critical to the reaction. Although these reactions occur on unactivated, out-of-the-bottle alumina, higher yields of products are formed on the activated solid. Surprisingly these reactions do not occur on hydrated or dehydrated silica gel. The reaction of the alkenes with HI only occurs on the surface. When cyclohexene is treated with a solution of I_2 in petroleum ether (bp 35–36 °C), which had previously been refluxed

(6) Attempts to cleave aryl methyl ethers with I_2/Al_2O_3 without simultaneously iodinating the aryl ring have yielded discouraging results. Diethyl ether is cleaved rapidly by I_2/Al_2O_3, but a complex mixture of products results. One clearly cannot use ethers as solvents in reactions involving I_2/Al_2O_3.

(7) Some of this work has appeared in preliminary form: Stewart, L. J.; Gray, D.; Pagni, R. M.; Kabalka, G. W. *Tetrahedron Lett.* **1987**, *28*, 4497. See also ref 8.

(8) Pagni, R. M.; Kabalka, G. W.; Boothe, R.; Gaetano, K.; Stewart, L. J. In *Physical Organic Chemistry* **1986**; Kobayashi, M., Ed.; Elsevier: Amsterdam, 1987; p 399.

Table II. Reaction of Alkenes with I_2 on Al_2O_3 and SiO_2[a]

reactant	metal oxide used[b]	iodinated product	% yield of alkyl iodide (reaction time, h)
cyclopentene	activated Al_2O_3	cyclopentyl iodide	42 (1.75)
cyclohexene	activated Al_2O_3	cyclohexyl iodide	85 (2)
cyclohexene	unactivated Al_2O_3	cyclohexyl iodide	39 (2)
cyclohexene	unactivated Al_2O_3	cyclohexyl iodide	76 (3)
cyclohexene	unactivated SiO_2	none[c]	0 (2)
cyclohexene	activated SiO_2	none[c]	0 (2)
cycloheptene	activated Al_2O_3	cycloheptyl iodide	49 (6)
cyclooctene	activated Al_2O_3	cyclooctyl iodide	36 (32.5)
1-octene	activated Al_2O_3	2-iodooctane	83 (2)
3,3-dimethyl-1-butene	activated Al_2O_3	2,3-dimethyl-2-iodobutane	30 (2)
2,3-dimethyl-2-butene	activated Al_2O_3	2,3-dimethyl-2-iodobutene	36 (2)
norbornene	activated Al_2O_3	none	0 (6)
norbornene	activated Al_2O_3	none in refluxing cyclohexane	0 (4)
trans-stilbene	activated Al_2O_3	none	0 (4)
styrene	activated Al_2O_3	none, polymer forms instead	0 (4)

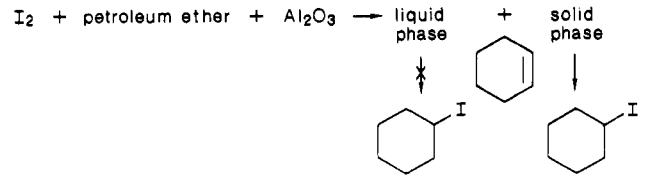
[a] Reactions were run in refluxing low-boiling petroleum ether (35–36 °C) unless otherwise noted. [b] The solids were activated by heating at 400 °C under vacuum for at least 20 h. [c] There is evidence that 1,2-diiodocyclohexane is formed in this reaction.

Table III. Reaction of Alkynes with I_2/Al_2O_3[a]

alkyne	reaction conditions	product (yield, %)
1-hexyne	reflux, 4 h	(*E*)-1,2-diiodo-1-hexene (86)
1-hexyne	rt,[b] 4 h	(*E*)-1,2-diiodo-1-hexene (92)
1-hexyne	rt,[b] 12 h, no Al_2O_3	(*E*)-1,2-diiodo-1-hexene (trace)
3-hexyne	reflux, 2 h	(*E*)-3,4-diiodo-3-hexene (97)
phenylacetylene	reflux, 2 h	(*E*)-α,β-diiodostyrene (96)
5-chloro-1-pentyne	reflux, 2 h	(*E*)-5-chloro-1,2-diiodo-1-pentene (82)
3-hydroxypropyne	reflux, 5 h	(*E*)-α,β-diiodoallyl alcohol (84)
propiolic acid	reflux, 24 h	(*E*)-2,3-diiodoacrylic acid (23)
dimethyl acetylenedicarboxylate	reflux, 2 h	dimethyl diiodofumarate (50)

[a] Reactions were run in low-boiling petroleum ether using activated alumina (400 °C for 2 h under vacuum). [b] rt = room temperature.

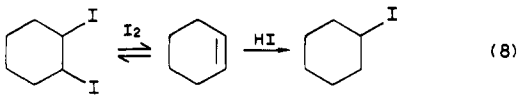
with dehydrated Al_2O_3, no iodocyclohexane is generated (eq 7). Had HI diffused into petroleum ether, iodo-



(7)

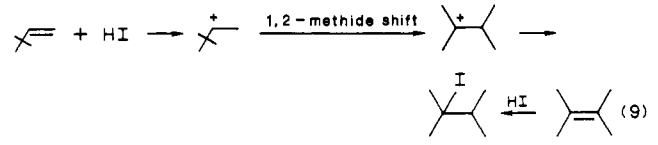
cyclohexane would have been formed in this experiment. By the same token, when a solution of cyclohexene in petroleum ether (bp 35–36 °C) is refluxed for 2 h with the dehydrated Al_2O_3 from the above experiment, iodocyclohexane is formed in 38% yield.

The facile addition of I_2 to the alkenes easily competes with the addition of HI but, because the addition of I_2 is reversible and the addition of HI is not, ultimately all of the alkene molecules afford the HI addition product (eq 8). The addition of HI occurs by an ionic mechanism



(8)

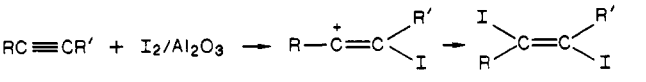
involving carbocations (eq 6): 3,3-dimethyl-1-butene affords the rearranged 2,3-dimethyl-2-iodobutane (eq 9), for example.



(9)

In conclusion, the ease with which this reaction can be run, even on unactivated alumina, make this procedure an attractive method for the preparation of alkyl iodides from alkenes.

Chemistry of Alkynes with I_2 on Alumina.[9] Unlike alkenes, which react reversibly with I_2, alkynes are known to react in solution irreversibly with I_2 to form (*E*)-1,2-diiodoalkenes, perhaps by a free-radical mechanism.[10,11] This reaction also occurs under very mild conditions on dehydrated Al_2O_3 to afford (*E*)-diiodoalkenes in synthetically useful yields (Table III). Because the addition reactions does not occur in the nonpolar petroleum ether (bp 35–36 °C) in the absence of alumina, whose surface is polar, and because electron-withdrawing groups on the alkyne retard the reaction, the surface reaction undoubtedly occurs by an ionic mechanism (eq 10).



(10)

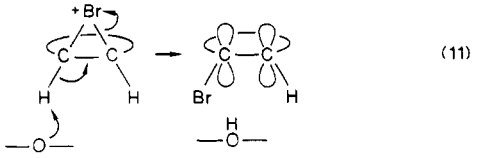
Bromination of Cyclohexene on Alumina. Because the chemistry of I_2 on Al_2O_3 with a variety of unsaturated compounds proved to be interesting and synthetically useful in many cases, the chemistry of Br_2 with cyclohexene was explored. Unlike the previous reactions with I_2/Al_2O_3, where no chemistry occurs in the absence of the solid, the bromination of alkenes, of course, occurs readily in solution to yield vicinyl dibromoalkanes by the anti addition of the two bromine atoms. If the surface bromination were to yield the same product as in solution, there is no advantage in running the surface reaction. If, on the other hand, the

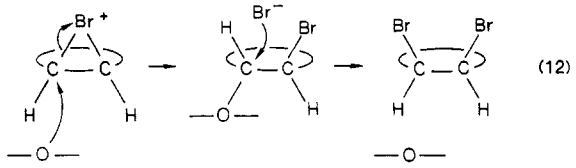
(9) Some of this work has appeared in preliminary form: Larson, S.; Luidhardt, T.; Kabalka, G. W.; Pagni, R. M. *Tetrahedron Lett.* **1985**, *26*, 35.

(10) Hollins, R. A.; Campos, M. P. A. *J. Org. Chem.* **1979**, *22*, 3931.

(11) Heasley, V. L.; Shellhamer, D. F.; Heasley, L. E.; Yaeger, D. B.; Heasley, G. E. *J. Org. Chem.* **1980**, *45*, 4649.

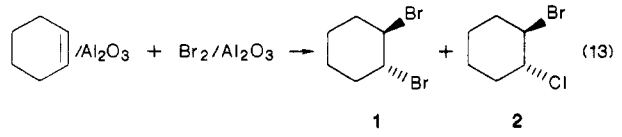
surface reaction were to yield products that are not observed in solution, e.g. vinyl bromides or *cis*-dibromides as shown in eq 11 and 12, the reactions might have synthetic utility.


(11)


(12)

The only previous example of the bromination of an alkene on a metal oxide surface was the selective bromination of styrene in a mixture of styrene and cyclohexene in carbon tetrachloride with Br_2 adsorbed in the cavity of 5A zeolite.[12] This selectivity was originally attributed to the ionic bromination of styrene inside the zeolite cavity where only styrene fits. Subsequently this reaction was shown to occur[13] by a free-radical mechanism involving low concentrations of Br_2 leached into solution.[14] Even though this reaction occurred in solution, the presence of the zeolite still affected product selectivity.

Because Br_2 and cyclohexene react with each other in solution, the surface reaction must be run in the absence of solvent. When cyclohexene adsorbed onto Al_2O_3 (cyclohexene/Al_2O_3) was mixed with Br_2/Al_2O_3, which was prepared by treating the solid with a solution of Br_2 in CCl_4, two products were formed: *trans*-1,2-dibromocyclohexane (1) and, unexpectedly, *trans*-1-bromo-2-chloro-cyclohexane (2) (eq 13).


(13)

As the dry reaction required workup with solvent (CCl_4), how can one be certain the two products are formed on the alumina and not during workup? Two experiments resolved this question.

When Br_2/Al_2O_3, prepared from a solution of Br_2 in CCl_4, was first slurried in CCl_4 and then the solid removed by filtration, the resulting solution yielded the dibromide 1, exclusively, when treated with cyclohexene. Thus, 1 may be formed on workup by extraction of Br_2 and cyclohexene into solution where they react rapidly with one another. Because the bromo chloride 2 was not formed in this experiment, it must form on the alumina surface. These ideas were supported by an additional experiment.

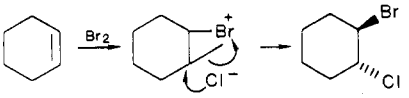
If 2 were formed on the surface and 1 on workup, the 2 to 1 ratio will increase as the time between reaction commencement and workup increases. As the reaction time increases, the amount of Br_2 and cyclohexene on the surface will decrease because of their reaction to form 2. On workup there will be less cyclohexene and Br_2 available to extract into solution and react to form 1. This is what is observed. For two reactions run identically except for the time the reactants were on the surface, the 2 to 1 ratio varied from 0.58:1 at 1 h to 99:1 at 24 h.

Table IV. Comparison of the Distribution of 1 and 2 for Br_2-CCl_4/Al_2O_3 and Br_2-Et_2O/Al_2O_3

reaction mixture[a-c]	reactn time, h	rel yield, % 2	1
15 g of Br_2-CCl_4/Al_2O_3+ 15 g of cyclohexene/Al_2O_3	1	45	55
	2	45	55
	4	59	41
15 g of Br_2-ether/Al_2O_3 + 15 g of cyclohexene/Al_2O_3	1	8	92
	2	19	81
	4	36	64

[a] Br_2 was adsorbed at a concentration of 3.4×10^{-5} mol per gram of Al_2O_3 and was dissolved in 5 mL of either CCl_4 or ether for adsorption. The solvent was not removed before reaction. [b] Cyclohexene was adsorbed at a concentration of 6×10^{-4} mol per gram of Al_2O_3. [c] Reactions were performed at room temperature.

Where does the chlorine in 2 arise? A logical choice is Cl^- (eq 14), generated in the reaction of CCl_4, the solvent used to absorb Br_2 onto the solid, with surface oxide, i.e. $O^{-2} + CCl_4 \rightarrow Cl^- + OCCl_3^-$.


(14)

If the chlorine in 2 arises form Cl^-, running the bromination reaction on alumina containing adsorbed NaCl should increase the ratio of 2 to 1, and this is observed. Furthermore, if CCl_4 is the source of Cl^- by its reaction with oxide, there will be an increase in the weight of the solid when Al_2O_3 is first contacted with CCl_4 and then dried under vacuum, and this is also observed.[15]

A second source of chlorine in 2 is the alumina itself. Analysis provided by the manufacturer (Fisher Scientific) showed that there are 0.03 mequiv of chlorine/gram of Al_2O_3. To prove that this chlorine is also reactive in the bromination of cyclohexene, a reaction was performed on a mixture of Br_2/Al_2O_3, prepared from a solution of Br_2 in ethyl ether (Br_2-Et_2O/Al_2O_3), and cyclohexane/Al_2O_3. For comparison, the reaction of Br_2-CCl_4/Al_2O_3 with cyclohexene/Al_2O_3 was also performed. The results are summarized in Table IV. These data show unambiguously that the intrinsic chlorine is available for the formation of 2. Moreover, the data show that the amount of 2 increases as a function of time, as one would expect if 2 is formed on the surface and 1 in solution during workup. Not surprisingly the amount of 2 is greater when Br_2-CCl_4/Al_2O_3 is used, because now Cl^- arises from two sources.

Because of the way in which the reaction is run, one or more of the reactants must hop to a grain of alumina containing its reaction partners for 2 to be formed. It is possible to deduce the intergranular mobility of Br_2, Cl^-, and cyclohexene on alumina from a very simple experiment. As already noted, adsorbing NaCl onto Br_2-CCl_4/Al_2O_3 increases the ratio of 2 to 1, specifically from 1.45:1 to 8:1 for a given reaction time. If the reaction is run identically except that NaCl is now adsorbed onto cyclohexene/Al_2O_3, the ratio of 2 to 1 remains at 1.45:1. Had Cl^- been very mobile, the ratio of 2 to 1 would have been the same in both cases. More revealing, however, is the relative mobility of Br_2 and cyclohexene on alumina.

(12) Risbood, P. A.; Ruthren, D. M. *J. Am. Chem. Soc.* **1978**, *100*, 4919.
(13) Dessau, R. M. *J. Am. Chem. Soc.* **1979**, *101*, 1344.
(14) There are several bromination reactions not involving alkenes that occur on metal oxide surfaces. See (a) Onaka, M.; Izumi, Y. *Chem. Lett.* **1984**, 2007 and references cited therein. (b) Guillemin, J. C.; Denis, J. M.; *Synthesis* **1985**, 1131. (c) Smith, K.; Batters, M. *Synthesis* **1985**, 1157. (d) Mistry, A. G.; Smith, K.; Bye, M. R. *Tetrahedron Lett.* **1986**, *27*, 1051.
(15) The weight increase corresponds to 3.5×10^{20} molecules of CCl_4/gram of Al_2O_3.

When the NaCl is on Br_2–CCl_4/Al_2O_3, the ratio of **2** to **1** goes up but when the added Cl^- is on cyclohexene/Al_2O_3 the ratio is not affected. This will only occur if cyclohexene hops to the grains containing Br_2 and Cl^-, where reaction occurs. Br_2 must be immobile or the ratio of **2** to **1** would have also been altered in the experiment where NaCl was adsorbed on the cyclohexene/Al_2O_3 grains.

It is clear that the reaction of Br_2 with cyclohexene on alumina is currently not synthetically useful. The results demonstrate, nonetheless, that it is possible to perform reactions on surfaces between components that are very reactive with one another in solution and that the products can be different in the two media.

Experimental Section

Analytical Techniques. Nuclear magnetic resonance spectra were recorded at 60 and 200 MHz in acetone-d_6 and $CDCl_3$ with tetramethylsilane as internal standard. Gas chromatography was performed on a 12-ft × $^1/_4$-in. column packed with 15% SE-30 by weight on Chromosorb W as the solid support; He was employed as the carrier gas. The gas chromatographs were calibrated (for yield determination) with known mixtures of the substrates and an internal standard.

Preparation and Characterization of Dehydrated Alumina. Brockmann activity grade 1 neutral alumina (Fisher Scientific Co.) was employed in all reactions. This material has a surface area of 155 m^2/g; water slurried with the solid has pH 7.0. The alumina was dehydrated at 400 °C under vacuum (<6 × 10^{-3} mm) for 20 h as reported earlier.[16] The dehydrated solid has a surface area of 300 m^2/g.[16] Water (50 mL) slurried with 30 g of the solid had pH 5.23 and pCl 1.00, while the water itself had pH 6.63 and pCl 3.15.[17]

Reaction of Arenes with I_2 on Dehydrated Alumina. When the arene and I_2 were treated by the solid method, a solution of I_2 in the liquid arene was added to the dehydrated alumina through a dropping funnel. To insure even adsorption of the compounds, the alumina was shaken with a vibramixer during the adsorption process. When the arene was a solid, it and I_2 were added to the alumina in a small amount of benzene. Because benzene also reacts with I_2 under these conditions, the yield of iodoarene is diminished. When the reaction was complete, the compounds were removed from the solid by Soxlet extraction, often with the arene itself or diethyl ether. The organic layer was extracted with aqueous $Na_2S_2O_3$ to remove unreacted I_2, dried over anhydrous $MgSO_4$, and analyzed by GC, GC/MS, or column chromatography. All products were compared by GC, GC/MS, and NMR to authentic materials. A typical procedure follows.

N,N-Dimethylaniline was adsorbed onto dehydrated alumina at a concentration of 6 × 10^{-4} mol of *N,N*-dimethylaniline/gram of Al_2O_3, and I_2 in *N,N*-dimethylaniline was adsorbed onto alumina at a concentration of 1 × 10^{-5} mol of I_2/gram of Al_2O_3. The *N,N*-dimethylaniline used to dissolve the I_2 was not removed; thus the I_2/Al_2O_3 had *N,N*-dimethylaniline adsorbed at a concentration of 3.9 × 10^{-4} mol/gram of Al_2O_3. The aniline/Al_2O_3 (10 g) was mixed with 50 g of I_2/Al_2O_3 and allowed to stand at room temperature for 20 h. The alumina was then extracted with 100 mL of diethyl ether. The ether was collected, extracted with aqueous $Na_2S_2O_3$, dried over $MgSO_4$, and removed by rotoevaporation. The resulting liquid was analyzed by ^1H NMR spectroscopy and MS and found to contain two compounds. One compound was identified as *N,N*-dimethylaniline, and the other, identified by comparison to a known sample, as *p*-iodo-*N,N*-dimethylaniline. The known *p*-iodo-*N,N*-dimethylaniline was synthesized from *N,N*-dimethylaniline via the method of Brewster.[18] The yield of product was determined by GC.

In a typical solution reaction 0.147 g of I_2 dissolved in 50 mL of aromatic substrate was stirred with 20 g of Al_2O_3 for 20 h at room temperature. Workup and analysis were similar to what is described above.

Effect of Al_2O_3 Activation Time on the Reaction of Benzene and Iodine. Benzene was adsorbed onto 50 g of the alumina, which had been dehydrated at 400 °C for 1 h,[16] at a concentration of 6 × 10^{-4} mol of benzene/gram of Al_2O_3. I_2 in 10 mL of benzene was adsorbed onto another 100 g of the dehydrated alumina to give a concentration of 1 × 10^{-5} mol of I_2/gram of Al_2O_3. Ten grams of benzene/Al_2O_3 was mixed with 100 g of I_2/Al_2O_3, and the mixture allowed to stand for 20 h at room temperature. After 20 h, the alumina was extracted with 100 mL of diethyl ether. The ether was collected, dried over $MgSO_4$, and concentrated by rotoevaporation. To the resulting liquid was added 0.005 mL of 3-iodoanisole as internal standard, and, following calibration of the gc column with known samples of iodobenzene and 3-iodoanisole, GC was performed on the sample at 120 °C. No iodobenzene was produced. This procedure was then repeated with alumina, which had been dehydrated for 2, 5, 17, 24, and 48 h, with 0%, 0%, 2.5%, 6.3%, and 7.0% iodobenzene being generated, respectively.

50-g batches of alumina were also heated at 400 °C under vacuum (<6 × 10^{-3} mmHg) for various times, and the water was collected and weighed as previously described.[16] The following results [time (h), grams of H_2O/50 grams of Al_2O_3] were obtained: 1, 0.10; 3, 0.22; 6, 0.32; 19, 0.68; 24, 0.83; and 40, 1.13.

Effect of Reaction Temperature on the Reaction of Benzene and I_2. Benzene was adsorbed onto 50 g of alumina, which had been dehydrated at 400 °C for 20 h,[16] at a concentration of 6 × 10^{-4} mol of benzene/gram of Al_2O_3, and I_2 dissolved in 10 mL of benzene was adsorbed onto another 150 g of dehydrated solid at a concentration of 1 × 10^{-5} mol of I_2/gram of Al_2O_3. Four batches of 10 g of benzene/Al_2O_3 and 50 g of I_2/Al_2O_3 were prepared and mixed, and each batch was allowed to react for 20 h, one at 0 °C, one at 22 °C, another at 65 °C, and the fourth at 110 °C. After 20 h each alumina mixture was extracted with 100 mL of diethyl ether. Workup and analysis, as previously described, yielded the following results (temperature, percent yield of iodobenzene): 0 °C, 0%; 22 °C, 4.7%; 65 °C, 18%; and 110 °C, 26%.

Reaction of Alkenes with I_2. In a typical reaction, a mixture of 3.87 g (56.8 mmol) of cyclopentene and 16.5 g (65 mmol) of I_2 in 120 mL of petroleum ether (bp 35–36 °C, distilled) was refluxed for 2 h with 50 g of dehydrated alumina (400 °C, 2 h under vacuum). After removal of the solid, the organic phase was washed with aqueous $Na_2S_2O_3$, dried, concentrated by distillation, and analyzed by GC. Authentic cyclopentyl iodide was prepared by treating cyclopentanol with PI_3.

Reactions on unactivated alumina, activated and unactivated silica gel (chromatography grade), and without alumina were carried out as described above. Silica gel was activated by heating at 400 °C for 20 h under vacuum.[16]

Reaction of Alkynes with I_2. The reactions were run in petroleum ether as described in the previous section. All products were identical with known compounds.

Preparation of Bromine-Adsorbed Alumina. A solution of Br_2 in CCl_4 was added to dehydrated alumina under vacuum. Because the adsorption is extremely exothermic, the solid must be cooled to room temperature before adsorption begins. After the addition, the alumina is again cooled to room temperature and the CCl_4 removed on a rotoevaporator. A similar procedure was used to prepare Br_2–ether/Al_2O_3.

Preparation of Olefin-Adsorbed Alumina. The olefin was added to dehydrated alumina under vacuum and shaken to allow complete mixing.

Reaction of Cyclohexene/Al_2O_3 with Br_2/Al_2O_3. The brominated alumina was mixed with olefin-adsorbed alumina by using a vibramixer. At the end of the reaction time, the mixture was extracted with carbon tetrachloride and filtered through a fritted-glass funnel.

Gas chromatography of the solution at 140 °C yielded two compounds with retention times of 8.9 and 12.3 min. The slower moving compound was collected and identified as *trans*-1,2-bromocyclohexane (**1**) by comparison with an authentic sample.

The faster moving compound, which was identified as *trans*-1-bromo-2-chlorocyclohexane (**2**), had the following properties: mass spectrum, *m/e* (relative intensity) 196 (3), 198 (5); ^1H NMR δ 1.44–2.00 (m, 6 H, CH_2), 2.07–2.50 (m, 2 H, CH_2), 4.10–4.26 (m, 2 H, CH); ^{13}C NMR (proton decoupled) δ 22.57, 23.36, 32.81, 33.33, 55.49, and 62.91. Single frequency off resonance decoupled ^{13}C

(16) Gaetano, K.; Pagni, R. M.; Kabalka, G. W.; Bridwell, P.; Walsh, E.; Hassaneen, H. M. *J. Org. Chem.* **1981**, *46*, 1513.
(17) Boothe, R. M.S. Thesis, University of Tennessee, 1986.
(18) Brewster, R. Q. *Org. Synth.* **1931**, *11*, 62.

NMR spectrum showed that the two downfield peaks split into doublets and the four upfield peaks into triplets. Anal. Calcd for $C_6H_{10}BrCl$: C, 36.36; H, 5.44. Found: C, 36.38; H, 5.26.

The *trans*-1-bromo-2-chlorocyclohexane obtained from the surface reaction was identical with authentic material prepared by the reaction of cyclohexene with Br_2/HCl in carbon tetrachloride.

Technique Used To Determine the Br_2 Adsorption Isotherm. A standard plot of bromine concentration (in carbon tetrachloride) versus absorbance (at 410 nm) was prepared using solutions from 0.0001 to 0.01 M in Br_2. The absorbance was determined using a Bauch and Lomb Spec 21 visible spectrometer.

Brockmann activity I neutral grade alumina was dehydrated as previously described. The dehydrated alumina was transferred to an inert atmosphere and added in 20-g samples to 100-mL solutions of bromine in carbon tetrachloride. The concentrations ranged from 0.02 to 0.001 M Br_2 in carbon tetrachloride. The solutions were stoppered, and the flasks were covered with aluminum foil to avoid contact with light. After 3 days, aliquots of each solution were removed and the absorbance of Br_2 was determined. By comparing the absorbance of each solution to the standard plot of absorbance versus concentration, the equilibrium concentration of Br_2 for each sample was determined. By determining the difference between the initial and equilibrium concentrations, the amount of bromine adsorbed on alumina was determined.

A plot of p_a/V, where p_a equals the equilibrium Br_2 concentration and V equals the moles of Br_2 adsorbed per gram of Al_2O_3, versus p_a yields a straight line with a slope equal to $1/V_\infty$ and an intercept equal to $1/KV_\infty$.[19,20] Thus, V_∞, which corresponds to a monolayer coverage of Br_2, equals 3.8×10^{-5} mol of Br_2/gram of Al_2O_3 or 2.3×10^{19} molecules of Br_2/gram of Al_2O_3 and K, the equilibrium constant, is 5.2×10^2. If one eliminates one point, which deviates substantially from the straight line, one get $V_\infty = 3.7 \times 10^{-5}$ mol of Br_2/gram of Al_2O_3 and $K = 8.3 \times 10^2$ with a correlation coefficient of 0.994. Most reactions were run with Br_2 concentrations $\leq V_\infty$.

Determination of Bromo Chloride Formation Site. A solution of 0.2 mL of bromine in 10 mL of CCl_4 was adsorbed onto 100 g of alumina. Twenty grams of this alumina was washed with 50 mL of CCl_4, and the resulting liquid was mixed with 5 mL of cyclohexene, which was allowed to stand for 10 h at room temperature. After most of the CCl_4 was removed by rotoevaporation, the resulting liquid was found to contain cyclohexene and *trans*-1,2-dibromocyclohexane.

(19) Adamson, A. W. *Physical Chemistry of Surfaces*, 4th ed.; Wiley: New York, 1982.
(20) Atkins, P. W. *Physical Chemistry*; Freeman: San Francisco, 1978.

pH and pCl Measurements. Hydrogen ion and chloride ion concentrations were determined with a pH meter (Fisher Scientific Co., Accument Model 810) with pH and chloride electrodes.

Preparation of NaCl Aluminas. An aqueous solution of NaCl was added to alumina and mixed. The water was removed first on a rotoevaporator and then by heating under vacuum at 400 °C. Typical concentrations were 6×10^{-4} mol of NaCl/gram of Al_2O_3. Once the NaCl had been adsorbed in this fashion, Br_2 and cyclohexene were adsorbed as previously described. CCl_4 was adsorbed prior to the adsorption of NaCl.

Adsorption of Br_2 on Silica Gel and Its Reaction with Cyclohexene/Silica Gel. One hundred grams of silica gel were dehydrated by the same method used to dehydrate alumina, after which 3.5×10^{-5} mol of Br_2/gram of silica gel was adsorbed along with 1 mL of CCl_4. The Br_2/SiO_2 was reacted with cyclohexene/SiO_2 for 24 h. The mixture was extracted with CCl_4, and the solution was analyzed by gas chromatography. Only *trans*-1,2-dibromocyclohexane was detected.

Acknowledgment. This research was supported by the Department of Energy. C.D., S.L. and T.L. thank the University of Tennessee Science Alliance Center of Excellence for summer support.

Registry No. 1, 7429-37-0; 2, 13898-96-9; benzene, 71-43-2; iodobenzene, 591-50-4; toluene, 108-88-3; *o*-iodotoluene, 615-37-2; *m*-iodotoluene, 625-95-6; *p*-iodotoluene, 624-31-7; phenol, 108-95-2; *o*-iodophenol, 533-58-4; *p*-iodophenol, 540-38-5; anisole, 100-66-3; *o*-iodoanisole, 529-28-2; *m*-iodoanisole, 766-85-8; *p*-iodoanisole, 696-62-8; aniline, 62-53-3; acetanilide, 103-84-4; *N,N*-dimethylaniline, 121-69-7; *p*-iodo-*N,N*-dimethylaniline, 698-70-4; bromobenzene, 108-86-1; naphthalene, 91-20-3; 1-iodonaphthalene, 90-14-2; azulene, 275-51-4; 1-iodoazulene, 76279-71-5; 1,3-diiodoazulene, 36044-42-5; azobenzene, 103-33-3; nitrobenzene, 98-95-3; cyclopentene, 142-29-0; cyclopentyl iodide, 1556-18-9; cyclohexene, 110-83-8; cyclohexyl iodide, 626-62-0; cycloheptene, 628-92-2; cycloheptyl iodide, 2404-36-6; cyclooctene, 931-88-4; cyclooctyl iodide, 1556-10-1; 1-octene, 111-66-0; 2-iodooctane, 557-36-8; 3,3-dimethyl-1-butene, 558-37-2; 2,3-dimethyl-2-iodobutane, 594-59-2; 2,3-dimethyl-2-butene, 563-79-1; alumina, 1344-28-1; norbornene, 498-66-8; *trans*-stilbene, 103-30-0; styrene, 100-42-5; 1-hexyne, 693-02-7; (*E*)-1,2-diiodo-1-hexene, 115482-64-9; 3-hexyne, 928-49-4; (*E*)-3,4-diiodo-3-hexene, 87161-05-5; phenylacetylene, 536-74-3; (*E*)-α,β-diiodostyrene, 71022-74-7; 5-chloro-1-pentyne, 14267-92-6; (*E*)-5-chloro-1,2-diiodo-1-pentene, 115482-65-0; 3-hydroxypropyne, 107-19-7; (*E*)-α,β-diiodoallyl alcohol, 71264-49-8; propiolic acid, 471-25-0; (*E*)-diiodoacrylic acid, 14092-48-9; dimethyl acetylene dicarboxylate, 762-42-5; dimethyl diiodofumarate, 20697-49-8; iodophenol, 30587-23-6.

Preparation of Aryl, Alkynyl, and Vinyl Organocopper Compounds by the Oxidative Addition of Zerovalent Copper to Carbon–Halogen Bonds

Greg W. Ebert[1] and Reuben D. Rieke*[2]

Department of Chemistry, University of Nebraska—Lincoln, Lincoln, Nebraska 68588-0304

Received March 23, 1988

A highly reactive copper slurry can be prepared by the reduction of CuI·PEt_3 with 1 equiv of lithium naphthalide. The highly reactive copper is found to undergo rapid oxidative addition to alkyl, aryl, alkynyl, and vinyl halides under mild conditions. The aryl, alkynyl, and vinyl organocopper compounds are stable at room temperature. These organocopper compounds can be prepared with a variety of functional groups such as nitro, nitrile, ester, and ketone.[3,4] The arylcopper compounds can be cross-coupled in moderate to high yields with acid chlorides and with alkyl halides. A comparison of different methods for producing activated copper is presented, and the scope and limitations are discussed.

Organocopper and lithium alkyl cuprate reagents are finding ever increasing usage in organic synthesis. Normally, these reagents are produced from the reaction of an organolithium or Grignard reagent with an appropriate

0022-3263/88/1953-4482$01.50/0