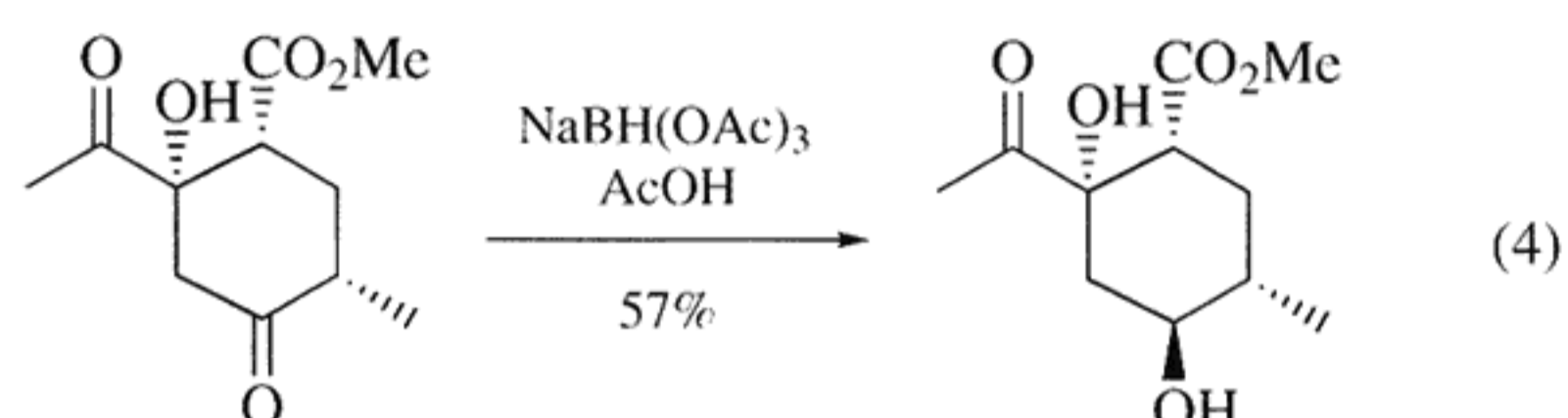
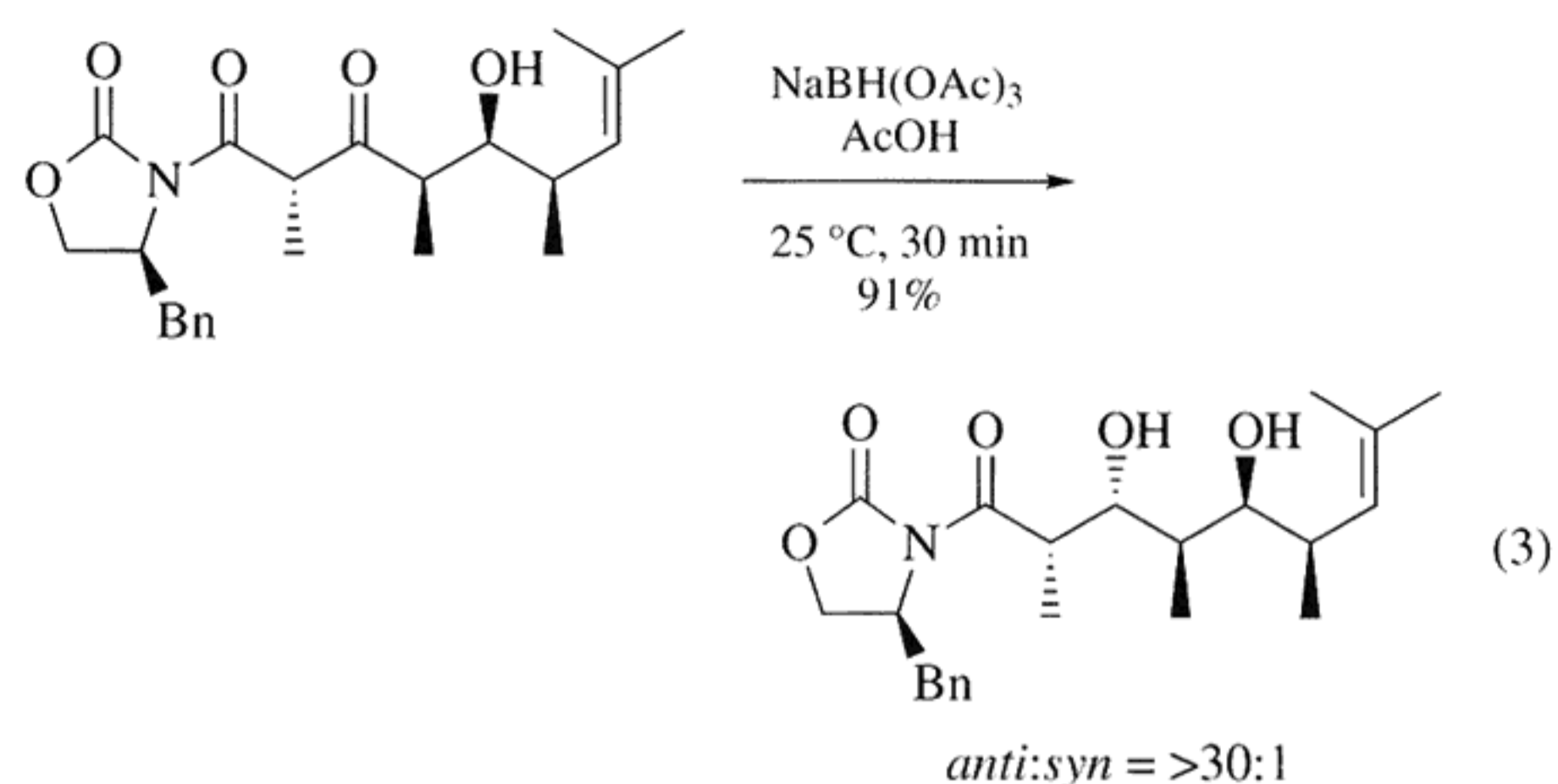
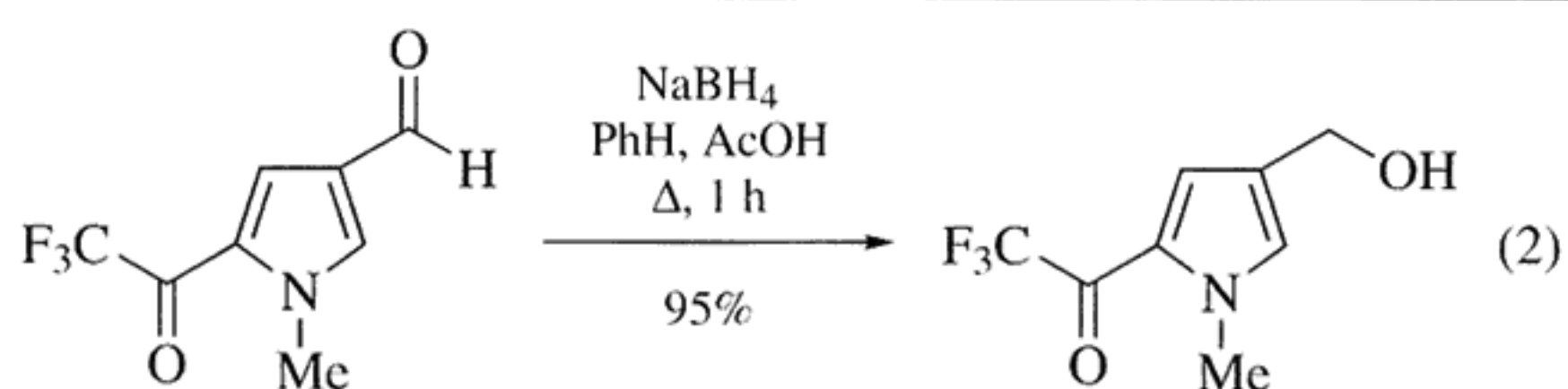


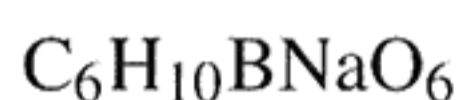
S. D. Burke & R. L. Danheiser (Ed.)
Handbook of Reagents for Organic Synthesis:
Oxidizing and Reducing Agents, pp. 429-432
 John Wiley & Sons, Chichester, UK (1999)



Sodium Triacetoxyborohydride¹



[56553-60-7]



(MW 211.96)

(the prototype of a class of NaBH(OCOR)_3 reagents that are selective reducing agents for a number of functional groups¹ and heterocycles;¹ alkylation of amines;¹⁻⁴ hydroboration¹)

Physical Data: mp t 116–120 °C (dec); the related NaBH_3OAc has not been fully characterized.

Solubility: NaBH(OAc)_3 and related acyloxyborohydrides are rapidly destroyed by H_2O and protic solvents; H_2 is liberated. Cosolvents that have been employed are benzene, toluene, THF, dioxane, CH_2Cl_2 , $\text{ClCH}_2\text{CH}_2\text{Cl}$.

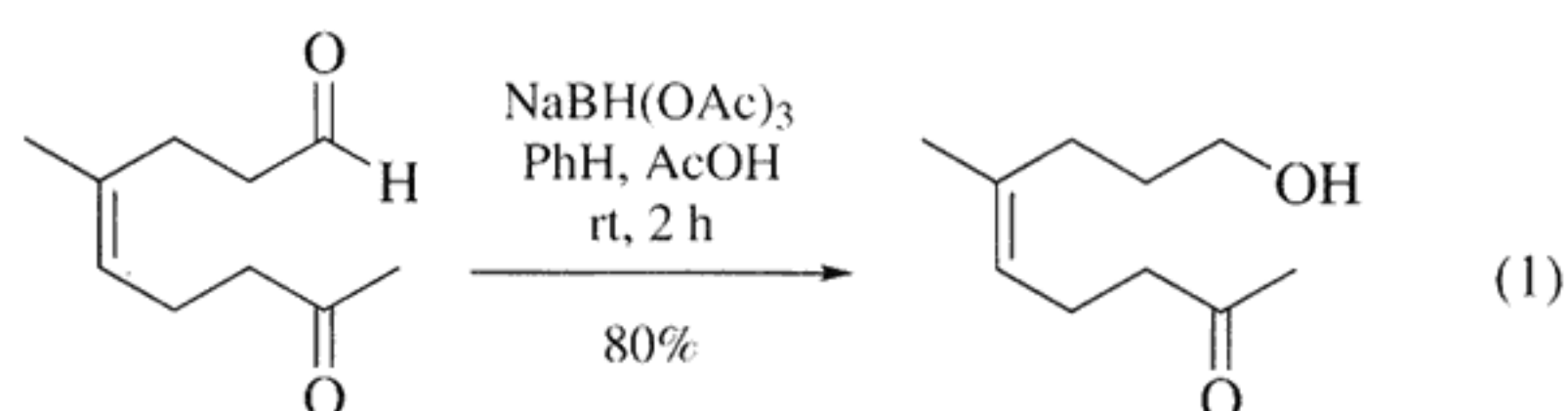
Form Supplied in: NaBH(OAc)_3 and the related **Tetramethylammonium Triacetoxyborohydride** are commercially available as colorless powders.

Preparative Method: NaBH(OAc)_3 and NaBH_3OAc can be easily prepared in situ from the appropriate amount of acetic acid and NaBH_4 .

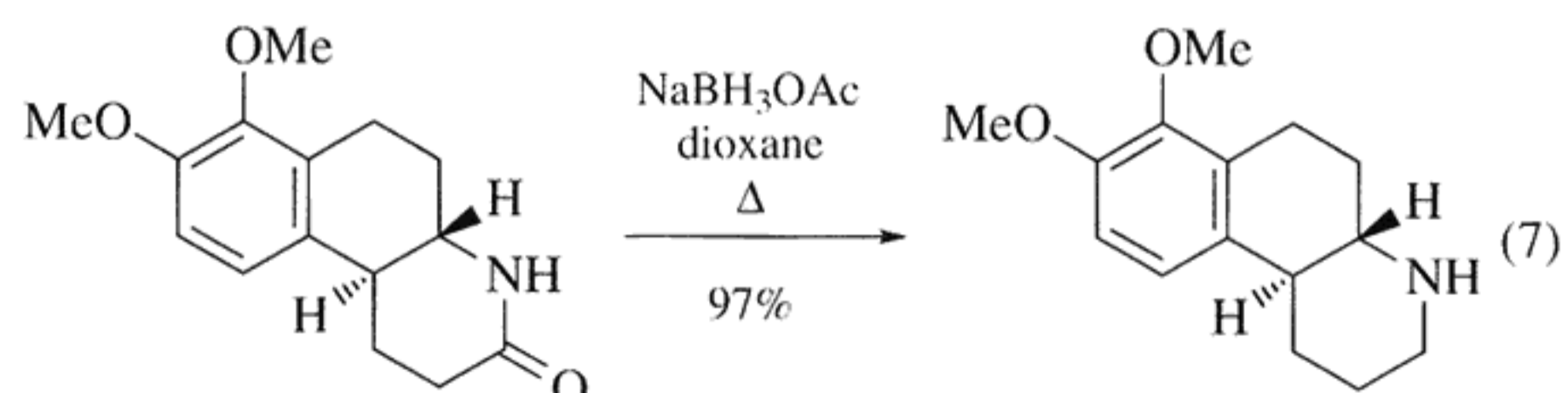
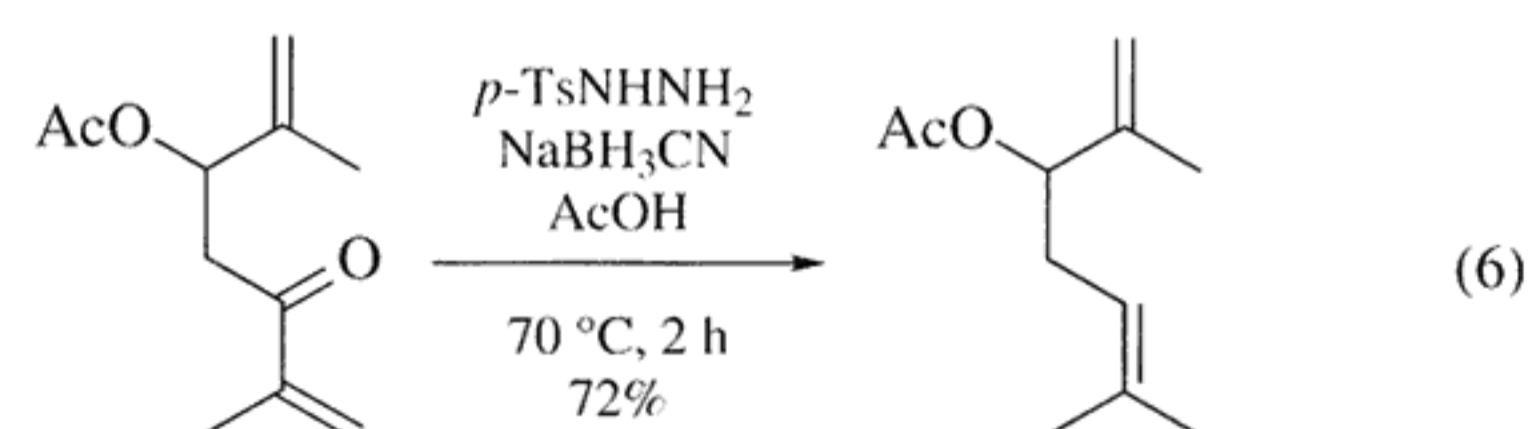
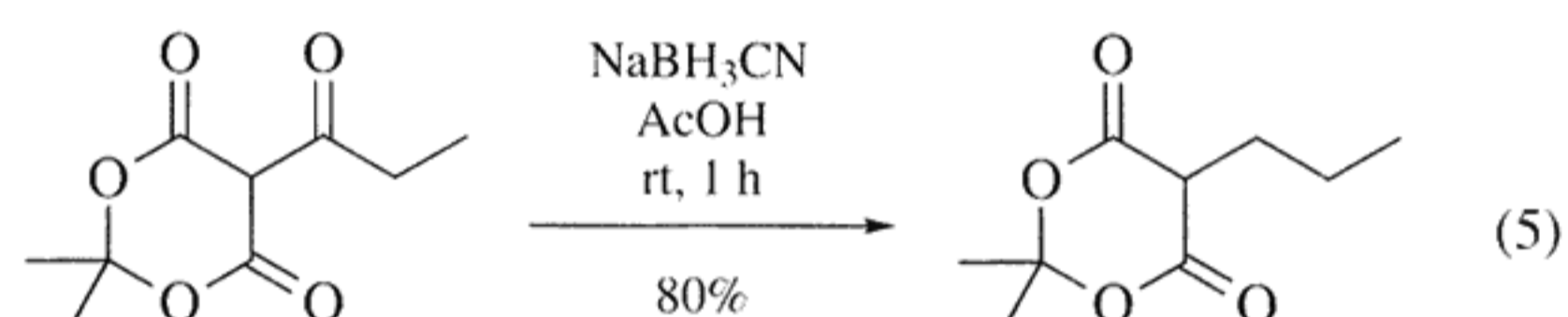
Analysis of Reagent Purity: NaBH(OAc)_3 has been characterized by elemental analysis, IR, and ^1H , ^{13}C , and ^{11}B NMR.

Handling, Storage, and Precautions: because H_2 is liberated during the preparation of these reagents, all handling and storage of acyloxyborohydrides should take place under an inert atmosphere.

Functional Group Reductions. NaBH(OAc)_3 selectively reduces aldehydes but not ketones^{5,6} (eqs 1 and 2),^{7,8} even with excess reagent. However, α - and β -hydroxy ketones are reduced to the *anti*-diols by hydroxy-directed hydride delivery^{6,9,10} (eqs 3 and 4).^{11,12} Diastereoselectivities are generally excellent, although $\text{Me}_4\text{NBH(OAc)}_3$ seems to be a superior reagent in this regard.⁹ Several recent examples of NaBH(OAc)_3 in the stereoselective reduction of hydroxy ketones attest to the power of this reagent.¹³



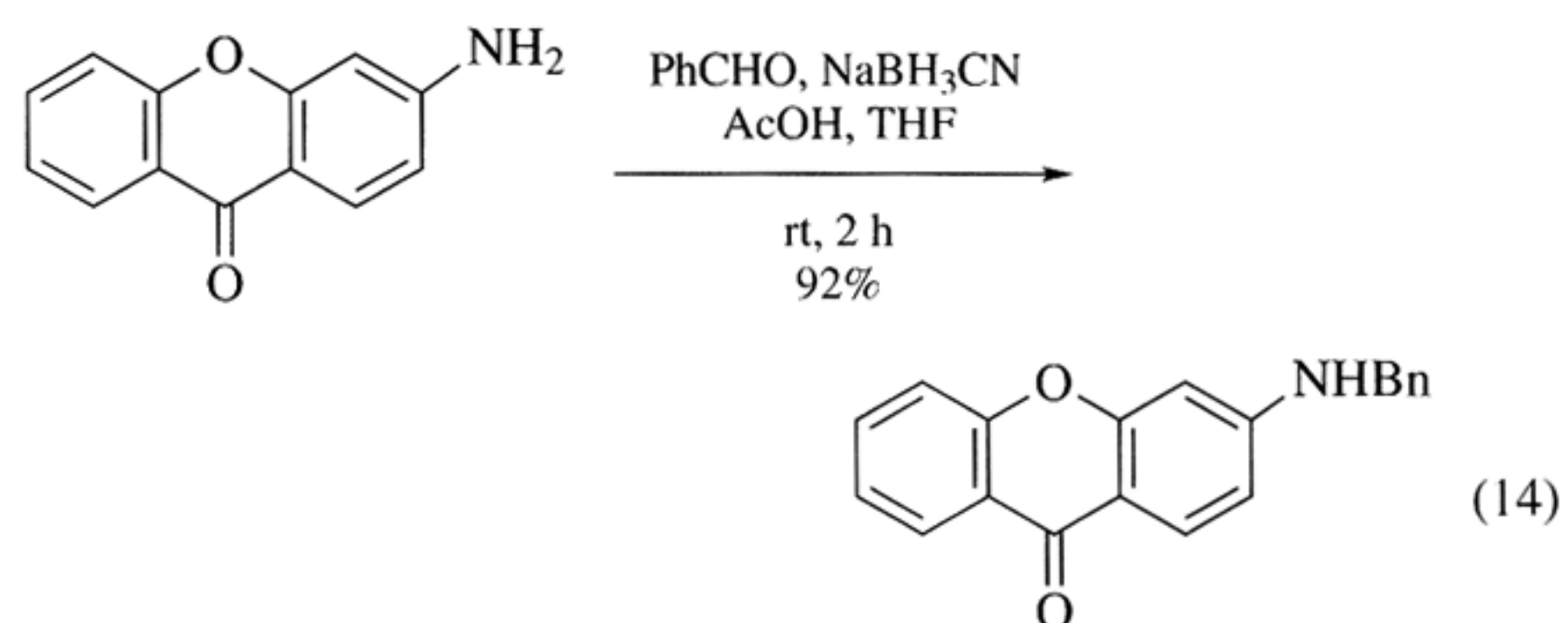
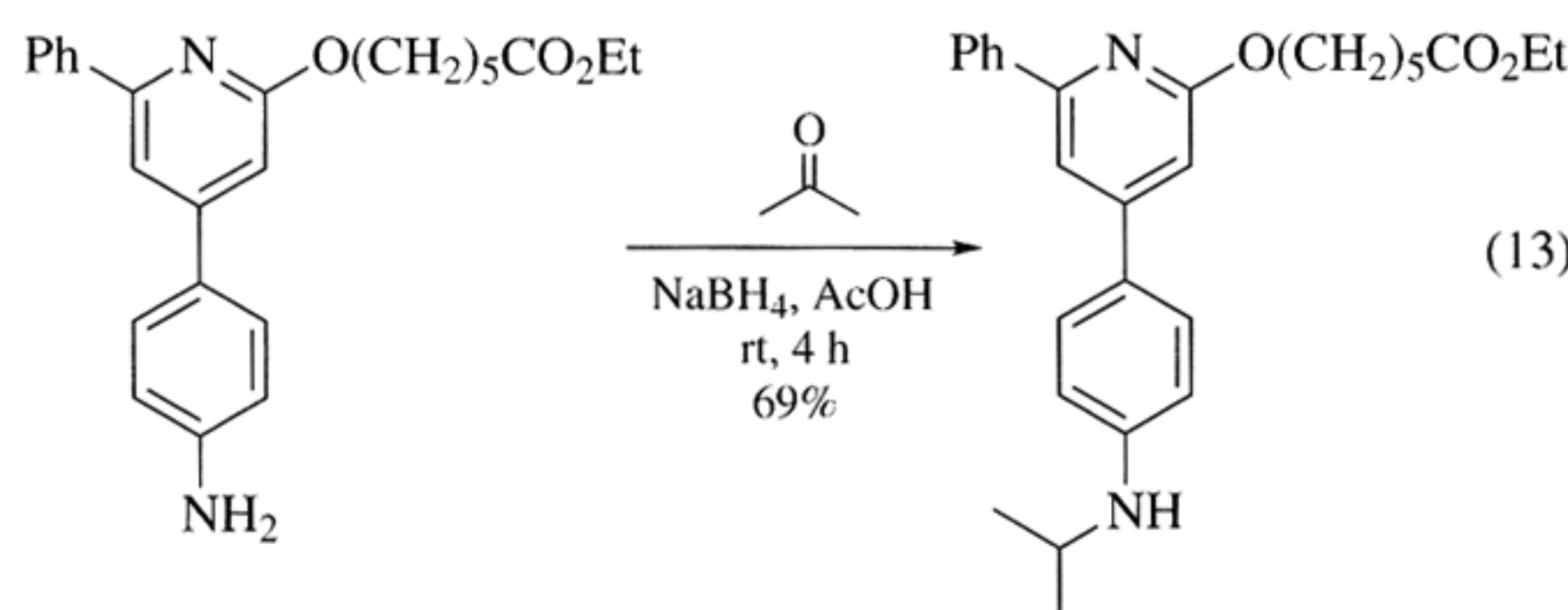
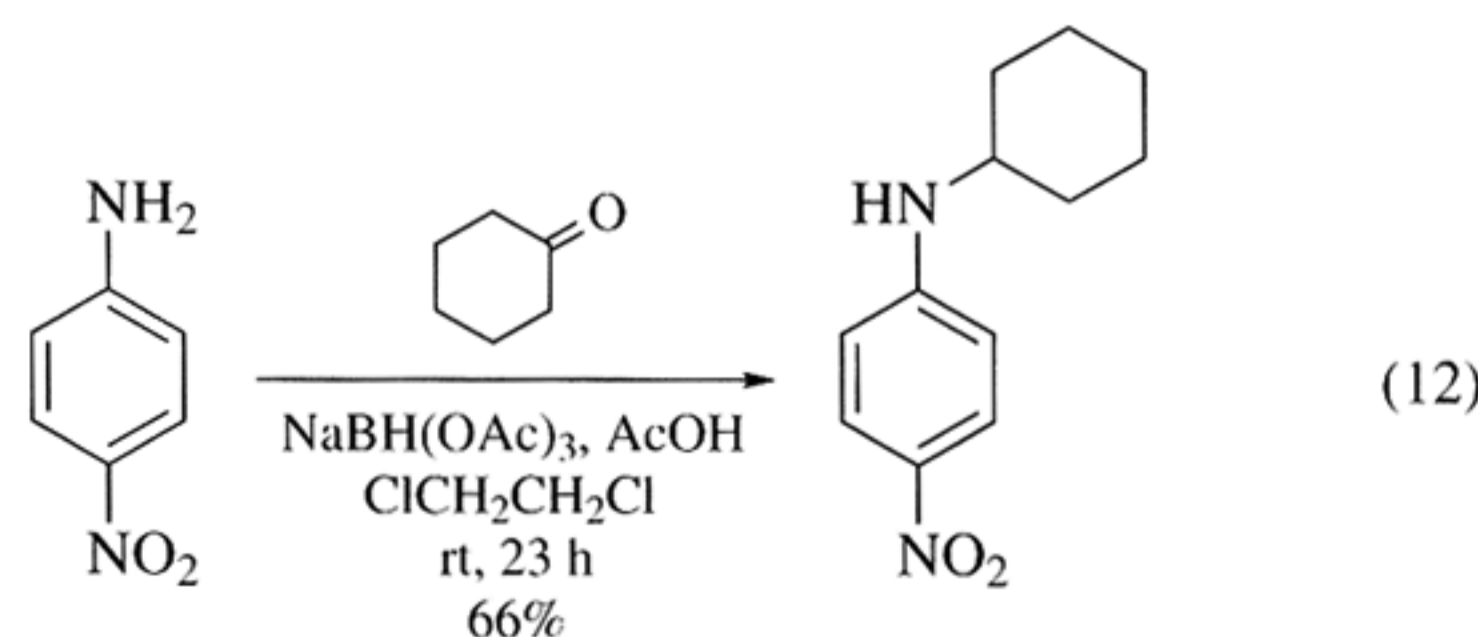
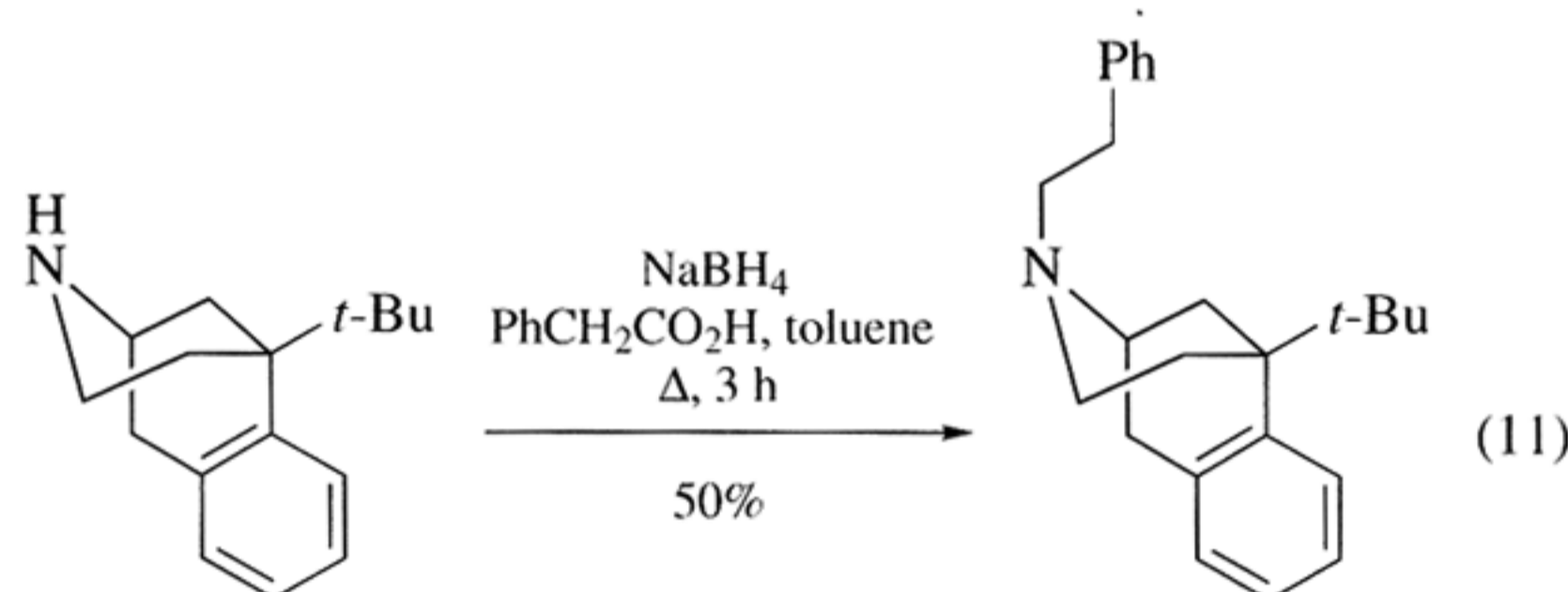
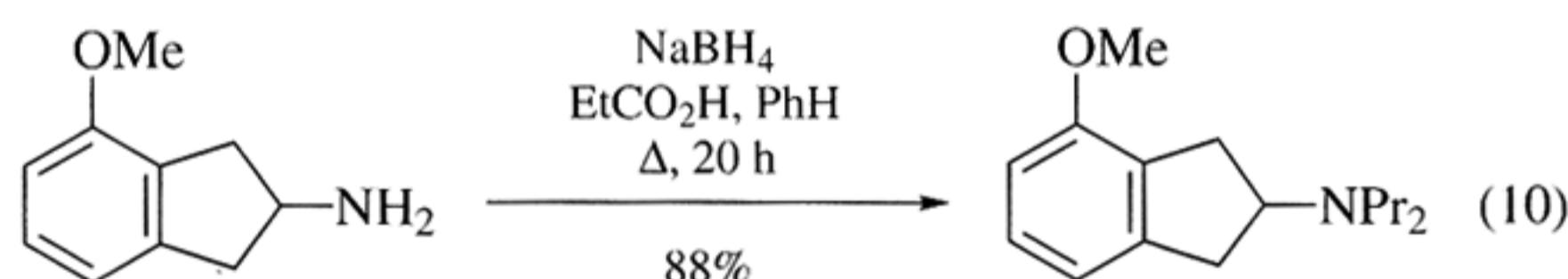
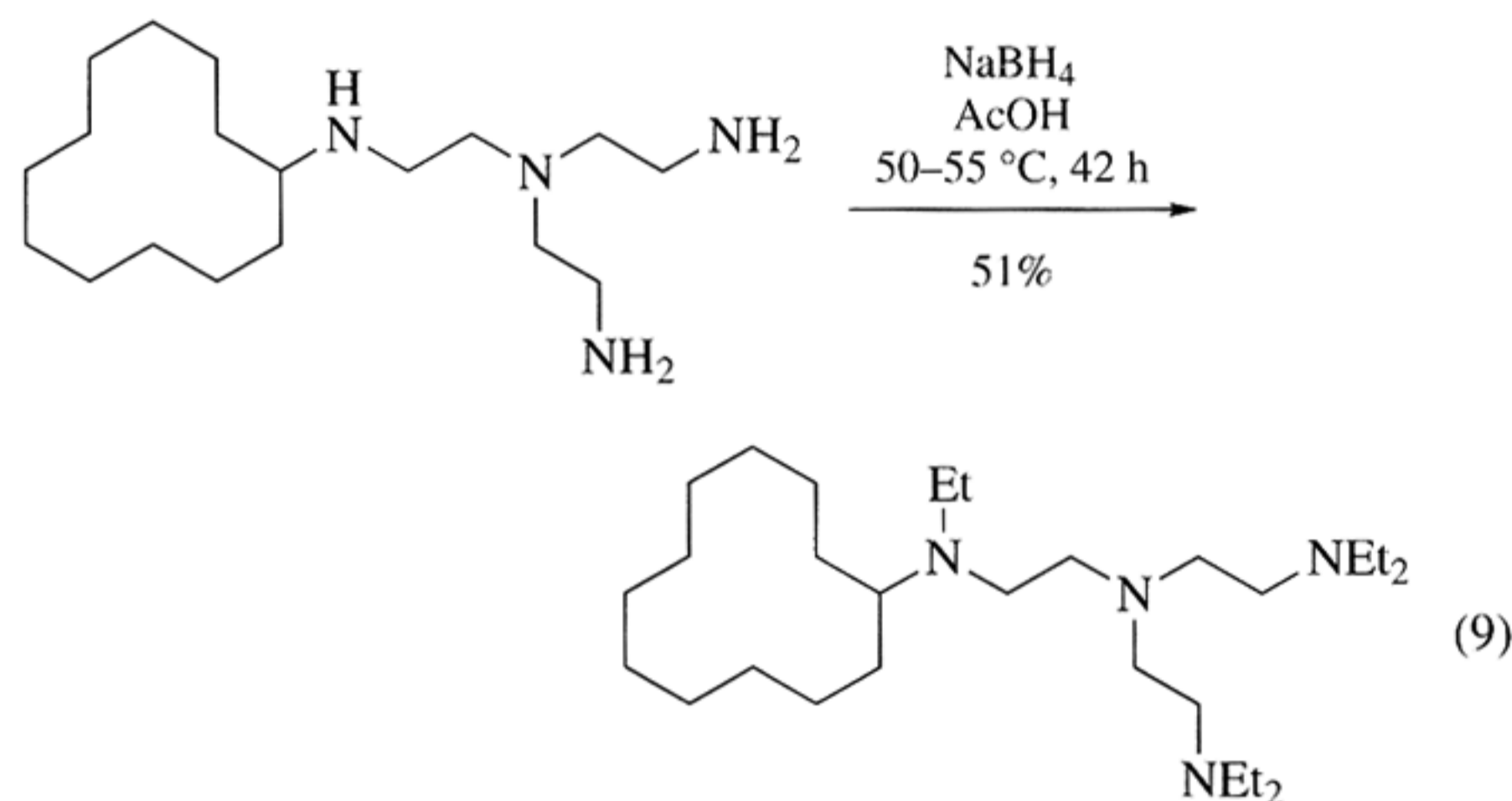
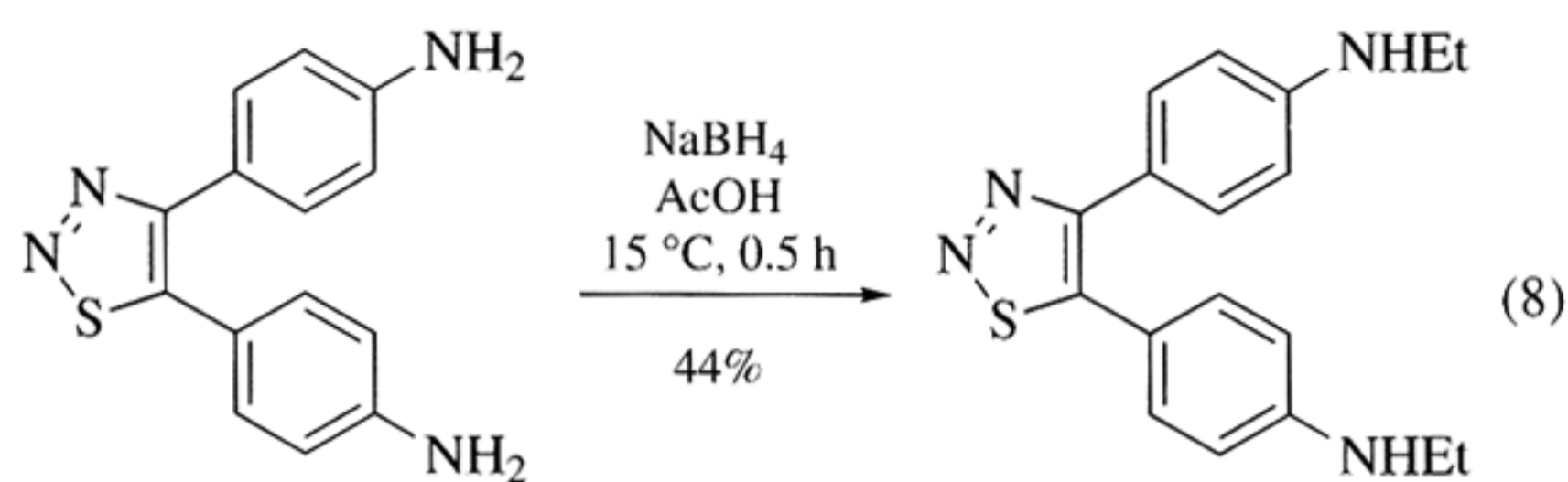
The hydroxy-directed NaBH(OAc)_3 reduction of an imide has been described.¹⁴ The more reactive NaBH_3OAc reduces enones to allylic alcohols,¹⁵ and some ketones can be reduced to alcohols with **Sodium Borohydride**–tartaric acid.¹⁶ The combination of NaBH_4 or **Sodium Cyanoborohydride**–Acetic Acid serves to deoxygenate tricarbonyl systems (eq 5)¹⁷ and tosylhydrazones of ketones and aldehydes (eq 6).¹⁸ Primary and secondary amides are reduced to amines by the action of NaBH_3OAc (eq 7),^{19,20} while tertiary amides require **Sodium Trifluoroacetoxyborohydride**.



Amine Alkylation (Reductive Amination). By a pathway that may involve the generation of free aldehyde, the combination of NaBH_4 and carboxylic acids is capable of *N*-alkylation of amines.¹⁻⁴ Recent examples abound (eqs 8–11). At lower temperature, monoalkylation is generally observed (eq 8),²¹ while at 50–55 °C, primary and secondary amines are converted into tertiary amines (eqs 9 and 10).^{22,23} Neat carboxylic acid (eqs 8 and 9) or a cosolvent (eq 10) may be used. In the latter event, solid carboxylic acids function well (eq 11).²⁴ **Formic Acid** may be employed for *N*-methylation.^{1,25} A useful variation is the reductive

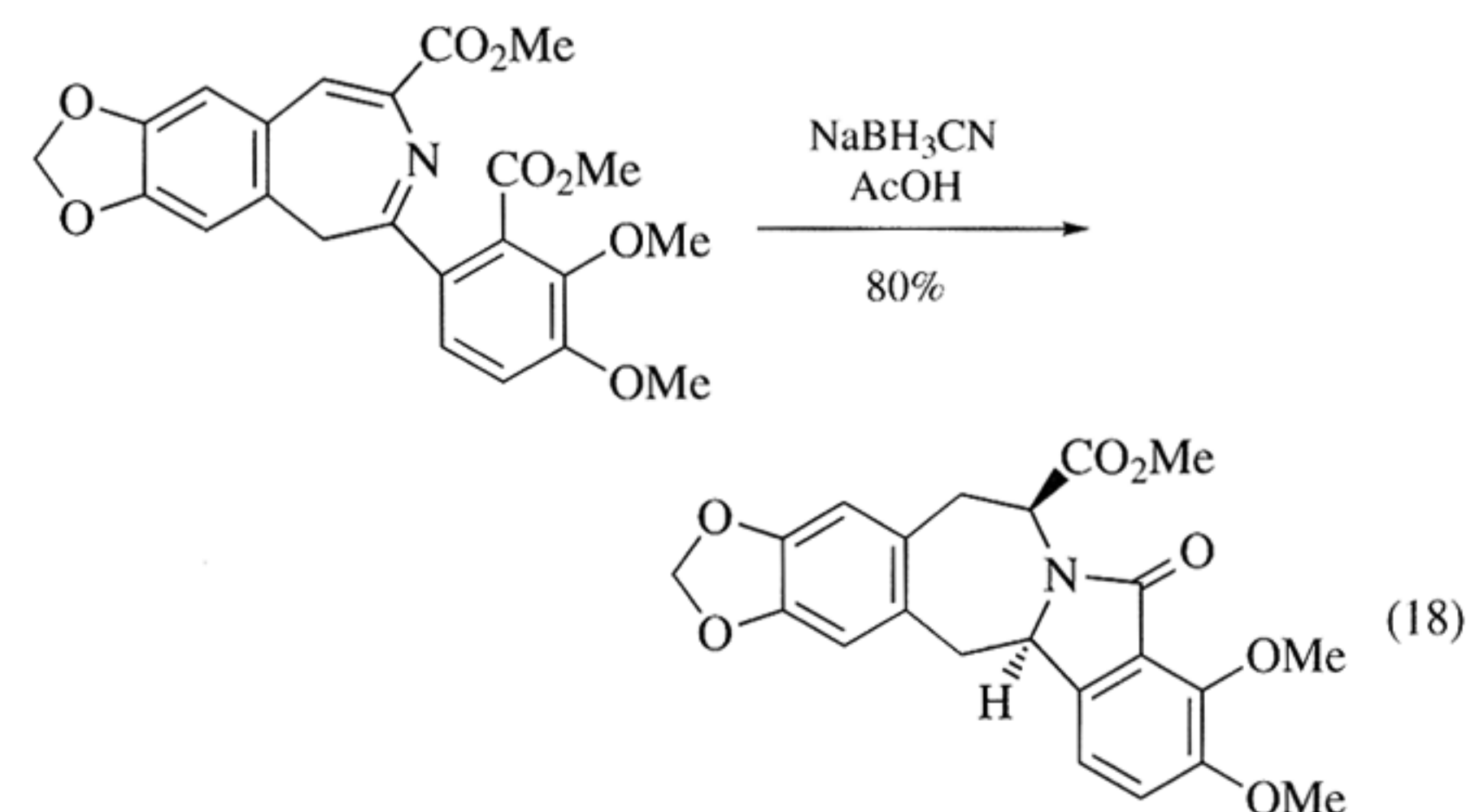
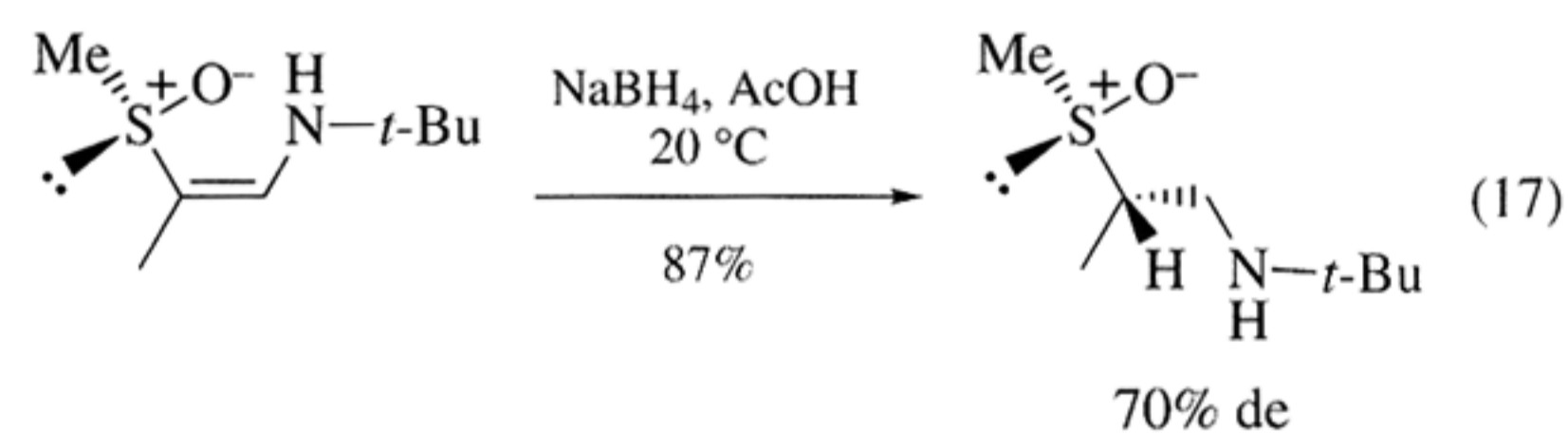
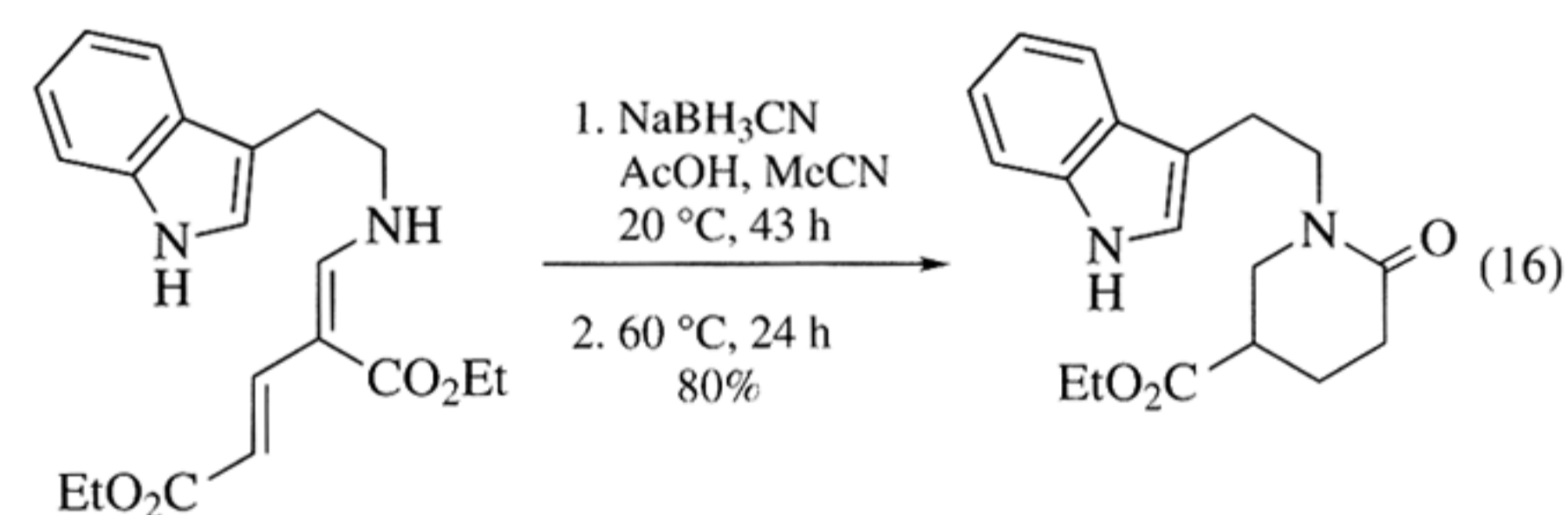
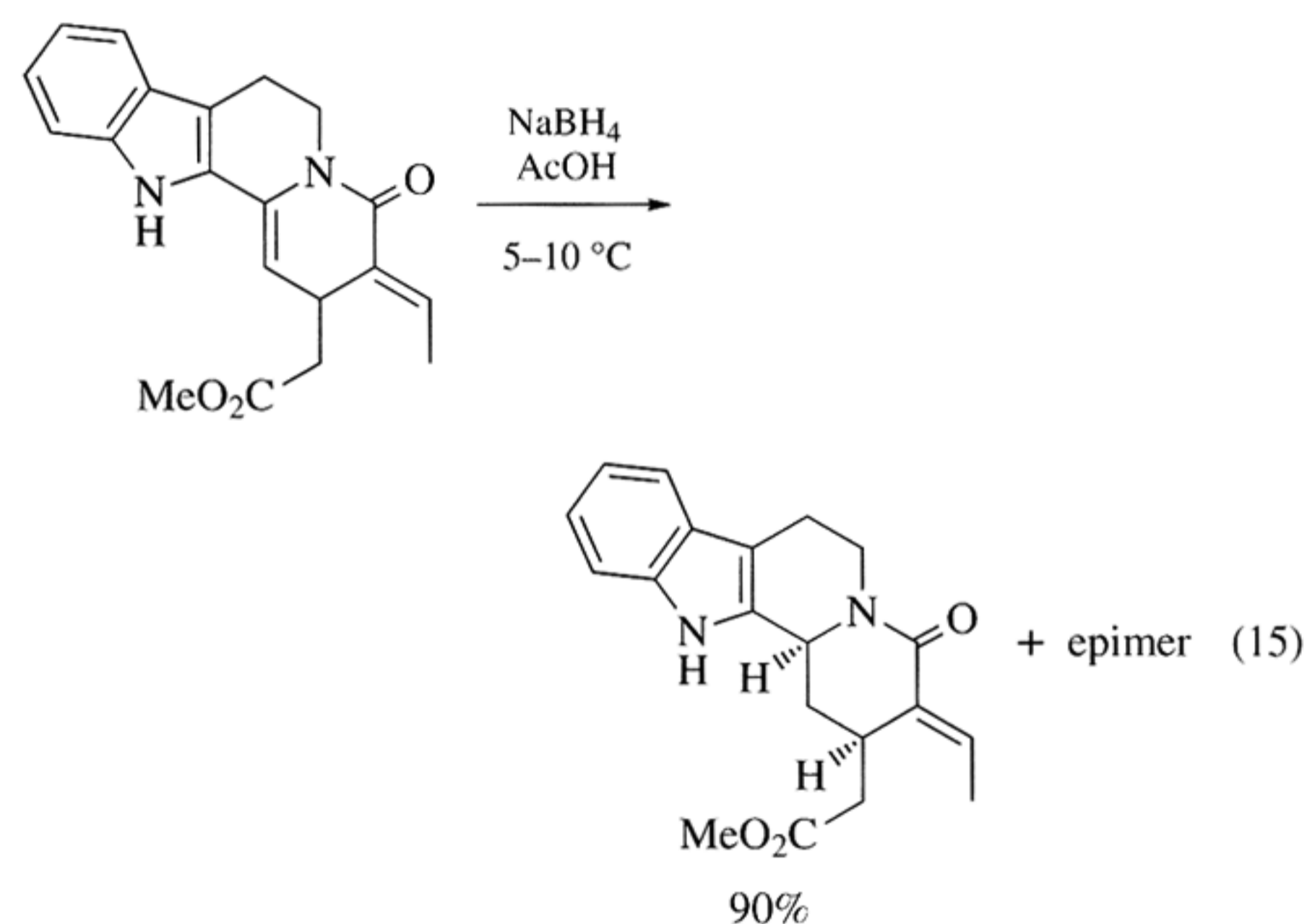
amination of aldehydes and ketones (eqs 12–14),^{1,26–29} a method which is claimed to be superior to that using NaBH₃CN–MeOH.²⁶

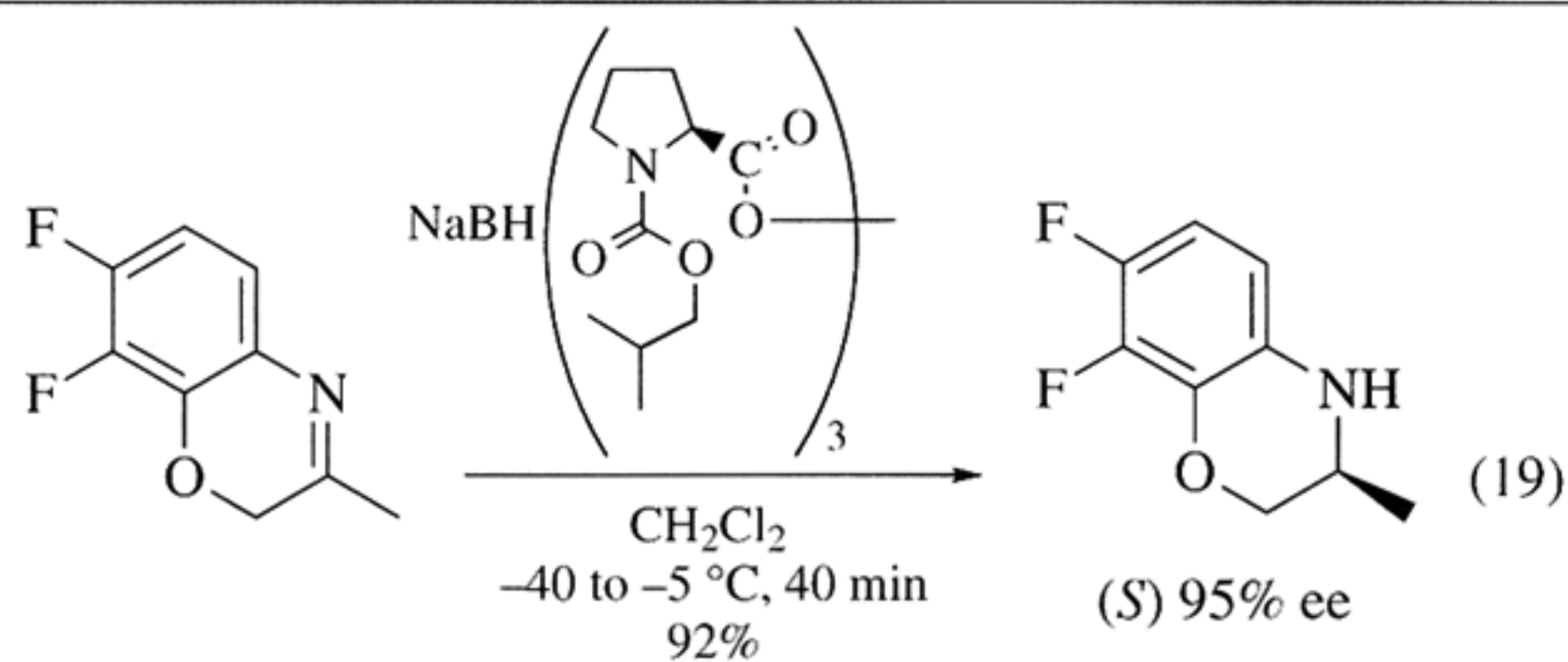
Paraformaldehyde serves as a convenient source of HCHO for *N*-methylation in this protocol.^{30,31}



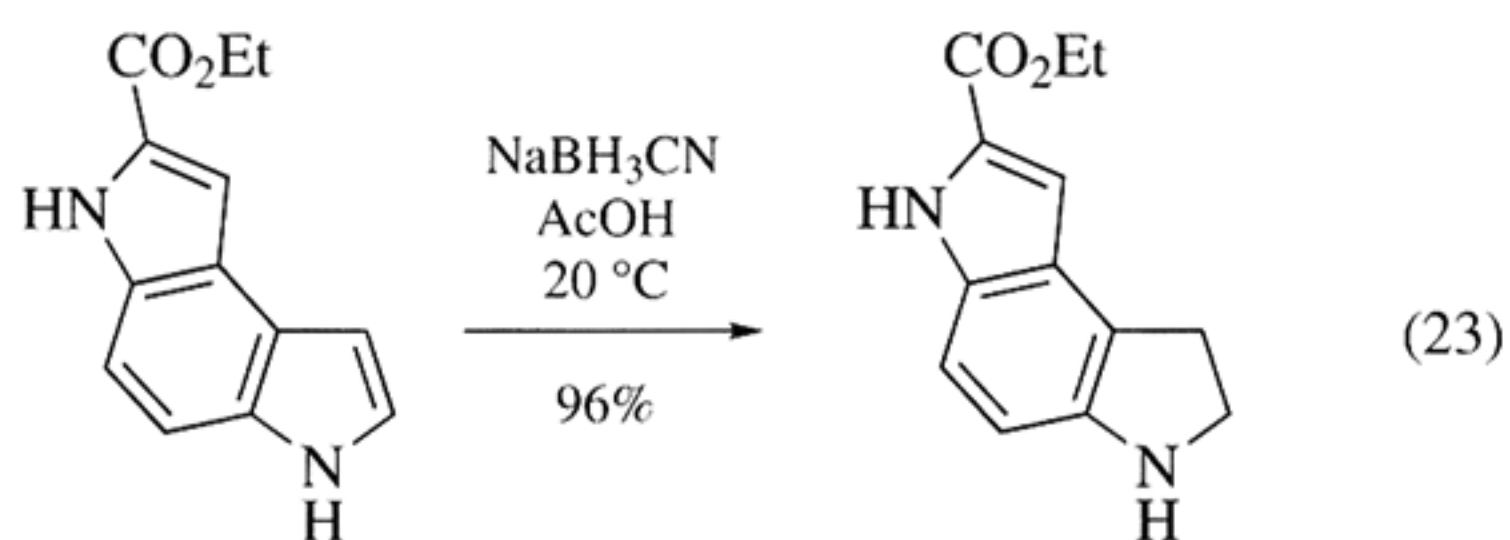
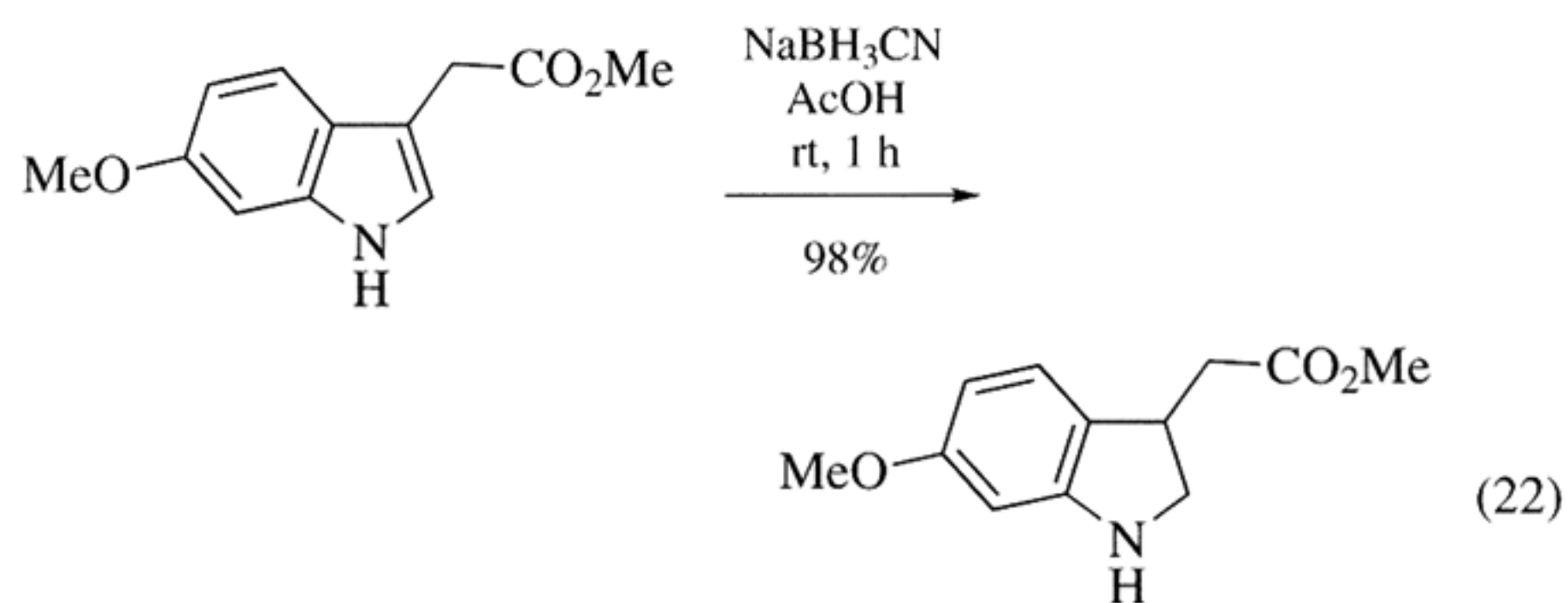
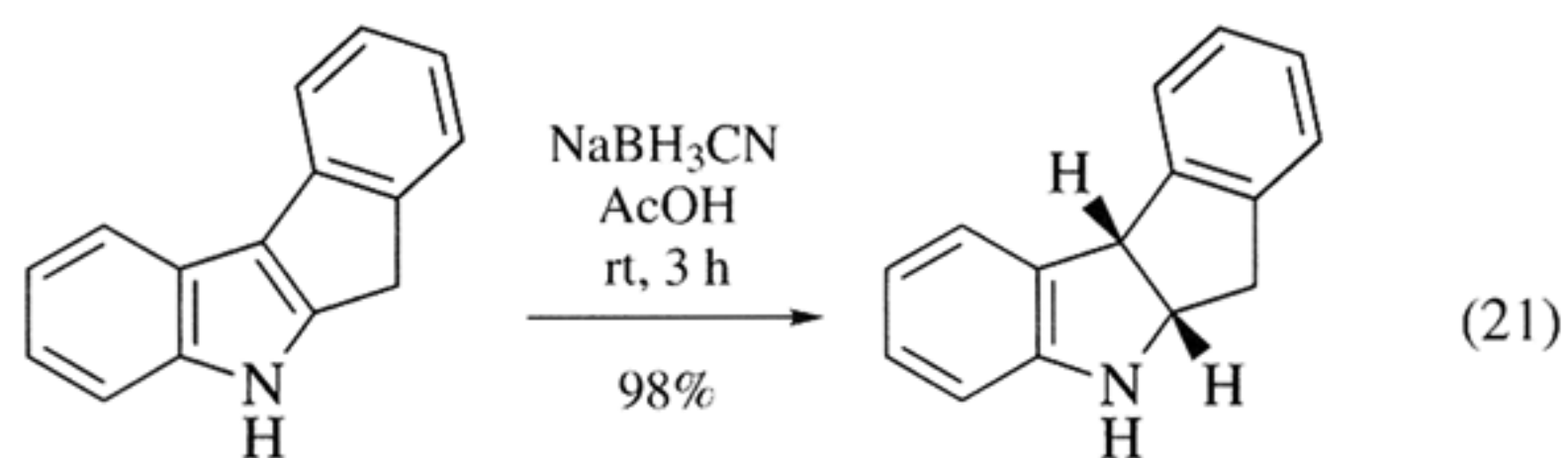
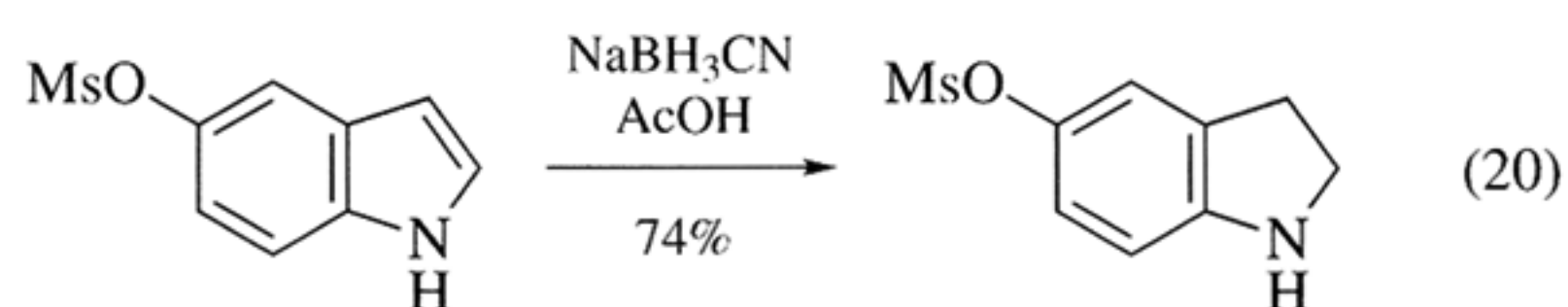
Carboxylic acids are reduced to alcohols with NaBH₄ in THF,³² although the use of CF₃CO₂H in this regard is superior, and there is one report of an ester reduction to a primary alcohol with NaBH₄–HOAc.³³

Enamine, Imine, Iminium Ion, and Enamide Reduction. The first reported use of NaBH₄–HOAc was in the reduction of dienamines,³⁴ and this application has found extensive use in synthesis¹ (eqs 15–19).^{35–39}

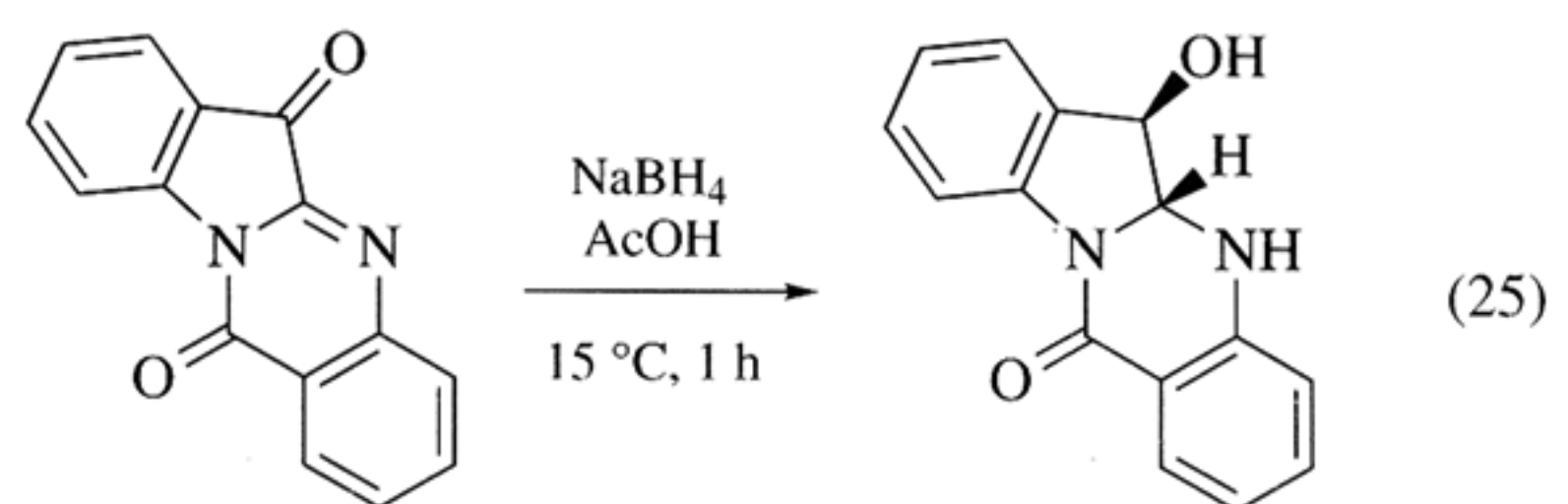
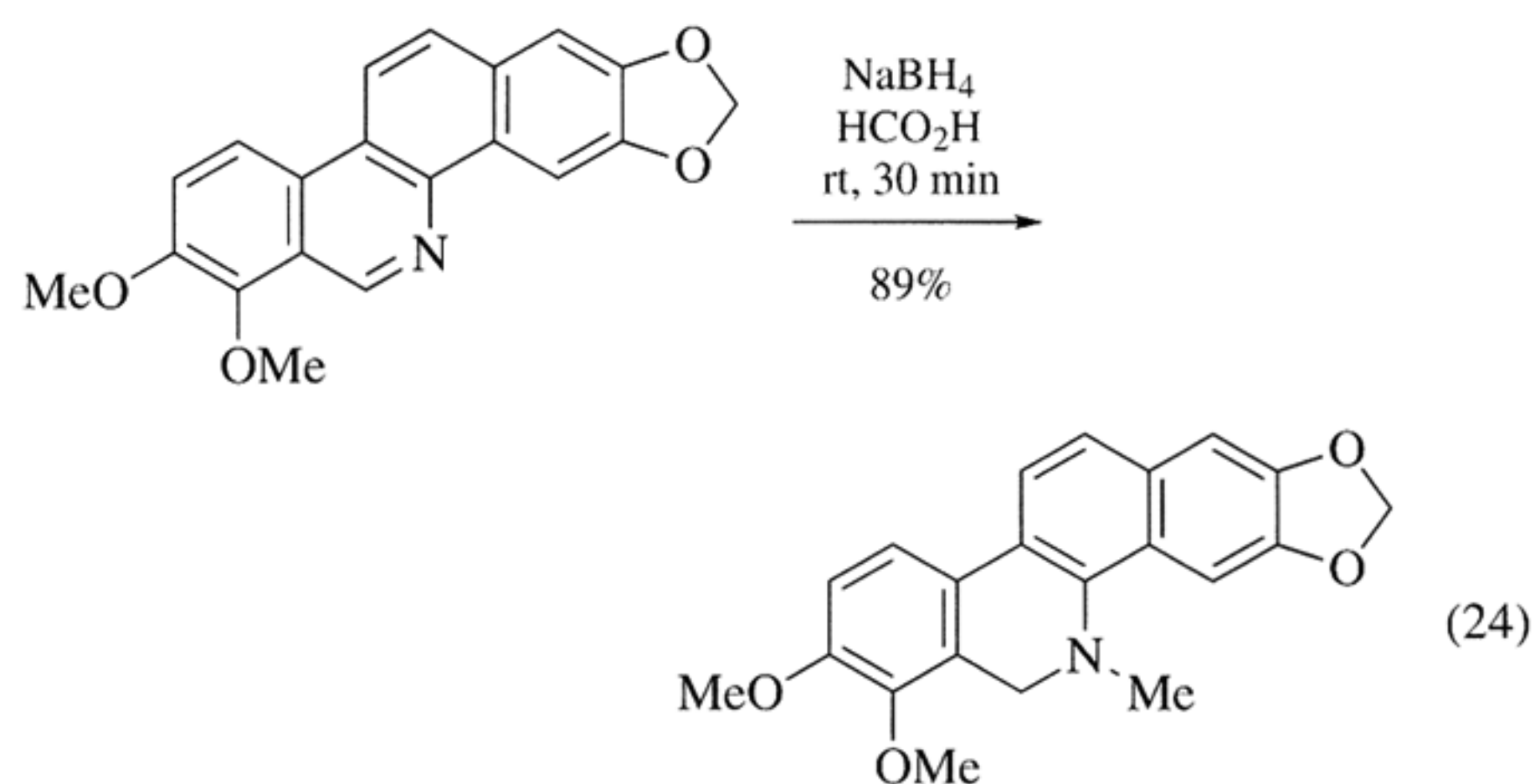




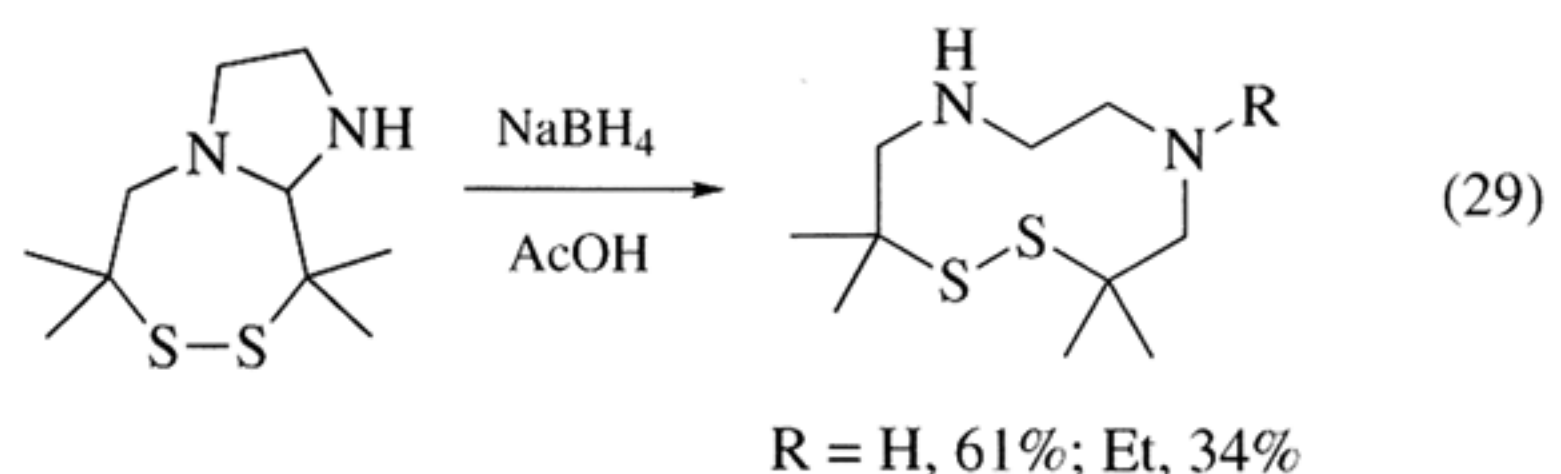
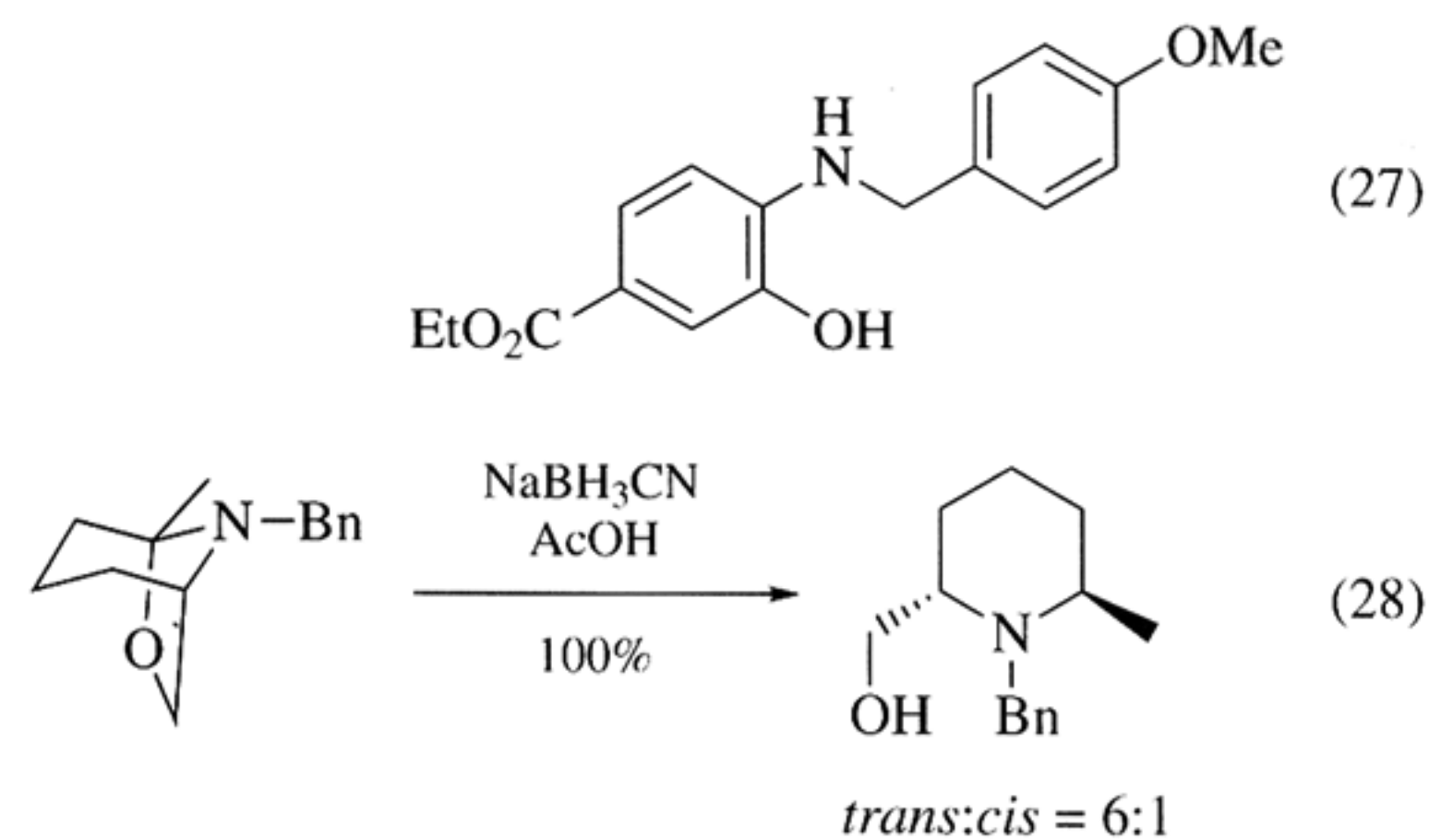
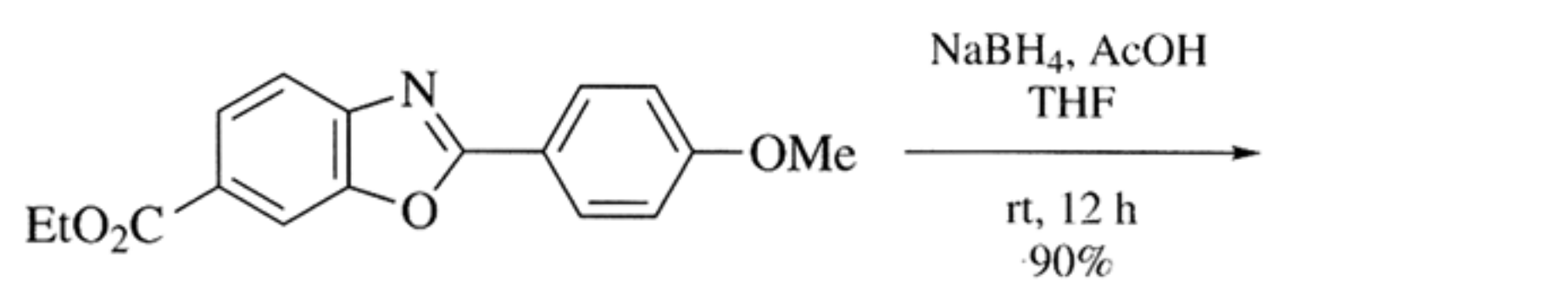
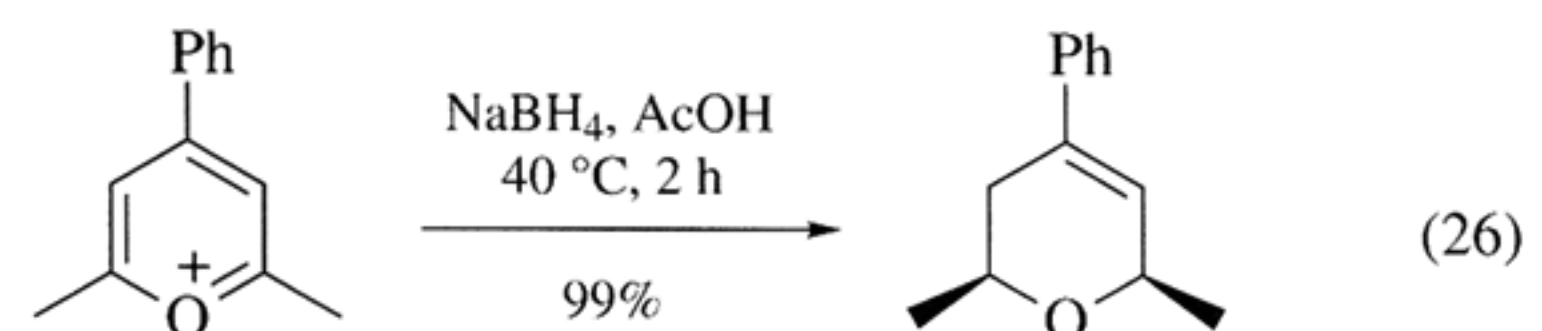
Indole Reduction. Indole is smoothly reduced to indoline under the influence of $\text{NaBH}_3\text{CN}\text{-HOAc}$;² the reaction is quite general^{1,40} and has been employed often (eqs 20–22),^{41–43} especially in the synthesis of CC-1065, PDE, and analogs where only the more basic indole ring is reduced (eq 23).^{44,45} *N*-Substituted indoles are reduced to indolines with $\text{NaBH}_4\text{-HOAc}$,^{1,2} and the action of $\text{NaBH}_4\text{-RCO}_2\text{H}$ on *N*-unsubstituted indoles affords *N*-alkylindolines by *N*-alkylation of the initially formed indoline.^{1,2}



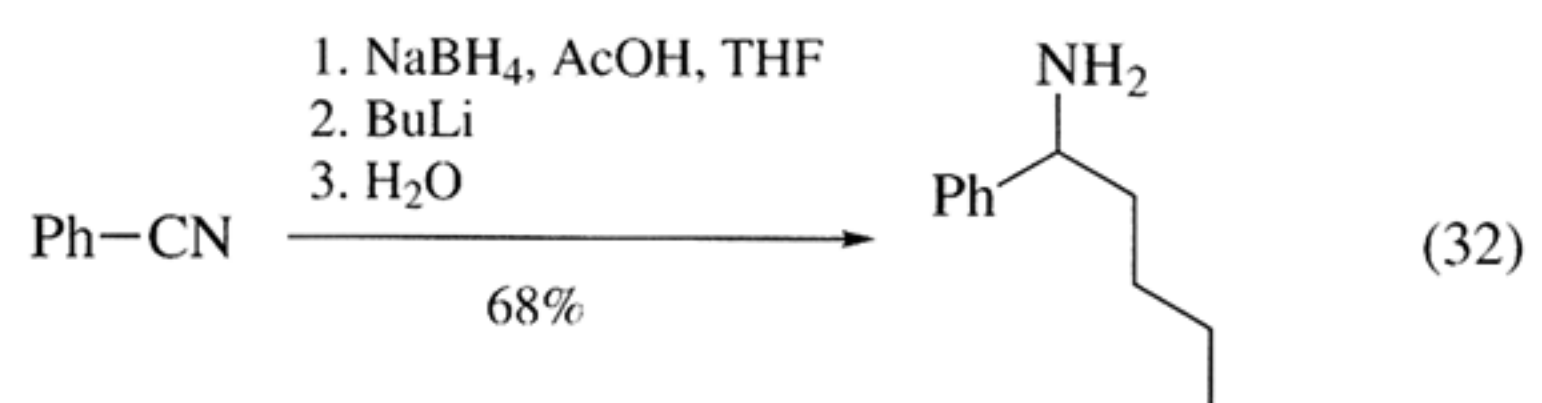
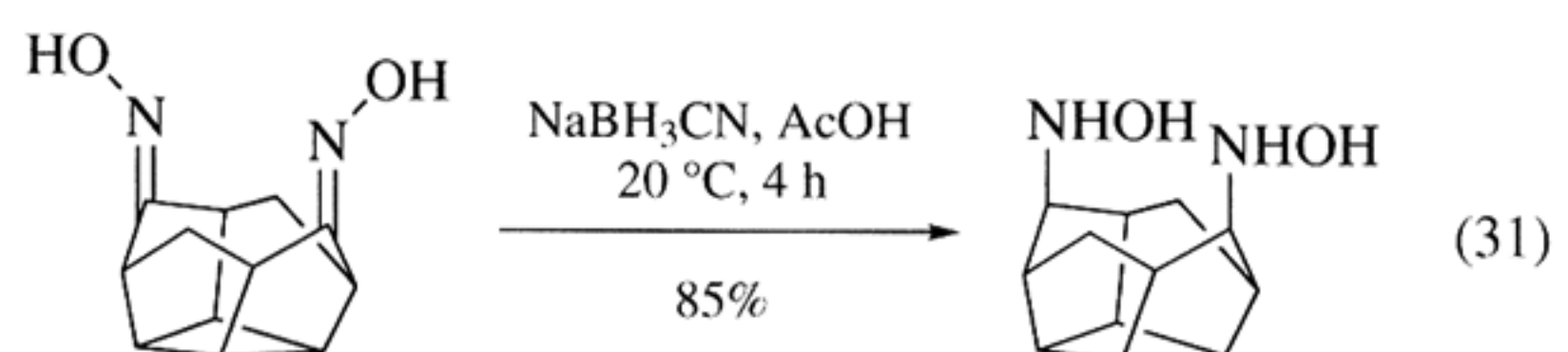
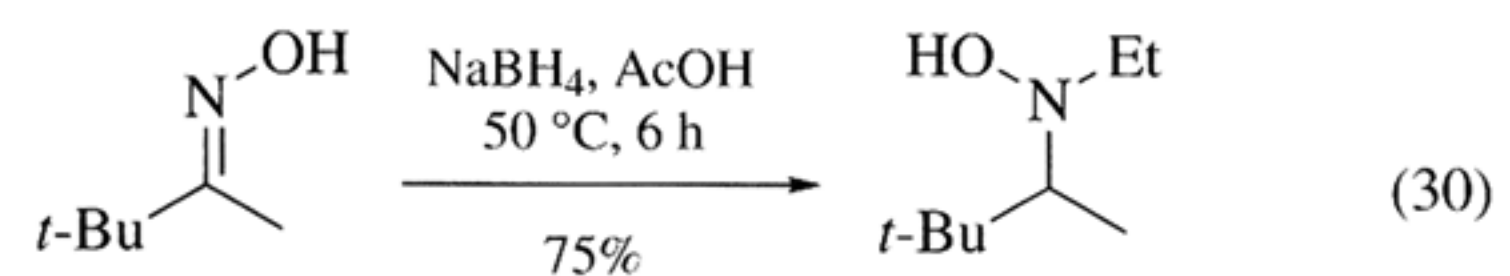
Reduction of Other Heterocycles. Quinolines and isoquinolines are reduced to the corresponding tetrahydro derivatives with NaBH_3CN or $\text{NaBH}_4\text{-RCO}_2\text{H}$, the latter combination affording the *N*-alkylated compounds.^{1,46} Related heterocycles have been subjected to this protocol (eqs 24 and 25).⁴⁷



The reduction of pyrylium salts (eq 26),⁴⁸ the reductive cleavage of benzoxazoles (eq 27)⁴⁹ and of saturated nitrogen heterocycles (eqs 28 and 29),^{1,50,51} and the reduction of other π -deficient nitrogen heterocycles¹ are known.



Reduction of Oximes. Oximes can be alkylated or reduced, depending on whether NaBH_4 or NaBH_3CN is employed, to give hydroxylamines^{1,52} (eqs 30 and 31).^{52,53} Oxime ethers are also reduced under these conditions,^{1,54} and the hydroxy-directed reduction of oxime ethers has been reported using $\text{Me}_4\text{NBH}(\text{OAc})_3$.⁵⁵ Nitriles are converted into primary amines by the tandem action of acyloxyborohydrides and alkyl lithium reagents (eq 32).⁵⁶



Hydroboration of Alkenes. The second reported reaction of acyloxyborohydrides was the hydroboration of alkenes,^{1,57} and this reaction has been further refined.⁵⁸ In a similar vein, the reduction of organomercurials by NaBH(OAc)₃ has been described.⁵⁹

Related Reagents. See Classes R-2, R-3, R-5, R-6, R-8, R-10, R-12, R-13, R-17, R-20, R-29, and R-35, pages 1–10. Sodium Borohydride; Sodium Cyanoborohydride; Sodium Trifluoroacetoxyborohydride; Sodium Tris(trifluoroacetoxy)borohydride; Tetramethylammonium Triacetoxyborohydride.

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