problems. Path a involves solvolysis of a primary halide and requires that a ketal alkoxy group ends up as the ether. In fact, when photolytically generated methyl ketal in methanol was placed in a large excess of ethanol and warmed to ca. 40 °C, appreciable 4-ethoxy-2-butanone was formed, even when the ethanol contained sodium bicarbonate (so as to prevent ketal exchange). Path b would explain such incorporation of the solvent at the 4-position, but it invokes a chloronium ion within a four-membered ring, a ring size that other workers have claimed is particularly disfavored for chlorine participation.[11] Finally, path c would explain the very facile substitution of the chloride by conversion of the ketal to a highly reactive allylic halide, but this mechanism requires that a ketal to enol ether transformation occur under unusually mild conditions.[12] Further studies are clearly needed before this issue can be resolved.

Experimental Section

^{1}H NMR spectra were recorded on a Perkin-Elmer R-32 (90 MHz) or a Nicolet NT-470 (470 MHz) spectrometer. ^{13}C NMR spectra were obtained on a Varian XL-200 instrument. Mass spectra were obtained with a Finnigan automated GC EI/CI mass spectrometer. Gas chromatography utilized a Varian Model 90P instrument for preparative work and Models 1200 or 1400 FID chromatographs with a Hewlett-Packard 3380 or 3380A digital integrator for quantitiative studies. Most photolyses were carried out in a Model RPR-100 Rayonet Reactor (New England Ultraviolet Corp.) with an MGR merry-go-round and 300-nm lamps; the ambient temperature in a covered reactor is ca. 40 °C, and removal of the cover allowed for photolysis at lower temperatures (28 ± 2 °C). Some experiments used a Pyrex filtered Canrad-Hanovia 450-W medium-pressure mercury lamp (Model 679A), with a merry-go-round in a thermostatted cooling bath set to maintain temperatrures from 5 to 20 °C. All photolyses employed matched sets of 10 mm i.d. Pyrex photolysis tubes, and the solutions were degassed with argon for 15 min prior to photolysis. Quantitative experiments included tetradecane in the photolysis solution as an internal standard for GC analysis; complete experimental details for these may be found in the Ph.D. thesis of L.D.C. 4-Chloro-2-butanone (**4-CB**)[13,14] was prepared by bubbling dry HCl gas through a solution of methyl vinyl ketone in sulfur dioxide at −78 °C. The methanol was Burdick and Jackson, Distilled in Glass, Spectrograde.

Photolytic Conversion of 4-CB to 1-Chloro-3,3-dimethoxybutane (4-CK). Aliquots of a 1 M solution of **4-CB** in 3 mL of methanol that had been dried over molecular seives were photolyzed in the Rayonet Reactor with 16 300-nm lamps for 1 h at 28 °C. Gas chromatographic analysis on a 2 ft × 0.125 in. 3% FFAP on 60/80 AW-DMCS Chromosorb W column at 110 °C showed formation of **4-CK** at 6.8 min (other retention times: **4-CB**, 7.8 min; 4-methoxy-2-butanone, 4.7 min). The limiting amount of **4-CK** formation was ca. 20% (the remainder being **4-CB**) with attempts to generate higher conversions leading to diminished **4-CK** and the formation of 4-methoxy-2-butanone. The solutions were either transferred to 10-mm NMR tubes for ^{13}C NMR spectroscopy or subjected to GC/mass spectral analysis. (In general, solutions were 0.1 M in **4-CB**, and somewhat higher conversions to **4-CK** (25%–30%) could be obtained with the medium-pressure lamp and a reaction temperature of 5 °C.) All attempts to purify **4-CK** lead to the isolation of 4-methoxy-2-butanone.

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Registry No. 4-CB, 6322-49-2; 4-CK, 111772-63-5; 4-methoxy-2-butanone, 6975-85-5.

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Communications

Disproportionation of (Acyloxy)borohydrides: A ^{11}B NMR Study of the Reaction between Sodium Borohydride and Isobutyric Acid

Summary: ^{11}B NMR confirms the existence of BH_4^- ions in large amounts in diglyme solutions of (acyloxy)borohydrides through disproportionation of both the mono- and bis(acyloxy) compounds. The equilibria are slow but need to be carefully examined when designing chiral reducing agents from $NaBH_4$.

Sir: In recent years some reports on the use of chirally modified $NaBH_4$ in asymmetric reductions have appeared.[1] Morrison[2] and Hirao[3] have independently studied a reagent prepared from $NaBH_4$, isobutyric acid, and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose. Optical yields as high as 83% ee were reported[3] in the reduction of propiophenone. These works raised the question whether the initially formed (acyloxy)alkoxyborohydrides disproportionate in the same way as the related lithium alkoxyaluminohydrides which we have previously studied in some detail using ^{27}Al and ^{7}Li NMR.[4] In this paper we report a similar ^{11}B NMR study of $NaBH_4$ modified with isobutyric acid in diglyme solution.

When $NaBH_4$ reacts with a carboxylic acid, hydrogen gas is evolved (eq 1). By measuring the quantity of hydrogen gas evolved we found, in line with previous work,[5,6]

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(3) Hirao, A.; Itsuno, S.; Owa, M.; Nagami, S.; Mochiguki, H.; Zoorov, H. H. A.; Niakahama, S.; Yamazaki, N. *J. Chem. Soc., Perkin Trans. 1* **1981**, 900.
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$$NaBH_4 + RCOOH \rightarrow NaBH_3OCOR + H_2 \quad (1)$$

that with many different carboxylic acids 2 molar equiv of hydride react rapidly, the third more slowly, and the fourth hydride does not react at all at room temperature. Unpon addition of H_2SO_4, however, all four hydrides react quantitatively. This cannot be explained on steric grounds alone.

In the NMR experiments, isobutyric acid in diglyme was added to a diglyme solution of $NaBH_4$ in portions of 0.2 equiv (acid to hydride), and the ^{11}B NMR spectra were recorded. The signal from the symmetrical BH_4^- anion is a well-resolved quintet with $J_{^{11}B-^1H} = 80$ Hz. The signals from the reaction products appeared at high frequency from BH_4^-. Due to lower symmetry around the ^{11}B nucleus, and consequently more rapid quadrupole relaxation, these signals were too broad to show any resolved fine structure from $^{11}B-^1H$ spin–spin coupling. In all cases, the total integral of the ^{11}B spectra (corrected for dilution) was constant during a titration.

Upon each addition of acid, the intensity of the signal from BH_4^- decreased initially as a result of reaction 1. However, thereafter the BH_4^- signal increased with time and finally reached a constant value. Establishment of equilibrium was verified by the results of back-titrations, i.e., adding the reactants in reversed order. When the mole ratio acid/BH_4^- = 1 more than 50% of the BH_4^- ions remained in solution at equilibrium. When the titration had proceeded to the mole ratio 2.5, the signal from BH_4^- disappeared initially after the addition but reappeared in the spectrum after 2 h and reached the equilibrium value, 10% of the total integral, after 12 h (Figure 1). Continued titration caused the definite removal of BH_4^- as evidenced by observing the spectra for more than 48 h.

These results suggest that the monoacyloxy compound initially formed slowly disproportionates according to eq 2 and 3. According to the results from hydrogen gas

$$2NaBH_3OCOR \underset{}{\overset{K_1}{\rightleftharpoons}} NaBH_2(OCOR)_2 + NaBH_4 \quad (2)$$

$$2NaBH_2(OCOR)_2 \overset{K_2}{\rightleftharpoons} NaBH_3OCOR + NaBH(OCOR)_3 \quad (3)$$

evolution experiments, the tetrakis(acyloxy) compound is not formed at room temperature, and it is therefore not necessary to take further disproportionation into account.

The titration curves did not depend on the initial $NaBH_4$ concentration in the range 0.1–0.4 M, which shows that formation of polynuclear species need not be considered. According to the model for disproportionation, (reactions 2 and 3) we have fitted calculated concentrations of BH_4^- to the experimental NMR data. The law of mass action was applied to reactions 2 and 3, and a system of equations, corresponding to the chemical equilibria and to the relations for the total concentrations of boron and acid, was set up. This procedure has been described in detail elsewhere.[4] The calculated BH_4^- concentrations were then fitted by a least-squares minimization method to the values obtained in ^{11}B NMR by varying the equilibrium constants. In the ^{11}B spectra, the broad peak was assigned to all boron-containing species except BH_4^-. The results from the best fit are shown in Figure 2. As can be seen, a good fit to experimental data is obtained with $K_1 = 19$ and $K_2 = 0.7$. In order to obtain a good fit, reaction 3 had to be included; i.e., disproportionation of both monoacyloxy and bis(acyloxy) compounds is indicated. A comparison

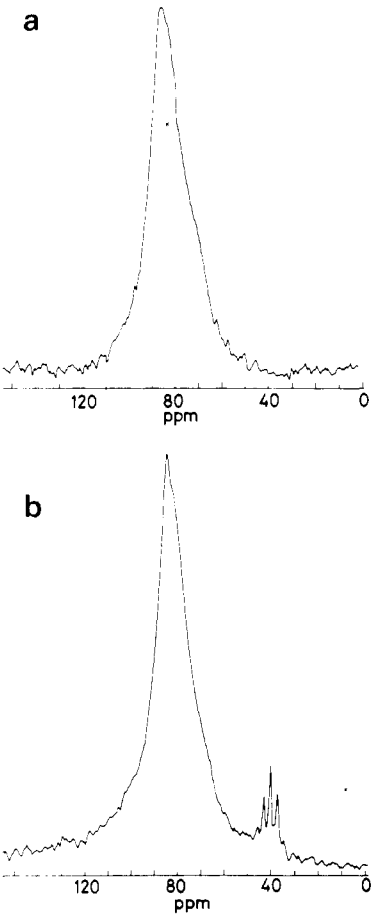

Figure 1. ^{11}B spectrum from a diglyme solution with molar ratio isobutyric acid/$NaBH_4$ = 2.5 registered 2 h (a) and 12 h (b) after the addition of the acid.

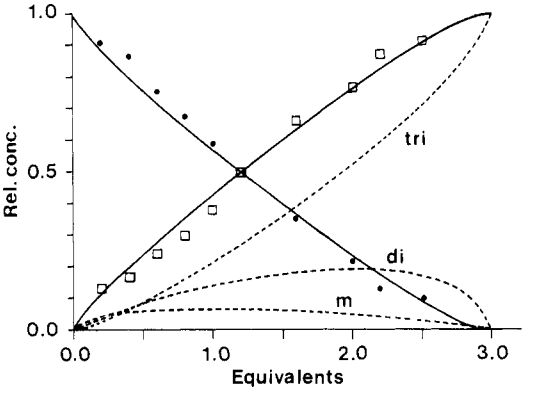

Figure 2. Concentrations of BH_4^-, mono-, bis- and tris(acyloxy)borohydrides obtained from the best fit to the experimental data: (●) experimental BH_4^- concentrations; (□) experimental concentrations of all other boron containing species.

of these results with similar studies of the reaction of $LiAlH_4$ with alcohols[4] shows a much higher degree of disproportionation for the (acyloxy)borohydrides, but the equilibria take longer time to establish. This means that in synthetic work, disproportionation can be suppressed by minimizing the time between preparation and use of the reagent. Thus, disproportionation is a factor to consider carefully when designing chiral reducing agents by modification of $NaBH_4$. If a multinuclear NMR spectrometer is available, ^{11}B NMR can be used very conveniently to study the composition of the reducing solution.

^{11}B NMR spectra were recorded at 28.8 MHz on a Bruker CXP-100 instrument using a high-power probe equipped with a quartz glass insert. Chemical shifts were

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(6) Gribble, G. W.; Ferguson, D. C. *J. Chem. Soc., Chem. Commun.* **1975**, 535.

related to BF_3·$(OEt)_2$ as an external standard.

$NaBH_4$ was recrystallized from diglyme.[7] The diglyme solutions were standardized prior to use by measuring the amount of hydrogen gas evolved upon hydrolysis in 2 M H_2SO_4. The reproducibility was always within ±2%. The solution was kept under dry nitrogen in storage bottles equipped with Teflon stop cocks and rubber septums. Aliquots were removed by syringe as needed. All glassware was carefully dried to exclude moisture. Isobutyric acid and diglyme were distilled under dry nitrogen prior to use.

Registry No. $NaBH_4$, 16940-66-2; $NaBH_3OCOCHMe_2$, 77979-89-6; $NaBH_2(OCOCHMe_2)_2$, 77979-90-9; $NaBH(OCOCHMe_2)_3$, 77979-91-0; isobutyric acid, 79-31-2.

(7) Brown, H. C.; Mead, E. J.; Subba Rao, B. C. *J. Am. Chem. Soc.* **1955**, *77*, 6209.

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Regiospecific Preparation of the Benz[*b*]xanthen-12-one Ring System: Total Synthesis of Bikaverin

Summary: The benz[*b*]xanthen-12-one ring system can be fabricated regiospecifically through condensation of (phenylsulfonyl)isobenzofuranones with chromones. This discovery was used to achieve a brief synthesis of the antiprotozoal agent bikaverin (1).

Sir: Bikaverin (1), a red pigment with significant and specific antiprotozoal activity, has been isolated from several fungi.[1-5] Although partial assignment of the structure through chemical and spectroscopic studies was possible,[4,6] X-ray analysis was required to establish unambiguously the substitution pattern.[7] Shortly after the structure was elucidated, an elegant regiospecific synthesis of 1 was reported by Barton et al.[8] and more recently two additional preparations have been described.[9,10]

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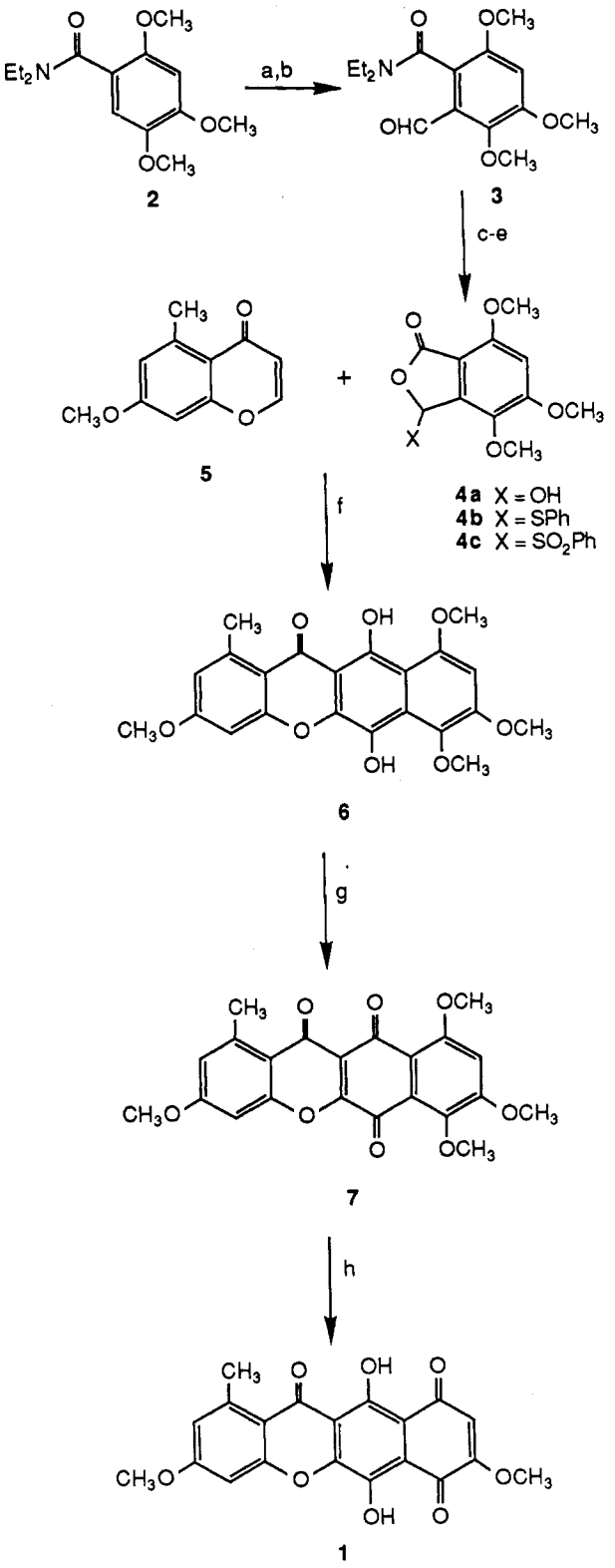
Scheme I[a]



[a] (a) *sec*-BuLi, TMEDA, THF; (b) DMF, 56%; (c) $H_3O^+Cl^-$, HOAc; 81%; (d) PhSH, catalytic TsOH; 91%; (e) MCPBA, CH_2Cl_2; 100%; (f) LiO-*t*-Bu, THF, −78 °C and reflux; 27%; (g) Ag_2CO_3–Celite; 91%; (h) LiI, DMF; 78%.

Our synthesis of 1, shown in Scheme I, was based on the expectation that condensation of (phenylsulfonyl)isobenzofuranones[11] with chromones would furnish regios-

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