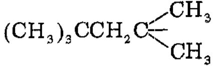
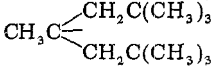
Table III. Comparison of Diazenes, *tert*-Butyl Peresters, and Alkyl Chlorides

R	RN=NR, rel rate, 100 °C	RCO_3-$C(CH_3)_3$, rel rate, 25 °C	RCl,[a] rel rate, 25 °C (80% ethanol)
$(CH_3)_3C$-	1	1[b]	1
 $(CH_3)_3CCH_2C(CH_3)_2$-	35	4.1[b]	21
 $CH_3C(CH_2C(CH_3)_3)_2$-	57000	5.7[c]	580

[a] E. N. Peters and H. C. Brown, *J. Am. Chem. Soc.*, **97**, 2892 (1975). [b] Reference 11. [c] Professor T. T. Tidwell, private communication.

project. The authors are grateful to Professors T. Tidwell and C. Rüchardt for unpublished results and useful discussions.

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(8) $\Delta G^{\ddagger}_6 \simeq \Delta G^{\ddagger}_1 - 2[2(\Delta G^{\ddagger}_1 - \Delta G^{\ddagger}_4) - (\Delta G^{\ddagger}_1 - \Delta G^{\ddagger}_5)] = 25.4$ kcal mol^{-1}.

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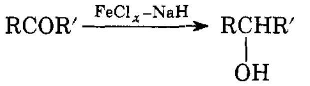
Iron Chloride–Sodium Hydride System as New Reducing Reagents of Carbonyl Compounds

Summary: Iron(II or III) chloride and sodium hydride in tetrahydrofuran provide an effective reagent system for the reduction of ketones and aldehydes to the corresponding alcohols under mild conditions.

Sir: Recently much attention has been paid toward reducing reagents consisting of a mixture of metal compounds. For example, an addition of metal salts to metal hydrides is known to modify the reducing ability.[1] Further, the reagents consisting of $TiCl_3$-$LiAlH_4$[2] or n-BuLi-WCl_6[3] have been demonstrated to be effective for the reductive coupling of carbonyl compounds to olefins and the reduction of epoxides to olefins. We have also described the deoxygenation of epoxides to olefins with $FeCl_3$-n-BuLi system using the strong affinity of iron to oxygen atom.[4] We now report the iron chloride–sodium hydride systems as effective reagents for the reduction of ketones and aldehydes to the corresponding alcohols under mild reaction conditions.

Sodium hydride is known as a strong base to abstract a proton from a carbonyl compound giving an enolate anion, but has, in general, little reducing ability for carbonyl compounds. A few exceptions reported so far are reductions of nonenolizable ketones under such drastic conditions as refluxing with sodium hydride in xylene[5] or as heating in an aprotic solvent.[6] Reductions of usual carbonyl compounds, however, were observed when they were added at room temperature to the yellow suspension generated by addition of iron(III) chloride to sodium hydride in tetrahydrofuran (THF). Table I reveals that the reagent is effective for aromatic aldehydes and ketones as well as aliphatic carbonyl compounds. The molar ratio of the hydride to the chloride seriously affected the yields of alcohols. The best result was obtained with the ratio of sodium hydride to iron(III) chloride being 3:1 and, above or below this ratio, diminished yields of alcohols were observed. It is important to note that the reducing procedure is specific, since no alcohol formation was observed when sodium hydride was added to a solution of a carbonyl compound and iron(III) chloride.

Table I. Reduction of Carbonyl Compounds



$$RCOR' \xrightarrow{FeCl_x\text{-}NaH} \underset{OH}{RCHR'}$$

R	R′	$FeCl_3$–NaH[a] Time, h	$FeCl_3$–NaH[a] Yield of alcohol,[c] %	$FeCl_2$–NaH[b] Time, h	$FeCl_2$–NaH[b] Yield of alcohol,[c] %
Ph	Me	30	82	45	72
Ph	Ph	43	81	45	0
n-C_6H_{13}	Me	42	75	48	88
-$(CH_2)_5$-		24	75	30	77
Ph	H	24	85	48	48
n-C_7H_{15}	H	24	79	24	77

[a] Typically, a solution of iron(III) chloride (14 mg equiv) in THF (20 ml) was added to a suspension of sodium hydride (42 mg equiv) in THF (5 ml), and the mixture was stirred for 4 h at room temperature under an atmosphere of argon. Then a solution of a carbonyl compound (2 mmol) in THF (2 ml) was added and stirring was continued at room temperature. [b] Iron(II) chloride (20 mg equiv) and sodium hydride (40 mg equiv) were mixed in THF (15 ml) at 0–5 °C; then a solution of carbonyl compound (2 mmol) in THF (2 ml) was added with continuous stirring at the same temperature. [c] Yields were determined by GLC.

The reducing system was prepared as follows. To a stirred solution of sodium hydride in THF, was added dropwise a solution of iron(III) chloride in THF. Evolution of molecular hydrogen was observed and a yellow suspension was obtained after one third the amount of hydrogen based on the hydride used was evolved. The stability of the reducing reagent depends on the solvent used. Ether cannot be used as a solvent, since fast decomposition of the reducing reagent prevents the reduction. Even in the case of using THF as the solvent, further evolution of hydrogen was observed when carbonyl compounds were added to the suspension. Thus, to obtain satisfactory results, an excess of the reducing reagent to carbonyl compounds was necessary. The reaction mixture became dark as the reduction proceeded. Although the reducing species is not exactly identified at present, it is considered to be some kind of iron hydride,[7] because no formation of coupling product, i.e., glycol derivatives,[8] which were obtained by the reduction of carbonyl compounds with lower valent metal compound,[9] were observed in the reduction.

It is interesting to note that the use of iron(II) chloride in place of iron(III) chloride in the reduction gave different results.[10] As shown in Table I, the reduction of enolizable aliphatic carbonyl compounds with iron(II) chloride[11]–sodium hydride system in THF gave also the corresponding alcohols in good yields, but the reaction manner and the reactivity are different from those of the reduction with iron(III) chloride–sodium hydride system. For example, the reduction was smoothly carried out at 0–5 °C with the iron(II) chloride–sodium hydride system consisting of 2:1 ratio of the hydride and the chloride, since the reducing species decompose easily with the evolution of hydrogen at room temperature to lower the yields of alcohols. Moreover, in the case of nonenolizable aromatic carbonyl compounds, a clear-cut difference was observed between the reactivities of the reducing reagents prepared from trivalent and divalent iron chloride. With iron(II) chloride–sodium hydride system, benzophenone was not reduced and benzaldehyde gave the reductive coupling product, 1,2-diphenylethylene glycol, in a 22% yield, along with benzyl alcohol in a 48% yield. This suggests that one of the reduction routes may proceed via anion radical intermediates, similar to that of the reduction of carbonyl compounds with the $FeCl_3$–*n*-BuLi system.[9]

In any case, complex species are considered to act as reducing reagent in the above reaction system, but it is of interest to note that the reducing ability of sodium hydride is modified by using with iron chloride.

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(8) In general, reductions of carbonyl compounds with metal hydrides give the corresponding alcohols; for example, see N. G. Gaylord, "Reduction with Complex Metal Hydrides", Wiley-Interscience, New York, N.Y., 1956. One exception is the reduction of fluorenone with sodium hydride that gives reductively coupled glycol as a main product; see ref 6a.

(9) The $FeCl_3$-*n*-BuLi system in THF reduced benzaldehyde to give benzyl alcohol (17%), 1,2-diphenylethylene glycol (46%), and stilbene (3%), which suggests that the reaction proceeds via anion radicals formed by lower valent iron; cf. ref 4.

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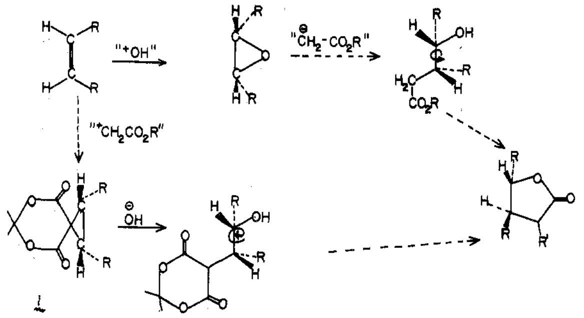
The Cyclopropane Route to Trans-Fused γ-Lactones

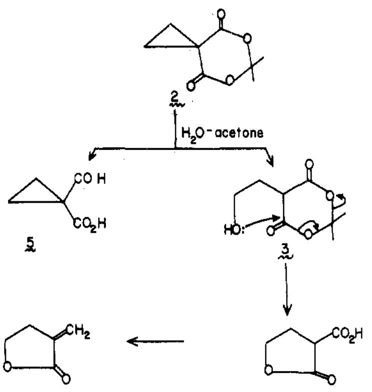
Summary: Suitably activated cyclopropanes can be converted to γ-lactones with inversion of configuration by solvolysis in aqueous acetone.

Sir: The usual route from olefins to trans γ-lactones involves epoxidation followed by nucleophilic attack by an equivalent of acetic acid carbanion.[1,2] Our findings concerning the remarkable electrophilic properties of spiroactivated cyclopropanes[3-5] suggested the feasibility of a conceptually different approach, wherein systems of the type 1 would be opened by hydroxide or an equivalent thereof. Clearly, the success of such a scheme depends, critically, on a stereospecific inversion result during the ring opening. A further requirement is that the ring opening be faster than hydrolytic cleavage of the activating acylal linkage. Below we report the results of testing this new approach in simple model systems. These results show that the two conditions cited above can be met and suggest that activated cyclopropanes may be of utility in the synthesis of the trans-fused γ-lactonic compounds present in a variety of biologically important natural products.[6-8]



When the parent cyclopropane acylal 2[4] was heated with 2:1 acetone–water under reflux for 40 h, there was obtained upon evaporation of the solvents, a 9:1 mixture (NMR analysis) of 3-carboxybutyrolactone (**4**) and cyclopropane-1,1-dicarboxylic acid (**5**). Thus, with water as the nucleophile, ring cleavage is faster than acylal cleavage to a synthetically usable extent. Presumably, the spiroacylal functions as an active ester in the cyclization of **3**, the initially formed 1,5 adduct, to produce the observed **4**. Compound **3** itself was not detected under these conditions.

Without purification, the total reaction mixture was subjected to α-methylenation: (i) formalin–diethylamine; (ii) sodium acetate–acetic acid.[9] The well-known α-methylenebutyrolactone (**6**)[8] was obtained in 40% yield from **2**.



An insight into the stereochemical course of the process was gained by studying the solvolysis of spiroacylal **9**. The starting material for its preparation was the known 7,7-dicarbomethoxynorcarane (**7**).[10] This was converted to diacid[11] **8**. Reaction of **8** with isopropenyl acetate–sulfuric acid at 0 °C[4] gave **9**,[12] mp 87–88 °C, in 51% yield. Heating compound **9** with 2:1 acetone–water under reflux for 7 h gave, in one step, the α-carboxylactone **11**[1] characterized as its methyl ester **12**,[13] mp 81–83 °C.

The yield from **9** → **12** (purified by silica gel chromatography) is 65%. That **11** and **12** are, in fact, trans fused was shown by conversion of the former by the Mannich procedure[9] to the α-methylenelactone **13**, identical with an authentic sample provided by Professor Grieco.

The stereochemical course of the ring opening has thus been shown to involve inversion of configuration by solvent (water). It will be noted that Hudrlik[14] observed retention of configuration in the rearrangement of cyclopropropylcarbinyl systems of the type **14**. This was explained by postulating intra-