

Notes

Reduction of Alkyl Halides with Lithium Gallium Hydride

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The discovery of sodium borohydride¹ and lithium aluminum hydride² had revolutionized the procedures utilized for the reduction of organic functional group. Since then, a number of methods for the effective reduction of alkyl halide were modified with various hydride reagents.³ And in the course of exploring the reducing properties of lithium gallium hydride, its reducing ability was found to be strong like those of lithium aluminum hydride.⁴ Especially alkyl halides, such as butyl chloride and bromide, were found to be reduced easily with lithium gallium hydride. So we decided to investigate the reduction of alkyl and aryl halides with lithium gallium hydride in detail. In this report, we described such systematic study, and the reducing ability of the reagent in this reduction was also compared with those of representative hydride reducing agents, such as lithium aluminum hydride and lithium borohydride.

Results and Discussion

In this experiment, we utilized a clear solution of lithium gallium hydride in THF, prepared in the previous paper.⁵ A representative series of organic halides with different structure feature were selected to evaluate the reducing ability of the reagent.

We first began the experiment by observing the rate of reduction for octyl halides as representative primary alkyl halides. The reagent readily reduced both octyl bromide and iodide to the corresponding alkane, octane, in 99% yields at 65 °C in 0.5 h, while octyl chloride was reduced to octane in a yield of 92% at a relatively slow rate (24 h). And 2-bromooctane, a secondary alkyl halide, was reduced to octane in 98% yield at 65 °C in 24 h. Like the reactivity pattern observed in the S_N2 reaction, the reagent shows a stronger reactivity toward primary alkyl halide than secondary one. Lithium aluminum hydride also reduced octyl bromide and iodide quantitatively to octane in 0.5 h at 25 °C, whereas octyl chloride was slowly reduced in 73% yield at 25 °C in 24 h. The reactivity of lithium borohydride toward octyl halides is far less than that of lithium gallium hydride or of lithium aluminum hydride.

In the case of cycloalkyl halides, the reduction of cyclohexyl iodide by lithium gallium hydride resulted in the quantitative formation of cyclooctane at 65 °C in 0.5 h, while cyclohexyl bromide was slowly reduced in 63% yield at 65 °C in 24 h. Cyclohexyl chloride was found to be essentially inert to this reagent under the reaction conditions adopted. The results clearly reveal that the rate of the reduc-

tion is in the order of RI > RBr > RCl. In the case of reduction with lithium aluminum hydride, cyclohexyl iodide was converted to cyclohexane in 93% at 65 °C in 6 h. Even cyclohexyl bromide was reduced in 96% in 12 h at 65 °C.

Benzyl halides, such as benzyl chloride and bromide, by lithium gallium hydride were readily reduced to toluene in a quantitative yield at 65 °C in 0.5 h. Lithium aluminum hydride also reduced benzyl bromide rapidly to toluene in a quantitative yield in 0.5 h at 25 °C.

A series of reductions were carried out utilizing the monohalobenzenes which are normally resistant to nucleophilic substitution. The reaction of such compound, iodobenzene, with lithium gallium hydride underwent the reduction smoothly, showing the 99% yield in 3 h at 65 °C. Similarly, the rate of the reduction markedly decreased as the halogen was changed from iodine to bromine and chlorine. Lithium aluminum hydride in a higher concentration also reduced bromobenzene quantitatively at 65 °C in 6 h.

The presence of the electron releasing substituents, such as *p*-methyl or *p*-methoxy group attached to the aromatic ring of halobenzene diminished the reduction rate. Thus, 4-iodotoluene and 4-iodoanisole required 6 h for complete reduction to the corresponding dehalogenated product at a slower reduction rate, compared to the 3 h reaction in the case of iodobenzene. Similarly, 4-bromotoluene and 4-bromoanisole were reduced slowly in 70 and 65% yields, respectively, at 65 °C in 24 h. Finally, 4-chlorotoluene and 4-chloroanisole were essentially inert toward this reagent. Lithium aluminum hydride also showed a similar trend.

In conclusion, lithium gallium hydride reduces effectively both primary and secondary alkyl bromides and iodides to the corresponding alkanes at 65 °C; the reduction of alkyl chlorides is relatively slow. The reducing power of lithium gallium hydride is much stronger than lithium borohydride. Therefore, lithium gallium hydride and lithium aluminum hydride can be reagents of choice for the hydrogenolysis of alkyl halides.

Experimental Section

Lithium gallium hydride was prepared by the known method.⁵ The following procedure for the reduction of octyl bromide was representative. An oven-dried, 50 mL-flask with a side arm capped with rubber stopple, a magnetic stirring bar and a reflux condenser connected to a mercury bubbler, was flushed with nitrogen and charged with 1 mL of 1.00 M octyl bromide-THF solution. To this solution, a

Table 1. Reduction of Alkyl Halides with LiGaH₄^a, LiAlH₄^b and LiBH₄^c in Tetrahydrofuran

Compound	Reducing agent	Temp (°C)	Reduction ^c , %					
			0.5h	1h	3h	6h	12h	24h
Octyl chloride	LiGaH ₄	65 °C	34	48	80	89	91	92
	LiAlH ₄ ^{1c}	25 °C		4	19	37	56	73
	LiBH ₄ ^{1c}	25 °C					0	0
Cyclohexyl chloride	LiGaH ₄	65 °C						tr
	LiAlH ₄ ^{1f}	25 °C			2	2	4	6
Benzyl chloride	LiGaH ₄	65 °C	98	98				
Chlorobenzene	LiGaH ₄	65 °C						3
	LiAlH ₄ ^{2b}	25 °C	0	0	4	8	8	15
4-Chlorotoluene	LiGaH ₄	65 °C						tr
4-Chloroanisole	LiGaH ₄	65 °C						tr
Octyl bromide	LiGaH ₄	65 °C	99					
	LiAlH ₄ ^{1c}	25 °C	97	99				
	LiBH ₄ ^{1c}	25 °C		3	11	14	22	39
2-Bromooctane	LiGaH ₄	65 °C	34	63	87	98		
	LiAlH ₄ ^{1f}	25 °C						97
Cyclohexyl bromide	LiGaH ₄	65 °C	5	10	25	42	59	63
	LiAlH ₄ ^{1f}	25 °C		0	4	4	8	16
Benzyl bromide	LiGaH ₄	65 °C	99					
	LiAlH ₄ ^{1f}	25 °C	100	100				
Bromobenzene	LiGaH ₄	65 °C	5	18	37	56	71	76
	LiAlH ₄ ^{1f,2b}	25 °C		6	10	14	20	28
		65 °C	36	46	79	100		
4-Bromotoluene	LiGaH ₄	65 °C	4	12	34	52	67	70
	LiAlH ₄ ^{2b}	25 °C	0	6	8	12	14	20
4-Bromoanisole	LiGaH ₄	65 °C	2	8	22	40	62	65
	LiAlH ₄ ^{2b}	25 °C	0	0	4	7	13	17
Octyl iodide	LiGaH ₄	65 °C	99					
	LiAlH ₄ ^{1c}	25 °C	100	100				
	LiBH ₄ ^{1c}	25 °C	13	22	50	53	72	75
Cyclohexyl iodide	LiGaH ₄	65 °C	99					
	LiAlH ₄ ^{1f}	25 °C	2	7	20	30	49	74
Iodobenzene	LiGaH ₄	65 °C	62	84	99			
	LiAlH ₄ ^{2b}	25 °C	6	11	18	31	41	50
4-Iodotoluene	LiGaH ₄	65 °C	15	29	68	98		
4-Iodoanisole	LiGaH ₄	65 °C	12	30	70	99		

^aSolutions were 0.125 M in lithium gallium hydride and alkyl halide. ^bSolutions were 0.25 M in lithium aluminum hydride or lithium borohydride, and alkyl halide. ^cReactions were followed by GC using a suitable internal standard. ^dThe concentration of lithium aluminum hydride was 1.00 M.

solution of lithium gallium hydride (1.72 mL, 0.58 M, 1 mmol) in THF and dodecane as a internal standard were added and refluxed. At the appropriate interval, an aliquot of reaction mixture was hydrolyzed with 1 mL of 2 N sulfuric acid. The aqueous layer was saturated with sodium chloride, and organic layer was separated, dried with anhydrous magnesium sulfate, and finally subjected to GLC analysis on a Chromosorb-WHP, 10% SE-30, 2 m, 1/8 inch column, indicating the presence of octane in 99% yield.

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