mg (33%) of unreacted cyclohexanone: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 (t, J = 2.8 Hz, 1 H), 2.56 (t, J = 7.1 Hz, 1 H), 2.37 (heptet, J = 7.4 Hz, 1 H), 2.30–2.21 (ddd, J = 15.5, 7.6, and 3.0 Hz, 1 H), 1.96–1.87 (ddt, J = 15.5, 8.3, and 2.0 Hz, 1 H), 1.72–1.24 (m, 11 H), 1.23–1.20 (m, 2 H), 1.02 (d, J = 6.9 Hz, 3 H), 0.86 (t, J = 7.4 Hz, 3 H); m/z calcd (M^+) 208.1827, obsd 208.1799.

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Registry No. **2**, 96689-55-3; **3**, 96689-56-4; **4**, 5682-72-4; **5**, 76047-58-0; **5** (azine derivative), 96689-53-1; **6**, 76047-57-9; **7a**, 96689-35-9; **7b**, 96689-36-0; **8**, 96689-37-1; **9**, 96689-38-2; **10**, 96689-39-3; **11a**, 96689-40-6; **11b**, 96689-41-7; **12**, 96689-42-8; **13**, 96689-43-9; *cis*-**14**, 96689-54-2; *trans*-**14**, 96689-44-0; **15**, 96689-45-1; **16**, 96689-46-2; **17**, 96689-47-3; **18**, 96689-48-4; **20**, 96689-49-5; **21**, 96689-50-8; **22**, 96689-51-9; **23**, 96689-52-0; TMG, 80-70-6; NH_2NHSO_2Tris, 39085-59-1; NH_2NHTos, 1576-35-8; CH_3Li, 917-54-4; I_2, 7553-56-2; *n*-BuLi, 109-72-8; Me_3SnCl, 1066-45-1; Me_3SiCl, 75-77-4.

Reaction of Diisobutylaluminum Hydride with Selected Organic Compounds Containing Representative Functional Groups

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The approximate rates and stoichiometry of the reaction of excess diisobutylaluminum hydride (DIBAH) with 69 selected organic compounds containing representative functional groups were examined under standardized conditions (toluene, 0 °C) in order to compare its reducing characteristics with aluminum hydride previously examined and to enlarge the scope of its applicability as a reducing agent. In general, the data confirm the results already available in the literature but provide data in a single solvent with controlled concentration and temperature. Primary, secondary, and tertiary alcohols, simple phenols, and thiols evolve hydrogen rapidly and quantitatively. However, DIBAH reacts with only one active hydrogen in primary amines. Aldehydes and ketones of diverse structure are reduced rapidly and quantitatively to give the corresponding alcohols. Reduction of norcamphor gives 7% *exo*- and 93% *endo*-norborneol. Conjugated aldehydes and ketones such as cinnamaldehyde, methyl vinyl ketone, and isophorone are rapidly and cleanly reduced to the corresponding allylic alcohols. Anthraquinone is mainly reduced to 9,10-dihydro-9,10-anthracenediol. Hexanoic acid, benzoic acid, and crotonic acid liberate hydrogen rapidly, but only partially, and the reduction proceeds very slowly. The acid chlorides and esters tested are all reduced rapidly and quantitatively to the corresponding alcohols. Alkyl halides, such as *n*-octyl iodide, and aromatic halides, such as *p*-bromotoluene, are all inert toward this reagent. However, epoxides are reduced rapidly with an uptake of 1 equiv of hydride. Styrene oxide is reduced to give 27% 1- and 73% 2-phenylethanol. Tertiary amides are reduced rapidly in 0.5 h, whereas primary amides are reduced only very slowly. Nitriles consume 1 equiv of hydride rapidly but further hydride uptake is very sluggish. Nitro compounds, azobenzene, and azoxybenzene were reduced moderately. Cyclohexanone oxime liberates hydrogen rapidly, consuming 1.2 equiv of hydride for reduction. However, further reduction is very slow. Phenyl isocyanate is rapidly reduced to the imine stage. Pyridine reacts at a moderate rate with an uptake of one hydride in 12 h; however, further reaction is very slow. Disulfides are rapidly reduced, whereas sulfide, sulfone, and sulfonic acid are inert to this reagent under these reaction conditions. Dimethyl sulfoxide is reduced at a moderate rate. *n*-Octyl tosylate is quantitatively reduced to *n*-octane within 0.5 h at 0 °C, whereas cyclohexyl tosylate undergoes elimination, liberating 1 equiv of hydrogen rapidly to give a 95% yield of cyclohexene.

Nearly 25 years after Ziegler's pioneering work,[1] DIBAH has secured its place as a common reducing agent in organic synthesis[2] and its popularity has risen considerably, especially after safe and easy-to-handle solutions of DIBAH in toluene and hexane became available. However, most of the data available are for reactions carried out for preparative purposes, with the concentrations of the reactants, the temperature of the reaction, and the reaction time not specified.

Some time ago, systematic studies of various complex metal hydrides were undertaken, and now more than 15 hydride systems[3] have been examined systematically as to the approximate rates and the stoichiometry for the reaction with a standard list of representative compounds containing the more common functional groups under standard conditions, usually in tetrahydrofuran (THF) at 0 °C, with the concentration of hydride and compound

(1) Ziegler, K. *Angew. Chem.* **1964**, *76*, 545.

(2) For comprehensive reviews, see: (a) Winterfeldt, E. *Synthesis* **1975**, 617. (b) Bruno, G. "The Use of Aluminum Alkyls in Organic Synthesis"; Ethyl Corp.: Baton Rouge, LA, 1968. (c) Bruno, G. "The Use of Aluminum Alkyls in Organic Synthesis, 1969–1972 Supplement"; Ethyl Corp.: Baton Rouge, LA, 1972. (d) "Speciality Reducing Agents"; Texas Alkyls.

(3) (a) Brown, H. C.; Weissman, P. M.; Yoon, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 1458. (b) Brown, H. C.; Weissman, P. M. *J. Am. Chem. Soc.* **1965**, *87*, 5614. (c) Brown, H. C.; Weissman, P. M. *Isr. J. Chem.* **1963**, *1*, 430. (d) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 1464. (e) Yoon, N. M.; Cha, J. S. *J. Korean Chem. Soc.* **1977**, *21*, 108. (f) Pyun, C.; Son, J. C.; Yoon, N. M. *Bull. Korean Chem. Soc.* **1983**, *4*, 3. (g) Brown, H. C.; Mathew, C. P.; Pyun, C.; Son, J. C.; Yoon, N. M. *J. Org. Chem.*, in press. (h) Brown, H. C.; Kim, S. C.; Krishnamurthy, S. *J. Org. Chem.* **1980**, *45*, 1. (i) Brown, H. C.; Cha, J. S.; Nazar, B.; Kim, S. C.; Kirshnamurthy, S.; Brown, C. A. *J. Org. Chem.* **1984**, *49*, 885. (j) Yoon, N. M.; Lee, H. J.; Kim, H. K.; Kang, J. *J. Korean Chem. Soc.* **1976**, *20*, 59. (k) Yoon, N. M.; Lee, H. J.; Chung, J. S. *J. Korean Chem. Soc.* **1973**, *17*, 275. (l) Brown, H. C.; Heim, P.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 1637. (m) Brown, H. C.; Heim, P.; Yoon, N. M. *J. Org. Chem.* **1972**, *37*, 2942. (n) Brown, H. C.; Bigley, D. B.; Arora, S. K.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 7161. (o) Brown, H. C.; Krishnamurthy, S.; Yoon, N. M. *J. Org. Chem.* **1976**, *41*, 1778.

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Table I. Reaction of DIBAH with Representative Alcohols, Phenols, Amines, and Thiols in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
1-hexanol	0.5	0.97	1.00	0.03
	1.0	0.97	1.00	0.03
benzyl alcohol	0.5	1.01	1.01	0.00
	1.0	1.01	1.00	0.01
3-hexanol	0.5	0.99	1.01	0.02
	1.0	0.99	1.01	0.02
3-ethyl-3-pentanol	0.5	1.01	1.01	0.00
	1.0	1.01	1.01	0.00
phenol	0.5	0.98	1.00	0.02
	1.0	0.98	1.00	0.02
2,6-di-*tert*-butylphenol	0.5	0.99	0.99	0.00
	1.0	0.99	0.99	0.00
1-hexanethiol	0.5	1.01	1.00	0.01
	1.0	1.01	1.00	0.01
benzenethiole	0.5	1.02	1.00	0.02
	1.0	1.02	1.01	0.01
n-hexylamine	0.5	0.44	0.44	0.00
	1.0	0.61	0.61	0.00
	3.0	0.87	0.87	0.00
	6.0	0.99	1.00	0.01
	12.0	1.00	1.00	0.00
	24.0	1.02	1.02	0.00
2-aminoethanol[c]	0.5	1.98	1.98	0.00
	1.0	2.00	2.02	0.02
	3.0	2.00	2.00	0.00
	24.0	2.00	2.00	0.00

[a] Three mmoles of compound (3 mmol) was added to 12 mmol of DIBAH in 12 mL of solution (0.25 M in compound and 1.0 M in hydride). [b] In mmol/mmol of compound. [c] Reverse addition.

being 1.0 and 0.25 M, respectively. In order to understand better the reducing characteristics DIBAH and hopefully to enlarge the scope of its applicability as a reducing agent, we decided to undertake a similar systematic study of DIBAH in toluene at 0 °C, with the concentration of hydride and compound being 1.0 and 0.25 M, respectively. We chose a toluene solution of the reagent since the 1.5 M solution in toluene (1.0 M solution in THF is not adequate to make the reaction mixture 1.0 M in DIBAH) is commercially available and it is more stable than the tetrahydrofuran solution.

Results and Discussion

In order to define the reduction characteristics of DIBAH, we undertook a systematic study of the DIBAH with selected organic compounds containing representative functional groups under standardized conditions (toluene, 0 °C). The general procedure adopted was to add 3.0 mmol of the organic compounds to 12.0 mmol of DIBAH, both in toluene, to give 12 mL of solution at 0 °C. This makes the reaction mixture 1.0 M in DIBAH and 0.25 M in the compound under examination. The hydrogen evolved on adding the compound to the reagent was noted. The reaction mixture was maintained at 0 °C and aliquots were removed at appropriate intervals and analyzed for "residual hydride" with methanol at 0 °C.[4] In this way, it was possible to establish both the rate at which reduction proceeds and the stoichiometry of the reaction, i.e., the number of hydrides utilized per mole of compound when the reaction comes to an effective halt.

In some cases the hydride-to-compound ratio of 4:1 was inadequate to achieve complete reduction. In such cases the hydride concentration was maintained constant, but the concentration of compound was reduced to give a higher ratio.

(4) Methanol does not attack aluminum–carbon bonds at temperatures of 5–15 °C.[2d]

Table II. Reaction of DIBAH with Representative Aldehydes and Ketones in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
n-hexanal	0.5	0.03	1.04	1.01
	1.0	0.04	1.04	1.00
benzaldehyde	0.5	0.01	1.01	1.00
	1.0	0.01	1.01	1.00
2-heptanone	0.5	0.04	1.02	0.98
	1.0	0.04	1.02	0.98
norcamphor	0.5	0.01	0.98	0.97
	1.0	0.01	0.99	0.98
camphor	0.5	0.02	0.94	0.92
	1.0	0.02	1.02	1.00
acetophenone	0.5	0.00	0.98	0.98
	1.0	0.00	0.98	0.98
benzophenone	0.5	0.00	0.99	0.99
	1.0	0.00	0.99	0.99
cinnamaldehyde	0.5	0.01	0.98	0.97
	1.0	0.01	1.00	0.99
	3.0	1.01	0.99	0.98
	24.0	0.03	1.05	1.02
methyl vinyl ketone	0.5	0.02	1.05	1.03
	3.0	0.04	1.05	1.02
	24.0	0.04	1.06	1.02
isophorone	0.5	0.04	1.05	1.01
	3.0	0.04	1.06	1.02
	24.0	0.04	1.06	1.02

[a,b] See corresponding footnotes in Table I.

Alcohols, Phenols, Amines, and Thiols. All of the alcohols, phenols, and thiols examined liberated hydrogen instantly and quantitatively. On the other hand, *n*-hexylamine required 6 h for the liberation of only 1 equiv of hydrogen, and no more hydrogen was evolved for 24 h. Similarly, DIBAH evolved 2 equiv of hydrogen rapidly with 2-aminoethanol. These results indicate DIBAH reacts with only one active hydrogen in primary amine (eq 1 and 2). In contrast, aluminum hydride (AlH_3) evolved 1.1

$$CH_3(CH_2)_4CH_2NH_2 + (i\text{-}Bu)_2AlH \rightarrow CH_3(CH_2)_4CH_2NH\ Al(i\text{-}Bu)_2 + H_2 \quad (1)$$

$$HOCH_2CH_2NH_2 + 2(i\text{-}Bu)_2AlH \rightarrow (i\text{-}Bu)_2AlOCH_2CH_2NHAl(i\text{-}Bu)_2 + 2H_2 \quad (2)$$

equiv of hydrogen rapidly in 15 min and 1.87 equiv in 24 h at 0 °C.[3d] The results are summarized in Table I.

Aldehydes and Ketones. All of the aliphatic and aromatic aldehydes and ketones examined took up 1 equiv of hydride rapidly, indicating clean reductions to the corresponding alcohol stage (eq 3). Cinnamaldehyde,

$$R_2CO + (i\text{-}Bu)_2AlH \rightarrow R_2CHOAl(i\text{-}Bu)_2 \xrightarrow{H_3O^+} R_2CHOH \quad (3)$$

methyl vinyl ketone, and isophorone utilized one hydride rapidly in 30 min with no sign of uptake of a second hydride even after 24 h. This suggests clean reduction to the corresonding allylic alcohols. Indeed, we obtained a 94% yield (isolated) of cinnamyl alcohol without contaminating by hydrocinnamyl alcohol. Ziegler[1,5] reported that 1 mol of DIBAH can reduce 3 mol of benzaldehyde or cinnamaldehyde to the corresponding alcohols, involving reduction by isobutyl groups. However, under these standard conditions (toluene, 0 °C, with excess DIBAH), no participation of isobutyl groups is apparent, as shown by the clean one hydride uptake. The results are summarized in Table II.

(5) Ziegler, K.; Schneider, K.; Schneider, J. *Justus Liebigs Ann. Chem.* **1959**, *623*, 9.

Table III. Stereochemistry of the Reduction of Representative Cyclic and Bicyclic Ketones with DIBAH in Toluene at 0 °C

ketone[a]	less stable isomer	%[b]
2-methylcyclohexanone	cis	51 (26)
4-*tert*-utylcyclohexanone	cis	39 (13)
norcamphor	endo	93 (93)
camphor	exo	84 (90)

[a] See corresponding footnotes in Table I. [b] The figures in parentheses are results with AlH_3 in THF.[6]

Table IV. Reaction of DIBAH with Representative Quinones in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
p-benzoquinone[c,d]	0.5	0.25	1.46	1.21
	1.0	0.29	1.53	1.24
	3.0	0.37	1.62	1.25
	6.0	0.41	1.66	1.25
anthraquinone[c,e]	0.5	0.04	1.50	1.46
	1.0	0.08	1.87	1.79
	3.0	0.12	2.12	2.09
	6.0	0.21	2.24	2.03

[a] Four mmoles of DIBAH was added to 1.0 mmol of compound in 4 mL of solution (0.25 M in compound and 1.0 M in hydride). [b] In mmol/mmol of compound. [c] Batch reaction. [d] Dark violet precipitate. [e] Green, gelatinous, and fluorescent precipitate.

Stereochemistry of the Reduction of Monocyclic and Bicyclic Ketones with DIBAH. The stereoselectivity of the reagent toward representative cyclic ketones was also studied. The reaction conditions were the same as those of the rate and stoichiometry studies. The reductions of 2-methylcyclohexanone and 4-*tert*-butylcyclohexanone appear to involve more equatorial attack than those with AlH_3, yielding 51% and 39% cis isomers, respectively, compared to the 26% and 13% cis isomers with the latter reagent.[6] However, Ashby has reported that AlH_3 in diethyl ether gives 46% cis alcohol in the reaction with 4-*tert*-butylcyclohexanone.[7] Therefore, the more equatorial attack observed with DIBAH also may be due to the solvent difference (toluene vs. tetrahydrofuran). Reduction of bicyclic ketones such as norcamphor and camphor proceeds with preferential attack of DIBAH from the less hindered site, yielding the less stable isomers of the two possible isomers predominantly (93% *endo*-2-norborneol and 84% isoborneol, respectively). Aluminum hydride shows similar stereoselectivity as DIBAH with these bicyclic ketones.[6] The results are summarized in Table III.

Quinones. *p*-Benzoquinone rapidly consumed 1.46 equiv of hydride per mol of compound, of which 85% was utilized for reduction and the remaining 15% for hydrogen evolution. This value indicates that the reaction does not involve simple reduction either to hydroquinone or to 1,4-dihydroxycyclohexadiene. Anthraquinone consumed 2.03 equiv of hydride for reduction and 0.21 equiv for hydrogen evolution. These data indicate that the reaction proceeded mainly to give 9,10-dihydro-9,10-anthracenediol.[3h,o] In the case of aluminum hydride, the reduction of *p*-benzoquinone proceeded to give a 50:50 distribution between hydroquinone and 1,4-dihydroxycyclohexadiene, whereas anthraquinone appeared to be reduced cleanly to 9,10-dihydro-9,10-anthracenediol. The experimental data are summarized in Table IV.

(6) Yoon, N. M.; Brown, H. C. *J. Am. Chem. Soc.* **1968**, *90*, 2927.
(7) Ashby, E. C.; Sanders, J. R.; Claudy, P.; Schwarz, R. *J. Am. Chem. Soc.* **1973**, *95*, 6485.

Table V. Reaction of DIBAH with Representative Carboxylic Acids and Acyl Derivatives in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
hexanoic acid	0.5	0.88	1.65	0.77
	6.0	0.88	2.09	1.21
	24.0	0.88	2.26	1.38
	48.0	0.88	2.34	1.46
	6.0[d]	0.84	2.69	1.85
	12.0[d]	0.84	2.81	1.97
benzoic acid[c]	0.5	0.43	1.13	0.70
	6.0	0.43	1.44	1.01
	24.0	0.43	1.78	1.35
	48.0	0.43	2.00	1.57
	6.0[d]	0.36	2.22	1.86
	12.0[d]	0.36	2.36	2.00
crotonic acid	0.5	0.85	1.86	1.01
	3.0	0.85	2.10	1.25
	24.0	0.85	2.54	1.69
	48.0	0.85	2.69	1.84
	0.5[d]	0.71	2.12	1.41
	1.0[d]	0.71	2.49	1.78
	3.0[d]	0.71	2.74	2.03
	12.0[d]	0.71	2.78	2.07
lithium benzoate[c]	0.5	0.04	0.05	0.01
	1.0	0.04	0.05	0.01
	3.0	0.04	0.05	0.01
	6.0	0.04	0.05	0.01
acetic anhydride[e]	0.5	0.00	3.55	3.55
	1.0	0.00	3.55	3.55
	3.0	0.00	3.80	3.80
	6.0	0.00	4.01	4.01
succinic anhydride[e,f]	0.5	0.04	0.78	0.74
	1.0	0.04	1.84	1.80
	3.0	0.08	2.70	2.62
	6.0	0.12	3.06	2.96
	24.0	0.17	3.25	3.08
phthalic anhydride[e,f]	0.5	0.04	2.26	2.22
	1.0	0.08	2.26	2.58
	3.0	0.12	2.84	2.72
	6.0	0.17	2.97	2.80
	24.0	0.29	3.15	2.86
hexanoyl chloride	0.5	0.00	1.98	1.98
	1.0	0.00	2.01	2.01
benzoyl chloride	0.5	0.00	1.97	1.97
	1.0	0.00	1.97	1.97
	3.0	0.00	1.97	1.97

[a,b] See corresponding footnotes in Table I. [c] Reverse addition. [d] At 25 °C. [e] Hydride:compound = 6:1. [f] Batch reaction.

Carboxylic Acids and Derivatives. Hexanoic acid and crotonic acid evolved 0.88 and 0.85 equiv of hydrogen, respectively, whereas benzoic acid evolved only 0.43 equiv of hydrogen, suggesting that the isobutyl groups in DIBAH must be reacting with active hydrogen. One hydride uptake with these acids (corresponding to the reduction to the aldehyde stage) proceeded rapidly, with further reductions very slow. Indeed, Zakharkin has reported a 40–70% yield of aldehydes.[8] However, hexanoic acid and benzoic acid could be reduced to the alcohol stage in 12 h at room temperature, and crotonic acid also could be reduced to the crotyl alcohol in 3 h with no sign of further hydride uptake after 12 h. Lithium benzoate was inert to this reagent. Acetic anhydride consumed four hydrides in 6 h, whereas phthalic anhydride and succinic anhydride consumed about three hydrides at a moderate rate for reduction with only a very slow reduction thereafter. In contrast, carboxylic acids and acid anhydrides are rapidly reduced with AlH_3 in 3 h. Acid chlorides, both hexanoyl and benzoyl chloride, were rapidly reduced to the alcohol stage with either DIBAH or aluminum hydride. The re-

(8) Zakharkin, L. I.; Khorlina, I. M. *Zh. Obshch. Khim.* **1964**, *34*, 1029; *Chem. Abstr.* **1964**, *60*, 15724*f*.

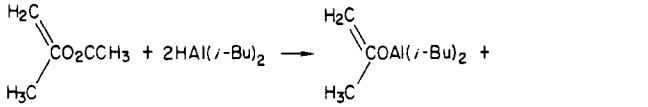
Table VI. Reaction of DIBAH with Representative Esters and Lactones in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
ethyl hexanoate	0.5	0.00	1.99	1.99
	1.0	0.00	1.99	1.99
ethyl benzoate[c]	0.5	0.02	2.01	1.99
	1.0	0.02	2.04	2.02
	3.0	0.02	2.05	2.03
ethyl crotonate[d]	0.5	0.02	2.04	2.02
	3.0	0.03	2.04	2.01
	24.0	0.03	2.06	2.03
phenyl acetate	0.5	0.00	1.99	1.99
	1.0	0.00	1.99	1.99
γ-butyrolactone	0.5	0.00	1.98	1.98
	1.0	0.00	1.98	1.98
	3.0	0.00	1.97	1.97
phthalide[c]	0.5	0.02	1.98	1.96
	1.0	0.02	1.98	1.96
	3.0	0.02	1.98	1.96
isopropenyl acetate	0.05	0.01	1.98	1.97
	1.0	0.01	1.98	1.97
	3.0	0.01	1.98	1.97
	6.0	0.01	2.01	2.00

[a,b] See corresponding footnotes in Table I. [c] Utilizing 2 equiv (5% excess) of hydride; benzyl alcohol and 1,2-benzenedimethanol were obtained 86% and 81% (isolated) yield from ethyl benzoate and phthalide, respectively. [d] GLC analysis showed 98% crotyl alcohol and 2% 1-butanol.

sults are summarized in Table V.

Esters and Lactones. All of the esters and lactones examined reacted rapidly with the uptake of 2 equiv of hydride per mol. Indeed, we obtained an 86% yield (isolated) of benzyl alcohol from ethyl benzoate by reacting 2 equiv (5% excess) of DIBAH in 3 h at 0 °C. 1,2-Benzenedimethanol was also isolated in 81% yield from the reduction of phthalide utilizing 2 equiv (5% excess) of hydride. With 1 equiv of hydride at −78 °C, excellent yields of aldehydes from the reduction of esters have been reported;[2] however, no sign of the formation of aldehyde was observed under these standard conditions (toluene, 0 °C, with excess DIBAH). Ethyl crotonate raidly consumed 2.02 equiv of hydride per mol with no sign of further hydride uptake after 24 h, yielding 98% crotyl alcohol and 2% 1-butanol. Isopropenyl acetate also took up 2 equiv of hydride cleanly, suggesting the formation of an aluminum enolate (eq 4). However, Schmitt reported that



$CH_3CH_2OAl(i\text{-}Bu)$ (4)

2,4-pentanediol was obtained in 80% yield after a 3-h reaction at 20 °C.[9] Apparently the reaction does not seem to proceed simply as shown in eq 4. The results are summarized in Table VI.

Halides and Epoxides. All of the alkyl halides examined and *p*-bromotoluene were inert toward DIBAH. The epoxides examined all reacted very fast, an uptake of 1 hydride per mol of epoxide being essentially complete within 30 min at 0 °C. In the case of styrene oxide, hydride attacked the more hindered carbon, yielding 27% 1-phenylethanol and 73% 2-phenylethanol.[10] However, when lithium chloride was added, the product distribution

Table VII. Reaction of DIBAH with Representative Halides and Epoxides in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
n-octyl iodide	3.0	0.01	0.02	0.01
	6.0	0.01	0.02	0.01
	12.0	0.02	0.08	0.06
	24.0	0.02	0.13	0.11
n-octyl bromide	3.0	0.02	0.04	0.02
	6.0	0.02	0.05	0.03
	12.0	0.02	0.08	0.06
	24.0	0.02	0.13	0.11
n-octyl chloride	3.0	0.03	0.04	0.01
	6.0	0.03	0.05	0.02
	12.0	0.03	0.05	0.02
	24.0	0.03	0.06	0.03
p-bromotoluene	3.0	0.02	0.04	0.02
	6.0	0.02	0.04	0.02
	12.0	0.05	0.08	0.03
	24.0	0.05	0.08	0.03
1,2-butylene oxide	0.5	0.01	0.99	0.98
	1.0	0.01	0.99	0.99
cyclohexene oxide	0.5	0.00	1.00	1.00
	1.0	0.00	1.00	1.00
styrene oxide	0.5	0.03	1.04	1.01
	1.0	0.03	1.04	1.01
	3.0[c]	0.03	1.01	0.98
1-methyl-1,2-cyclohexene oxide	0.5	0.04	1.04	1.01
	1.0	0.04	1.05	1.01
	3.0[d]	0.04	1.05	1.01

[a,b] See corresponding footnotes in Table I. [c] GLC analysis showed 27% 1-phenylethanol and 73% 2-phenylethanol. [d] GLC analysis showed 90% 1-methylcyclohexanol and 10% *cis*-2-methylcyclohexanol.

was dramatically reversed, yielding 86% 1- and 14% 2-phenylethanol. These results strongly suggest that the system is in equilibrium with a basic type of hydride[11a,b] (eq 5).

$$(i\text{-Bu})_2AlH + LiCl \rightleftharpoons Li(i\text{-Bu})_2AlHCl \quad (5)$$

Previously we observed that the major reduction product of styrene oxide with AlH_3 in THF is the secondary alcohol (74% 1- and 26% 2-phenylethanol). 1-Methyl-1,2-cyclohexene oxide yielded 90% 1-methylcyclohexanol and 10% *cis*-2-methylcyclohexanol, very similar to the results with AlH_3.[12] The results are summarized in Table VII.

Amides and Nitriles. Primary amides, similar to *n*-hexylamine, evolved only about 1 equiv of hydrogen rapidly, but the second active hydrogen was inert to the reagent. Reduction of both primary amides tested was sluggish; hexanamide utilized 1.37 equiv of hydride, and benzamide utilized only 0.59 equiv of hydride for reduction, both in 24 h. On the other hand, tertiary amides took up 2 equiv of hydride rapidly in 0.5 h at 0 °C. Zakharkin has reported 75–95% yields of tertiary amines from the reduction of the corresponding amides.[13] Hexanenitrile, benzonitrile, and acrylonitrile utilized 1 equiv of hydride rapidly, and further reductions were very slow or did not proceed at all. These results confirm that DIBAH is a superior reagent for the synthesis of aldehydes from nitriles. Such formation of aldehydes by the reduction of nitriles with DIBAH were reported by Zakharkin[14a] and

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(10) Previously 21% 1-phenylethanol and 79% 2-phenylethanol were reported: Zakharkin, L. I.; Khorlina, I. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1965**, 862; *Chem. Abstr.* **1965**, *63*, 5574*f*.

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(12) More recent work has established that AlH_3 gives 91.3% 1-methylcyclohexanol and 8.7% *cis*-2-methylcyclohexanol and not the 100% 1-methylcyclohexanol reported in ref 3d.

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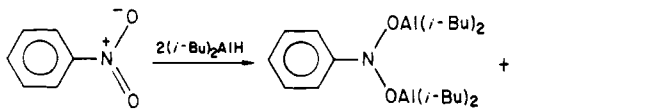
Table VIII. Reaction of DIBAH with Representative Amides and Nitriles in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
hexanamide[c]	0.5	0.89	1.22	0.33
	1.0	0.89	1.38	0.49
	3.0	0.89	1.42	0.53
	6.0	0.89	1.70	0.81
	12.0	0.89	2.17	1.28
	24.0	0.89	2.26	1.37
benzamide[c]	0.5	0.96	0.99	0.03
	1.0	0.96	0.99	0.03
	3.0	0.96	1.01	0.05
	6.0	0.96	1.11	0.15
	12.0	0.97	1.52	0.55
	24.0	0.97	1.56	0.59
N,N-dimethylhexanamide	0.5	0.26	2.18	1.92
	1.0	0.26	2.29	2.03
N,N-dimethylbenzamide	0.5	0.07	2.09	2.02
	1.0	0.07	2.07	2.00
hexanenitrile	0.5	0.00	1.04	1.04
	1.0	0.00	1.04	1.04
	3.0	0.00	1.08	1.08
	6.0	0.00	1.14	1.14
benzonitrile	0.5	0.04	1.04	1.00
	1.0	0.04	1.04	1.00
	3.0	0.04	1.03	0.99
	6.0	0.04	1.04	1.00
acrylonitrile	0.5	0.03	1.03	1.00
	3.0	0.03	1.09	1.06
	24.0	0.03	1.19	1.16

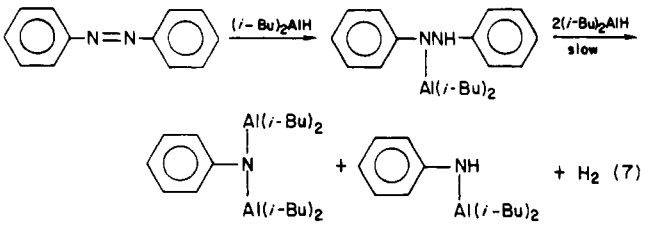
[a,b] See corresponding footnotes in Table I. [c] Reverse addition.

Miller.[14b] The results are listed in Table VIII.

Nitro Compounds and Their Derivatives. Nitropropane and nitrobenzene rapidly consumed a total of 3 equiv of hydride, with 2 equiv of hydride being utilized for reduction and 1 equiv for hydrogen evolution. This corresponds to the reduction to the hydroxylamine stage (eq 6).



Azobenzene utilized 1 equiv of hydride in 3 h and the second equivalent of hydride quite slowly with the slow evolution of hydrogen. This suggests the fast reduction to the hydrazobenzene stage, followed by the slow reduction (N–N bond cleavage) to aniline (eq 7).



Azoxybenzene evolved 0.76 equiv of hydrogen and took up 2 equiv of hydride for reduction in 9 h. This stoichiometry indicates that azoxybenzene is reduced to the hydrazobenzene stage. These results are in contrast to the behavior of AlH_3, which is inert to nitro compounds, azobenzene, and azoxybenzene.

Interesting color changes were observed in these reductions. At the initial stage of the reduction of nitrobenzene, the solution became brown immediately, and the color changed to a light brown within 20 min. Similarly, at the initial stage, the nitropropane solution became brown, and the color then faded out with hydrogen evolution within 5 min. In the cases of azobenzene and azoxybenzene, the solution became reddish black within 15 min, and the color gradually changed to dark brown. The results are summarized in Table IX.

Table IX. Reaction of DIBAH with Representative Nitro Compounds and Their Derivatives in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
nitrobenzene[c]	3.0	1.08	2.70	1.62
	6.0	1.08	2.86	1.78
	24.0	1.08	2.95	1.93
nitropropane[d]	1.0	0.80	2.55	1.75
	6.0	0.80	2.61	1.81
	24.0	0.80	2.82	2.02
azobenzene[e]	3.0	0.04	1.13	1.09
	6.0	0.04	1.16	1.12
	24.0	0.21	1.34	1.13
	48.0	0.37	1.69	1.32
azoxybenzene[e]	3.0	0.73	1.91	1.18
	6.0	0.76	2.10	1.34
	9.0	0.76	2.77	2.01
	24.0	0.76	2.84	2.08

[a,b] See corresponding footnotes in Table I. [c] A brown color developed on the addition of compound, changed to light brown in 20 min. [d] A brown color, developed on the addition of compound, faded out with hydrogen evolution within 5 min. [e] Solution became reddish black and changed to dark brown.

Other Nitrogen Compounds. Cyclohexanone oxime rapidly liberated 0.89 equiv of hydrogen and took up 1.2 equiv of hydride for reduction with only a slow further reduction thereafter. However, acetophenone oxime underwent a rapid reduction in 0.5 h at 0 °C. Yamamoto[15] reported that the Beckmann-type rearranged secondary amine, *N*-ethylaniline, was obtained from acetophenone oxime in a 92% yield in 2 h at 0 °C. This is quite a contrast to our earlier observations with AlH_3 in THF. In the reduction of acetophenone oxime with AlH_3 in THF, only 4.3% *N*-ethylaniline, together with 82% α-phenylethylamine, an unrearranged amine,[6] was obtained. Phenyl isocyanate consumed 2.3 equiv of hydride rapidly. Pyridine underwent a reaction at a moderate rate, utilizing about 1 equiv of hydride in 24 h.[16] Pyridine *N*-oxide rapidly consumed two hydrides for reduction and evolved 0.45 equiv of hydrogen. The partial hydrogen evolution suggests the participation of isobutyl groups. Since two hydride consumptions, one hydride uptake, and one hydrogen evolution with pyridine *N*-oxide correspond to the reduction to pyridine, this stoichiometry suggests the reduction to 1,2-dihydropyridine. However, more detailed study is required for a definite conclusion. The results are summarized in Table X.

Sulfur Compounds. Disulfides were reduced to the thiol stage, utilizing 2 mol of hydride, 1 mol for reduction and 1 mol for hydrogen evolution. It is interesting to note that DIBAH reduced di-*n*-butyl disulfide significantly faster than diphenyl disulfide. With many other reducing agents, such as $Li(t\text{-}BuO)_3AlH$,[3c] AlH_3,[3d] $LiBH_4$,[3e] $K(i\text{-}PrO)_3BH$,[17] and $(C_6H_5)_3P$,[18] aromatic disulfides could be reduced selectively in the presence of aliphatic disulfides.

(15) Sasatani, S.; Miyazaki, T.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1983**, *27*, 4711.
(16) It is known that quinoline can be reduced to dihydroquinoline and tetrahydroquinoline, depending upon the amount of DIBAH and the reaction temperature: (a) Neuman, W. P. *Justus Liebigs Ann. Chem.* **1958**, *618*, 90. (b) Neuman, W. P. *Angew. Chem.* **1958**, *70*, 401.
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Table X. Reaction of DIBAH with Other Representative Nitrogen Compounds in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
cyclohexanone oxime	1.0	0.89	2.09	1.20
	6.0	0.89	2.13	1.24
	24.0	0.89	2.25	1.44
	48.0	0.89	2.47	1.58
acetophenone oxime	0.5	0.82	2.68	1.86
	3.0	0.85	2.68	1.83
	6.0	0.85	2.69	1.84
	24.0	0.85	2.69	1.84
phenyl isocyanate	0.5	0.01	2.32	2.31
	1.0	0.01	2.35	2.34
	6.0	0.01	2.35	2.34
	24.0	0.05	2.51	2.46
pyridine	3.0	0.05	0.51	0.46
	6.0	0.05	0.93	0.88
	24.0	0.11	1.29	1.14
	48.0	0.13	1.40	1.23
pyridine *N*-oxide[c]	0.5	0.45	2.41	1.96
	1.0	0.45	2.41	1.96
	3.0	0.46	2.40	1.96

[a,b] See corresponding footnotes in Table I. [c] Reverse addition.

Dimethyl sulfoxide was moderately reduced; however, tetramethylene sulfoxide was reduced rapidly to give a 95% yield of tetramethylene sulfide in 0.5 h at 0 °C. Although sulfones are reported to be reduced to sulfides in a moderate yield at elevated temperature,[19,20] diphenyl sulfone was inert to DIBAH under standard conditions. Both methanesulfonic acid and *p*-toluenesulfonic acid liberated hydrogen quantitatively. However, no reduction was observed.

p-Toluenesulfonic acid monohydrate liberates 3 equiv of hydrogen with most metal hydrides.[3a-o] DIBAH and $LiEt_3BH$ are two rare examples that liberate only 2 equiv of hydrogen. We examined the reaction of water with 4 equiv of DIBAH and observed only 1 equiv of hydrogen evolution. Apparently diisobutylaluminum hydroxide (A) is inert to DIBAH, as shown in eq 8.

$$(i\text{-Bu})_2\text{AlH} + \text{H}_2\text{O} \rightarrow \underset{\text{A}}{(i\text{-Bu})_2\text{AlOH}} + \text{H}_2$$

$$\underset{\text{A}}{(i\text{-Bu})_2\text{AlOH}} + (i\text{-Bu})_2\text{AlH} \rightarrow \text{no reaction} \qquad (8)$$

n-Octyl tosylate was rapidly reduced to *n*-octane in a 97% yield in 1 h at 0 °C; however, cyclohexyl tosylate evolved 1 equiv of hydrogen rapidly, suggesting an elimination reaction. Indeed, we identified the products as 95% cyclohexene and 5% cyclohexane after 6 h at 0 °C. The rapid reduction of *n*-octyl tosylate and the inertness of *n*-octyl halides (Table VII) promise an important selective reduction of tosylates in the presence of halides.

Many other hydrides, such as $LiAlH_4$,[21] $LiEt_3BH$,[22] and $NaBH_4$,[23] can be used for tosylate reduction; however, they have almost no chemoselectivity between tosylates and halides. We are going to study this possibility more in detail. The results are summarized in Table XI.

Table XI. Reaction of DIBAH with Representative Sulfur Derivatives in Toluene at 0 °C

compd[a]	time, h	hydrogen evolved[b]	hydride used[b] total	hydride used[b] for red.
di-*n*-butyl disulfide	0.5	1.00	1.95	0.95
	1.0	1.00	1.99	0.99
diphenyl disulfide	0.5	0.51	1.00	0.50
	1.0	0.65	1.30	0.65
	6.0	0.97	1.97	1.00
methyl *p*-tolyl sulfide	0.5	0.00	0.01	0.01
	1.0	0.01	0.04	0.03
	3.0	0.01	0.03	0.02
dimethyl sulfoxide	3.0	0.71	1.51	0.80
	6.0	0.85	1.72	0.87
	24.0	0.85	1.85	1.00
diphenyl sulfone[c]	0.5	0.00	0.00	0.00
	3.0	0.00	0.00	0.00
methanesulfonic acid[c]	0.5	0.99	0.99	0.00
	1.0	0.99	0.00	0.00
p-toluenesulfonic acid monohydrate[c]	0.5	2.03	2.04	0.01
	1.0	2.03	2.04	0.01
	6.0	2.03	2.04	0.01
n-octyl tosylate[d]	0.5	0.02	1.05	1.03
	6.0	0.04	1.05	1.01
	24.0	0.04	1.05	1.01
cyclohexyl tosylate[c]	0.5	0.91	0.97	0.06
	1.0	0.98	1.04	0.06
	6.0[e]	1.03	1.12	0.09

[a,b] See corresponding footnotes in Table I. [c] Reverse addition. [d] GLC analysis showed a 97% yield of *n*-octane in 1 h at 0 °C. [e] GLC analysis showed a 95% yield of cyclohexene and a 5% yield of cyclohexane.

Conclusion

The reducing characteristics of DIBAH in toluene have been studied systematically with 69 selected organic compounds containing representative functional groups. In general, the data confirm the results already available in the literature but provide data in a single solvent with controlled concentration and temperature. This permits ready comparison of the rates and stoichiometry of the reactions of DIBAH and of many other metal hydrides[3a-o] already studied so that definite conclusions can be drawn as to the particular reagent that would be most advantageous to apply for specific reduction. The data for the reduction of representative functional groups with this reagent in toluene at 0 °C are summarized in Table XII.

Experimental Section

Materials. DIBAH was purchased from Aldrich Chemical Co. as a 25% solution in toluene. Most of the organic compounds utilized in this study were commercial products of the highest purity. They were further purified by distillation or recrystallization when necessary. All glassware was dried thoroughly in a drying oven and cooled under a dry nitrogen atmosphere. Hypodermic syringes were used to transfer solutions.[24]

Procedure for Rates and Stoichiometry. All the reactions and solutions were maintained under a dry nitrogen atmosphere. The reduction of styrene oxide is described as an example of the experimental procedure. A 50-mL flask was oven-dried and cooled in a dry stream of nitrogen. The flask was equipped with a reflux condenser connected to a gas buret. The flask was immersed in an ice bath, and 1.6 mL of toluene was introduced into the reaction flask, followed by 7.4 mL (12 mmol) of a 1.62 M solution of DIBAH in toluene. Finally, 3 mL (3.0 mmol) of a 1.0 M solution of styrene oxide and *n*-dodecane was injected into the reaction flask. *n*-Dodecane was added as an internal standard. Now the reaction mixture was 1.0 M in DIBAH and 0.25 M in styrene oxide. The hydrogen evolved was collected in the buret and measured (0.03 mmol). After 30 min, a 2-mL aliquot of the reaction mixture (0.5 mmol of the compound) was removed with a hypodermic syringe and injected into a hydrolyzing solution of methanol, which was precooled to 0 °C in an ice bath. The hydrogen evolved amounted

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Table XII. Reduction of Representative Functional Groups with Diisobutylaluminum Hydride in Toluene at 0 °C

functional group	hydride used[a]	time, h	products and remarks	ref
aldehyde	1	0.5	alcohol	2
ketone	1	0.5	alcohol	2
cinnamaldehyde	1	0.5	cinnamyl alcohol[c]	2
benzoquinone	1.6 (0.4)	3	hydroquinone and 1,4-dihydroxycyclohexadiene[b]	
anthraquinone	2.1 (0.1)	3	mostly 9,10-dihydroxy-9,10-dihydroanthracene[b]	
carboxylic acid	2.8 (0.8)	12	at room temp, alcohol	2
carboxylic acid salt	0	6	no reaction	
anhydride	4	6	alcohol	2
anhydride (cyclic)	3	24	slow red. to alcohol	2
acyl chloride	2	0.5	alcohol	2
ester	2	0.5	alcohol[c]	2
lactone	2	0.5	glycol[c]	
isopropenyl acetate	2	0.5	2,4-pentanediol	9
alkyl halide	0	24	no reaction	
aryl halide	0	24	no reaction	
epoxide	1	0.5	alcohol[c]	10
primary amide	2.3 (0.9)	24	slow red. to amine[b]	
tertiary amide	2	0.5	amine	13
nitrile	1	0.5	aldehyde	14
nitro	3 (1)	24	hydroxylamine[b]	
azo	1	3	hydrazobenzene[b]	
azoxy	3 (1)	9	hydrazobenzene[b]	
cyclohexanone oxime	2 (0.9)	1	hydroxylamine[b]	
acetophenone oxime	2.7 (0.8)	0.5	secondary amine	15
pyridine	1.2 (0.1)	24	1,2-dihydropyridine	16
pyridine *N*-oxide	2.4 (0.4)	0.5	1,2-dihydropyridine[b]	
disulfide	2 (1)	1	thiol[b]	
sulfoxide	2 (1)	1	sulfide[c]	
n-octyl tosylate	1	0.5	*n*-octane[c]	
cyclohexyl tosylate	1 (1)	0.5	cyclohexene[c]	

[a] Total hydride used per mole of compound. Numbers in parentheses indicate hydrogen evolution. [b] Products deduced from the stoichiometry. [c] Products confirmed by identification.

to 1.49 mmol as compared to 2.01 mmol for a blank reaction (in which 3 mL of toluene was substituted for the 3 mL of the solution of the compound). The difference of 0.52 mmol represented the number of mmoles of hydride used per 0.5 mmol of compound added. Aliquots were also removed and hydrolyzed after 1 and 3 h of reaction time. Both produced 0.52 and 1.51 mmol of hydrogen, indicating 1 equiv of hydride had been consumed. At the end of 3 h, the remaining mixture was hydrolyzed with methanol, followed by hydrochloric acid solution (2.0 M). The organic layer was separated, and analysis by GLC with a 5% Carbowax 20M column, 6 ft × 0.125 in., showed 27% 1-phenylethanol and 73% 2-phenylethanol.

General Procedure for Stereochemistry Study. The reduction of 2-methylcyclohexanone is representative. To a 50-mL flask fitted with a side arm and capped by a rubber septum were added 7.4 mL (12 mmol) of 1.62 M DIBAH in toluene and 1.6 mL of toluene. The flask was kept at 0 °C with the aid of an ice bath. To this was added 3 mL (3 mmol) of a 1.0 M solution of 2-methylcyclohexanone and *n*-dodecane (as an internal standard). The reaction mixture was kept at 0 °C for 3 h. It was then hydrolyzed by the addition of methanol, followed by hydrochloric acid solution (2.0 M). The organic layer was separated and dried with anhydrous potassium carbonate. The dry organic solution was subjected to GLC analysis on 10% diglycerol column, 17 ft × 0.125 in., showing 51% *cis*- and 49% *trans*-2-methylcyclohexanol.

Preparative Procedures for Reduction of Organic Compounds with DIBAH. In most cases, the identities of the products were established by GLC analysis, as described above. However, in some cases, the reaction mixtures were then worked up to isolate and characterize the reduction products. Three representative examples are described to illustrate the procedure.

Reduction of Cinnamaldehyde to Cinnamyl Alcohol. A magnetic stirring bar was placed in a 250-mL flask equipped with reflux condenser connected to a mercury bubbler, and 25 mL (40.5 mmol) of 1.62 M DIBAH in toluene was introduced. An ice bath was placed under the flask, and 40 mL (20 mmol) of a 0.5 M solution of cinnamaldehyde in toluene was added. After 2 h, 20 mL of toluene–methanol (1:1) solution was added slowly, with cooling, followed by 20 mL of 2.0 M hydrochloric acid solution, and the resulting mixture was stirred at 0 °C for 30 min. The solid aluminum salts were filtered, the organic layer was separated, the aqueous layer was extracted twice with 20-mL portions of ether, and the combined organic layer was dried over anhydrous potassium carbonate. The solvents were evaporated on a rotary evaporator to give a colorless oil which solidified upon cooling in an ice bath. The resulting precipitate was recrystallized with *n*-pentane–ether to give 2.52 g (94%) of cinnamyl alcohol as a white solid, mp 33–34 °C (lit.[25] mp 33–35 °C), >99% pure by GLC.

Reduction of Ethyl Benzoate to Benzyl Alcohol. In a 250-mL flask, typically equipped as above, 26 mL (42.1 mmol) of 1.62 M DIBAH in toluene was placed, and 10 mL of toluene was introduced. An ice bath was placed under the flask, and 20 mL (20 mmol) of 1.0 M ethyl benzoate in toluene was added. After 3 h, the product was decomposed with 20 mL of toluene–methanol (1:1) solution, followed by 20 mL of 2.0 M hydrochloric acid solution. The solid aluminum salts were filtered, the organic layer was separated, the aqueous layer was extracted with ether (2 × 15 mL), and the combined organic layer was dried over anhydrous potassium carbonate. Distillation of the organic product gave 1.85 g (86%) of benzyl alcohol, bp 89–91 °C (7 mm), n^{20}_D 1.5384, (lit.[25] n^{20}_D 1.5396), >98% pure by GLC.

Reduction of Phthalide to 1,2-Benzenedimethanol. A typical reaction setup was assembled. Then 13.0 mL (21.1 mmol) of DIBAH in toluene was introduced into the 250-mL flask. An ice bath was placed under the flask, and 20 mL (10 mmol) of a 0.5 M phthalide solution in toluene was slowly added with vigorous stirring. After 1 h, the reaction mixture was worked up as described in the reduction of cinnamaldehyde. The solvents were removed under water aspirator and finally over the vacuum pump, and the resulting precipitate was recrystallized with hexane–ether to give 1.119 g (81%) of 1,2-benzenedimethanol as a white solid, mp 62 °C (lit.[25] mp 63–65 °C). The identity of the product was further confirmed by NMR and IR.

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Registry No. DIBAH, 1191-15-7; $CH_3(CH_2)_5OAl(i\text{-}Bu)_2$, 96503-31-0; $PhCH_2OAl(i\text{-}Bu)_2$, 41329-29-7; $CH_3CH_2CH(CH_2CH_2CH_3)OAl(i\text{-}Bu)_2$, 96503-32-1; $CH_3CH_2CH(CH_2CH_3)OAl(i\text{-}Bu)_2$, 96503-33-2; $PhOAl(i\text{-}Bu)_2$, 4165-53-1; 2,6-$(t\text{-}Bu)_2C_6H_4OAl(i\text{-}Bu)_2$, 76229-55-5; $CH_3(CH_2)_5SAl(i\text{-}Bu)_2$, 96503-34-3; $PaSAl(i\text{-}Bu)_2$, 96503-35-4; $CH_3(CH_2)_5NHAl(i\text{-}Bu)_2$, 96503-36-5; $(i\text{-}Bu)_2AlOCH_2CH_2NHAl(i\text{-}Bu)_2$, 96503-37-6; 1-hexanol, 111-27-3; benzyl alcohol, 100-51-6; 3-hexanol, 623-37-0; 3-ethyl-3-pentanol, 597-49-9; phenol, 108-95-2; 2,6-di-*tert*-butylphenol, 128-39-2; 1-hexanethiol, 111-31-9; benzenethiol, 108-98-5; *n*-hexylamine, 111-26-2; 2-aminoethanol, 141-43-5; *n*-hexanal, 66-25-1; benzaldehyde, 100-52-7; 2-heptanone, 110-43-0; norcamphor, 497-38-1; camphor, 1195-79-5; acetophenone, 98-86-2; benzophenone, 119-61-9; cinnamaldehyde, 104-55-2; methyl vinyl ketone, 78-94-4; isophorone, 78-59-1; 2-methylcyclohexanone, 583-60-8; 4-*tert*-butylcyclohexanone, 98-53-3; *p*-benzoquinone, 106-51-4; anthraquinone, 84-65-1; hexanoic acid, 142-62-1; benzoic acid, 65-85-0; crotonic acid, 3724-65-0; lithium benzoate, 553-54-8; acetic anhydride, 108-24-7; succinic anhydride, 108-30-5; phthalic anhydride, 85-44-9; hexanoyl chloride, 142-61-0; benzoyl chloride, 98-88-4; ethyl hexanoate, 123-66-0; ethyl benzoate, 93-89-0; ethyl crotonate, 10544-63-5; phenyl acetate, 122-79-2; γ-butyrolactone, 96-48-0; phthalide, 87-41-2; isopropenyl acetate, 108-22-5; *n*-octyl iodide, 629-27-6; *n*-octyl bromide, 111-83-1; *n*-octyl chloride, 111-85-3; *p*-bromotoluene, 106-38-7; 1,2-butylene oxide, 106-88-7; cyclohexene oxide, 286-20-4; styrene oxide, 96-09-3; 1-methyl-1,2-cyclohexene oxide, 1713-33-3; hexanamide, 628-02-4; benzamide, 55-21-0; *N,N*-dimethylhexanamide, 5830-30-8; *N,N*-dimethylbenzamide, 611-74-5; hexanenitrile, 628-73-9; benzonitrile, 100-47-0; acrylonitrile, 107-13-1; nitrobenzene, 98-95-3; nitropropane, 108-03-2; azobenzene, 103-33-3; azoxybenzene, 495-48-7; cyclohexanone oxime, 100-64-1; acetophenone oxime, 613-91-2; phenyl isocyanate, 103-71-9; pyridine, 110-86-1; pyridine *N*-oxide, 694-59-7; diphenyl disulfide, 882-33-7; methyl *p*-tolyl sulfide, 623-13-2; dimethyl sulfoxide, 67-68-5; diphenyl sulfone, 127-63-9; methanesulfonic acid, 75-75-2; *p*-toluenesulfonic acid, 104-15-4; *n*-octyl tosylate, 3386-35-4; cyclohexyl tosylate, 953-91-3; benzenemethanol, 100-51-6; 2-heptanol, 543-49-7; bicyclo[2.2.1]heptan-2-ol, 1632-68-4; 1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol, 10385-78-1; 1-phenylethanol, 98-85-1; diphenylcarbinol, 91-01-0; cinnamyl alcohol, 104-54-1; 3-hydroxy-1-butene, 598-32-3; 3,5,5-trimethyl-2-cyclohexen-1-ol, 470-99-5; *cis*-2-methylcyclohexanol, 7443-70-1; *trans*-2-methylcyclohexanol, 7443-52-9; *cis*-4-*tert*-butylcyclohexanol, 937-05-3; *trans*-4-*tert*-butylcyclohexanol, 21862-63-5; hydroquinone, 123-31-9; 1,4-dihydroxycyclohexadiene, 63453-92-9; 9,10-dihydro-9,10-anthracenediol, 58343-58-1; crotyl alcohol, 6117-91-5; ethanol, 64-17-5; 1,4-dihydroxybutene, 110-64-5; 1,2-benzenedimethanol, 612-14-6; 2,4-pentanediol, 625-69-4; 1,2-dihydroxybutane, 584-03-2; 1,2-dihydroxycyclohexane, 931-17-9; 2-phenylethanol, 60-12-8; 1-methylcyclohexanol, 590-67-0; 1-aminohexane, 111-26-2; benzylamine, 100-46-9; *N,N*-dimethylhexanamine, 4385-04-0; *N,N*-dimethylaniline, 121-69-7; acrylaldehyde, 107-02-8; *N*-hydroxyaniline, 100-65-2; *N*-hydroxy-1-propanamine, 627-38-3; hydrazobenzene, 122-66-7; *N*-hydroxycyclohexanamine, 2211-64-5; *N*-ethylaniline, 103-69-5; *N*-methylenebenzenamine, 100-62-9; 1,2-dihydropyridine, 22694-45-7; butyl mercaptan, 109-79-5; methyl mercaptan, 74-93-1; *p*-tolyl mercaptan, 106-45-6; dimethyl sulfide, 75-18-3; 1,4-dihydroxybutane, 110-63-4; octane, 111-65-9; cyclohexene, 110-83-8; hydrogen, 1333-74-0; di-*n*-butyl disulfide, 629-45-8; tetramethylene sulfoxide, 1600-44-8; tetramethylene sulfide, 110-01-0.

Synthesis of Pyrrolo[3,4-*d*]imidazoles. A New Fluorescent Heterocyclic System[1]

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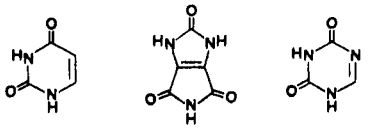
Pyrrolo[3,4-*d*]imidazoles (**9**), "stretched-up" pyrimidine analogues, have been prepared by a two-step procedure from the corresponding pyrrolo[3,4-*d*]imidazolines (**5**). The new heterocyclic system displays exceptional fluorescence properties. Large Stokes shifts are observed in both polar and nonpolar solvents, and the emission maxima are sensitive to solvent. *N*-Ribosyl derivatives have been prepared in both series (**12** and **13**). The planarity of the substituted pyrrolo[3,4-*d*]imidazole ring system has been established by X-ray crystallographic analysis.

Research in our laboratory has focused on the synthesis of fluorescent and dimensionally extended analogues of adenine, adenosine, and adenosine phosphates. The interactions of these analogues with selected enzyme systems have provided insights into the geometric and electronic requirements of enzyme binding sites.[2] We are now extending such studies to include analogues of pyrimidines. Our first goal is the synthesis of a heterocycle that maintains both the array of hydrogen bond donors and acceptors found in a pyrimidine such as uracil (**1**) and the planarity of the system. The first structure targeted, pyrroloimidazole **2**, incorporates these features (albeit on both sides of the molecule), but the sites of hydrogen bonding are set apart and are at slightly different angles. We have chosen the term "stretched-up" to describe this type of analogue. Obviously, the analogy is imperfect: heterocycle **2** contains extra nitrogen and carbonyl groups. Nevertheless, the symmetry of the compound presents the same type of hydrogen-bonding potentiality on each side. Closer analogy of **2** might be to the azapyrimidine 5-azauracil (**3**), which has been found to inhibit protein synthesis and to be incorporated as its riboside into RNAs,[3] or to cyanuric acid.



1 **2** **3**

The ring structure of two fused, copolanar five-membered rings may interfere with pyrimidine metabolic processes through similar or competitive enzyme binding based on spatial requirements. At the same time, the

(1) Casteel, D. A.; Leonard, N. J. "Abstracts of Papers", 188th National Meeting of the American Chemical Society, Philadelphia, PA, Aug 1984; American Chemical Society: Washington, DC, 1984; ORGN 119.

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