precipitated CrO_3.[2b] The final volume was 336 mL (3.36 M with respect to CrO_3).

General Oxidation Procedure Using the Jones Reagent. To a two-necked, 300-mL Morton flask, fitted with a high-speed mechanical stirrer and immersed in an ice bath, was added 0.02 mol of the hydrocarbon in 50 mL of acetone. The cooled mixture was stirred[6a] vigorously during the addition of 46 mL of Jones reagent over a period of 30 min. The temperature of the reaction mixture was maintained between 5 and 15 °C throughout the reaction. As the green $Cr_2(SO_4)_3$ began appearing, 8.4 g (0.07 mol) of anhydrous $MgSO_4$ was added. The maximum yield was observed with this quantity. As stated earlier, this treatment minimized stirrer imbalance resulting from adhering salts. The use of 50 g of oven-dried (120–130 °C) silica (50 mol/mol of hydrocarbon) as a substitute for anhydrous magnesium sulfate proved equally effective.[6b]

Samples were withdrawn at intervals, treated with anhydrous sodium carbonate, filtered, and analyzed by gas chromatography (Table I) to determine the completeness of reaction. In most cases, 6–8 h of reaction time was adequate for complete consumption of starting hydrocarbon. Additional Jones reagent was added to those hydrocarbons that oxidized slowly, and stirring was continued for a total of 10 h.

On disappearance of starting material, excess Jones reagent was destroyed by adding isopropyl alcohol.[2b] The contents of the flask were filtered through Dicalite to remove suspended chromium salts. The filter cake was washed, as needed, with acetone and ether. The filtrate was rotary evaporated, the reaction product was dissolved in ether, and the ether solution was washed with sodium bicarbonate solution to remove any remaining sulfuric acid and acetic acid formed through the oxidation of acetone. The ether extract was dried ($MgSO_4$), filtered, and concentrated to obtain the ketone of interest.

Yield Optimization in Converting Tetralin to 1-Tetralone. Five experiments were carried out in which all conditions, including the amount of $MgSO_4$, were held constant except that the molar ratio of CrO_3:tetralin ranged from 4:1 to 10:1. The maximum yield of 1-tetralone was obtained with a ratio of 7:1. The theoretical chromium trioxide:tetralin ratio is 4:3.

Stability of 1-Tetralone during Jones Oxidation. 1-Tetralone (2.92 g, 0.02 mol) and 46.0 mL of Jones reagent in 50 mL of acetone were stirred for 4 h at ice-bath temperature. The isolation was carried out as described in the general procedure. The product showed a single GLC peak (1-tetralone), and the recovered yield (85%) of 1-tetralone was determined by GLC analysis using added tetralin as an internal standard.

Chromium Trioxide Consumed and Acetic Acid Formed during Blank Runs. Samples of actone (50 mL, 1.17 mol) were stirred with 10 mL of Jones reagent for 4, 8, and 12 h, under conditions typical of those used to oxidize hydrocarbons. At the end, the excess Jones reagent was destroyed by adding isopropyl alcohol, and the contents were steam-distilled. Several 100-mL distillation fractions were collected and titrated with 0.1 N NaOH to the phenolphthalein end point. These data are found in Table II.

The amount of chromium trioxide consumed for the same oxidation was also determined by repeating the reaction for 4, 8, and 12 h under identical experimental conditions and rotary evaporating the remaining acetone. The residue was diluted to 1000 mL, and several 50-mL portions were titrated with standardized sodium thiosulfate solution after the addition of potassium iodide and 1% starch solution for end point determination.[8] Again, the results are shown in Table II.

Acknowledgment. We thank Drs. O. C. Dermer and R. A. Bunce for their interest in this work and for reading the manuscript.

Registry No. **1a**, 119-64-2; **1b**, 529-34-0; **2a**, 101-81-5; **2b**, 119-61-9; **3a**, 86-73-7; **3b**, 486-25-9; **4a**, 1685-82-1; **4b**, 1685-81-0; **4c**, 6682-69-5; **5a**, 42044-22-4; **5b**, 42981-75-9; **5c**, 42981-74-8; **6a**, 42044-24-6; **6b**, 51015-35-1; **6c**, 51015-36-2; **7a**, 5325-97-3; **7b**, 13250-73-2; **7c**, 75490-06-1; **8**, 1559-81-5; **9**, 14944-28-6; **10**, 19832-98-5; **12**, 66405-16-1.

Synthesis of a Representative Cis/Trans Pair of 4,5-Disubstituted Cyclopentenyllithium Reagents

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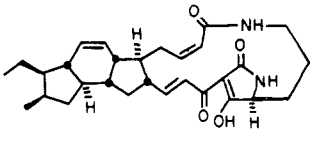
Received January 14, 1985

A useful procedure for effecting the conversion of 2,3-disubstituted cyclopentanones to cis- and trans-4,5-disubstituted cyclopentenyllithium reagents has been developed. The preferred sequence of reactions (at least for obtaining the cis isomer) involves *uncatalyzed* tosylhydrazone formation and conversion by the Shapiro reaction to epimeric vinylstannanes that are readily separable by spinning band distillation. Of particular relevance is the ease and high efficiency of the subsequent iodination and metalation of these pivotal intermediates. This methodology is amenable to reasonable scale-up and convenient to implement in practice.

Utilization of the anionic oxy-Cope rearrangement in organic synthesis most often relies upon preliminary condensation of a β,γ-unsaturated ketone with a vinyl organometallic reagent.[2] While notable achievements have been made through proper application of vinyllithium, vinylmagnesium bromide, and related simple nucleophilic reagents, acquisition of complex natural products understandably can become limited by the availability of stereochemically more ornate substrates. In connection with a convergent approch to ikarugamycin (1) being pursued



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(1) Postdoctoral Fellow of the Deutscher Akademischer Austauschdienst (NATO), 1983–1984.

(2) For example: (a) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765. (b) Still, W. C. *Ibid.* **1977**, *99*, 4186. (c) Jung, M. E.; Hudspeth, J. P. *Ibid.* **1978**, *100*, 4309. (d) Evans, D. A.; Nelson, J. V. *Ibid.* **1980**, *102*, 774. (e) Kahn, M. *Tetrahedron Lett.* **1980**, *21*, 4547. (f) Koreeda, M.; Tanaka, Y.; Schwartz, A. *J. Org. Chem.* **1980**, *45*, 1172. (g) Schreiber, S. L.; Santini, C. *Tetrahedron Lett.* **1981**, *22*, 4651. (h) Geetha, P.; Huq, C. A. M. A.; Rajagopalan, K.; Swaminathan, S. *Ibid.* **1982**, *23*, 569.

0022-3263/85/1950-2438$01.50/0

Table I. Catalytic Hydrogenation of 4[a]

conditions	solvent	5:6
10 wt % of 10% Pd-C	CH_2Cl_2	1.1:1
10 wt % of 10% Pd-C	C_2H_5OH	4.5:1
10 wt % of 5% Rh-C	petroleum ether	9:1
10 wt % of 5% Rh-C and 2.5 wt % of Na_2CO_3	petroleum ether	18:1

[a] Reactions were uniformly carried out on 1 g of substrate, and product determinations were performed by analytical VPC.

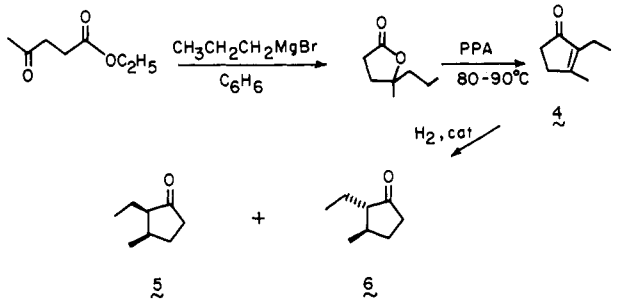
along these lines in this laboratory, the need immediately arose for a reliable source of (*cis*-4-methyl-5-ethylcyclopentenyl)lithium (**2**). To our knowledge, no attention has

2

3

previously been paid to gaining access to synthons of this type. We therefore describe here preparatively useful routes to **2** and its trans isomer **3** that are expected to prove equally serviceable for obtaining higher homologues.

Although the conjugate addition of lithium dimethylcuprate to 2-cyclopentenone followed by in situ condensation with ethyl iodide could prove expeditious in providing 3-methyl-2-ethylcyclopentanone, the dominant isomer was certain to be trans.[3] For this reason, attention was focused upon securing the readily available **4**[4] and

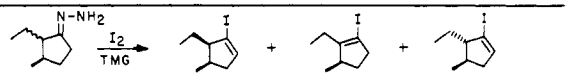


5 **6**

subjecting this enone to catalytic hydrogenation. The distribution of **5** and **6** was found to be highly dependent upon the conditions of reduction (Table I), a direct result of the sensitivity of the cis isomer to epimerization. In ancillary experiments, samples highly enriched (90%) in **5** were readily transformed into mixtures dominated by **6**, especially when acidic reagents were involved. In the presence of bases such as triethylamine, epimerization was much slower (see Experimental Section). The isomers were separated by means of gas chromatography and further identified on the basis of their ^1H NMR spectra.[5]

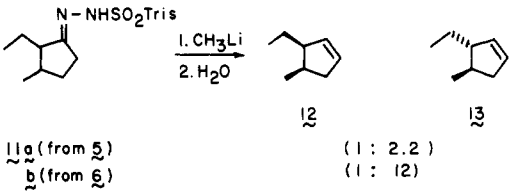
Despite the shortcomings arising from the obvious thermodynamic instability of **5**, the preceding experiments failed to provide information concerning the fate of the cis ketone under reaction conditions having a significant element of kinetic control. To gain some insight into this question, **5** (90% stereochemical purity) was treated with a 50-fold excess of hydrazine hydrate in refluxing ethanol containing triethylamine. Under these conditions, a 56% yield of hydrazone **7** and 28% yield of azine was realized. Direct exposure of **7a** to the action of iodine and tetramethylguanidine in ether[6] afforded in 78% yield a three-component mixture of the isomeric vinyl iodides **8–10** (Table II) which were separated by preparative VPC. Repetition of this reaction scheme with **6** (85% isomerically enriched) gave hydrazone **7b** (78%) and subsequently **8–10** (78%). The indicated structural assignments follow

Table II. Iodine-Promoted Oxidation of Hydrazones 7[a]



	8	**9**	**10**
7a	1	3.5	4.5
7b	1	7	8

[a] Product determinations were achieved by means of analytical VPC.



12 **13**

from ^1H NMR analysis, combustion/mass spectral data, and (for **8** and **10**) expectations based on the stereochemistry of the starting ketone. The obvious loss of stereochemical integrity and difficulty associated with ready fractionation of the vinyl iodides signaled that a more controlled functionalization scheme had to be devised.

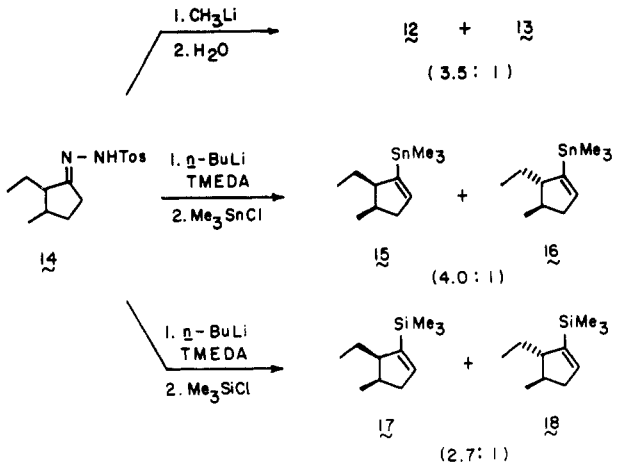
Since the Shapiro reaction[7] exhibits a strong predilection for conversion of a ketone sulfonylhydrazone to the less substituted vinyllithium derivative, the independent conversion of **5** and **6** to their (triisopropylbenzenesulfonyl)-hydrazones (**11a** and **11b**, respectively) was next examined.[8] Despite the fact that neither heat nor acid catalysis was applied during the derivatization reactions, considerable loss of stereochemical integrity was again apparent (^1H NMR analysis) in the crystalline solids that precipitated from solution. Thus, the 300 MHz of **11a** exhibited, in addition to the overlapping methyl signals of the cis isomer centered at δ 0.75, the characteristic absorptions for the C-3 methyl (δ 0.98) and CH_3CH_2 groups (0.53) of the trans isomer. When the individual trisylhydrazones were degraded with methyllithium and ultimately quenched with water, cyclopentenes **12** and **13** resulted. VPC analysis showed **13** to be present in excess in both cases, with substantially greater enrichment arising expectedly from **11b**.

The unanticipated results of this study demanded clarification. A clue to the source of the complication was located in a recent report wherein the inherent instability of triisopropylbenzenesulfonylhydrazine was closely scrutinized.[9] Remarkably, this reagent was noted to have a half-life of only 50 min in methanol. Given the sensitivity of **5** (and presumably also *cis*-**11**; see below) to acids, the resultant cis → trans conversion might well be attributed to the relatively rapid liberation of the benzenesulfinic acid! The instability of this sulfonylhydrazine was further reflected in our inability to isolate **11a** and **11b** in yields greater than 50%.[10]

(3) Smith, A. B., III; Wexler, B. A.; Slade, J. A. *Tetrahedron Lett.* **1980**, *21*, 3237.
(4) Rai, C.; Dev, S. *J. Indian Chem. Soc.* **1957**, *34*, 178.
(5) Pfeffer, P. E.; Osman, S. F. *J. Org. Chem.* **1972**, *37*, 2425.
(6) Barton, D. H. R.; Bashiardes, G.; Fourrey, J.-L. *Tetrahedron Lett.* **1983**, *24*, 1605.
(7) Shapiro, R. H. *Org. React. (N.Y.)* **1975**, *23*, 405.
(8) Chamberlin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147.
(9) Cusack, N. J.; Reese, C. B.; Risius, A. C.; Roozpukar, B. *Tetrahedron* **1976**, *32*, 2157.
(10) For complications of a related type involving this functionality, see Daniels, R. G.; Paquette, L. A. *Organometallics* **1982**, *1*, 1449.

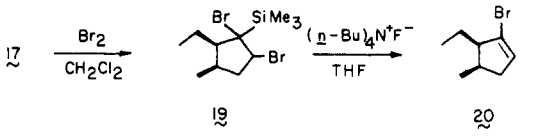
By comparable standards, (*p*-toluenesulfonyl)hydrazine is much less prone to decomposition.[9] Accordingly, suitable condensation of this reagent with **5** was investigated. Condensation in methanol at room temperature during 12 h afforded colorless crystals of **14** in 99% yield. Recrystallization from petroleum ether–ether (4:1) afforded a product melting sharply at 84–85 °C. Although this substance is very probably not isomerically pure, its ^{1}H NMR spectrum in $CDCl_3$ suggested that 60% of the trans isomer was present. Immediate recovery of the material from the NMR tube gave crystals melting at 98–105 °C. As a direct consequence of this obvious lability, **14** was utilized directly as it precipitated from solution for the ensuing experiments.

Perhaps the best indicator of the stereochemical character of **14**, at least in a synthetically usable sense, is the relative distribution of **12** and **13** which results from its Shapiro degradation. Subsequent to such handling of freshly prepared **14**, the cyclopentene mixture was found to be enriched to the extent of 78% in the cis isomer. Comparable product distributions were observed upon conversion to the trimethylstannyl (**15**/**16**) and trimethylsilyl (**17**/**18**) derivatives by means of a protocol



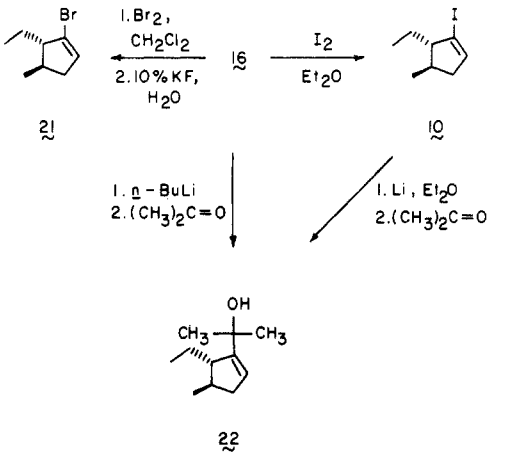
earlier described.[11] Their ratios have proven to be variable and entirely dependent on the technique employed for isolation of **14**. *Importantly, these reactions can be scaled up with ease and the individual isomers conveniently separated by spinning band distillation.* This fractionation serves as the simultaneous entry point to both series of 4,5-disubstituted 1-cyclopentenyl reagents.

Although the conversion of vinylsilanes into vinyl halides is purported to be a general reaction,[12] only one example is known where a five-membered ring compound has undergone a transformation of this type.[13] Indeed, direct iodination[14] of **17** could not be accomplished. Also, while conversion to the highly unstable dibromide **19** proceeded smoothly, neither sodium ethoxide[15] nor alumina[15] was effective in delivering the desired **20**. In contrast, tetra-*n*-butylammonium fluoride in tetrahydrofuran proved serviceable and provided **20** in approximately 50% overall yield from **17**. Trans isomer **21** could be obtained in



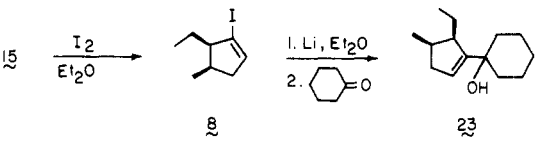
analogous fashion. With both isomers in hand, it was quite clear (VPC, 300 MHz ^{1}H NMR) that no stereochemical cross-contamination had taken place during this sequence of steps.

The preceding limitations did not surface when the more reactive trimethylstannane derivatives were employed. For example, low-temperature bromination of **16** and ensuing treatment with aqueous potassium fluoride solution gave rise to **21** in 92% yield. Conversion to iodide **10** by direct



iodination proceeded straightforwardly and efficiently (97%). In fact, the sequential formation of **10**, halogen–lithium exchange, and condensation with acetone proved to be a more efficacious route to allylic alcohol **22** (83%) than that mediated by the direct metalation of **16** with *n*-butyllithium (30%).

Iodide **8**, which is formed from **15** in 95% yield under equally mild conditions, likewise undergoes ready halogen–metal exchange as a preclude to nucleophilic activation. The 1,2-addition of cyclohexanone leading to **23** is illustrative of the reactivity of this cyclopentenyllithium reagent.



The chemistry described herein establishes that 1-cycloalkenyllithium reagents that carry flanking chiral centers can be prepared in stereochemically pure form from the derived ketones. The problem of safeguarding the thermodynamically less stable configuration is resolvable if tosylhydrazone formation is resorted to. The vinylsilanes and vinylstannanes can be prepared on a reasonable scale and efficiently separated by distillation. Where trimethylstannanes are concerned, no difficulties are involved in subsequent activation for use as nucleophilic reagents. The tin-mediated scheme, particularly attractive for its high yields, emerges as the method of choice for preparing this class of organolithium reagents.

Experimental Section

Typical Catalytic Hydrogenation of 4. A solution of **4**[4] (3.4 g, 27.4 mmol) in petroleum ether (50 mL) containing 5% rhodium on carbon (0.4 g) and powdered sodium carbonate (0.5 g) was stirred vigorously under an atmosphere of hydrogen. Progress of the reaction was monitored by VPC (10% SE-30, 80 °C) and

(11) (a) Taylor, R. T.; Degenhardt, C. R.; Melega, W. P.; Paquette, L. A. *Tetrahedron Lett.* **1977**, 159. (b) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. *J. Org. Chem.* **1980**, *45*, 3017.

(12) Miller, R. B.; Reichenbach, T. *Tetrahedron Lett.* **1974**, 543.

(13) Paquette, L. A.; Wells, G. J.; Horn, K. A.; Yan, T.-H. *Tetrahedron Lett.* **1982**, *23*, 263; *Tetrahedron* **1983**, *39*, 913. For application of this process to larger rings, consult: Snider, B. B.; Cartaya-Marin, C. P. *J. Org. Chem.* **1984**, *49*, 153.

(14) Review: Chan, T. H.; Fleming, I. *Synthesis* **1979**, 701.

(15) Miller, R. B.; McGarvey, G. *Synth. Commun.* **1977**, *7*, 475.

noted to be complete after 12 h. Three peaks were observed in the ratio of 1:9:0.4 (6:5:unknown compound, respectively). After filtration and solvent evaporation, the residue was distilled to give 3.2 g (92.3%) of product, bp 87 °C (22 torr). No change in product composition occurred during this processing. A pure sample of **5** was isolated by prepative VPC (12 ft, 10% SE-30, 75 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (m, 1 H), 2.24–2.18 (m, 2 H), 2.11–1.93 (m, 2 H), 1.77–1.67 (m, 2 H), 1.31–1.21 (m, 1 H), 0.96 (t, J = 7.4 Hz, 3 H), 0.87 (d, J = 7.15 Hz, 3 H).

Acid-Catalyzed Epimerization of 5. A 10-g sample of the preceding 9:1 mixture of **5** and **6** was dissolved in methanol (20 mL), treated with 0.5 mL of concentrated hydrochloric acid, and stirred at room temperature for 2 h. At this point, VPC analysis indicated the **5**:**6** ratio to be 1:7. The solvent was evaporated, and a small quantity of **6** was isolated by preparative VPC as above; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.39–2.27 (m, 2 H), 2.16–1.99 (m, 2 H), 1.97–1.84 (m, 1 H), 1.61 (m, 2 H), 1.47–1.33 (m, 1 H), 1.15 (d, J = 6.4 Hz, 3 H), 0.91 (t, J = 7.4 Hz, 3 H).

Triethylamine-Catalyzed Epimerization of 5. A solution of **5** (0.5 g, 4.0 mmol, 91% stereochemical purity) and triethylamine (0.5 mL) in ethanol (8 mL) was heated at the reflux temperature. Progress of the reaction was monitored by VPC (10% SE-30, 80 °C). The following **5**:**6** ratios were observed: after 60 min, 4.4:1; after 100 min, 1:1; after 9 h, 0.4:1.

Formation of Hydrazones 7. A solution of **5** (88% stereochemical purity) (2.50 g, 19.8 mmol), hydrazine hydrate (50 mL, 1 mmol), and triethylamine (10 mL) in ethanol (30 mL) was heated at the reflux temperature for 12 h, cooled, poured into water (150 mL), and extracted with dichloromethane (3 × 50 mL). The combined organic layers were washed with water, dried, and evaporated. The remaining liquid was distilled to give 1.55 g (56%) of hydrazone **7a**, bp 61 °C (0.5 torr), and 0.70 g (28%) of the azine, bp 123 °C (0.5 torr).

For **7a**: IR (neat, cm^{-1}) 3360, 3200, 2950, 2945, 2865, 2825, 1658, 1614, 1460, 1423, 1377, 1183, 1065; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.81 (br s, 2 H), 2.32–1.69 (m, 5 H), 1.62–1.52 (m, 2 H), 1.30–1.23 (m, 1 H), 1.0–0.75 (m, 6 H); m/z calcd (M^+) 140.1313, obsd 140.1327.

By means of an analogous procedure, a sample enriched in **6** (87%) was transformed into **7b**.

Oxidation of 7 with Iodine. To a solution of 1,1,3,3-tetramethylguanidine (17.6 g, 153 mmol) in anhydrous ether (150 mL) was added dropwise during 90 min a solution of iodine (8.35 g, 32.9 mmol) in the same solvent. Subsequently a solution of **7a** (2.00 g, 14.3 mmol) in dry ether (30 mL) was introduced slowly over 80 min. The dark reaction mixture was stirred at room temperature for 30 min and freed of ether by distillation under a nitrogen atmosphere. An additional 10 mL of guanidine base was added, and the black mixture was heated at 80–90 °C for 2 h, cooled to room temperature, and treated with ether (20 mL). The organic phase was washed with 2 N hydrochloric acid (2 × 30 mL), dilute sodium bisulfite solution (2 × 30 mL), saturated sodium bicarbonate solution (50 mL), and brine (30 mL). Following solvent removal, the residue was taken up in petroleum ether (5 mL), filtered through a plug of Florisil, and analyzed by VPC (10% SE-30, 100 °C). Three peaks were seen in a 4.5:3.5:1 ratio. When the solvent was evaporated, there remained 2.63 g (78%) of a clear, colorless oil which turned pink upon standing for 1 hr at room temperature. After 24 h, the color had changed to black-green. The individual vinyl iodides could be isolated in a pure state by preparative VPC (12 ft 10% SE-30, 80 °C).

For **10** (major component): ^{1}H NMR (30 MHz, $CDCl_3$) δ 6.03 (ABXq, J_{AX} = 2.3 Hz, 1 H), 2.58–2.46 (m, 1 H), 2.26–2.08 (m, 2 H), 1.88 (d of m, J = 16.4 Hz, 1 H), 1.71–1.57 (m, 1 H), 1.40–1.25 (m, 1 H), 1.08 (d, J = 6.9 Hz, 3 H), 0.88 (t, J = 7.4 Hz, 3 H); m/z calcd (M^+) 236.0021, obsd 236.0026.

Anal. Calcd for $C_8H_{13}I$: C, 40.70; H, 5.55. Found: C, 40.94; H, 5.76.

For **9**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.73–2.50 (m, 3 H), 2.31–2.05 (m, 3 H), 1.54–1.42 (m, 1 H), 1.04 (d, J = 6.8 Hz, 3 H), 0.97 (t, J = 7.6 Hz, 3 H); m/z calcd (M^+) 236.0021, obsd 236.0069.

For **8** (minor component): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.16 (ABXq, J_{AX} = 2.4 Hz, 1 H), 2.60–2.34 (m, 3 H), 1.93 (d of m, J = 17 Hz, 1 H), 1.64–1.52 (m, 1 H), 1.49–1.34 (m, 1 H), 1.02 (d, J = 6.6 Hz, 3 H), 0.91 (t, J = 7.4 Hz, 3 H); m/z calcd (M^+) 236.0021, obsd 236.0081.

Anal. Calcd for $C_8H_{13}I$: C, 40.70; H, 5.55. Found: C, 40.76; H, 5.70.

Comparable handling of **7b** provided the results summarized in Table II.

(2,4,6-Triisopropylbenzenesulfonyl)hydrazone Preparation. A solution containing **6** (87% stereochemical purity) (4.7 g, 37.3 mmol) and (2,4,6-triisopropylbenzenesulfonyl)hydrazine (12.0 g, 40.3 mmol) in methanol (25 mL) was prepared and allowed to stand for 1.5 h. The precipitated white crystals were separated by filtration. Partial concentration of the filtrate provided additional crystals, which were also collected. Following washing of the combined crops with cold methanol, there was obtained 7.3 g (52%) of **11b**, mp 142–144 °C dec: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (br s, 1 H), 7.15 (s, 2 H), 4.23 (heptet, J = 6.7 Hz, 2 H), 2.89 (heptet, J = 6.9 Hz, 1 H), 2.36–2.21 (m, 1 H), 2.10–1.84 (m, 3 H), 1.73–1.34 (m, 4 H), 1.26 (6 singlets, total 24 H) 0.98 (d, J = 6.4 Hz, 3 H), 0.53 (t, J = 7.4 Hz, 3 H). Also observed was a multiplet centered at δ 0.75 clearly due to the cis isomer; m/z calcd (M^+) 406.2654, obsd 406.2662.

***trans*-3-Ethyl-4-methylcyclopentene (13).** To a vigorously stirred cold (−50 °C) suspension of **11b** (5.0 g, 12.3 mmol) in anhydrous ether (100 mL) was added methyllithium (30 mL of 1.25 N in ether, 37.5 mmol) during 15 min. The clear yellow solution which resulted was allowed to warm and was stirred at room temperature for 2 h. Water (100 mL) was carefully added, the organic phase was separated, and the aqueous phase was extracted with ether (100 mL). The combined organic layers were dried and distilled slowly through a Vigreux column to remove the ether. Distillation of the residue afforded 0.80 g (59%) of colorless hydrocarbon. VPC analysis (12 ft 10% SE-30, 40 °C) showed **13** and **12** to be present in a 12:1 ratio. Pure **13** was isolated; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.63 (br s, 2 H), 2.57–2.47 (m, 1 H), 2.17–2.05 (m, 1 H), 1.93–1.81 (m, 2 H), 1.46–1.22 (m, 2 H), 1.05 (d, J = 6.6 Hz, 3 H), 0.92 (t, J = 7.4 Hz, 3 H).

Anal. Calcd for C_8H_{14}: C, 87.19; H, 12.81. Found: C, 87.15; H, 12.80.

***cis*-3-Ethyl-4-methylcyclopentene (12).** Reaction of **11a** (3.0 g, 7.4 mmol), prepared analogously from **5** (88% stereochemically pure) with methyllithium (20 mL of 1.25 N in ether) as described above provided 0.60 g (74%) of hydrocarbon product consisting of **12** and **13** in a 1:2.2 ratio. Preparative VPC isolation of **12** was achieved readily; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.71 (m, 2 H), 2.45–2.26 (m, 3 H), 1.90 (d of m, J = 14 Hz, 1 H), 1.50–1.36 (m, 1 H), 1.26–1.13 (heptet, J = 7.4 Hz, 1 H), 0.91 (d, J = 6.6 Hz, 3 H), 0.90 (t, J = 7.3 Hz, 3 H); m/z calcd (M^+) 110.1096, obsd 110.1080.

Anal. Calcd C_8H_{14}: C, 87.19; H, 12.81. Found: C, 87.06; H, 12.91.

2-Ethyl-3-methylcyclopentanone Tosylhydrazone (14). A solution of **5** (88% stereochemically pure) (1.5 g, 12 mmol) and tosylhydrazine (2.4 g, 12.9 mmol) in methanol (20 mL) was stirred at room temperature for 12 h. After evaporation of the solvent and washing of the residue with a small amount of cold methanol, 3.5 g (99%) of **14** was isolated as colorless crystals, which were used immediately without further purification.

A small sample of **14** was recrystallized from petroleum ether–ether (4:1), mp 84–85 °C; IR (KBr, cm^{-1}) 3210, 2955, 2870, 1655, 1600, 1492, 1460, 1402, 1332, 1290, 1203, 1182, 1157, 1088, 1018, 922, 859, 805, 741, 700, 668, 570, 558. The following 300-MHz ^{1}H NMR spectrum which was recorded in $CDCl_3$ suggested the substance to be a 3:2 trans/cis mixture: δ 8.3 (d, J = 8.2 Hz, 2 H), 7.29 (d, J = 8.2 Hz, 2 H), 7.12 (br s, 1 H), 2.42 (br s, 3 H), 2.3–1.4 (m, 7 H), 1.32–1.15 (m, 1 H), 1.00 (d, J = 6.5 Hz) and 0.70 (d, J = 6.8 Hz, total 3 H), 0.86 (t, J = 7.4 Hz) and 0.75 (t, J = 7.4 Hz, total of 3 H).

Evaporation of the $CDCl_3$ gave crystals, mp 98–105 °C; m/z calcd (M^+) 294.1402, obsd 294.1444.

Shapiro Degradation of 14. Reaction of freshly prepared **14** (3.7 g, 12.6 mmol) with methyllithium (33 mL of 1.25 N in ether) as described above delivered 0.90 g (65%) of hydrocarbon mixture. VPC analysis showed **12** and **13** to be present in a ratio of 3.5:1.

***cis*- and *trans*-4-Methyl-5-ethyl-1-(trimethylstannyl)-cyclopentenes (15 and 16).** To a cold (−60 °C), stirred solution of freshly prepared **14** (34.1 g, 0.13 mmol) in dry *N,N,N',N'*-tetramethylethylenediamine (TMEDA) was added *n*-butyllithium

in hexane (325 mL of 1.6 N, 0.52 mol) during 60 min. The deep red solution was allowed to warm to room temperature where it was maintained for 3 h. Nitrogen evolution began at −20 °C. The reaction mixture was recooled to −20 °C, and solid trimethylstannyl chloride (80 g, 0.40 mol) was added in one portion. After 15 h of stirring at room temperature, the reaction mixture was treated carefully with a few drops of water and poured into 500 mL of ice water. Following extraction with petroleum ether (3 × 500 mL), the combined organic phases were washed thoroughly with water, saturated cupric sulfate solution, and brine. Drying and solvent evaporation provided a residue which was distilled to give a 4.0:1 mixture of **15** and **16** (21.2 g, 61%), bp 58–67 °C (10 torr). The isomers could be separated by spinning band distillation, with **16** being the more volatile constituent.

For **15**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dd, J = 4.3 and 2.2 Hz, 1 H), 2.58–2.30 (m, 3 H), 1.98 (d of m, J = 13.0 Hz, 1 H), 1.49–1.02 (m, 2 H), 0.91–0.87 (m, 6 H), 0.20 (s, 3 H), 0.11 (s, 3 H), 0.02 (s, 3 H); m/z calcd ($M^+ - CH_3$) 259.0505, obsd 259.0485.

Anal. Calcd for $C_{11}H_{22}Sn$: C, 48.40; H, 8.12. Found: C, 48.37; H, 8.19.

For **16**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77 (dd, J = 4.2 and 2 Hz, 1 H), 2.67–2.57 (m, 1 H), 2.29–2.23 (m, 1 H), 2.00–1.91 (m, 2 H), 1.57–1.45 (m, 1 H), 1.34–1.21 (m, 1 H), 1.02 (d, J = 6.7 Hz, 3 H), 0.88 (t, J = 7.4 Hz, 3 H), 0.22 (s, 3 H), 0.13 (s, 3 H), 0.04 (s, 3 H); m/z calcd ($M^+ - CH_3$) 259.0505, obsd 259.0526.

Anal. Calcd for $C_{11}H_{22}Sn$: C, 48.40; H, 8.12. Found: C, 48.47; H, 8.12.

***cis*- and *trans*-4-Methyl-5-ethyl-1-(trimethylsilyl)cyclopentenes (17 and 18).** To a cold (−60 °C) stirred solution of freshly prepared **14** (50 g, 18.8 mmol) in TMEDA (50 mL) was added *n*-butyllithium in hexane (50 mL of 1.6 N, 80 mmol) during 40 min. The deep red solution was allowed to warm to room temperature where it was maintained for 3 h. Dry trimethylsilyl chloride (8.0 mL, 63 mmol) was added in one portion, and the reaction mixture was stirred at room temperature for 15 h. The predescribed workup, followed by distillation, gave a 2.7:1 mixture of **17** and **18** (2.31 g, 68%), bp 80–84 °C (20 torr).

For **17**: IR (neat, cm^{-1}) 3030, 2970, 2930, 2880, 2845, 1585, 1450, 1380, 1248, 1020, 875, 830, 800, 750; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.99 (ABXq, J = 2.2 Hz, 1 H), 2.62 (m, 1 H), 2.47–2.32 (m, 2 H), 1.97 (d of m, J = 10.4 Hz, 1 H), 1.69–1.54 (m, 1 H), 1.50–1.35 (m, 1 H), 0.91 (d, J = 6.8 Hz, 3 H), 0.86 (t, J = 7.4 Hz, 3 H), 0.08 (s, 9 H).

Anal. Calcd for $C_{11}H_{22}Si$: C, 72.44; H, 12.16. Found: C, 72.22; H, 12.14.

For **18**: IR (neat, cm^{-1}) 3025, 2960, 2920, 2875, 2850, 1590, 1460, 1378, 1248, 1055, 1028, 875, 835, 750, 688; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (ABXq, J = 2.2 Hz, 1 H), 2.60 (ddt, J = 16.9, 8.0, and 2.2 Hz, 1 H), 2.27–2.24 (m, 1 H), 2.00 (m, 1 H), 1.88 (d of m, J = 17 Hz, 1 H), 1.61–1.52 (m, 1 H), 1.26–1.16 (m, 1 H), 0.96 (d, J = 6.9 Hz, 3 H), 0.87 (t, J = 7.4 Hz, 3 H), 0.08 (s, 9 H).

Anal. Calcd for $C_{11}H_{22}Si$: C, 72.44; H, 12.16. Found: C, 72.63; H, 12.25.

***cis*-1-Bromo-4-methyl-5-ethylcyclopentene (20).** To a cold (−30 °C), stirred solution of **17** (1.83 g, 10.1 mmol) in dry dichloromethane (10 mL) was added a solution of bromine (1.80 g, 11.1 mmol) in the same solvent (8 mL) during 20 min. The reaction mixture was allowed to warm to room temperature, stirred for 30 min, and washed with dilute sodium bisulfite solution. Following drying and solvent evaporation, the dark blue residue was added immediately to an ice-cold, stirred solution of dry tetra-*n*-butylammonium fluoride (3.0 g, 11.5 mmol) in anhydrous tetrahydrofuran (15 mL). After 3 h, the black solution was washed with water and brine, dried, and freed of solvent by distillation at atmospheric pressure. The residue was taken up in pentane and filtered through Florisil. Solvent evaporation gave 0.81 g (43%) of **20**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dd, J = 4.1 and 2.4 Hz, 1 H), 2.58–2.50 (m, 2 H), 2.41–2.32 (m, 1 H), 1.93–1.84 (d of m, J = 15.7 Hz, 1 H), 1.63–1.58 (m, 1 H), 1.45 (m, J = 7.2 Hz, 1 H), 1.01 (d, J = 6.7 Hz, 3 H), 0.92 (t, J = 7.4 Hz, 3 H); m/z calcd (M^+) 188.0200, obsd 188.0214.

***trans*-1-Bromo-4-methyl-5-ethylcyclopentene (21). A. From Vinylsilane 18.** To a cold (−30 °C), stirred solution of **18** (490 mg, 2.7 mmol) in dry dichloromethane (5 mL) was added a solution of bromine (0.17 mL, 3.3 mmol) in the same solvent (2 mL) during 10 min. The reaction mixture was allowed to warm to room temperature, stirred for 30 min, and washed with dilute sodium bisulfite solution. Following drying and solvent evaporation, the dark blue residue was added immediately to an ice-cold, stirred solution of dry tetra-*n*-butylammonium fluoride (0.60 g, 2.3 mmol) in anhydrous tetrahydrofuran (10 mL). After 5 h, the black solution was washed with water and brine, dried, and freed of solvent by distillation at atmospheric pressure. The residue was taken up in pentane and filtered through Florisil. Solvent evaporation gave 0.25 g (45%) of **21**, an analytical sample of which was obtained by preparative VPC (12 ft 10% SE-30, 100 °C): IR (neat, cm^{-1}) 3080, 2960, 2920, 2870, 1622, 1455, 1382, 1330, 1312, 1275, 1140, 995, 978, 913, 830, 800; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.77 (q, J = 4.3 Hz, 1 H), 2.56–2.42 (m, 1 H), 2.26–2.09 (m, 2 H), 1.84 (d of m, J = 16 Hz, 1 H), 1.71–1.60 (m, 1 H), 1.46–1.32 (heptet, J = 6.6 Hz, 1 H), 1.08 (d, J = 6.8 Hz, 3 H), 0.90 (t, J = 7.4 Hz, 3 H); m/z calcd (M^+) 188.0201, obsd 188.0213.

Anal. Calcd for $C_8H_{13}Br$: C, 50.81; H, 6.93. Found: C, 51.19; H, 7.13.

B. From Vinylstannane 16. A solution of bromine (0.3 g, 1.88 mmol) in dichloromethane (5 mL) was added during 10 min to a cold (−40 °C), stirred solution of **16** (0.50 g, 1.83 mmol) in the same solvent (10 mL). Immediate decoloration was noted. The clear, colorless reaction mixture was allowed to warm to room temperature, stirred for 15 min, and thoroughly washed with 10% potassium fluoride solution and brine. After drying, the solvent was evaporated, and the dark blue residue was filtered through Florisil (pentane solution). The filtrate was evaporated to give 320 mg (92%) of pure **21**, identical in all respects with the substance isolated in A.

***trans*-1-Iodo-4-methyl-5-ethylcyclopentene (10).** A solution of iodine (0.50 g, 2.0 mmol) in dry ether (20 mL) was added over 5 min to a cold (0 °C), stirred solution of **16** (0.50 g, 1.83 mmol) in the same solvent (10 mL). The reaction mixture was stirred an additional 20 min at room temperature and treated with saturated sodium bisulfite solution. The colorless organic phase was washed thoroughly with 10% potassium fluoride solution, dried, and evaporated. There was isolated 417 mg (97%) of pure **10**, identical in all respects with the substance isolated earlier.

1-(*trans*-4-Methyl-5-ethylcyclopentenyl)dimethylcarbinol (22). Method A. From 16. A cold (−65 °C), stirred solution of **16** (0.50 g, 1.83 mmol) in dry ether (5 mL) was treated with *n*-butyllithium (1.5 mL of 1.55 N in hexane, 2.3 mmol). The reaction mixture was stirred for 1 h at −65 °C and 2 h at room temperature, recooled to −50 °C, and quenched with acetone (0.16 g, 2.8 mmol). Following return to room temperature, water and saturated ammonium chloride solution were carefully introduced, and the organic phase was dried and evaporated. MPLC purification (silica gel, elution with 20% ethyl acetate in petroleum ether) provided 90 mg (50%) of **22**: ^{1}H NMR (30 MHz, $CDCl_3$) δ 5.52 (br s, 1 H), 2.57–2.49 (ddt, J = 16.5, 7.6, and 2.1 Hz, 1 H), 2.19–2.16 (m, 1 H), 2.08–2.03 (m, 1 H), 1.79–1.68 (m, 2 H), 1.59 (br s, 1 H), 1.38 (s, 3 H), 1.34 (s, 3 H), 1.40–1.25 (m, 1 H), 0.95 (d, J = 7.0 Hz, 3 H), 0.89 (t, J = 7.4 Hz, 3 H); m/z calcd (M^+) 168.1514, obsd 168.1494.

Method B. From 10. A solution of **10** (0.75 g, 3.18 mmol) in dry ether (10 mL) was stirred with finely cut lithium metal (80 mg, 11 mmol) under nitrogen for 15 h, and the resulting organometallic reagent was removed by syringe and added to a cold (−60 °C), stirred solution of acetone (0.25 g, 4.3 mmol) in dry ether (10 mL). After 30 min, the usual workup was implemented, and 442 mg (83%) of **22** was isolated.

***cis*-1-Iodo-4-methyl-5-ethylcyclopentene (8).** Treatment of **15** (3.13 g, 11.5 mmol) with iodine (3.13 g, 12.3 mmol) in the predescribed manner afforded 2.63 g (97%) of **8**, identical in all respects with the substance isolated earlier.

1-(*cis*-4-Methyl-5-ethyl-1-cyclopentenyl)cyclohexanol (23). A solution of **8** (0.2 g, 0.85 mmol) in dry ether (8 mL) was stirred with finely cut lithium metal (100 mg, 14.3 mmol) for 15 h. The resulting organometallic reagent was removed by syringe and added to a cold (−60 °C), stirred solution of cyclohexanone (60 mg, 0.61 mmol) in dry ether (8 mL). After stirring at −60 °C for 1.5 h and at room temperature for an additional 2 h, the reaction mixture was quenched with water (20 mL), and the organic layer was separated and dried. After removal of the solvent by evaporation, MPLC purification (silica gel, elution with 20% ethyl acetate in petroleum ether) provided 58 mg (46%) of **23** and 20

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

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