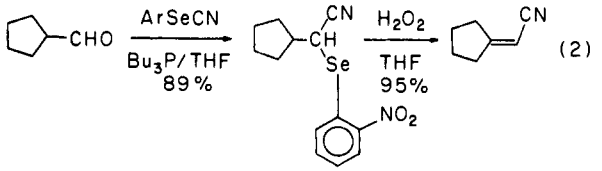
trophenyl selenocyanate[2b]) react rapidly at room temperature with aldehydes in the presence of tri-*n*-butylphosphine to give cyano selenides, **1**, in excellent yields (Table I).

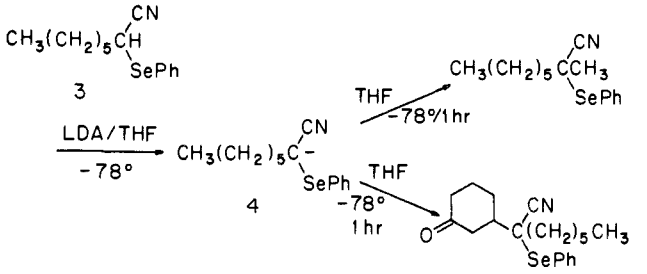
The one-carbon homologation of an aldehyde to a nitrile possessing an α-arylseleno substituent represents a synthetically useful reaction which permits a variety of synthetic transformations.[3] For example, cyclopentylmethanal was converted directly (eq 2) into the α,β-unsaturated nitrile **2** in



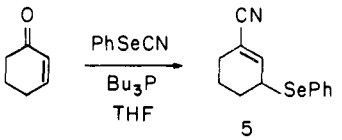
(2)

high overall yield. Similarly dodecanal was converted to a 55:45 (trans:cis) mixture of its corresponding α,β-unsaturated nitrile in 84% overall yield.

The cyanoselenenylation of *n*-heptanal with phenyl selenocyanate provided **3** in high yield which when treated with 1.2 equiv of lithium diisopropylamide in tetrahydrofuran at −78 °C generated anion **4**. Anion **4** undergoes (a) smooth alkylation with methyl iodide (87%) and (b) Michael addition to cyclohexenone in 91% yield.

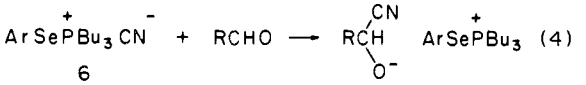


In contrast to aldehydes ketones do not undergo cyanoselenenylation but rather give rise to cyanohydrin formation. However, cyclohexenone does undergo reaction with phenyl selenocyanate in the presence of tributylphosphine giving rise to the rearranged product **5** in 50% yield (eq 3). Other α,β-unsaturated ketones (e.g., methyl vinyl ketone, cyclopentenone) gave similar results in only modest yield.

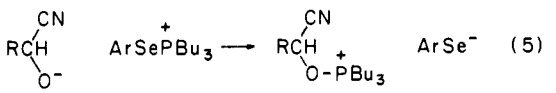


(3)

As illustrated in Table I, aldehydes require ~2.5 h for complete conversion to cyano selenide. If, however, the reaction is worked up after 10–15 min, the corresponding cyanohydrin contaminated with ~10% cyanoselenenylated product can be isolated in very high yield. The formation of the observed products is believed to involve, upon mixing tributylphosphine and the aryl selenocyanate, instantaneous formation of selenophosphonium cyanide **6** which rapidly reacts with the aldehyde as indicated in eq 4. The resulting species gives rise to the products by oxaphosphonium salt formation (eq 5) followed



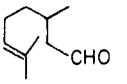
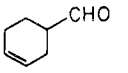
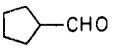
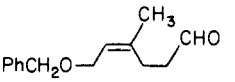
(4)



(5)

by aryl selenide displacement of tributylphosphine oxide which produces the cyanoselenenylated product. The mechanism of this reaction is very similar to the mechanism involved in the direct conversion of alcohols to aryl alkyl selenides with aryl selenocyanates and tributylphosphine.[4]

Table I. Cyanoselenenylation of Aldehydes Using *o*-Nitrophenyl Selenocyanate

Aldehyde	% yield of product[a-c]
dodecanal	93
heptanal	94
	96
	99
	89
	76

[a] All compounds were fully characterized by spectral methods. [b] Yields reported are for isolated, chromatographically pure substances. [c] All reactions were performed at room temperature over 2.5 h in tetrahydrofuran using 1.5 equiv of aryl selenocyanate and 1.5 equiv of tri-*n*-butylphosphine.

The following general procedure indicates the simplicity of the method. A solution of aldehyde in tetrahydrofuran containing 1.5 equiv of aryl selenocyanate at room temperature is treated with a solution of 1.5 equiv of tri-*n*-butylphosphine in tetrahydrofuran. After the addition is complete, the reaction is allowed to stir for 2.5 h. Evaporation of the solvent gives the crude product which is filtered through silica gel to remove tributylphosphine oxide and minor impurities.

Acknowledgment. We thank the National Institutes of Health (CA 13689-05), Glidden Organics, and Shell Development Co. for generous support of this research.

References and Notes

(1) For a review of organoselenium chemistry, see K. B. Sharpless, K. M. Gordon, R. F. Lauer, D. W. Patrick, S. P. Singer, and M. W. Young, *Chem. Scr.*, **8A**, 9 (1975); see also H. J. Reich, J. M. Renga, I. L. Reich, *J. Am. Chem. Soc.*, **97**, 5434 (1975).
(2) (a) O. Behaghel and H. Seibert, *Ber.*, **65**, 812 (1932); (b) H. Bauer, *Ber.*, **46**, 92 (1913). We have found that the crude crystalline material obtained from the procedure of Bauer can be sublimed at 100 °C (0.2 mmHg) providing yellow crystals of *o*-nitrophenyl selenocyanate, mp 144 °C.
(3) Nitriles have previously been selenenylated using 2 equiv of base: D. N. Brattesani and C. H. Heathcock, *Tetrahedron Lett.* 2279 (1974).
(4) P. A. Grieco, S. Gilman, and M. Nishizawa, *J. Org. Chem.*, **41**, 1485 (1976).
(5) Fellow of the Alfred P. Sloan Foundation.

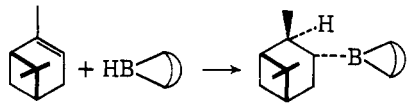
Paul A. Grieco,*[5] Yuusaku Yokoyama
Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260
Received March 11, 1977

Preparation of Optically Active Benzyl-α-*d* Alcohol via Reduction by *B*-3α-Pinanyl-9-borabicyclo[3.3.1]nonane. A New Highly Effective Chiral Reducing Agent

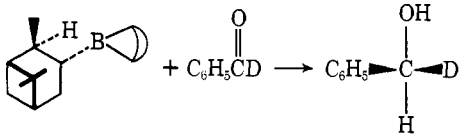
Sir:

B-3α-Pinanyl-9-borabicyclo[3.3.1]nonane, readily prepared by hydroboration of (+)-α-pinene with 9-borobicy-

clo[3.3.1]nonane (9-BBN), rapidly reduces benzaldehyde-α-*d* to (*S*)-(+)-benzyl-α-*d* alcohol of 90% enantiomeric excess (eq 1 and 2). Since the starting α-pinene was only 92% enantiomerically pure, the results represent an essentially quantitative asymmetric induction.



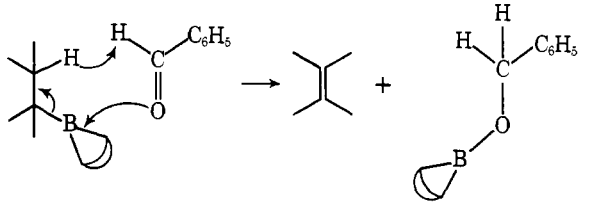
(1)



(2)

Optically active benzyl-α-*d* alcohol has been used extensively for mechanistic studies of chemical and biochemical reactions.[1] This compound is usually prepared by the fermenting yeast reduction of benzaldehyde-α-*d*.[2] Although high enantiomeric purities are obtained, the process is tedious at best. Chemical reducing agents have invariably given low enantiomeric purities. For example, diisopinocampheylborane[3] has been reported to give 6% (*R*)-(−)-benzyl-α-*d* alcohol by one group[4a] but 30% *S*-(+) alcohol by another group.[4b] The highly selective reducing agent made from lithium aluminum hydride and (+)-(2*S*,3*R*)-4-dimethylamino-3-methyl-1,2-diphenyl-2-butanol gives only a 40% enantiomeric purity.[5] The highest optical rotations have been reported for reductions using isobornyloxymagnesium bromide which is reported to give between 45[6a] and 62% e.e.[6b] However, the product of these reductions is usually contaminated with an alcohol of high optical rotation which is difficult to remove.

We have recently found that certain *B*-alkyl-9-borobicyclo[3.3.1]nonane compounds reduce benzaldehyde at a rate which is much faster than that of the corresponding trialkylborane.[7] Alkyl groups containing a tertiary β hydrogen generally give the fastest rates. The reaction seems to involve a cyclic process in which only the *B*-alkyl group is eliminated as an olefin (eq 3).



(3)

Using the chiral organoborane from (+)-α-pinene and 9-BBN we have achieved asymmetric reductions of benzaldehyde-α-*d* in enantiomeric yields which approach those obtained with enzymes. The process is operationally simple and can be done on a large scale. The reaction is over within 2 h at room temperature when a slight excess of organoborane is used. To facilitate isolation of the product, the excess organoborane is destroyed with acetaldehyde. The pinene which is liberated may then be removed under a vacuum. Addition of 1 mol of ethanolamine then precipitates the 9-BBN as an adduct[8] and liberates the benzyl alcohol.

The organoborane from (+)-α-pinene produces (*S*)-(+)-benzyl-α-*d* alcohol. The opposite enantiomer may in principal be prepared from benzaldehyde-α-*d* using (−)-α-pinene. More conveniently, the *R* enantiomer may be prepared using the organoborane made from (+)-α-pinene and *B*-deuterio-9-borobicyclo[3.3.1]nonane.[9,10] This route not only gives the benzyl-α-*d* alcohol in high enantiomeric purity (81%, 90% corrected for deuterium incorporation) but also eliminates the need to prepare benzaldehyde-α-*d*.

The following procedure was used for the preparation of benzyl-α-*d* alcohol. A dry, 1000-mL flask fitted with a side arm covered with a rubber stopple, a reflux condenser, and a magnetic stirring bar was flushed with nitrogen.[11] The flask was charged with 25 g (0.205 mol) of solid 9-BBN.[9] Then 400 mL of dry THF was added by a double-ended needle. This was followed by 35 mL of α-pinene[9] (0.22 mol, $[\alpha]^{22}_D$ +46.6° (neat, *l* = 1) 92% e.e.),[12] which had been distilled under vacuum from a small amount of lithium aluminum hydride. The mixture was stirred at a gentle reflux for 2 h. The flask was then cooled to room temperature and 19 mL of benzaldehyde-α-d[13] (0.185 mol, 99% deuterated) was added by syringe. The solution became slightly yellow. After 10 min the solution was refluxed for 1 h to ensure completion of the reaction. Then 5 mL of acetaldehyde was added and the mixture cooled to room temperature. The THF was removed with a water aspirator. The pinene was then removed on a vacuum pump (0.05 mm, 2 h) with the flask surrounded by a warm water bath (40 °C). Nitrogen was admitted to the flask and 150 mL of diethyl ether added. The solution was cooled to 0 °C and 12.4 mL (0.205 mol) of ethanolamine added. A white precipitate formed and was removed on a Büchner funnel. The precipitate was washed with 2 × 20 mL of ether. The ether solution was washed with water, then dried ($MgSO_4$), and removed under vacuum. The resulting liquid was distilled through a 10-cm Vigreux column to give 16.5 g of benzyl-α-*d* alcohol (81.6%), bp 110 °C (30 mm), $[\alpha]^{25}_D$ +1.56 ± 0.05° (neat, *l* = 1), n^{25} 1.5318 (lit.[2] $[\alpha]^{24}_D$ +1.58°, n^{20}_D 1.5350). The compound appeared to be pure by VPC and ^{1}H NMR (60 MHz, CCl_4) δ 2.0 (s, 1 H), 4.6 (t, 1 H, J_{HCD} = 1.8 Hz), 7.33 (s, 5 H). Examination in the presence of an optically active shift reagent[5] indicated a mixture of 6% *R* and 94% *S*. Repetition of the reaction at room temperature produced alcohol of 5% *R* and 95% *S* purity. The alcohol may be further purified as the phthalate ester to give a product with a rotation of $[\alpha]^{25}_D$ +1.39 ± 0.05° (88% e.e).

The *B*-alkyl-9-borobicyclo[3.3.1]nonane compounds represent a new class of reducing agents which show great promise of being highly enantioselective, stereoselective, and chemoselective. For example, preliminary results have shown that certain organoboranes will reduce aldehydes within minutes but will not reduce ketones over a period of several days. We are actively exploring the full scope of these reductions.

References and Notes

(1) D. Arigoni and E. L. Eliel in "Topics in Stereochemistry", Vol. 4, E. L. Eliel and N. L. Allinger, Ed., Wiley-Interscience, New York, N.Y., 1969, pp 127–244; L. Verbit in "Progress in Physical Organic Chemistry", Vol. 7, R. Streitwelser and R. W. Taft, Ed., Wiley-Interscience, New York, N.Y., 1970, pp 51–127; K. S. Y. Lau, P. K. Wong, and J. K. Stille, *J. Am. Chem. Soc.*, **98**, 5832 (1976); E. Caspi and C. R. Eck, *J. Org. Chem.*, **42**, 767 (1977), and references therein.

(2) V. E. Althouse, D. M. Feigl, W. A. Sanderson, and H. S. Mosher, *J. Am. Chem. Soc.*, **88**, 3595 (1966).

(3) This reagent has been used to hydroborate cis olefins with nearly quantitative enantioselectivity: H. C. Brown, N. R. Ayyangar, and G. Zweifel, *J. Am. Chem. Soc.*, **86**, 397 (1964).

(4) (a) K. R. Varma and E. Caspi, *Tetrahedron*, **24**, 6365 (1968); (b) S. Wolfe and A. Rauk, *Can. J. Chem.*, **44**, 2591 (1966).

(5) C. J. Relch, G. R. Sullivan, and H. S. Mosher, *Tetrahedron Lett.*, 1505 (1973).

(6) (a) A. Streitwieser, Jr., J. R. Wolfe, Jr., and W. D. Schaeffer, *Tetrahedron*, **6**, 338 (1959); (b) H. Gerlach, *Helv. Chim. Acta*, **49**, 2481 (1966).

(7) M. M. Midland, A. Tramontano, and S. A. Zderic, *J. Organomet. Chem.*, in press; B. M. Mikhailov, Yu N. Bubnov, and V. G. Kiselev, *J. Gen. Chem. USSR*, **36**, 65 (1966).

(8) S. Krishnamurthy and H. C. Brown, *J. Org. Chem.*, **42**, 1197 (1977).

(9) Available from Aldrich Chemical Co.

(10) The reaction times used for [*B*-D]-9-BBN were twice those used for [*B*-H]-9-BBN.

(11) For a discussion of the handling of air-sensitive reagents see H. C. Brown, G. W. Kramer, A. B. Levy, and M. M. Midland, "Organic Syntheses via Boranes", Wiley-Interscience, New York, N.Y., 1975, Chapter 9.

(12) (+)-α-Pinene of 100% optical purity may be prepared: H. C. Brown and N. M. Yoon, *Israel J. Chem.*, in press. Essentially none of the *R* enantiomer

could be detected by NMR when high-purity α-pinene ($[\alpha]^{25}_D + 51.5°$) was used.

(13) A. W. Burgstahler, D. E. Walker, Jr., J. P. Kuebrich, and R. L. Schowen, *J. Org. Chem.*, **37**, 1272 (1972).

(14) Recipient of a University of California, Riverside, Undergraduate Research Grant.

M. Mark Midland,* Alfonso Tramontano, Stephen A. Zderic[14]
Department of Chemistry, University of California
Riverside, California 92521
Received March 21, 1977

Dipole-Stabilized Carbanions. Direct Lithiation of the Methyl Group of a Methyl Ester

Sir:

The preparation of synthetically useful α-oxoorganometallics by deprotonation has been reported for allyl and vinyl ethers, cases in which stabilization of the formal carbanion is provided by unsaturation.[1,2] We now wish to report direct metalation of the methyl group of a methyl ester, a case in which stabilization of the carbanion may be attributed in part to the formally positive oxygen of the ester dipole.[3] Since the metalation can be followed by reaction with an electrophile and subsequent cleavage of the substituted ester, the overall sequence provides a method for nucleophilic oxomethylation.

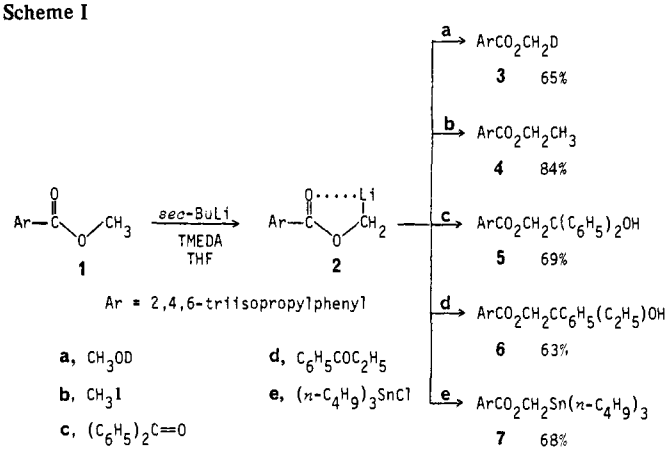
Reaction of methyl 2,4,6-triisopropylbenzoate (**1**) with *sec*-butyllithium/tetramethylethylenediamine (TMEDA) at −75 or −98 °C for 2 to 2.5 h provides **2.** Subsequent addition of an electrophilic trapping agent gives the expected products **3–7** in the yields indicated in Scheme I.[4] Yields have not been optimized.[5]

The formally dipole-stabilized carbanion **2** provides the oxymethylene synthon $LiCH_2OH$.[6] For example, reaction of **2** with benzophenone to give **5** may be followed by reduction with lithium aluminum hydride in tetrahydrofuran to give the diol **8** in 49% yield from **1.** In an alkylation sequence *n*-butyl iodide undergoes reaction with **2** to give *n*-pentyl 2,4,6-triisopropylbenzoate (**9**) which can be reduced with lithium aluminum hydride to 2-pentanol, followed by acylation with 3,5-dinitrobenzoyl chloride to give the known derivative **10** in 61% yield from **1.**

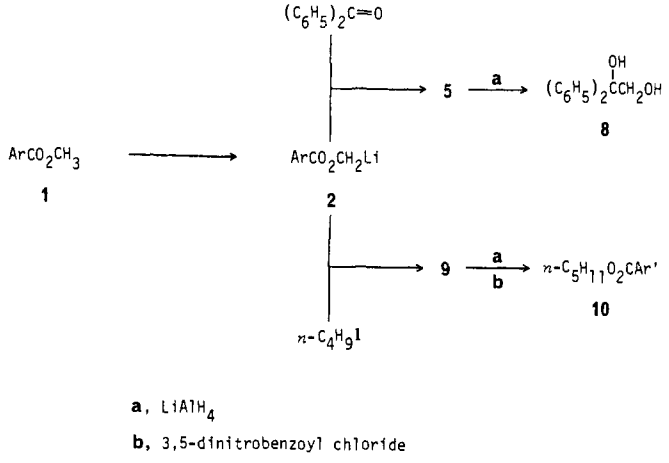
The present results show the ester function to be capable of activating the position α to the bivalent oxygen toward metalation to give a formal dipole-stabilized carbanion.[7] The fact the ester function retains its structure in the face of possible stabilizing rearrangements is also interesting. The α-acyloxy carbanion **2** is analogous to intermediates which have been proposed in the self-condensations of benzyl, allyl, and vinyl benzoate[8] and to carbanions which could be involved in the formation of α-acyloxy carbeneoids on reaction of the α-acyloxychloro ester function with lithium 2,2,6,6-tetramethylpiperidide.[9] The general synthetic utility of **2** and its derivatives,[10] questions about kinetic and thermodynamic acidities, and the role of the metal ion in the formation of such species are being explored.

Acknowledgment. We are grateful to David B. Reitz for stimulating discussions and to the National Institutes of Health for support of this work.

Scheme I



Scheme II



References and Notes

(1) For allyl cases, see D. A. Evans, G. C. Andrews, and B. Buckwalter, *J. Am. Chem. Soc.*, **96**, 5560 (1974); W. C. Still and T. C. Macdonald, *ibid.*, 5561 (1974); J. Hartmann, M. Stähle, and M. Schlösser, *Synthesis*, 888 (1974); G. Sturz, B. Corbel, and J. P. Paugam, *Tetrahedron Lett.*, **47** (1976); W. Oppolzer and R. L. Snowden, *ibid.*, 4187 (1976), and references cited therein.

(2) For vinyl cases, see U. Schöllkopf and P. Hänssle, *Justus Liebigs Ann. Chem.*, **763**, 2 (1972); J. E. Baldwin, G. A. Höfle, and O. William Lever, Jr., *J. Am. Chem. Soc.*, **96**, 7125 (1974); C. G. Chavdarian and C. H. Heathcock, *ibid.*, **97**, 3822 (1975); J. E. Baldwin, O. William Lever, Jr., and N. R. Tzodikov, *J. Org. Chem.*, **41**, 2874 (1976), and references cited therein.

(3) For formation of analogous species from amides and thioesters, see P. Beak and R. Farney, *J. Am. Chem. Soc.*, **95**, 4771 (1973); P. Beak, G. R. Brubaker, and R. F. Farney, *ibid.*, **98**, 3621 (1976); D. Seebach and W. Lubosch, *Angew. Chem., Int. Ed. Engl.*, **15**, 313 (1976); P. Beak, B. G. McKinnie, and D. B. Reitz, *Tetrahedron Lett.*, in press.

(4) Yields are for analytically pure materials. The assigned structures were confirmed by IR, NMR, and mass spectral properties.

(5) Trapping of **2** also took place with benzaldehyde, allyl bromide, cyclohexanone, and cyclopentanone in 40–60% yields as indicated by the NMR of the crude products. Isolation and characterization of these materials has been deferred until optimal conditions are achieved.

(6) For an alternative preparation of this synthon from formaldehyde, see D. Seebach and N. Meyer, *Angew. Chem., Int. Ed. Engl.*, **15**, 438 (1976).

(7) Apparently the activating effect of the ester is sufficient to overcome the usually deactivating effect of oxygen toward α-carbanion formation. For discussions, see F. G. Bordwell, M. Van Der Puy, and N. R. Vanier, *J. Org. Chem.*, **41**, 1885 (1976); D. H. Hunter, Y. Lin, A. L. McIntyre, D. J. Shearing, and M. Zvagulis, *J. Am. Chem. Soc.*, **95**, 8327 (1973), and references cited therein. For general discussions, see E. Buncel, "Carbanions: Mechanistic and Isotopic Aspects", Elsevier, New York, N.Y., 1975, Chapter 2; M. Schlösser, "Struktur und Reaktivität Polar Organometallic", Springer-Verlag, Berlin, 1973, Chapter 2; D. J. Peterson, *Organometal. Chem. Rev.*, **A7**, 295 (1972).

(8) C. J. Upton and P. Beak, *J. Org. Chem.*, **40**, 1094 (1975).

(9) R. A. Olofson, K. D. Lotts, and G. N. Barber, *Tetrahedron Lett.*, 3381 (1976).

(10) Reaction of ethyl 2,4,6-trlisopropyl benzoate with *sec*-BuLi/TMEDA in THF at −75 °C for 2 h followed by addition of methanol-d_1 gave an 85% recovery of the starting ester with 57% of one methylene proton exchanged for deuterium. The location and extent of deuteration was established by nmr and mass spectral determinations. Extensions of this observation will follow when optimal conditions and functionality for the formation of oxygen dipole-stabilized carbanions have been found.

Peter Beak,* B. Gary McKinnie
Roger Adams Laboratory, University of Illinois
Urbana, Illinois 61801
April 11, 1977