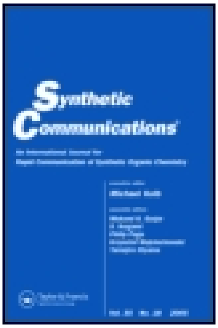


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Effect of the Temperature on the Stoichiometry of Borane Dimethyl Sulfide Reduction of Secondary and Tertiary Amides

M. Bonnat [a], A. Hercouet [a] & M. Le Corre [a]

[a] Laboratoire de Synthèse Organique, associé au CNRS, Université de Rennes, Avenue du Général Leclerc, 35042, Rennes, France

Version of record first published: 23 Sep 2006.

To cite this article: M. Bonnat, A. Hercouet & M. Le Corre (1991): Effect of the Temperature on the Stoichiometry of Borane Dimethyl Sulfide Reduction of Secondary and Tertiary Amides, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 21:15-16, 1579-1582

To link to this article: http://dx.doi.org/10.1080/00397919108021056

SYNTHETIC COMMUNICATIONS, 21(15&16), 1579-1582 (1991)

EFFECT OF THE TEMPERATURE ON THE STOICHIOMETRY OF BORANE DIMETHYL SULFIDE REDUCTION OF SECONDARY AND TERTIARY AMIDES

M. Bonnat, A. Hercouet, and M. Le Corre *

(Laboratoire de Synthèse Organique, associé au CNRS, Université de Rennes,
Avenue du Général Leclerc, 35042 Rennes, France).

Abstract : A simple procedure has been described for the reduction of secondary and tertiary amides to amines using borane-dimethyl sulfide in theoretical amounts.

Numerous chemicals of interest and importance in chemistry have been preparated through an amide reduction with a borane reagent (1).

Borane-tetrahydrofuran (2) and borane-dimethyl sulfide (3) have proven to be the reagents of choice for most reductions of carboxylic amides to amines.

Primary amides are reduced to primary amines by borane-dimethyl sulfide (BMS) used in theoretical amounts (3,4)

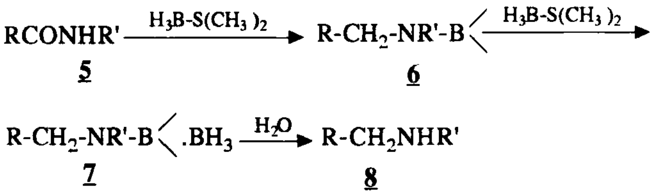
$$(1)\quad \underset{\underline{1}}{\mathrm{RCONH_2}} + \underset{\underline{2}}{\mathrm{4/3\ BH_3.\ S(CH_3)_2}} \xrightarrow{\mathrm{THF}} \underset{\underline{3}}{\mathrm{R\text{-}CH_2\text{-}N(B\langle\ )_2}} \xrightarrow{\mathrm{H_2O}} \underset{\underline{4}}{\mathrm{R\text{-}CH_2NH_2}}$$

In the same conditions, the amine-borane adducts 7 and 11 corresponding to secondary and tertiary amides are inert towards further hydride transfer reaction. Hence for the complete reduction, six or five equiv. of hydride (H-B) was needed to reduce secondary or tertiary amides respectively (eq 2 and 3).

---

* To whom correspondence should be addressed.

(2)



$$\underset{\underline{9}}{\text{RCONR'R''}} \xrightarrow{2/3\ H_3B\text{-}S(CH_3)_2} \underset{\underline{10}}{\text{RCH}_2\text{-NR'R''}} \xrightarrow{H_3B\text{-}S(CH_3)_2} \underset{\underline{11}}{\text{R-CH}_2\text{NR'R''.BH}_3} \xrightarrow{H_2O} \underset{\underline{12}}{\text{R-CH}_2\text{NR'R''}} \quad (3)$$

To use reduced amounts of BMS in the reduction of these amides, Brown et al. (3,5) described a method in which BMS is used for reduction purposes and boron trifluoride etherate for the complexation with 6 or 10.

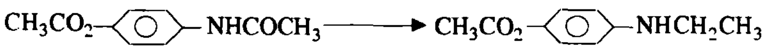
In the course of studying the stability of the amine-borane adduct, we discovered that the stoichiometry of the reduction of secondary and tertiary amides is largely dependent on the temperature.

In refluxing toluene we observe that amides do not require an additional mole of BMS for the complexation, thus :

- secondary amides are reduced with one mole of BMS,
- tertiary amides need only two equivalents of hydride (2/3 mole of BMS).

The above stoichiometry is dependent on the temperature and not the solvent. If we decrease the temperature of toluene to 65-70°, we observe only partial reduction of amides as in the case of reduction in THF. On the other hand the reduction in dibutyl ether at 115-120° gave a high yield of amine (90% for the transformation 9d-12d).

Finally N - acetyl p - acetoxy aniline was examined to test the utility of this procedure for selective reduction. The amine - ester was obtained in 95 % yield, confirming the value of this procedure for selective reduction.



From a practical point of view, our procedure offers two advantages :

- distillation from the reaction mixture of dimethyl - sulfide is not necessary,
- there is no need for final decomplexation of amine-borane complex.

The results are summarized in table :

Table - Reduction of secondary and tertiary amides with borane-dimethyl sulfide in toluene.

$$R\text{-}CONR'R'' \longrightarrow R\text{-}CH_2NR'R''$$

Amide	R	R'	R"	Reaction time (h)	Yield[a] (%)
5a	CH_3	C_6H_5	H	2	87
b	C_2H_5	C_6H_5	H	4	80
c	C_6H_5	C_6H_5	H	2	97
d	$4\text{-}O_2N\text{-}C_6H_4$	cyclohexyl	H	2	82
e	$2\text{-}Cl\text{-}C_6H_5$	$n\text{-}C_4H_9$	H	2	81
9a	CH_3	C_2H_5	$CH_2\text{-}C_6H_5$	4[b]	78
b	C_2H_5	$i\text{-}C_3H_7$	$i\text{-}C_3H_7$	2	80[c]
c	C_6H_5	C_2H_5	C_2H_5	4[b]	85
d	C_6H_5	C_2H_5	$CH_2\text{-}C_6H_5$	2	93
e	C_6H_5	$CH_2\text{-}C_6H_5$	$CH_2\text{-}C_6H_5$	2	83

a : yields represent pure isolated products. All of the products were fully characterised by ^1H NMR spectra and physical constants (bp/mp).

b: complete reduction (100%) required 12h.

c: this amine was isolated by extraction of the toluene solution with hydrochloric acid.

General Procedure :

Borane-dimethylsulfide (10,5 mM, 1,05 mL, 5% excess) was added dropwise under nitrogen at 0°C to a stirred suspension (or solution) of amide (10 mM for 5, 15 mM for 9) in toluene (10 mL).

The reaction mixture was stirred at 0°C for 15 min. and then was refluxed. After 2-4h, the flask was cooled at room temperature, 15mL of 10% aqueous sodium carbonate was added and the reaction mixture was stirred at 20°C (100°C in the case of compounds 9a and 9c) for 30 min. The toluene layer was separated and dried (sodium sulfate), and the solvent was evaporated. The crude amine was distilled with a Kugelrohr apparatus.

References :

1. F . C. Lane, Chemical Reviews 1976, 76, 773,
2. H. C. Brown, P. Heim, J. Org. Chem. 1973, 38, 912,
3. H. C. Brown, J. M Choi, J. Org. Chem. 1982, 47, 3153,
4. H. C. Brown, S.. Narasimhan, J. M Choi, Synthesis 1981, 441,
5. H. C. Brown, S. Narasimhan, J. M. Choi, Synthesis 1981, 996.

(Received in UK 15 April, 1991)