under vacuum to a small volume, and then petroleum ether (bp 40–60°) was added. O-Carbobenzoxyalanylglycolic acid (**3**) precipitated (0.2 g, 70% yield), mp 85°.

Anal. Calcd for $C_{13}H_{15}O_6N$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.66; H, 5.68; N, 5.18.

Rearrangement of DL-Alanylaminoxyacetic Acid.—DL-Alanylaminoxyacetic acid[2] (mp 197°) (0.162 g, 0.001 mol) was dissolved in water (1 ml) and cooled to 10° $NaNO_2$ (0.069 g, 0.001 mol) was added portionwise during 10 min. The solution was stirred at room temperature for 30 min until the effervescence of gas stopped, was acidified to pH 3, and was cooled overnight. A solution of 5% $NaHCO_3$ (5 ml) was added together with carbobenzoxychloride (0.38 g, 0.0015 mol) and stirred overnight at 10°. After washing with ether the solution was acidified to congo red. The precipitated O-carbobenzoxy-DL-alanylglycolic acid (**3**) was collected and recrystallized from ethyl acetate–petroleum ether (0.1 g, 35%), mp 86°. A mixture melting point and ir spectrum showed this product to be identical with that which is described in the preceding preparation.

Rearrangement of Glycylaminoxyacetic Acid.—Glycylaminoxyacetic acid[4] (mp 150°) (0.148 g, 0.001 mol) was treated as the alanyl derivative above, yielding O-carbobenzoxyglycylglycolic acid (0.07 g, 30% yield), mp 110° (lit. 105–106°).[5]

Registry No.—**2**, 21347-35-3; **3**, 21343-30-6.

Rearrangement of a 4,4-Disubstituted Homophthalimide to the Benzo[*b*]phenanthridine System

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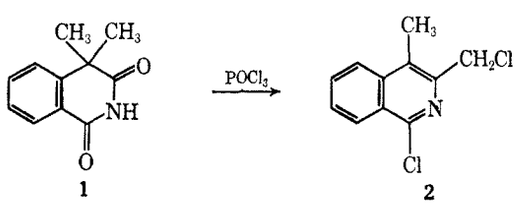
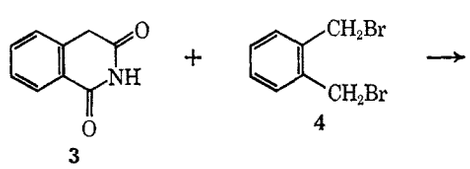
Heating 4,4-dimethylhomophthalimide (**1**) with phosphorus oxychloride produces dichloride $C_{11}H_9Cl_2N$,[1] which has been shown to be 1-chloro-3-chloromethyl-4-methylisoquinoline (**2**).[2–4] We have now succeeded in



1 2

utilizing a skeletal rearrangement analogous to the **1** to **2** process for the generation of the benzo[*b*]phenanthridine system. Homophthalimide (**3**),[5] on alkylation with 1,2-bis(bromomethyl)benzene (**4**), gives spiro compound **5**.[6] When the spiro compound is heated at



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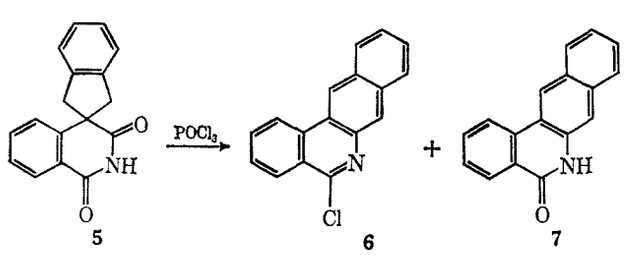
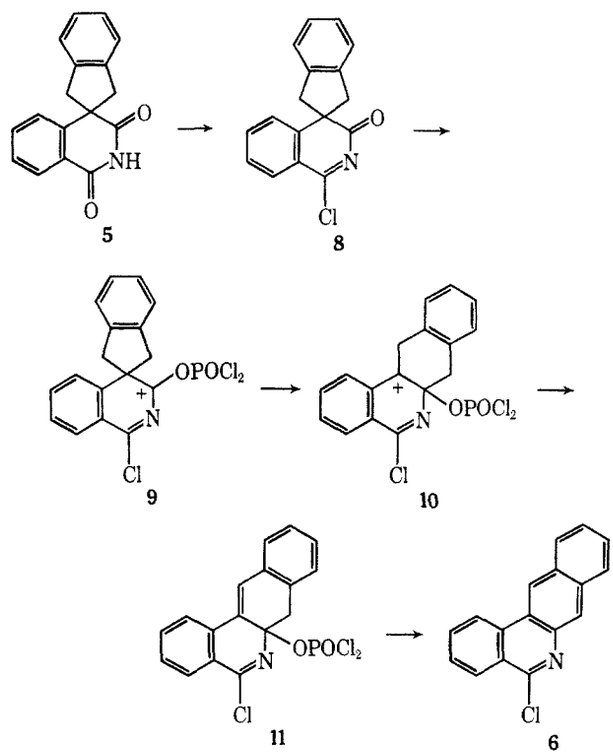


5 6 7

130° with phosphorus oxychloride, products **6** and **7** as well as unchanged starting material **5** were isolated. Direct comparison of the 6H-benzo[*b*]phenanthridin-5-one (**7**) with the same substance prepared in a different way established its structure as shown.[7]

We suggest a reaction sequence in which the spiro compound **5** is first converted with phosphorus oxychloride into chloro compound **8**. Further reaction with phosphorus oxychloride gives carbonium ion **9**, skeletal rearrangement of which forms **10**. Loss of a

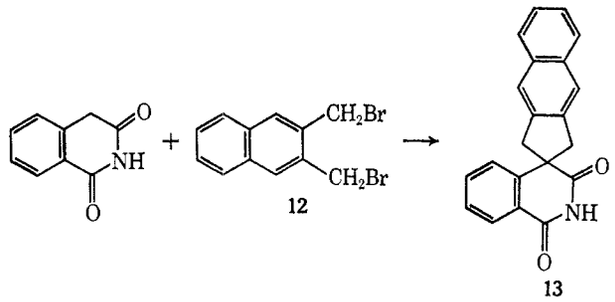


proton would give the stilbene-like intermediate **11**, and subsequent loss of the oxyphosphoryl grouping and a second proton would lead to the fully aromatic product **6**. Since oxo compound **7** can be derived readily from chloro compound **6** by acid-catalyzed hydrolysis, possibly, though not necessarily, the oxo compound originates from **6** during the processing of the reaction mixture.[4]

We intend to exploit this kind of rearrangement for the preparation of other polycyclic nitrogen compounds and, in this connection, have prepared spiro compound **13** by alkylating homophthalimide with 2,3-bis(dibromomethyl)naphthalene (**12**). Also, during the course of this work we have developed conditions for the original rearrangement of 4,4-dimethylhomo-

(1) S. Gabriel, *Chem. Ber.*, **20**, 1205 (1887).
(2) G. Jones, *J. Chem. Soc.*, 1896 (1960).
(3) N. Wang and H. R. Snyder, Jr., unpublished work.
(4) F. H. Marquardt and M. D. Nair, *Helv. Chim. Acta*, **50**, 1469 (1967); F. H. Marquardt, *ibid.*, **50**, 1477 (1967).
(5) S. Gabriel, *Chem. Ber.*, **19**, 1653, 2354 (1886); A. S. Bailey and D. L. Swallow, *J. Chem. Soc.*, 2477 (1956); A. Meyer and R. Vittenet, *Ann. Chim.*, [10], **17**, 271 (1932).
(6) Reported by C. Fournier and J. Decombe, *Bull. Soc. Chim. Fr.*, 364 (1968), after this work was completed.
(7) L. H. Klemm and A. Weisert, *J. Heterocycl. Chem.*, **2**, 15 (1965).

phthalimide that give 1-chloro-3-chloromethyl-4-methylisoquinoline (2) in over 80% yield. Since catalytic hydrogenolysis easily removes both chloro groups,[3] clearly the most convenient way to make 3,4-



dimethylisoquinoline,[1,8] is now through this two-stage rearrangement-hydrogenolysis sequence.

Experimental Section

General.—Melting points were determined with the sample between two cover glasses on a metal block. Analyses for elements were performed by Dr. S. M. Nagy and his associates at Massachusetts Institute of Technology, Cambridge, by Dr. C. K. Fitz, Needham Heights, Mass., and by Galbraith Laboratories, Inc., Knoxville, Tenn. Nuclear magnetic resonance spectra were taken with a 60-MHz instrument with the sample generally as a 10% solution.

Spiro[homophthalimide-4,2′-indan] (5).—A solution of 4.0 g (15 mmol) of 1,2-bis(bromomethyl)benzene (4), mp 93–94°, in 20-30 ml of benzene was added to a bright yellow solution of 2.45 g (15 mmol) of homophthalimide (3)[5] in 135 ml of 95% ethanol and 15 ml of water containing 2.44 g (45 mmol) of potassium hydroxide. The mixture was boiled for 2.5 hr. Periodic titration of small aliquots showed that alkali was consumed during the first 1.5 hr but not thereafter. The reaction mixture was concentrated in a rotary evaporator to a volume of *ca.* 100 ml. Dilute hydrochloric acid was then added until the solution was acid to litmus, and the concentration was continued until the volume was about 50 ml. Filtration gave a product, which after air drying weighed 3.7 g (95%) and showed mp 170–203°. Several wasteful crystallizations from tetrahydrofuran yielded 2.2 g (56%) of spiro[homophthalimide-4,2′-indan] (5), mp 210–211° (capillary). Crystallization from acetic anhydride gave material with mp 214–216° (lit.[6] mp 211°).

Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98. Found: C, 77.5; H, 5.2.

The infrared absorption spectrum (KBr) shows peaks at 3443, 3220, 3090, 1720, 1685, and 1600 cm^{-1}; uv max (6×10^{-5} *M* in absolute C_2H_5OH) 243 mμ (log ε 4.05), 267 (3.45), 275 (3.46), 285 (3.35), 292 (3.33); nmr (10% in F_3CCOOH) δ 8.36–7.33 ppm (complex, aromatic H's), 4.25, 3.97, 3.60, 3.30) (estd 4 H, AB quartet with two intense inside peaks accompanied by outside satellites, aliphatic H's). The quartet of signals may be associated with two equivalent pairs in the two methylene groups in which the protons of each pair have δ 4.07 ppm (1 H, d, J_{gem} = 17.5 Hz) and 3.48 ppm (1 H, d, J_{gem} = 17.5 Hz), respectively.

Action of Phosphorus Oxychloride on Spiro[homophthalimide-4,2′-indan] (5).—A mixture of 33.8 mg (0.13 mmol) of spiro compound 5 and 0.5 ml (3.3 mmol) of phosphorus oxychloride, sealed in a small glass tube, was heated in a 128–130° oil bath for 39 hr. The colorless phosphorus oxychloride was a sample of Baker product taken from a bottle that had been first opened 15 months before but kept carefully stoppered while not in use. After most of the excess reagent had been removed in a stream of nitrogen, 2 ml of water–methanol (1:1) was added, and the mixture was brought to pH 5 with aqueous sodium hydroxide. The solids were collected, dried at 110°, and dissolved in 2 ml of tetrahydrofuran. The tan solution was streaked on a preparative chromatography plate coated with a 2-mm layer of silica gel containing a phosphor (Brinkmann). Development with benzene produced six bands visible under ultraviolet light. The first band at R_F 0.0–0.07 corresponded to 6H-benzo[*b*]phenanthridin-5-one (7), the second at R_F 0.08–1.7 to unchanged starting material 5, and the fourth at R_F 2.6–4.0 to 5-chlorobenzo[*b*]-phenanthridine (6).

Bands 1, 2, and 4 were scraped from the plate, and the separate fractions were exhaustively extracted; band 4 was extracted with benzene, and bands 1 and 2 with tetrahydrofuran that had been freshly distilled from lithium aluminum hydride to remove peroxides.

Crystallization of the solvent-free material from band 2 from tetrahydrofuran afforded 7.7 mg (23%) of unchanged starting material 5 as white crystals, mp 212–214° (capillary).

Crystallization of the material from band 4 from dimethylformamide gave 14.1 mg (41%) of 5-chlorobenzo[*b*]phenanthridine (6), mp 161–162° (capillary).

Anal. Calcd for $C_{17}H_{10}ClN$: C, 77.41; H, 3.82; N, 5.31. Found: C, 77.52; H, 3.91; N, 5.26.

This material shows relatively minor infrared absorption peaks (KBr) at 1600, 1575, and 1490 cm^{-1}; uv max (1.8×10^{-5} *M* in 95% C_2H_5OH) 220 mμ (log ε 4.85), 249 (4.99), 256.5 (5.03), 265 (4.94), 275.5 (4.91), 287 (5.05), 299 (4.98), 326 (3.98), and 340.5 (4.05); nmr signals (F_3CCOOH) are seen as broad multiplets between δ 8.80–7.00 ppm with peaks at 8.65, 8.30, 7.82, 7.43 ppm.

Crystallization of the material from band 1 from glacial acetic acid gave 4.1 mg (11%) of 6H-benzo[*b*]phenanthridin-5-one (7), mp over 320° [lit.[7] mp 304.5–306°].

Anal. Calcd for $C_{17}H_{11}NO$: C, 83.25; H, 4.52; N, 5.71. Found: C, 83.09; H, 4.63; N, 5.68.

Infrared absorption maxima (KBr) appear at 3050, 1660, 1630, and 1610 cm^{-1}; uv max (1.3×10^{-5} *M* in 95% C_2H_5OH) 224 mμ (log ε 4.47), 252 (4.68), 259.5 (4.76), 269 (4.75), 358 (3.28), and 375 (2.89); nmr signals (F_3CCOOH solution) are seen as complex multiplets between δ 8.20–6.80 ppm with prominent peaks at 7.98, 7.30, and 6.98 ppm.

A small sample of 6H-benzo[*b*]phenanthridin-5-one (7) prepared by an altogether different method[7] was crystallized from glacial acetic acid. The fine white needles did not melt up to 320° and showed an infrared absorption spectrum identical with that obtained for the above product. As already reported,[7] the ultraviolet absorption spectra of the two samples of 7 are identical. When spotted on the same thin-layer chromatography plate (silica gel), both samples produced single spots, with R_F 0.02 when developed with benzene and with R_F 0.22 when developed with ether. The nmr spectra of the two materials are the same over the δ 8.3–4.5 ppm region; some minor signals appeared between 4.5–0.8 ppm in the comparison sample that were absent in the product obtained from 5.

6H-Benzo[*b*]phenanthridine-5-one (7) from 5-Chlorobenzo[*b*]-phenanthridine (6).—Three drops of glacial acetic acid containing 1.1 mg of chloro derivative 15 was held at 100° for 20 min. The white crystals that appeared at room temperature were collected and dried. This material (0.93 mg or 94%) melted above 320°. Its identity was shown by an infrared absorption spectrum (KBr) identical with that of 6H-benzo[*b*]phenanthridin-5-one (7).

The same process performed by warming 1 mg of chloro compound 6 in 5 drops of 6 *M* hydrochloric acid plus 6 drops of methanol at 70° for 20 min gave incomplete hydrolysis and, as shown by silica gel thin layer chromatography, produced a mixture of 6 and 7.

Spiro[homophthalimide-4,2′-benzo[*f*]indan] (13).—A solution of 0.27 g (1.7 mmol) of homophthalimide in 20 ml of water–ethanol (1:9) containing 0.29 g (5.2 mmol) of potassium hydroxide was mixed with a solution of 0.54 g (1.7 mmol) of 2,3-bis(bromomethyl)naphthalene (12)[9] in 5 ml of benzene. After a 2-hr period at the reflux temperature, the cooled reaction mixture was brought to pH 5 with hydrochloric acid and then was concentrated under reduced pressure to a volume of 5 ml. The mixture, diluted with 10 ml of water, was filtered. The dry, pale yellow product (0.5 g) was crystallized twice from tetrahydrofuran to give fine white needles of spiro compound 13, mp 287–288° (capillary), in low recovery.

Anal. Calcd for $C_{21}H_{15}NO_2$: C, 80.49; H, 4.82; N, 4.47. Found: C, 80.24; H, 4.72; N, 4.37.

Infrared absorption maxima (KBr) were observed at 3190, 3080, 1705, 1685, and 1600 cm^{-1}; uv max (5.6×10^{-6} *M* in 95% C_2H_5OH) 230 mμ (log ε 6.00), 271.5 (4.89), 282 (4.93), 290

(8) B. Witkop, *J. Amer. Chem. Soc.*, **70**, 1424 (1948).

(9) W. Ried and H. Bodem, *Chem. Ber.*, **91**, 1981 (1958).

(4.81), 3.08 (4.15), and 322 (4.20); nmr (10% solution in F_3-CCOOH) δ 8.2–7.4 (complex, aromatic H's), 4.35, 4.07, 3.68, 3.40 (estd 4 H, AB quartet with relatively intense inside peaks, aliphatic H's). The quartet arises from two equivalent pairs of methylene protons in which the protons of each pair have calculated δ 4.18 (1 H, d, J_{gem} = 17 Hz) and 3.57 ppm (1 H, d, J_{gem} = 17 Hz), respectively.

4,4-Dimethylhomophthalimide (1) with Phosphorus Oxychloride.—4,4-Dimethylhomophthalimide (1), mp 118–119°, was prepared from homophthalimide[5] by a method similar to one already described.[10] After crystallization from acetic acid–water (1:4), product was obtained in yields as high as 60%; ir (KBr) 3185, 3077, 1720, 1695, and 1605 cm^{-1}; uv max (6.0×10^{-5} *M* in 95% C_2H_5OH) 243 mμ (log ϵ 4.07), 282 (3.13), and 290 (3.17). A mixture of 5.0 g of the dimethyl compound 1 (0.027 mol) with 25 ml of phosphorus oxychloride was sealed in a glass tube and heated for 7.5 hr in an oil bath at 180 ±1°. Removal of excess reagent from the clear brown reaction mixture by distillation under reduced pressure left a residue, to which 40 ml of 95% ethanol was added. After cooling the mixture in an ice bath, the precipitate was collected, dried, and freed of acid by washing its benzene solution with several portions of dilute aqueous potassium hydroxide. When the product was brought out of benzene, 5.0 g (82%) of 1-chloro-3-chloromethyl-4-methylisoquinoline (2), mp 165–168°, was obtained. A sample for analysis, mp 169–170°, was prepared by further crystallization from the same solvent.

Anal. Calcd for $C_{11}H_9Cl_2N$: C, 58.43; H, 4.00. Found: C, 58.4; H, 4.0.

Dichloro compound 2 has been reported before with mp 165–166°,[1] 166°,[2] and 162–164°.[4]

When the reaction temperature was 170°, the yield of dichloro compound 2 was much lower, while at 210–220° only tar was obtained. With any given set of conditions, the yield of dichloro compound was lower when Merck and Co. "Reagent Grade" or Matheson Coleman and Bell phosphorus oxychloride (both colorless) was used than when J. T. Baker Chemical Co. "Analyzed Reagent" (slightly yellow) was used. Experiments with phosphorus oxychloride from a freshly opened bottle plus a few drops of concentrated hydrochloric acid showed no improvement in yield. Thus, we cannot support the suggestions that either hydrogen chloride or the partial hydrolysis products of phosphorus oxychloride are responsible.[11] Addition of a little lithium chloride to the reaction had very little effect.

The reported[12] high-yield conversion of homophthalimide to 1,3-dichloroisoquinoline by heating with benzenephosphonyl dichloride could be repeated without difficulty. However, experiments with 4,4-dimethylhomophthalimide (1) using 4–10 molar equiv of benzenephosphonyl dichloride at several temperatures ranging from 160–240° and for periods ranging from 1.5–96 hr gave no dichloro product 2.[13] Starting material was recovered at 160 and at 190°. One reaction at 240° gave small amounts of crystalline 3-chloromethyl-4-methylisocarbostyril, mp 251–254°.[4]

Registry No.—**5**, 6116-54-7; **6**, 21371-76-6; **7**, 2178-32-7; **13**, 21347-41-1.

Acknowledgment.—We wish to acknowledge the help of Professor L. H. Klemm, who provided us with a sample of 6H-benzo[*b*]phenanthridin-5-one (7) as well as with pertinent information prior to its publication.[7] National Science Foundation provided funds for the purchase of an nmr spectrometer (Research Equipment Grant GP 3618), for which we are grateful.

(10) S. Gabriel, *Chem. Ber.*, **19**, 2363 (1886); **20**, 1198 (1887).

(11) Jones[2] reported that old specimens of reagent gave better results and proposed that free acid accelerates the process. Others have noted that the effectiveness of phosphorus oxychloride in related processes depends on aging and exposure to air. *Cf.* H. E. Baumgarten, *J. Amer. Chem. Soc.*, **77**, 5109 (1955); A. Albert and W. Gledhill, *J. Soc. Chem. Ind.*, **64**, 169 (1945). H. R. Snyder and F. X. Werber [*J. Amer. Chem. Soc.*, **72**, 2962 (1950)] have suggested that polyphosporic acid may be implicated in explaining the efficacy of "old" reagents. Marquardt and Nair[4] deliberately add some concentrated hydrochloric acid to their phosphorus oxychloride.

(12) M. M. Robison, *J. Amer. Chem. Soc.*, **80**, 5481 (1958).

(13) The experiments with benzenephosphonyl dichloride were performed by Gerald Katz.

Heterocyclic Boronium Ions. The Reactions of Diamine Salts with Sodium Borohydride

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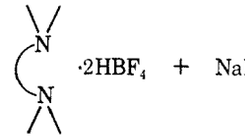
In recent years, several methods for synthesizing bis(amine)boronium ions, $(R_3N)_2BH_2^+$, have been reported.[1] One of the most versatile of these is the method of Miller and Muetterties involving the fusion of an amine–borane with an appropriate salt of a tertiary amine (eq 1). We now wish to report a

$$R_3N{-}BH_3 + R_3NH^+X^- \longrightarrow (R_3N)_2BH_2^+X^- + H_2 \quad (1)$$

modification of the Miller–Muetterties reaction which is particularly well suited for the preparation of heterocyclic boronium ions (2).

We have found that the fusion of equimolar amounts of the disalt of a 1,2- or 1,3-diamine (1) with sodium borohydride affords the corresponding five- or six-membered heterocyclic boronium ion (2) in reasonably good yields (eq 2). For example, the difluoroborate



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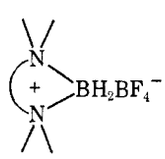

2

Diamine

a, N,N,N′N′-tetramethylethylenediamine

b, N,N,N′,N′-tetramethyl-1,2-propanediamine

c, N,N,N′,N′-tetramethyl-1,3-propanediamine

d, *trans*-N,N,N′,N′-tetramethyl-1,2-diaminocyclohexane

e, N,N,N′,N′-tetramethyl-*o*-phenylenediamine

f, N,N′-dimethylpiperazine

salt[2] of N,N,N′,N′-tetramethylethylenediamine (**1a**) reacts with sodium borohydride[3] at 180–200° to yield **2a**. The small amount (<5%) of diborane adduct of the diamine which is also formed can be readily separated from the other products by extraction with hot benzene. Experimentally it was found desirable to use a slight excess of borohydride to ensure that there is no unreacted disalt present in the product mixture, as it is not easily separated from the boronium salt. Separa-

(1) (a) J. E. Douglass, *J. Amer. Chem. Soc.*, **84**, 121 (1962); (b) H. Nöth, H. Beyer, and H. J. Vetter, *Ber.*, **97**, 110 (1964); (c) N. E. Miller and E. L. Muetterties, *J. Amer. Chem. Soc.*, **86**, 1033 (1964); (d) J. E. Douglass, *ibid.*, **86**, 5431 (1964); (e) G. E. Ryschkewitsch, *ibid.*, **89**, 3145 (1967); (f) J. E. Douglass, G. R. Roehrig, and O. H. Ma, *J. Organometal. Chem.*, **8**, 421 (1967); (g) K. C. Nainan and G. E. Ryschkewitsch, *J. Amer. Chem. Soc.*, **91**, 330 (1969).

(2) Fluoroborate salts were chosen because of their relatively low melting points and because the boronium fluoroborates are stable, easily crystallizable compounds.

(3) In general, lithium borohydride mixtures fuse at slightly lower temperatures and give slightly better yields; experimentally, however, it is more convenient to use the less sensitive sodium borohydride.