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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(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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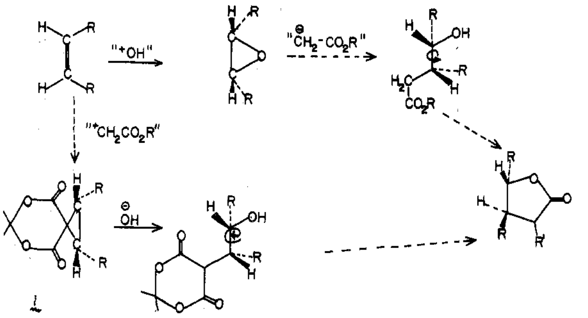
Received January 5, 1976

The Cyclopropane Route to Trans-Fused γ-Lactones

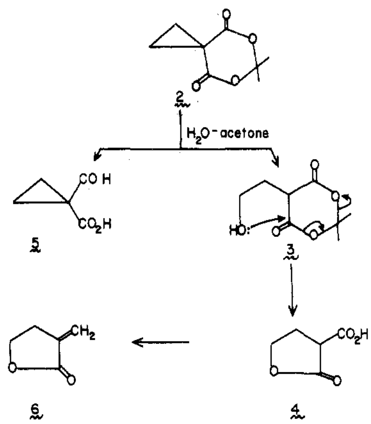
Summary: Suitably activated cyclopropanes can be converted to γ-lactones with inversion of configuration by solvolysis in aqueous acetone.

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.

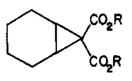
Without purification, the total reaction mixture was subjected to α-methylenation: (i) formalin–diethylamine; (ii) sodium acetate–acetic acid.[9] The well-known α-methylenebutyrolactone (6)[8] was obtained in 40% yield from 2.



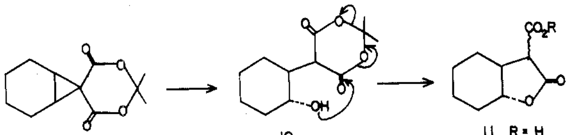
An insight into the stereochemical course of the process was gained by studying the solvolysis of spiroacylal 9. The starting material for its preparation was the known 7,7-dicarbomethoxynorcarane (7).[10] This was converted to diacid[11] 8. Reaction of 8 with isopropenyl acetate–sulfuric acid at 0 °C[4] 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.

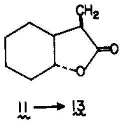
The stereochemical course of the ring opening has thus been shown to involve inversion of configuration by solvent (water). It will be noted that Hudrlik[14] observed retention of configuration in the rearrangement of cyclopropropylcarbinyl systems of the type 14. This was explained by postulating intra-



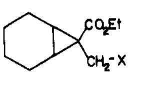
7 R = Me
8 R = H



9 **10** **11** R = H
12 R = Me



11 → **13**



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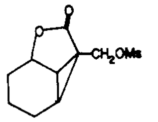


15

molecular capture of the electron-deficient homoallylic carbon by the proximate ester oxygen.

Ziegler[15] was the first to demonstrate inversion of configuration in the course of acetolysis of the cyclopropylcarbinyl system, **15**. While this result is potentially of considerable interest in the control of stereochemistry of oxygen functionality adjacent to α-methylenelactones,[16] we believe that the transformation of **9** → **11** represents the first instance of using activated cyclopropanes for the de novo synthesis of a γ-lactone in the trans series.

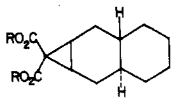
Parenthetically it will be noted that the cyclization of **10** → **11** is apparently[17] uncatalyzed and is occurring under conditions which must be regarded as quite mild for the closure of a trans-fused γ-lactone.[2] Again this is suggestive of particularly strong acylating powers of the cyclic acylal linkage.

A finer understanding of the stereochemical pathway of the solvolytic opening of spiroactivated cyclopropanes was possible in the context of the conformationally defined *trans*-decalin system, **18**. *trans*-Δ^2-Octalin was converted to the cyclopropane derivative **16**[12] (76%) by the action of dimethyl diazomalonate under the influence of copper bronze (3 equiv of diazo compound to 1 equiv of olefin, 150 °C). This was hydrolyzed to give diacid **17**, mp 195–197 °C,[12a] in 83% yield, which was converted to **18**,[12] mp 145–148 °C, in 82% yield via isopropenyl acetate.[4]

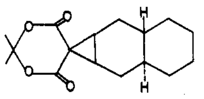
Compound **18** was heated in 1:1 acetone–water for 24 h under reflux. NMR analysis indicated the presence of two or more acidic components. Accordingly, the total reaction mixture was heated in pyridine[2] under reflux for 0.5 h thereby achieving decarboxylation. At this stage, an acidic product, identified as **20**, mp 117–120 °C (lit.[2] mp 116–117 °C), was isolated in 60% yield. A neutral product, mp 52–53 °C, shown to be Johnson's boat lactone **21** (lit.[2] 49.6 °C) was isolated in 30% yield. Although an authentic sample of **21** by the original method of synthesis[2] was not available, the lactone so produced was identical with the same compound obtained from the opening of the epoxide, **22**,[2] with diethyl ethoxyethynylalane.[18] Furthermore, **21** was also obtained by the cyclization of **20** by the method of Johnson (tosyl acid–xylene, reflux 30 min).

It is seen that a minimum of 90% of the solvolysis of **18** can be accounted for in terms of stereospecific opening of the activated cyclopropane to give trans-diaxial substitution. This is followed primarily by decarboxylation of the diacid produced by hydrolysis of the resultant acylal, **19**. To a small (but remarkable) extent, the acylal undergoes lactonization prior to the decarboxylation step with pyridine.

Application of this stereoelectronically specific conversion of fused spiroactivated cyclopropanes to trans-fused γ-lactones will be studied.



16 R = H
17 R = Me



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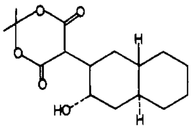

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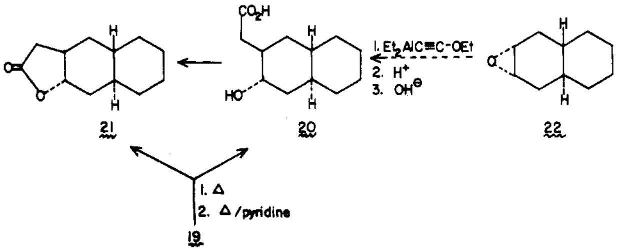

Acknowledgments. This research was supported by PHS Grant CA-12107-12. The authors wish to express their appreciation to the Andrew Mellon Foundation for a Fellowship to R.K.S. NMR services were maintained on instrumentation supported by RR-00292-06. Support from the Hoffmann-La Roche Company is gratefully acknowledged.

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Received January 6, 1976

Functionalized Alanes for the Conversion of Epoxides to Trans-Fused γ-Lactones

Summary: Aluminum derivatives of *tert*-butylacetate and ethoxyacetylene have been shown to be useful for the opening of oxidocycloalkanes.

Sir: In view of the large number of biologically active natural products containing trans-fused γ-lactones,[1,2] a general method of reaching such systems via oxidocycloalkanes could be useful. The traditional route involves the opening of an