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THE IODINATION OF AROMATIC SUBSTRATES ON ALUMINA

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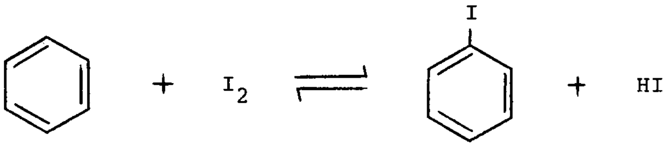
Abstract: The iodination of a wide variety of aromatic substrates has been attained on dehydrated alumina. The procedure is particularly well suited for arenes.

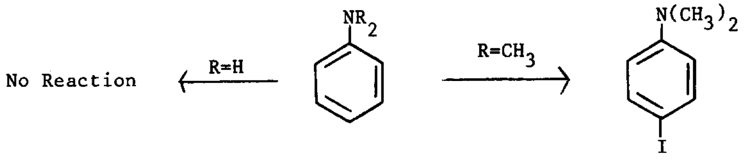
The direct iodination of aromatic substrates with molecular iodine has proven difficult because I_2 is the least reactive halogen in electrophilic aromatic substitution[1] and the reaction is reversible.[2] These problems have been circumvented by oxidation of I_2 to a more effective electrophile,[3] polarizing I_2 with a Lewis acid,[4] or removal of HI by precipitation of iodide.[5] The use of reagents such as ICl has also proven effective.[6]

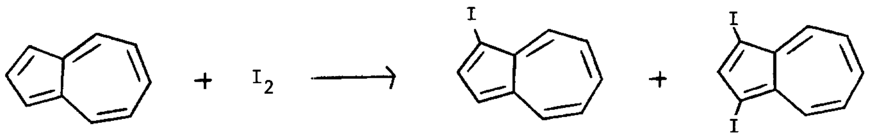


The dehydrated surface of γ-alumina (chromatography alumina) would appear to be an effective medium for electrophilic iodination because the surface contains[7] partially exposed Al^{+3}, which can polarize and activate the I_2 and O^{-2} which can react with the liberated HI. Furthermore O^{-2} and surface hydroxyl groups may react with I_2 to form OI^- and HOI, respectively, which can also function as electrophiles. These predictions are born out in fact. The new procedure represents an excellent method for iodinating aromatic substrates.

The iodinations have been carried out by two methods. These were: (1) the solution method in which a mixture of I_2 and a large excess of aromatic substrate is slurried with the solid,[8] and (2) the solid or dry method in which I_2 and the substrate are separately adsorbed[9] onto excess dehydrated alumina and the two solids thoroughly mixed. Depending on their adsorption characteristics, the products were removed from the solid by stirring with a polar solvent or Soxhlet extraction; unreacted I_2 was removed by treatment of the solution with aqueous sodium bisulfite.

The results of these experiments are summarized in Table 1. In the cases where both reaction procedures were attempted, the one giving the higher yield is reported. All reactions were run for 20 hours at room temperature. Because no attempt was made in these initial experiments to maximize yields, the results probably reflect relative reactivity of the substrate toward I_2. The experiments described below bear this out. In addition to the intermolecular reactivity, the distribution of isomers in the individual reactions clearly demonstrate that the iodinations occur by electrophilic aromatic substitution. Quite surprisingly aniline is unreactive towards I_2, even at 100°.[10] This is likely due to its reaction with surface Al^{+3} or HI (which is known to be generated on I_2/Al_2O_3) to generate an unreactive complex. N,N-Dimethylaniline, whose nitrogen is sterically blocked, reacts smoothly to generate *p*-iodo-N,N-dimethylaniline. Anisole, in addition to being iodinated, undergoes a competitive demethylation reaction, while acetanilide is preferentially cleaved to aniline. Azulene was an interesting substrate because, by varying reaction conditions, it was possible to get high yields of either 1-iodoazulene or 1,3-diiodoazulene.





Excess I_2, Room Temp.	0%	100%
Excess azulene, 100°	73%	7%

To examine what factors influence product yields, the iodination of benzene was examined in more detail. Three factors: reaction time, reaction temperature and the extent of dehydration of the alumina were examined. Benzene reacts with excess iodine by a pseudo first order process at room temperature. A plot of the yield of iodobenzene versus time shows that, even after 20 hrs, the standard reaction time for substrates in

Table 1. Reaction of Aromatic Substitutes with I_2 on Al_2O_3[1]

Substrate	Product	Yield	Distribution (Comments)
Benzene	Iodobenzene	26%[2]	
Toluene	Iodotoluenes	37%[3]	o:m:p = 32:4:64
Bromobenzene			(unreactive)
Iodobenzene			(unreactive)
Anisole	Iodoanisole (+ Phenols)	50%[3]	o:m:p = 41:14:45
Phenol	Iodophenols	8%[2]	o:m:p = 50:0:50
Aniline			(unreactive)
N,N-Dimethylaniline	*p*-Iodo-N,N-dimethylaniline	45%[2]	
Acetanilide	Aniline		
Naphthalene	1-Iodonaphthalene	10%[2]	
Azulene	1,3-Diiodoazulene	100%[2]	(excess I_2)
Azulene	1-Iodoazulene	7%[2]	(excess azulene)
Azulene[4]	Iodoazulenes	80%[2]	1-I:1,3-diI = 91:9 (excess azulene)

(1) The reactions were run at room temp. for 20 hrs. (2) Run by solid method. (3) Run by solution method. (4) Reaction run at 100°.

Table 1, the formation of product is only beginning to taper off. Longer reaction times, at room temperature, should be used for less reactive substrates. Temperature has a dramatic effect on yield. The yield of iodobenzene in reactions run at 100° is four to five times higher than for reactions run at ambient temperature. The time at which the alumina is dehydrated under vacuum at 400° also has a dramatic effect on the yield of iodobenzene in reactions run at room temperature for 20 hours. No reaction occurs on alumina dehydrated for less than five hours, even though a large amount of water is removed during this time. Maximum yields are obtained utilizing alumina which has been dehydrated 22 hours. Apparently physisorbed water is removed from Al_3O_3 below five hours and catalytic sites are not exposed. Above this time the chemisorbed surface hydroxyls react to give water and expose aluminum ions to the surface. After 22 hours, very little water is collected on dehydration, implying that the maximum number of catalytic sites has been attained.

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9. If the substrate was a liquid, it was injected directly onto the solid. Phenol was melted prior to introduction of it to the solid. Iodine was ordinarily dissolved in a small amount of liquid substrate and injected onto the solid. Azulene and naphthalene were introduced in benzene; in these cases I_2 was also introduced in benzene. Other solvents either reacted with I_2/Al_2O_3 or Al_2O_3.
10. At 100° aniline on alumina, under N_2 in a sealed tube, is converted into nitrobenzene and azobenzene. The oxidizing agent must be residual O_2 adsorbed to the alumina.

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