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Selectivities in Ionic Reductions of Alcohols and Ketones with Triethylsilane / Trifluoroacetic Acid

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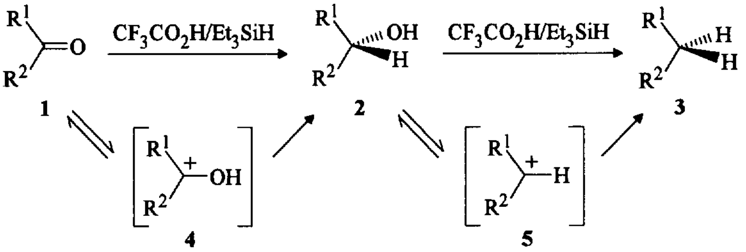
Abstract. The relative rates of reduction of alcohols and ketones by Et_3SiH/CF_3CO_2H have been determined by competition experiments in order to derive scope and selectivities of these reactions.

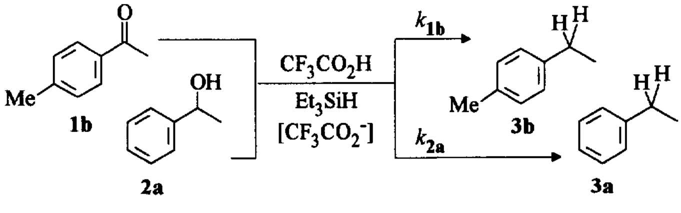
Mixtures of silanes and Brønsted acids are well-known reducing agents for a variety of functional groups,[1] but we are not aware of any systematic investigations on the selectivities of these reactions. In previous work we have studied the kinetics of hydride transfer reactions from silanes to carbenium ions[2] and we will now turn to the problem of selectivities in ionic hydrogenations.

Scheme 1. Ionic hydrogenations of ketones and alcohols



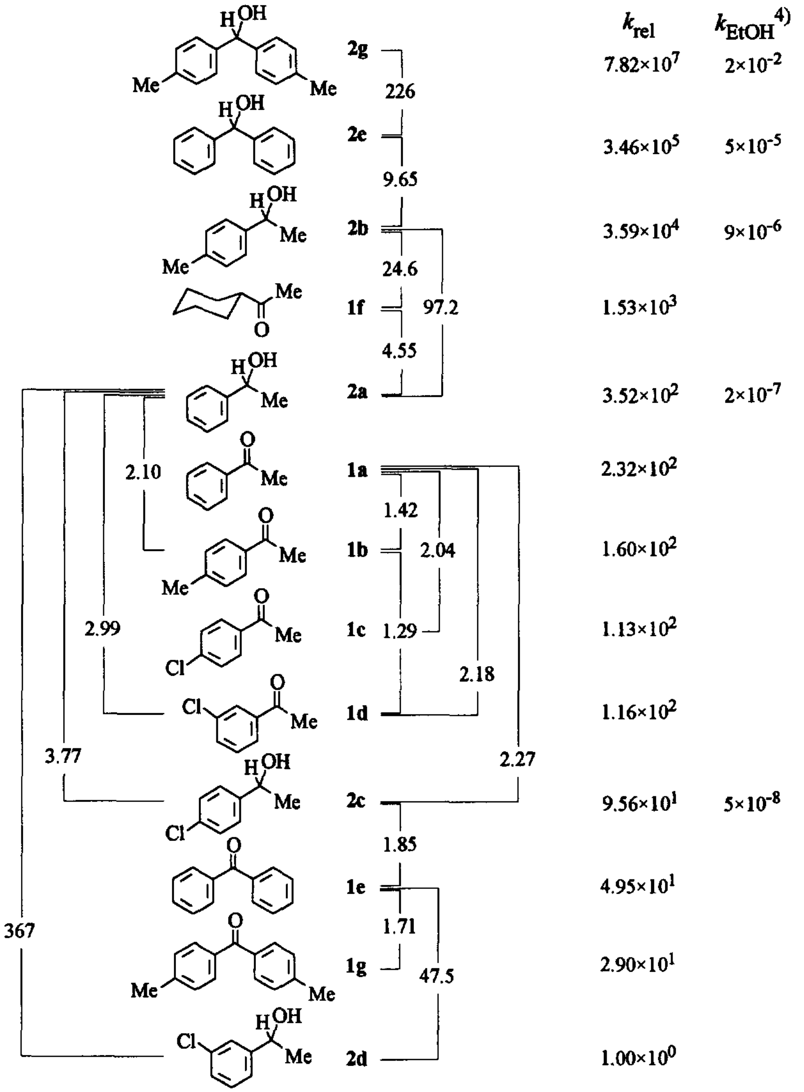
As shown in Scheme 1, alcohols **2** can be reduced to hydrocarbons **3** when the carbocations **5** are sufficiently stabilized to be generated as intermediates under the reaction conditions. The reduction of carbonyl groups may, therefore, either yield hydroxy or methylene groups,[3] depending on the relative reactivities of **1** and **2**.

Scheme 2. Competition experiment to determine $\kappa = k_{2a}/k_{1b}$



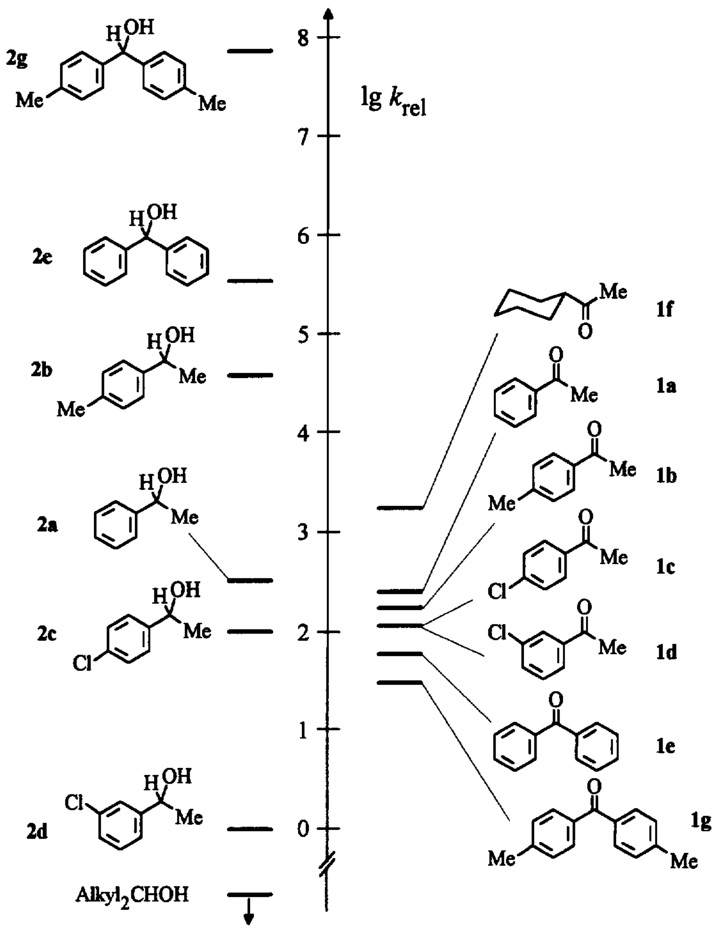
We will now report on the relative reactivities of alcohols and ketones in presence of CF_3CO_2H/Et_3SiH and derive a general rule for the outcome of such reactions. Preliminary experiments showed that the reactivity ratios of alcohols were dependent on the reaction conditions. Partial reduction of a mixture of **2a** and **2b**, for example, with Et_3SiH/CF_3CO_2H in dichloromethane, gave a ratio k_{2a}/k_{2b} which varied when the ratio of the reactants or the concentration of the reducing agent was altered. Competition *constants*, i.e. relative reactivities independent of the reaction conditions were obtained, however, when the reductions were performed in presence of 0.03 - 0.6 equivalents of tetraalkylammonium trifluoroacetate after converting the alcohols into their

Scheme 3. Competition constants and calculated relative rate constants for reductions of alcohols and ketones (Et_3SiH/CF_3CO_2H, 20 °C) and ethanolysis rate constants for the corresponding alkyl chlorides (25 °C).



trifluoroacetates. Competition experiments[5] as described in Scheme 2 yielded the reactivity ratios listed in Scheme 3 which have been subjected to a statistical treatment to give the relative rate constants given there.

Scheme 4. Relative reactivities of ketones and alcohols in ionic hydrogenations (CF_3CO_2H/Et_3SiH).



Scheme 4 orders these relative rate constants individually for alcohols and ketones. One can see that cyclohexyl methyl ketone (**1f**), a representative of dialkyl ketones, is approximately one order of magnitude more reactive that the acetophenones **1a** - **d** which hardly differ in reactivity, in accord with a previous report by Fukuzumi.[6] Obviously the substituent effects on the basicities of the acetophenones[7] are counterbalanced by the substituent effects on the electrophilicities of the intermediate hydroxycarbenium ions **4**. The well-known fact that the rate constants of acid catalyzed hydrolyses of ethyl benzoates are independent of the substituents at the arene ring (Hammet $\rho \approx 0$)[8] has been explained analogously. For the same reason, the reduction rates of the benzophenones hardly differ from those of the acetophenones. In contrast, dramatic substituent effects are observed for the reductions of the alcohols. The excellent correlation with the ethanolysis rate constants of the corresponding benzyl and benzhydryl chlorides (eq. 1) indicates a carbocation-like character of the transition states.

$$\lg k_{\mathrm{rel}} = 1.075 \lg k_{\mathrm{EtOH}} + 9.889 \qquad \text{(5 points, r = 0.997)} \qquad (1)$$

Scheme 4 now answers the initial question on the selectivities of ionic hydrogenations. Since dialkylcarbinols do not react under these conditions, dialkylketones are selectively reduced to secondary alcohols. The reactivity of the unsubstituted acetophenone (**1a**) differs only slightly from that of the corresponding alcohol (**2a**) indicating that the quantitative reduction of the acetyl group to the ethyl group is unproblematic if 2 equivalents of reducing agent is employed, but that the alcohol **2a** is not produced selectively from **1a** under the reaction conditions. The hundred-fold lower reactivity of the *m*-chloro substituted alcohol **2d** compared to **1d** implies that acceptor substituted acetophenones, in contrast to the parent and to the donor-substituted acetophenones may selectively be reduced to the corresponding alcohols. Since diphenylmethanol (**2e**) is 10^4 fold more reactive than benzophenone (**1e**), the ionic hydrogenation of benzophenones usually gives rise to the formation of diarylmethanes, and the isolation of the intermediate benzhydrols can only be expected for systems with strong electron acceptors.

The close similarity of the reduction rates of various types of ketones (Scheme 4) and aldehydes[6] in combination with eq. 1 gives rise to a rule of thumb: *Ionic hydrogenation of carbonyl compounds only yields alcohols selectively under the conditions described in this work, if the ethanolysis rate constants (25 °C) of the corresponding alkyl chlorides*[4] *are smaller than* 10^{-6} *to* 10^{-8} s^{-1}*. Otherwise, the carbonyl group is immediately reduced to a methylene group.*

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(5) In a typical experiment, ketone **1b** (0.4 mmol), alcohol **2a** (0.5 mmol), and *tert.*-butylcyclohexane (GC-standard) were combined with $Bu_4N^+CF_3CO_2^-$ (0.07 mmol) in CH_2Cl_2 (0.75 mL) and CF_3CO_2H (0.9 mL). After 10 min, when the alcohol was converted into the trifluoroacetate, triethylsilane (0.2 mmol) was added and the reaction was followed by taking 0.2-mL samples which were quenched with aqueous ammonia or saturated K_2CO_3 solution, and analyzed by GC. Four experiments with reactant ratios $[\mathbf{1b}]_0/[\mathbf{2a}]_0$ ranging from 0.7 to 4.1 yielded an averaged competition constant of $\kappa = k_{2a}/k_{1b} = 2.10 \pm 0.04$.

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