Hydroboration of Carbonyl Compounds with Borane–Methyl Sulfide

Enrico Mincione

Centro di Studio per la Chimica Delle Sostanze Organiche Naturali del C.N.R., c/o Istituto di Chimica Organica della Università di Roma, 00185 Roma, Italy

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Borane–methyl sulfide (BMS) is a new hydroborating complex which exists as a stable liquid.[1] We have investigated this complex as a selective reducing agent to be utilized in the presence of an olefinic bond.

In particular, we have examined the effectiveness of BMS toward a range of unsaturated carbonyl compounds. While it is known from the literature that the complex BH_3–THF hydroborates the α,β-unsaturated carbonyl compounds with a formation of saturated carbinol,[2] we have found that with using BMS selective reduction of the C=O group occurs in all α,β-unsaturated ketones examined, with the formation of the corresponding allylic alcohols in good yields (compounds I–V) (Table I). With unconjugated compounds VI and VII, we have observed selective reduction of the carbonyl group in VII, while in VI selective hydroboration of the olefinic double bond occurred, the more difficult being the reduction of a C=O group in a five-membered ring.[4]

Subsequently, a range of reducible functions such as acyl, anhydride, lactone, and ester was tested with BMS in an attempt to isolate the intermediate products of partial hydroboration.

However, we have observed complete reduction, under all conditions, in all cases except for *p*-nitrobenzoyl chloride, which produced the corresponding aldehyde in good yields (60%).

Finally, we have examined the reductive capacity of BMS toward some aromatic electron-rich carbonyl compounds. It is reported that these compounds suffer hydrogenolysis to hydrocarbon when reduced by diborane.[5] The reactions are reported to be catalyzed by the BF_3 present as an impurity.

We have thought it better to reduce these compounds with BMS, which we have found to be practically free from BF_3,[6] for a better understanding of the reaction. It is reported[7] that with anthraquinone at room temperature a very slow reaction occurs with BH_3–THF (1 mmol of compounds consumes 1 mmol of hydride in 7 days), whereas a fast reduction with hydrogenolysis to anthracene occurs after the addition of BF_3. However, using BMS we observed a fast hydrogenolysis with good yields in the formation of anthracene (70%) by raising the temperature to 30–40 °C. This result was confirmed by the fact that, when submitting anthraquinone to hydroboration with diborane developed from $NaBH_4$ and iodine, i.e., free from BF_3, fast hydrogenolysis at 50 °C with formation of anthracene in good yields (60%) occurred. Therefore, we deduced that hydrogenolysis can occur even in the absence of BF_3 by increasing the reaction temperature.

Likewise, we examined the behavior of *p*-dimethylaminobenzaldehyde (VIII) and of veratric aldehyde (IX) with BMS. Conflicting results have been reported for the hydroboration of these compounds with BH_3–THF. In particular, some authors reported the presence of BF_3 as determining the hydrogenolysis reaction and others pointed out that this reaction stopped at the alcohol stage or gave other products despite the presence of BF_3.[8,9]

In the experiments with BMS, we have observed that hydroboration of VIII yielded first the corresponding alcohol (70% after 1 h) and then, after prolonged stirring of the reaction mixture (6 h), the hydrogenolysis product in good yield (90%). Likewise, with IX we have obtained only the corresponding alcohol after 1 h; however, we have observed the formation of some hydrocarbon (30%) by keeping the reaction mixture at 40 °C for 1 day.

Experimental Section

General. Tetrahydrofuran was dried with excess of lithium aluminum hydride and distilled under nitrogen. BMS was used directly as obtained from Aldrich Chemical Co. and was transferred into the reaction vessel by a hypodermic syringe. The carbonyl compounds used were commercial products of the highest purity. All reduction experiments were carried out under a dry nitrogen atmosphere. Melting points were determined with a Kofler apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer 257 Infracord and NMR spectra with a Perkin-Elmer apparatus (90 MHz) in $CDCl_3$. For TLC, Kieselgel G from Merck was used. GLC analyses were carried out with a "Carlo Erba" Fractovap G-1 using a 60-m capillary column with 5% Carbowax as the stationary phase.

Reduction of α,β-Unsaturated Carbonyl Compounds. The following preparative procedure for the reduction of cinnamaldehyde to cinnamyl alcohol is representative. In a 10-mL flask equipped with a magnetic stirring bar and a reflux condenser, tetrahydrofuran (3 mL) was injected. In this solvent the compound was dissolved (297 mg, 2.25 mmol) and to this well-stirred solution under dry nitrogen atmosphere BMS (0.075 ml, 0.75 mmol) was added. After 1 h and 15 min at room temperature, water (0.5 mL) was added to destroy the excess hydride and the solution reaction was extracted by 6 × 10 mL of benzene. Organic extracts were dried (Na_2SO_4) and after evaporation of the solvent an organic residue was obtained, which was chromatographed on a silica gel column (10 g of silica gel from Merck). By elution with hexane–ethyl ether (80:20), cinnamyl alcohol (240 mg,

Table I. Results of the Reaction of BMS with Unsaturated Carbonyl Compounds

Compd[a]	Registry no.	Reaction temp, °C	Reaction time	Molar[b] ratio of reactive compds	Reaction products	Yields,[c] %	Registry no.
Cyclohexenone (I)	930-68-7	0	2 min	0,3	Cyclohexenol	94	822-67-3
Cinnamaldehyde (II)	104-55-2	20	1 h 15 min	0,3	Cynnamyl alcohol	82	104-54-1
10-Methyl-$\Delta^{1(9)}$-octalin-2-one (III)	826-56-2	20	45 min	0,3	10-Methyl-$\Delta^{1(9)}$-octalin-2-ol	65	26675-10-5
17β-Hydroxyandrost-4-en-3-one (IV)	58-22-0	0	1 h 45 min	1	Androst-4-ene-3β,17β-diol	79	1156-92-9
17β-Hydroxyestr-4-en-3-one (V)	434-22-0	0	10 min	0,6	Estr-4-ene-3β,17β-diol	60	19793-20-5
3β-Hydroxyandrost-5-en-17-one (VI)	53-43-0	0	20 min	0,6	3β,6α-Dihydroxy-5α-androstan-17-one	76	14895-71-7
					3β,6β-Dihydroxy-5β-androstan-17-one	18	65375-66-8
Pregn-5-en-3β-ol-20-one (VII)	145-13-1	0	12 min	0,6	Pregn-5-ene-3β,20α-diol	92	59042-34-1

[a] Tetrahydrofuran was used as solvent in all the experiments. [b] Millimole of BMS used per millimole of organic compound. [c] Yields by chromatography on silica gel column, except for cyclohexenol by GLC examination.

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82% yield, characterized by NMR spectroscopy and melting point), cinnamaldehyde (26 mg, 10% yield), and a third unidentified product (16 mg, 5% yield) were obtained. The absence of a possible reaction product, 3-phenylpropanol,[2] was confirmed by a chromatographic comparison of an authentic sample with the reaction mixture (silica gel–$AgNO_3$ plate, elution with hexane–ethyl ether, 80:20).

Reduction of Acyl, Ester, Lactone, and Anhydride Functions. The general technique was the same as described for the reduction of unsaturated ketones. *p*-Nitrobenzoyl chloride (185 mg, 1 mmol) was dissolved in 2 mL of tetrahydrofuran and treated (−18 °C) with 0.33 mmol of BMS under stirring. After 2.5 h, the reaction was stopped and the reaction mixture worked up. By chromatography of the crude mixture on Al_2O_3 (B III, neutral) (6 g) and by elution with hexane–ethyl acetate (95:5), *p*-nitrobenzaldehyde (110 mg, 60% yield) and *p*-nitrobenzyl alcohol (50 mg) were obtained. In other experiments, an increase in temperature (0 °C) led to an increase in yield of the alcohol. Benzyl chloride was unreactive at −18 °C. By raising the temperature to 0 °C, an effective reduction took place, yielding the corresponding alcohol (95%). Likewise, by the same procedure, phenyl methyl ester did not react at −18 °C; by raising the temperature to 15 °C a slow reduction to benzyl alcohol was observed. The phthalic anhydride did not react, even at room temperature. The undecalactone reacted very slowly at room temperature, giving the corresponding diol.

Hydrogenolysis of Electron-Rich Carbonyl Compounds. The following preparative procedures for hydrogenolysis of anthraquinone to anthracene are representative.

Method a (with BMS). This reduction was accomplished, with the general hydroboration procedures previously reported, by dissolving the compound (124 mg, 0.6 mmol) in tetrahydrofuran–benzene (1:1, 6 mL) and by adding, with stirring, BMS (0.08 mmol). The solution was stirred at 30–40 °C for 5 h. At the end of stirring, methanol (0.3 mL) was added and the solvent evaporated in vacuo. The residue was chromatographed on a silica gel column (6 g). By elution with hexane–ethyl ether (80:20), anthracene (72 mg, 70% yield), identical to an authentic sample (R_f value, melting point), and anthraquinone (24 mg, 25% yield) were obtained.

Method b (with Diborane Developed from Sodium Borohydride and Iodine). The compound (124 mg, 0.6 mmol) was dissolved in tetrahydrofuran–benzene (2:1, 12 mL), and the gaseous diborane [generated externally as described[7] using sodium borohydride (840 mg) and iodine (2.8 g)] was bubbled for 1 h in the reaction vessel at 50 °C with stirring. After 2.5 h of additional stirring, the reaction was stopped and the mixture worked up. By chromatography of the crude mixture on a silica gel column (6 g) eluting with hexane–ethyl ether (80:20), anthracene (68 mg, 66% yield) and anthraquinone (31 mg, 30% yield) were obtained. The reduction of aldehydes VIII and IX was accomplished with BMS according to method a using tetrahydrofuran as the only solvent. The crude reaction mixture was chromatographed on a silica gel column eluting with benzene–ethyl ether (90:10), and the reaction products were recognized by NMR spectroscopy and TLC comparison with authentic samples.

Registry No.—**VIII,** 100-10-7; **IX,** 120-14-9; BMS, 13292-87-0; *p*-nitrobenzoyl chloride, 122-04-3; benzyl chloride, 100-44-7; anthraquinone, 84-65-1; diborane, 19287-45-7.

References and Notes

(1) (a) L. M. Braun, R. A. Braun, H. Ray Crissman, M. Opperman, and R. M. Adams, *J. Org. Chem.*, **36,** 2388 (1971); (b) C. W. Kabalka and C. F. Lane, *CHEMTECH,* 325 (1976); (c) C. F. Lane, *Aldrichimica Acta,* **9,** 20 (1975).

(2) A selective reduction to allylic alcohols is otherwise possible by using butane derivatives with a greater steric crowding, such as the 9-BBN.[3]

(3) C. M. L. Gragg, "Organoboranes in Organic Synthesis", Marcel Dekker, New York, N.Y., 1973, p 171; S. Krishnamurthy and H. C. Brown, *J. Org. Chem.,* **40,** 1865 (1975).

(4) J. K. Norymberski and G. F. Woods, *J. Chem. Soc.,* 3426 (1955).

(5) Reference 3, p 331.

(6) We presume, reasonably, that the BMS used would be practically free from BF_3, since we observed a very slow reaction of this reactive with epoxides and lactones, which are both very sensitive to the presence of BF_3,[1a] whereas an effective and fast reaction took place after the addition of a catalytic drop of BF_3.

(7) H. C. Brown, P. Hein, and Nung Mim Yoon, *J. Am. Chem. Soc.,* **92,** 1637 (1970).

(8) K. M. Biswas and A. H. Jackson, *J. Chem. Soc. C.,* 1670 (1970).

(9) E. Breuer, *Tetrahedron Lett.,* **20,** 1849 (1967).

(10) A quantity of tetrahydrofuran higher than in method a was used to assure a satisfactory solubility of the gaseous diborane, which is little soluble in benzene.

Correlation of σ^+ and σ^- Substituent Constants with Carbon-13 Shieldings of β Carbons of Para-Substituted β,β-Dichlorostyrenes

Herman O. Krabbenhoft

Corporate Research and Development, General Electric Co., Schenectady, New York 12301

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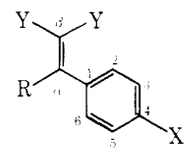
Carbon-13-NMR spectroscopy is an especially valuable tool for studying the electronic properties of aromatic systems.[1] Of particular interest are four recent reports in which the ^{13}C-NMR spectra for various para-substituted styrene derivatives (**1–5**) were presented.[2–4] For the substituted β,β-dicyanostyrenes (**4a–f**) an excellent linear correlation was found for the chemical shifts of the β carbons and σ^+ substituent constants[5] (ρ = 5.97; r = 0.995).[3] Likewise a correlation of δ ($^{13}C_\beta$) and the Brown–Okamoto σ^+ values[5] proved to be very successful (ρ = 3.37; r = 0.998) for the β-nitrostyrenes **5a–f.**[4] During the course of another study,[6] a number of para-substituted β,β-dichlorostyrenes (**6a–f**) were synthesized and analyzed by ^{13}C-NMR spectroscopy, the interesting results of which are discussed in this report.

Results and Discussion

Table I collects the ^{13}C-NMR chemical shifts for compounds **6a–f**; shielding assignments were made on the basis of relative signal intensities and general substituent effects established for substituted benzenes.[7] When the β ^{13}C chemical shifts for the β,β-dichlorostyrenes (**6a–f**) are plotted

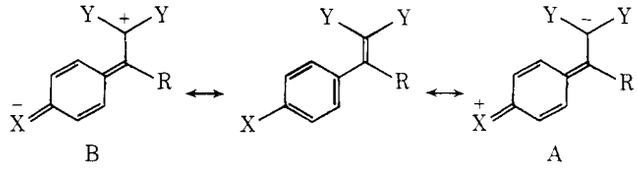


1, Y = R = H
2, Y = H; R = CH_3
3, Y = H; R = $C(CH_3)_3$
4, Y = CN; R = H
5, Y = NO_2, H; R = H
6, Y = Cl; R = H

a, X = H; b, X = CH_3; c, X = OCH_3; d, X = Cl; e, X = CN; f, X = NO_2

as a function of σ^+ substituent constants, a straight line is obtained (r = 0.989) with a ρ of 4.35. When the data for the styrenes (**1a–f**)[2a] or the α-methylstyrenes (**2a–d,f**)[2b] are subjected to a similar treatment, results (ρ = 4.55, r = 0.983 and ρ = 3.47, r = 0.974, respectively) analogous to those found for **6a–f** are obtained. The low correlation coefficients found for **1, 2,** and **6** are in marked contrast to the results found for **4** and **5.** Examination of the plots reveals that the poor correlations observed for **1, 2,** and **6** are attributable to the points for the 4-cyano and 4-nitro substrates.

In order to rationalize the above observations, it is necessary to consider that a para substituent on the aromatic ring of a styrene system can direct via resonance the distribution of the π electrons in either of two ways: (1) the substituent can *donate* the electrons to the ethylenic bond such that the β carbon acquires enhanced electron density (as in A), or (2) the substituent can *accept* electrons from the ethylenic bond with the



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