The *sym*-trinitrobenzene derivative, showed m.p. 157–159°.

Anal. Calcd. for $C_{34}H_{30}(C_6H_3N_3O_6)_2$: C, 63.88; H, 4.20; N, 9.72. Found: C, 63.58; H, 4.16; N, 9.72.

Concentration of the benzene filtrates gave the lower melting form, m.p. 198–200°, of **3,4-bis-(2-phenanthryl)-hexane (XV)**.

Anal. Calcd. for $C_{34}H_{30}$: C, 93.10; H, 6.89; mol. wt., 438. Found: C, 92.80; H, 6.80; mol. wt. (Rast's method), 428.

Reaction of α-(2-Phenanthryl)-*n*-propyl Bromide with Cuprous Cyanide and Pyridine.—A mixture of XIV (1.0 g.), cuprous cyanide (600 mg.) and pyridine (5 ml.) was heated at 160° for 24 hours. The reaction mixture was poured into dilute ammonium hydroxide and an ethereal extract of the resulting organic material was washed repeatedly with ammonium hydroxide solution until the aqueous layer did not develop a blue color. After being washed with dilute hydrochloric acid and then with water, the ether solution was dried over calcium chloride. Evaporation of the solvent gave a gummy material which, after several crystallizations from ethanol, gave 250 mg. of the unsaturated hydrocarbon XVI, m.p. 101–102°.

Anal. Calcd. for $C_{34}H_{28}$: C, 93.53; H, 6.47. Found: C, 93.83; H, 6.38.

Bromination of XVI.—A solution of bromine in carbon tetrachloride was added to 200 mg. of XVI dissolved in absolute ethanol, until a pale yellow color persisted. The mixture was allowed to stand for 8 hours. Concentration of the solution gave a solid which, after three crystallizations from ethanol, gave the pure tetrabromide, m.p. 145°, yield 60 mg.

Anal. Calcd. for $C_{34}H_{26}Br_4$: C, 54.14; H, 3.47. Found: C, 54.36; H, 3.73.

COMMUNICATIONS TO THE EDITOR

BIS-3-METHYL-2-BUTYLBORANE AS A SELECTIVE REAGENT FOR THE REDUCTION OF REPRESENTATIVE FUNCTIONAL GROUPS

Sir:

Bis-3-methyl-2-butylborane is a highly selective reagent for the hydroboration of olefins and dienes.[1] We now report that this reagent exhibits remarkable selectivity in its reducing action toward representative functional groups, permitting selective reductions not otherwise feasible.

The groups listed are reduced at 0° in 0.5 *M* solution in tetrahydrofuran (products in parentheses): aldehydes and ketones (alcohols), unhindered olefins and acetylenes (organoboranes), γ-lactones (hydroxyaldehydes) and N,N-dimethylamides (aldehydes). Nitrobenzene and nitriles react only slowly under these conditions.

These groups react to evolve hydrogen, but do not undergo reduction: alcohols, phenols, carboxylic acids, amides, and sulfonic acids. No reaction occurs under these conditions with esters, acid chlorides, acid anhydrides, azobenzene, sulfones and sulfonyl chlorides.

The failure of bis-3-methyl-2-butylborane to reduce carboxylic acids is unexpected in view of the very fast reaction with diborane.[2] It makes possible both selective reductions and hydroborations in the presence of unprotected carboxylic acid groups, as illustrated by the following conversion of 10-undecenoic acid to 11-hydroxyundecanoic acid.

Undecenoic acid, 25 mmoles, was treated with a solution of 50 mmoles of bis-3-methyl-2-butylborane[1] in tetrahydrofuran at 0°. Hydrogen (24 mmoles) was rapidly evolved. After 30 minutes, the reaction mixture was treated with alkaline hydrogen peroxide and the product was recrystallized from water. There was obtained 20.6 mmoles, 82% yield, of 11-hydroxyundecanoic acid, m.p. 68–69°.[3]

(1) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 3222 (1960).

(2) H. C. Brown and B. C. Subba Rao, *ibid.*, **82**, 681 (1960).

(3) P. Chuit and J. Hausser, *Helv. Chim. Acta*, **12**, 463 (1929), report m.p. 70–70.5°.

γ-Lactones react with one mole of the reagent, even when the latter is in excess. That the product is the hydroxyaldehyde was confirmed by demonstrating the reduction of γ-butyrolactone to ω-hydroxybutyraldehyde (73% yield of 2,4-dinitrophenylhydrazone, m.p. 198–199°). A representative procedure is given.

γ-Valerolactone, 50 mmoles, was treated with 0.5 *M* reagent for about 15 hours at 25°, followed by oxidation with alkaline (*p*H 8) hydrogen peroxide at 0°. γ-Hydroxyvaleraldehyde, b.p. 60–61° at 9 mm.,[4] was isolated, 38 mmoles, 76% yield.

The reaction of the reagent with these lactones is more rapid than its reaction with typical ketones. Consequently, it should be possible to achieve the selective reduction of such lactones in the presence of ketone, carboxylic acid or ester groups.

We continue to explore the full applicability of this versatile reagent.

Acknowledgment.—This study was made possible by a grant from the American Cyanamid Company. This support is gratefully acknowledged.

(4) B. Helferich, *Ber.*, **52**, 1123 (1919), reports b.p. 63–65° at 10 mm.

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RECEIVED DECEMBER 16, 1960

HYDROBORATION AS A CONVENIENT PROCEDURE FOR THE ASYMMETRIC SYNTHESIS OF ALCOHOLS OF HIGH OPTICAL PURITY

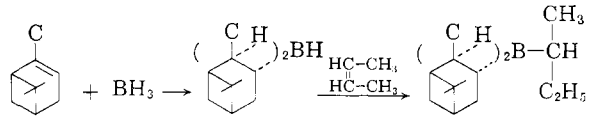
Sir:

We wish to report a new asymmetric synthesis which permits the conversion of olefins into optically active alcohols with optical purities in the neighborhood of 90%.

We previously observed that the hydroboration of hindered olefins proceeds rapidly to the dialkylborane stage and these compounds exhibit a remarkable selectivity for the hydroboration of olefins

of varying structure.[1] Accordingly, it appeared possible that dialkylboranes derived from optically active terpenes or steroids might convert olefins into organoborane moieties capable of being transformed into optically active derivatives.

α-Pinene was hydroborated to form di-isopinocampheylborane, and the product utilized for the hydroboration of a number of representative olefins.



Oxidation of the resulting organoborane with alkaline hydrogen peroxide produced the corresponding alcohols with exceptionally high optical purities—in the range of 83–91%. Since the optical purity of the α-pinene ($[\alpha]^{20}D$ + 47.6°) is probably no better than 90%,[2] *it appears that this procedure achieves nearly complete asymmetric stereoselectivity.*

A representative procedure is given: α-Pinene, 27.2 g. (0.200 mole) was dissolved in 75 ml. of a 1.00 *M* solution of sodium borohydride in diglyme and the mixture, cooled to 0°, was treated with 14.2 g., (0.100 mole) of boron trifluoride etherate to form the di-isopinocampheylborane. To the reagent at 0° was added 6.1 g., 0.100 mole, of *cis*-2-butene and the reaction mixture maintained at 0° for four hours, then left overnight at room temperature. Oxidation at 30–50° with 31 ml. of 3 *N* sodium hydroxide followed by 31 ml. of 30% hydrogen peroxide produced 6.7 g. of 2-butanol, a yield of 90%: b.p. 98° at 744 mm.; $n^{20}D$ 1.3975; $[\alpha]^{20}D$ −11.8°, indicating an optical purity of 87%.[3]

Similarly, *cis*-3-hexene, readily synthesized via the hydroboration reaction from 3-hexyne,[4] was converted in 81% yield to 3-hexanol: b.p. 135–136° at 752 mm.; $n^{20}D$ 1.4148, $[\alpha]^{20}D$ −6.5°, indicating an optical purity of 91%.[5]

Application of the procedure to norbornene produced *exo*-norborneol in a yield of 62%. The product, m.p. 125–126°, exhibited the rotation $[\alpha]^{20}D$ −2.0°; acetate, $\alpha^{20}D$ + 7.9°, indicating an optical purity of 83%.[6]

The results clearly demonstrate that a boron atom at the asymmetric center, RR′C*HB<, is capable of maintaining asymmetry without significant racemization over periods of several hours. The ease with which organoboranes may be converted into other derivatives with retention of configuration and the unusually high optical purity achieved should make this approach to optically active derivatives a most valuable one for the synthetic chemist.

(1) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 3222 (1960).

(2) F. H. Thurber and R. C. Thielke, *ibid.*, **53**, 1030 (1931), report $[\alpha]D$ +51.1° for α-pinene purified via the nitrosochloride.

(3) P. J. Leroux and H. J. Lucas, *ibid.*, **73**, 41 (1951), report for L(−)-2-butanol: b.p. 97.5–98° at 745 mm.; $n^{20}D$ 1.3970; $[\alpha]^{25}D$ −13.51°.

(4) H. C. Brown and G. Zweifel, *ibid.*, **81**, 1512 (1959).

(5) J. Kenyon and R. Poplett, *J. Chem. Soc.*, 273 (1945), report for 3-hexanol: b.p. 133–134°; $n^{20}D$ 1.4140; $[\alpha]^{18}D$ −7.13°.

(6) S. Winstein and D. Trifan, *J. Am. Chem. Soc.*, **74**, 1154 (1952), report for (−)-*exo*-norborneol: m.p. 126–126.8°; $[\alpha]^{24}D$ −2.41°; acetate, $\alpha^{25}D$ +10.39°.

Trans olefins and highly hindered olefins react only slowly with di-isopinocampheylborane. Consequently, we have undertaken both the development of less hindered reagents for the asymmetric hydroboration of such olefins and the investigation of the full scope of this new synthetic route to optically active derivatives.

We wish to acknowledge the generous gift of the α-pinene by Dr. R. A. Bankert of the Naval Stores Research Division of the Hercules Powder Company.

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STUDIES ON POLYPEPTIDES. XIII. THE SYNTHESIS OF A TRICOSAPEPTIDE POSSESSING ESSENTIALLY THE FULL BIOLOGICAL ACTIVITY OF NATURAL ACTH[1-3]

Sir:

As an outgrowth of our systematic studies[4] relating structure and function of peptides possessing melanophoretic and adrenocorticotropic activity, we have prepared seryltyrosylserylmethionylglutamylhistidylphenylalanylarginyltryptophylglycyllysylprolylvaline amide and seryltyrosylserylmethionylglutamylhistidylphenylalanylarginyltryptophylglycyllysylprolylvalylglycyllysyllysine amide and found these peptide derivatives which correspond to substantial portions of the N-terminal sequence of the corticotropins to possess, at best, a very low level of *in vivo* adrenocorticotropic activity (< 0.1 IU/mg.).[5] These results justify the conclusion that a sequence of more than 16 amino acid residues from the amino end of the corticotropin molecule is required for high adrenocorticotropic activity.

A recent communication by Li, *et al.*,[6] reporting *in vivo* adrenocorticotropic activity (29 IU/mg.) of a synthetic nonadecapeptide corresponding to the sequence of the 19 N-terminal amino acid residues of the corticotropins prompts us at this time to record further observations in this field.

We have prepared the tricosapeptide amide (I) and find that this compound possesses *in vivo* adrenocorticotropic activity. The most highly purified

		Formula	
I	R = H	R′ = OH	R″ = H
II	R = acetyl	R′ = NH_2	R″ = formyl

samples of the synthetic hormone derivative obtained to date exhibit 103 ± 10.4 IU/mg. of both ascorbic acid depleting and plasma corticosterone elevating

(1) Supported by grants from the U. S. Public Health Service, the National Science Foundation, the National Cancer Society and Armour and Company.

(2) The amino acid residues, except glycine, are of the L-configuration. In the interest of space conservation the customary L-designation of individual amino acid residues has been omitted.

(3) Amino acid analyses were carried out with a model 120 Beckman-Spinco amino acid analyzer. Unless noted otherwise, the R_f values refer to the Partridge system; S. M. Partridge, *Biochem. J.*, **42**, 238 (1948).

(4) See *J. Am. Chem. Soc.*, **82**, 3732 (1960), for Paper XVII in this series.

(5) K. Hofmann, "Brookhaven Symposia in Biology," Vol. 13, 184 (1960).

(6) C. H. Li, J. Meienhofer, E. Schnabel, D. Chung, T. Lo and J. Ramachandran, *J. Am. Chem. Soc.*, **82**, 5760 (1960).