# Alkylmetal Asymmetric Reduction. 18.[1] Starting Materials in the Preparation of New Chiral Reducing Agents: Synthetic Approach to Primary Alkyl Halides Derived from (+)-Camphor

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*Received April 25, 1986*

2,2-Dimethyl-3-(chloromethyl)bicyclo[2.2.1]heptane (camphanyl chloride), camphanyl bromide, 1,7,7-trimethyl-2-(chloromethyl)bicyclo[2.2.1]heptane [2-(chloromethyl)bornane], and 2-(bromomethyl)bornane were prepared from (+)-camphor. All these compounds were obtained as mixtures of exo and endo isomers in various ratios depending upon the synthetic path adopted. A loss of diastereomeric purity during the halogenations of corresponding alcohols was observed.

Recently we reported that optically active carbinols can be obtained by reducing the corresponding ketones with organometallic reagents of beryllium,[1,2] aluminum,[1,3] and gallium,[4] derived from β-pinene. In this context, an anomalous reversal of stereochemical course was observed on passing from the reduction of alkyl phenyl ketones to that of α-alkynyl ones.[1-5] It is noteworthy that such a reversal was not found when optically active 2-methylbutyl derivatives were employed.

To look for the origin of this discrepancy, we have undertaken the preparation of rigid, highly hindered, alkylmetal compounds, derived from camphor. Herein we report the preparation of camphanyl halides and 2-(halomethyl)bornanes.

These halides could be readily prepared from 2-methylenebornane (**1a**) and camphene (**2a**) via oxidative hydroboration, followed by conversion of the primary alcohol into the halide via its tosylate[3] (Chart I).

The alkene **1a** was obtained by methylation of (+)-camphor by two different routes.[6-8] A nonclassical Wittig reaction,[6] involving alkylzinc/titanium species gave **1a** in 73% conversion after 48 h at 25 °C. By prolonging the reaction time, the process afforded a byproduct (25%), which was identified as 2-methyl-2-bornene (GLC). Better results were obtained by the Wittig–Corey reaction,[7] which afforded **1a** in 73% recovered yield.

The (+)-(1*R*)-camphene (**2a**) was obtained in good yield from pyrolysis of the tosylate of (−)-isoborneol in pyridine at 100 °C:[9] (−)-(1*S*)-camphene was obtained in 70% yield by pyrolysis of the tosylate of (−)-borneol, rather than by methanolysis, as previously reported.[10]

The in situ oxidative hydroboration (diglyme) of **1a** afforded 2-(hydroxymethyl)bornane (**1b**) having an exo to endo isomer ratio of 80:20;[8] the same procedure on **2a** afforded *endo*-camphanol (*endo*-**2b**) containing the exo isomer (10%).[11]

The alcohols **1b** and **2b** were treated with *p*-TsCl in pyridine at room temperature. The tosylates **1c** and **2c** were then treated with LiCl in DMF at 85 °C. Table I shows the results obtained in these reactions along with the data of the preparation of *cis*-myrtanyl chloride (run 1).[3] It can be seen that tosylate **2c** is not appreciably affected and camphanyl chloride (**2d**) is only obtained in poor yield (run 3). 2-(Chloromethyl)bornane (**1d**) is formed, having a poor diastereomeric purity and in low chemical yield (run 2). In addition to the loss of epimeric purity from **1b** to **1d** the formation of considerable amounts of olefinic byproducts should be noted.

On the basis of these unsatisfactory results, we next turned our attention to the hydroboration–bromination of **1a** and **2a** in an attempt to prepare the target halides directly from the alkenes.[12] Contrary to what affirmed in literature (run 4),[12] as seen from the data in Table II, this procedure did not prove to be satisfactory as the yields of 2-(bromomethyl)bornane (**1e**) and camphanyl bromide (**2e**) were not higher than 30%. It is also noteworthy that the diastereomeric composition of the recovered samples of **1e** and **2e** was unlike that of the corresponding alcohols obtained from the oxidative hydroboration procedure above described. We noted that the reaction probably stopped when the borinic ester was formed: in fact, the oxidation ($H_2O_2/OH^-$) of both distillation residues of **1e** and **2e** afforded the alcohols **1b** and **2b** in ~60% yield.[13]

Finally, a third route for the preparation of the desired halides was investigated. Table III shows the experimental data obtained by treatment of alcohols **1b**, **2b**, and *cis*-myrtanol with triphenylphosphine and carbon tetra-

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(2) Giacomelli, G.; Falorni, M.; Lardicci, L. *Gazz. Chim. Ital.* **1985**, *115*, 289.
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(11) (a) Dulou, R.; Chretien-Bessiere, Y. *Bull. Soc. Chim. Fr.* **1959**, 1362. (b) Lohmme, J.; Ourisson, G. *Tetrahedron* **1968**, *34*, 3208. (c) Gream, G. E.; Pincombe, C. F. *Aust. J. Chem.* **1974**, *27*, 543. (d) Uzarewicz, I.; Uzarewicz, A. *Rocz. Chem.* **1976**, *50*, 1315.
(12) Brown, H. C.; Lane, C. F. *J. Am. Chem. Soc.* **1970**, *92*, 6660.
(13) The bromination of camphanylborole was also attempted: Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1971**, *93*, 1816. The bromide **2e** was recovered in a <10% yield (endo:exo = 80:20).

0022-3263/86/1951-5291$01.50/0 

**Chart I**

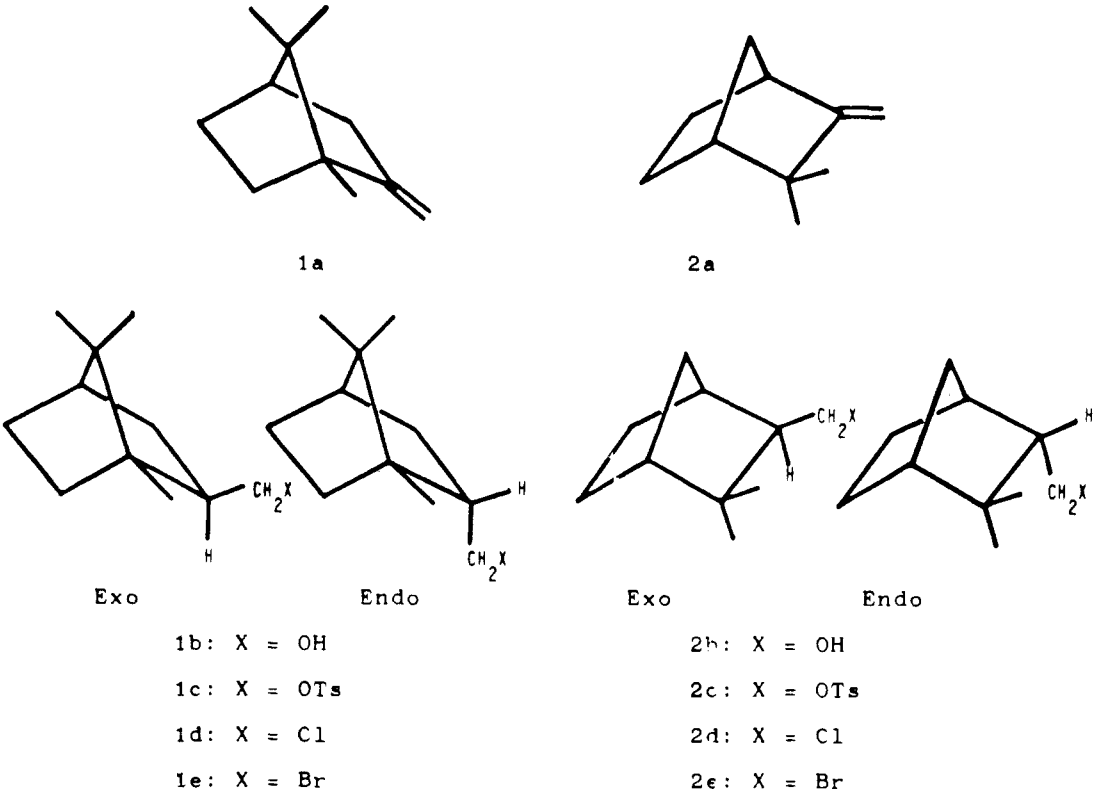


**Table I. Synthesis of Chlorides from Alcohols via Tosylate**

$$RCH_2OTs + LiCl \xrightarrow[DMF,\ 85\ °C]{} RCH_2Cl + LiOTs$$

| run | substrate | chloride, % conversion[a] | chloride, % yield[b] | chloride, % main isomer | olefinic[c] byproducts, % |
|---|---|---|---|---|---|
| 1 | *cis*-myrtanol | 100 | 60 | 90 (cis) | 10 |
| 2 | 2-(hydroxymethyl)bornane[d] (**1b**) | 100 | 37 | 55 (*exo*-**1d**)[c] | 50[e] |
| 3 | camphanol[f] (**2b**) | 10 | 25[c] | nd | 75 |

[a] Evaluated by $^1H$ NMR. [b] Recovered yield from alcohol. [c] Evaluated by GLC on the crude product. [d] Exo:endo = 80:20. [e] Mixture of **1a** and 2-methyl-2-bornene. [f] Endo:exo = 90:10.

**Table II. Synthesis of Alkyl Bromides from Olefins via Hydroboration-Bromination**

$$R_2C{=}CH_2 + BH_3 \rightarrow R_2CHCH_2B\langle \xrightarrow{Br_2,\ MeONa} R_2CHCH_2Br$$

| run | substrate | bromide, % conversion | bromide, % yield | bromide, % main isomer |
|---|---|---|---|---|
| 4 | β-pinene[a,b] | 65 | 59 | >90 (cis) |
| 5 | 2-methylenebornane (**1a**) | 15 | >90[c] | 60 (*exo*-**1e**)[c] |
| 6 | (+)-camphene (**2a**) | 30 | >95[c] | 75 (*endo*-**2e**)[c] |
| 7 | (+)-camphene (**2a**) | 5[d] | >90[c] | nd |

[a] See ref 12. [b] Reaction carried out in THF. [c] Evaluated by GLC. [d] Reaction carried out in diglyme.

halides.[14,15] The chemical yields were moderate or low (run 12),[16] and the generation of olefinic by products was still a major competitive event. However, in this case, the diastereomeric composition of the compound **2d** (run 13) changes smoothly with respect to the starting carbinol, while the loss of diastereomeric purity is large in the case of the products **1d** (runs 9 and 10) and **2e** (run 15).

The diastereomeric ratio of the products **1b** and **2b** from hydroboration process dependes on steric control:[17] consequently, the prevailing alcohols *exo*-**1b** and *endo*-**2b** have the hydroxymethyl group in the more hindered side of the molecule.

As shown in Table III, there is a change, generally loss, of the diastereomeric purity in the conversion of the alcohols to the halides; in addition, large amounts of alkenes are formed. This change can be ascribed to a competition between nucleophilic substitution to give the desired halide and elimination to afford an undesired alkene.

It is reasonable to suppose that the ratio of substitution/elimination will be smaller for the more hindered alcohols *exo*-**1b** and *endo*-**2b**. As a consequence the proportion of *endo*-**1d** and *exo*-**2d** in the derived chlorides should and actually does increase. For example, in run 9 alcohol **1b**, which contains only 20% of the endo isomer affords chloride **1d** comprised of 40% of the endo isomer; in run 11[18] alcohol **1b** containing 80% of the endo isomer yields chloride **1d** with 90% of the endo isomer present. Similarly, alcohol **2b** containing 10% of the exo isomer goes

(14) Weiss, R. G.; Snyder, E. I. *J. Org. Chem.* **1971**, *36*, 403.
(15) Snyder, E. I. *J. Org. Chem.* **1972**, *37*, 1466.
(16) The 2-methylenebornane **1a** was practically the only recovered product.
(17) Zweifel, G.; Ayyangar, N. R.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2073.
(18) A sample of alcohol **1b** (exo:endo = 80:20) was converted into its acid 3-nitrophthalate. This product, by slow recrystallization from ethyl acetate and saponification (KOH/EtOH), afforded **1b** (endo:exo = 80:20).

**Table III. Synthesis of Alkyl Halides from Alcohols via Treatment with Triphenylphosphine and Carbon Tetrahalides**

$$RCH_2OH + CX_4 + PPh_3 \xrightarrow[20\ °C]{} RCH_2X + CHX_3 + Ph_3PO$$

| run | substrate | X | halide, % conversion[a] (time, h) | halide, % yield[a] | halide, % main isomer | olefinic[a] byproducts, % |
|---|---|---|---|---|---|---|
| 8 | *cis*-myrtanol | Cl | 100 (72) | 50 | 90 (cis) | 50 |
| 9 | 2-hydroxymethylbornane (**1b**)[b] | Cl | 100 (72) | 40 | 60 (*exo*-**1d**)[a] | 60 |
| 10 | 2-hydroxymethylbornane (**1b**)[b] | Cl | 50 (24) | 40 | 60 (*exo*-**1d**)[a] | 60 |
| 11 | 2-hydroxymethylbornane (**1b**)[c] | Cl | 100 (72) | 70 | 90 (*endo*-**1d**)[a] | 30 |
| 12 | 2-hydroxymethylbornane (**1b**)[b] | Br | 100 (120) | <5 | nd | 90 |
| 13 | camphanol (**2b**)[d] | Cl | 100 (120) | 55 | 80 (*endo*-**2d**)[a] | 45 |
| 14 | camphanol (**2b**)[e] | Cl | 100 (120) | 50 | >95 (*endo*-**2d**)[a] | 50 |
| 15 | camphanol (**2b**)[d] | Br | 95 (20) | 50 | 70 (*endo*-**2e**)[a] | 30 |

[a] Evaluated by GLC on the crude product. [b] Exo:endo = 80:20. [c] Endo:exo = 80:20. [d] Endo:exo = 90:10. [e] Endo:exo > 97.

to chloride **2d** having 20% of the exo isomer.

The problem of the diastereomeric purity in the preparation of these halides could be solved by using pure alcohols. Unfortunately, the selectivity of hydroboration of **1a** and **2a** can be only slightly improved[8] and the separation of the endo and exo alcohols is tedious[8,11a,b] and scarcely convenient.[18,19]

In this light, the treatment of alcohols with triphenylphosphine and carbon tetrahalides appears to be the most convenient method,[20] even when the pure isomer is used (run 14, Table III).

However, for our purposes we do not need alcohols with very high diastereomeric purity, as good enantioselectivity has been observed using reducing organometallic compounds directly derived from mixtures of exo and endo halides. Preliminary results have in fact shown that camphanylberyllium chloride (from **2d**, endo:exo = 80:20) reduces isopropyl phenyl ketone with 61% enantioselectivity, whereas *cis*-myrtanylberyllium chloride gives isopropylpenylcarbinol with 38% enantioselectivity.[1]

## Experimental Section

Boiling and melting points are uncorrected; $^1H$ NMR (60 MHz) and $^{13}C$ NMR (25.2 MHz) Fourier transform were obtained with Varian T-60 and a Varian XL-100 spectrometers on $CDCl_3$ solutions with $Me_4Si$ as on internal standard. Optical rotations were measured on a Perkin-Elmer 142 automatic polarimeter; GLC analyses (Perkin-Elmer 3920 B) were performed with Carbowax 20 M and Apiezon M (3 mt) as a stationary phase and nitrogen as carrier gas. Mass spectra were obtained with a VG ANALYTICAL 7070E spectrometer. All solvents were reagent-grade materials, purified by standard methods, and redistilled before use. All new compounds gave satisfactory microanalyses for C, H, Cl, and Br (within ±0.3%). All reactions involving air-sensitive materials were conducted under an argon atmosphere. (+)-(1*R*)-Camphor [mp 177–179 °C; $[\alpha]^{20}_D$ +44.3° (*c* 10, EtOH)] and (−)-borneol [mp 207–208 °C; $[\alpha]^{20}_D$ −35.3° (*c* 5.3, EtOH)] were obtained by purification of commercial products. (+)-(1*R*)-Camphene (**2a**)[9] and *cis*-myrtanol[3] were prepared starting from (+)-camphor and from (−)-2-pinene, respectively, according previously reported procedures. 2-Methylenebornane (**1a**) was prepared starting from (+)-camphor according two different procedures already published.[6-8]

**(−)-(1*S*)-2,2-Dimethyl-3-methylenebicyclo[2.2.1]heptane [(−)-Camphene (2a)].** Under an anhydrous atmosphere, to a stirred solution of (−)-borneol (103.0 g, 667 mmol) in pyridine (500 mL) was added *p*-TsCl (140.0 g, 734 mmol). The mixture was kept at 100 °C for 8 h, then hydrolyzed with brine and HCl (pH 2), and extracted with ether. The organic layer was washed with $H_2O$, dried ($Na_2SO_4$), and concentrated. The distillation of the crude product afforded pure (GLC) **2a**: 75.2 g (83%); bp 155–160 °C; $[\alpha]^{25}_D$ −99.6° (*c* 2.7, benzene) [lit.[10] $[\alpha]^{20}_D$ −115.1° (*c* 5.6, benzene)].

**(1*R*,2*R*)-1,7,7-Trimethyl-2-(hydroxymethyl)bicyclo-[2.2.1]heptane (*exo*-1b).** To a well-stirred suspension of $NaBH_4$ (2.5 g, 62 mmol) and **1a** [22.6 g, 150 mmol, $[\alpha]^{25}_D$ −47.7° (*c* 3.2, benzene)] in diglyme (100 mL) was added dropwise (20 min), at −5 °C under argon, $BF_3{\cdot}Et_2O$ (10.5 mL, 11.8 g, 82 mmol). After being stirred at room temperature for 3 h, the mixture was oxidized in the usual manner (1 h, 50–60 °C) by the addition of NaOH (3 N, 20 mL) followed by $H_2O_2$ (36%, 18 mL). Workup by ether extraction, followed by distillation yielded *exo*-**1b**: 17.8 g (75%); mp 105–107 °C; bp 125–130 °C (13 mm); $[\alpha]^{25}_D$ −38.4° (*c* 2.6, benzene), containing the endo isomer (20%).

**(1*R*,3*S*)-2,2-Dimethyl-3-(hydroxymethyl)bicyclo[2.2.1]-heptane (*endo*-2b).** The preparation of **2b** was carried out as above, using $NaBH_4$ (5.1 g, 156 mmol), **2a** [40.8 g, 300 mmol, $[\alpha]^{25}_D$ +94.3° (*c* 4.3, benzene)], $BF_3{\cdot}Et_2O$ (23.4 g, 165 mmol). After the workup, distillation yielded *endo*-**2b**: 44.0 g (95%); mp 83 °C; bp 120 °C (15 mm); $[\alpha]^{25}_D$ −10.5° (*c* 0.9, benzene), containing the exo isomer (10%); $^1H$ NMR δ 3.62 (d, 2 H), 2.27 (m, 1 H), 1.80–1.08 (m, 9 H), 1.03 (exo, s, 0.3 H), 1.00 (endo, s, 2.7 H), 0.91 (exo, s, 0.3 H), 0.85 (endo, s, 2.7 H); $^{13}C$ NMR δ 60.9, 52.6, 49.1, 39.8, 37.1, 36.8, 32.6, 24.6, 20.5, 20.3; MS, *m/z* 154 ($M^+$).

**(1*R*,2*R*)-1,7,7-Trimethyl-2-(chloromethyl)bicyclo[2.2.1]-heptane (*exo*-1d). (A) Run 2.** To a solution of **1b** (17.8 g, 100 mmol, exo:endo = 80:20), in dry pyridine (90 mL), was added at −5 °C *p*-TsCl (23.0 g, 120 mmol) within 10 min. The resulting mixture was stirred at room temperature for 16 h, hydrolyzed with 10% HCl, extracted with ether, and dried ($Na_2SO_4$). The solvent was removed under reduced pressure, affording crude **1c** [26.0 g, 80 mmol (80%)] as a colorless oil: $^1H$ NMR ($CCl_4$) δ 7.50 (dd, 4 H), 4.20–3.57 (m, 2 H), 2.43 (s, 3 H), 2.00–0.67 (m, 17 H). Compound **1c** in anhydrous DMF (100 mL) was reacted at 85–90 °C with LiCl (4.2 g, 100 mmol) in DMF (100 mL). The mixture was stirred for 8 h at the same temperature, then cooled, hydrolyzed with $H_2O$, and extracted with ether. After distillation of the dried ($Na_2SO_4$) extracts, **1d** was recovered: 4.5 g (30%) exo:endo = 55:45, GLC; bp 56 °C (0.3 mm); $^1H$ NMR ($CCl_4$) δ 3.62–3.05 (m, 2 H), 2.17–0.73 (m, 17 H); MS, *m/z* 186 ($M^+$), and a mixture of **1a** and 2-methyl-2-bornene[21] (GLC).

**(B) Run 9.** A solution of $PPh_3$ (3.4 g, 12.3 mmol) in $CCl_4$ (5 mL) was added to a solution of **1b** (1.7 g, 10.5 mmol, exo:endo = 80:20) in $CCl_4$ (2 mL). The mixture was stirred at room temperature for 72 h and then extracted with pentane. After fractional distillation a mixture (1.5 g) of **1d** (40%, exo:endo = 60:40, GLC) and **1a** (60%, GLC) was recovered.

**(1*R*,3*S*)-2,2-Dimethyl-3-(chloromethyl)bicyclo[2.2.1]heptane (*endo*-2d). (A) Run 3.** The tosylate **2c** was prepared from **2b** (17.9 g, 116 mmol, endo:exo = 90:10) and *p*-TsCl (25.5 g, 130 mmol) in the usual manner. The crude product, purified by slow crystallization from methanol, gave chemically pure **2c**: 29.0 g (82%); mp 46–49 °C [lit.[22] mp 48–48.5 °C]; $^1H$ NMR δ 7.50 (dd,

(19) A sample of alcohol **2b** (endo:exo = 90:10) was converted into its acid 3-nitrophthalate. This product, by slow recrystallization from absolute ethanol and saponificaton (KOH/EtOH), afforded **2b** (endo:exo > 97).

(20) The bromination of alcohol **2b** with $PBr_3$ in pyridine was also attempted: Salvadori, P.; Lardicci, L.; Stagi, M. *Gazz. Chim. Ital.* **1968**, *91*, 428. The bromide **2e** was recovered in a <10% yield.

(21) Burgstahler, A. W.; Boger, D. L.; Naik, N. C. *Tetrahedron* **1976**, *32*, 309.

4 H), 4.00 (d, 2 H), 2.43 (s, 3 H), 2.17 (m, 1 H), 1.90–1.03 (m, 8 H), 0.93 (s, 3 H), 0.80 (s, 3 H); $^{13}C$ NMR δ 144.3, 133.2, 128.6, 127.6, 69.8, 48.9, 48.7, 40.0, 37.0, 32.1, 24.3, 23.7, 21.6, 20.4, 20.2. A solution of the tosylate **2c** (29.0 g, 95 mmol) in DMF (200 mL) was reacted with LiCl (5.0 g, 120 mmol) as above to give **2d** (1.0 g), containing camphene (50%, GLC) as impurity, after distillation of the crude product.

**(B) Run 13.** The preparation of **2d** was carried out starting from **2b** (4.2 g, 27.2 mmol, endo:exo = 90:10) and $PPh_3$ (8.8 g, 33.2 mmol) in $CCl_4$ (25 mL) as above described for **1d**. After 120 h, fractional distillation of the crude product gave *endo*-**2d**: 1.82 g (39%); bp 90–96 °C (10 mm); $[\alpha]^{25}_D$ −4.23° (*c* 3.9, benzene), containing the exo isomer (20%); $^1H$ NMR δ 3.42 (d, 2 H), 2.42–1.15 (m, 9 H), 1.02 (s, exo, 0.6 H), 0.98 (s, endo, 2.4 H), 0.92 (s, exo, 0.6 H), 0.85 (s, endo, 2.4 H); MS, *m/z* 217 ($M^+$).

**(1*R*,2*R*)-1,7,7-Trimethyl-2-(bromomethyl)bicyclo[2.2.1]heptane (*exo*-1e). Run 5.** Hydroboration was carried out bubbling gaseous $BH_3$ (4 h) in a solution of **1a** (30.4 g, 200 mmol) in THF (100 mL) at −5 °C. Excess hydride was destroyed by the addition of dry methanol (30 mL). Bromine (10.6 mL, 32.0 g, 200 mmol) was placed in an addition funnel, and sodium methoxide [metallic Na (6.0 g, 260 mmol) in methanol (150 mL)] was placed in a second funnel. The bromine and base were added simultaneously at a rate such that the reaction mixture was always orange (1.5 h, 20–25 °C). The reaction mixture was hydrolyzed (saturated $Na_2CO_3$) and extracted with ether; the distillation of dry ($Na_2SO_4$) organic layer afforded **1e**: 7.0 g (15%); bp 90–98 °C (15 mm); (exo:endo = 60:40, GLC; $^1H$ NMR δ 3.70–3.07 (m, 2 H), 2.30–0.98 (m, 8 H), 0.95–0.71 (m, 9 H); MS, *m/z* 231 ($M^+$). The solid residue of distillation was then oxidized with NaOH (3 N) and $H_2O_2$ (36%), affording **1b**, 21.6 g (65%).

**(1*R*,3*S*)-2,2-Dimethyl-3-(bromomethyl)bicyclo[2.2.1]heptane (*endo*-2e). (A) Run 6.** The preparation of **2e** was carried out starting from **2a** (68.2 g, 500 mmol) and gaseous $BH_3$ in THF (200 mL) as described above. The bromination was performed with bromine (25.6 mL, 80.0 g, 500 mmol) and sodium methoxide [metallic Na (15g, 660 mmol) in dry methanol (250 mL)]. After the usual workup, the distillation of crude product gave *endo*-**2e**: 29.1 g (27%); bp 74 °C (0.25 mm); endo:exo = 75:25, GLC; MS, *m/z* 217 ($M^+$). The solid residue of distillation was oxidized with NaOH (3 N) and $H_2O_2$ (36%), affording **2b**, 46.2 g (60%).

**(B) Run 15.** A solution of $PPh_3$ (31.5 g, 120 mmol) in $CH_2Cl_2$ (80 mL) was added to a solution of **2b** (15.4 g, 100 mmol, endo:exo = 90:10) and $CBr_4$ (46.5 g, 140 mmol) in $CH_2Cl_2$ (100 mL). The mixture was stirred at room temperature for 20 h and then treated with pentane. Fraction distillation of crude product afforded **2e**: 9.8 g (45%); bp 48 °C (0.1 mm); endo:exo = 70:30, GlC; $^1H$ NMR δ 3.83–3.03 (m, 2 H, 2.50–0.87 (m, 15 H).

**Acknowledgment.** We thank the Ministero della Pubblica Istruzione (Rome, Italy) for partial support of this work.

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# A General and Practical Synthesis of (*R*)-Phthalimido Aldehydes and D-α-Amino Acids from D-Mannitol

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*Received May 9, 1986*

A short and practical synthesis of five D-α-amino acids is described from D-mannitol as the chiral educt. The key steps in the sequence are (a) the erythro-selective addition of organometals to (*R*)-2,3-*O*-isopropylideneglyceraldehyde, (b) the Mitsunobu inversion substituting *N*-phthalimide for hydroxyl, and (c) acetonide hydrolysis and glycol cleavage to give the *N*-phthaloyl-(*R*)-α-aminoaldehydes **7**. These are oxidized under Jones conditions to give the N-protected amino acids **8**. The examples investigated (alanine, aminobutyric acid, norvaline, and allyl- and vinylglycine) demonstrate the general applicability of the method.

The synthesis of enantiomerically pure D-α-amino acids has received much attention in recent years. These compounds are of considerable biological interest,[1] but, in general, they cannot be procured in sufficient quantities from natural sources. D-α-Amino acids have been prepared by resolution of racemic mixtures,[2] by asymmetrically induced $sp^2 \rightarrow sp^3$ transformations using a variety of chiral auxiliaries,[3] by diastereoselective 2,3-sigmatropic rearrangement of optically active allyl selenates,[4] by $S_N2$ N-O exchange of (*S*)-α-hydroxy acids,[5] or by "ex-chiral-pool" synthesis starting from L-serine.[6] These methods except the last mentioned one either need expensive resolving agents or chiral auxiliaries[3] or they lack generality[5] and

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