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Observations on the Selective Deoxygenation of Epoxides to Olefins with Chlorotrimethylsilane and Zinc.

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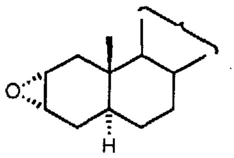
Key Words: Epoxide Deoxygenation; Chlorotrimethylsilane and Zinc

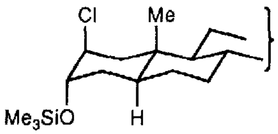
Abstract: Selective deoxygenation of epoxides to olefins using chlorotrimethylsilane and zinc can be accomplished via two distinct mechanistic pathways.

We have recently described a novel symmetrical dicarbonyl coupling reaction of aryl and α,β-unsaturated carbonyl compounds using chlorotrimethylsilane and zinc.[1] In contrast to the McMurry reaction,[2] vicinal diols or their derived trimethylsilyl ethers were shown to be inert. A mechanism involving the trapping of an organozinc carbenoid by a second molecule of carbonyl compound and subsequent deoxygenation of the resulting epoxide was proposed. Although the formation of stilbene (trans:cis; 83:17) from *trans*-stilbene oxide was demonstrated under the reactions conditions, it was of interest to examine the behaviour of other epoxides in which deoxygenation is not assisted by the doubly benzylic or allylic nature induced by the substrate.

In the first instance, we elected to screen a series of simple epoxides of varying substitution pattern using chlorotrimethylsilane (5 mol equiv.) and flame dried zinc amalgam (10 atom equiv.) in diethyl ether (substrate concentration 0.06 M) at room temperature. Under these conditions, reductive deoxygenation to alkenes was not observed for oxiranes derived from either mono- (1-octadecene oxide) or 1,2-disubstituted (*cis*- and *trans*-11-tetradecen-1-yl acetate oxides) substrates. In all of the above cases, however, ring opening to afford the derived trimethylsiloxychlorohydrins was an efficient process and use of $2\alpha,3\alpha$-epoxy-5α-cholestane (1) provided the opportunity to demonstrate that the stereoelectronically preferred mode of trans diaxial ring opening to give (2) (90%) was operating.[3]

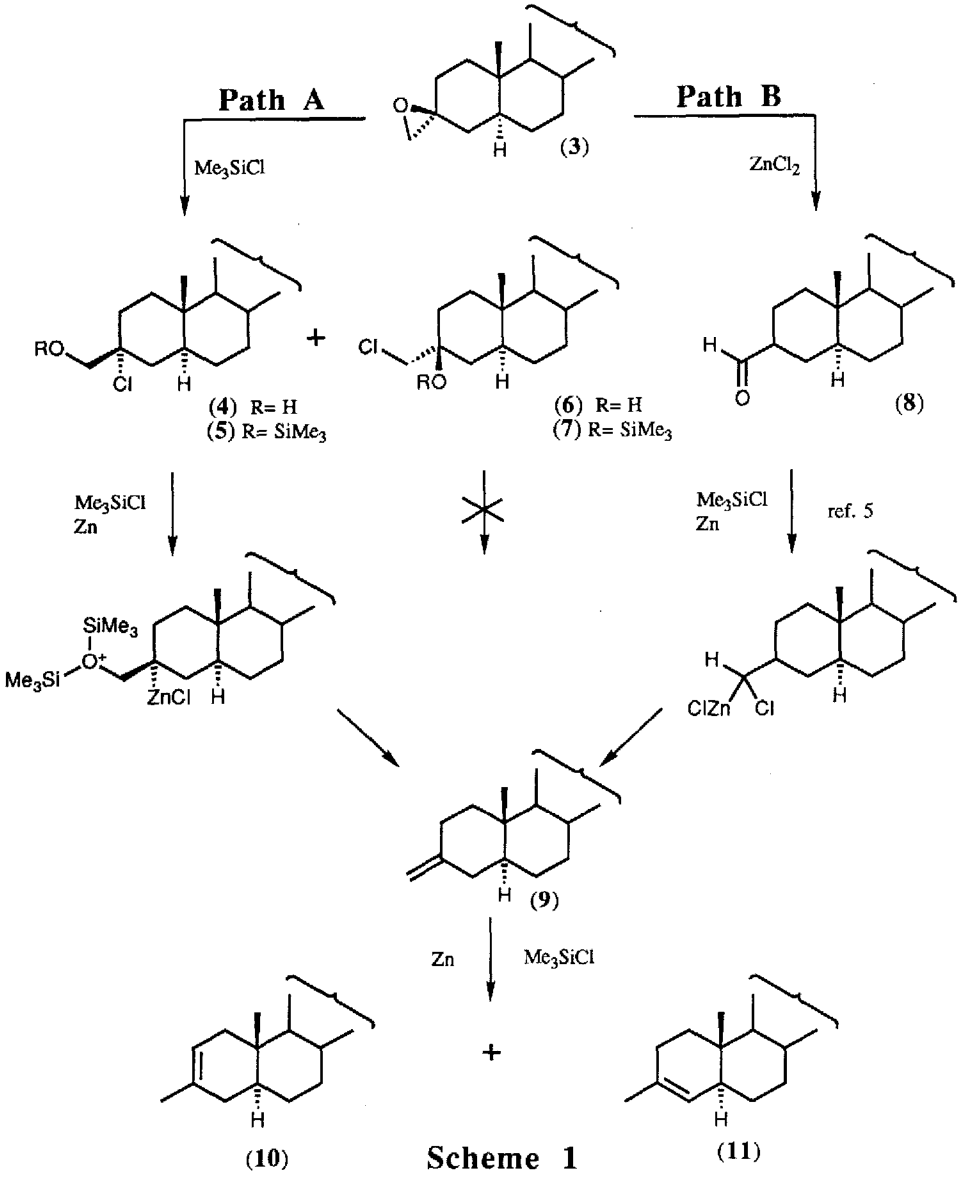


(1)

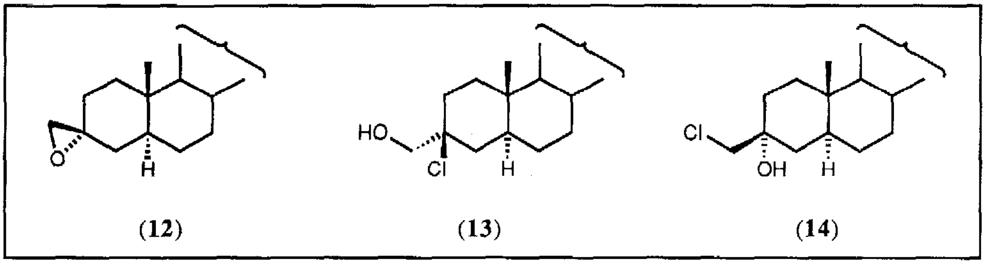


(2)

Such an outcome for deoxygenation is, of course, anticipated by analogy with the classical studies of Cornforth[4] on the necessity for the development of the *iodo*hydrin method (NaI, NaOAc, Zn, HOAc), since chlorohydrins were shown to be inert.

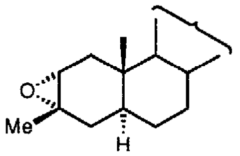

Path A
Path B
(3)
Me3SiCl
ZnCl2
RO
Cl
H
(4) R= H
(5) R= SiMe3
Cl
RO
H
(6) R= H
(7) R= SiMe3
H
O
H
(8)
Me3SiCl
Zn
Me3SiCl
Zn
ref. 5
SiMe3
Me3Si
O+
ZnCl
H
H
ClZn
Cl
H
H
(9)
Zn
Me3SiCl
+
H
(10)
H
(11)

Scheme 1

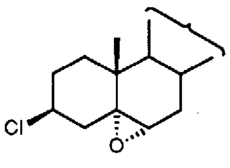

O
H
HO
Cl
H
Cl
OH
H
(12)
(13)
(14)

By way of contrast, however, a detailed study of 1,1-disubstituted spiro epoxide (**3**) proved to be most informative (Scheme 1). In this instance, reaction under the standard conditions (*vide supra*) for 5 days afforded alkenes (**10**) and (**11**) in good yields (72%, (**10**):(**11**); 10:1). Examination after hydrolytic workup following a shorter reaction time (22 hours) gave 3-methylene-5α-cholestane (**9**) as the major alkene (30%, (**9**):(**10**):(**11**); 16:5:1), together with chlorohydrins (**4**) and (**6**) (55%, (**4**):(**6**); 6:1) and the rearranged aldehydes (**8**) (12%, 3α:3β; 1:3). We consider that the formation of regioisomeric alkenes (**10**) and (**11**) is therefore most probably induced by Lewis acid mediated isomerisation of initially formed (**9**).[5]

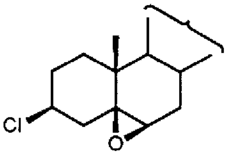
At this stage, the intriguing possibility therefore arose that alkene formation could occur by two distinct pathways: using either the trimethylsiloxychlorohydrins (**5**) and (**7**) (Path A) or *via* the aldehydes (**8**) (Path B). In order to examine path A, an experiment was performed whereby treatment of a mixture of the siloxychlorohydrins (**5**) and (**7**) ((**5**):(**7**); 1.1:1) with chlorotrimethylsilane and zinc afforded alkenes (**10**) and (**11**) (45%, (**10**):(**11**); 10:1) and chlorohydrin (**6**) (30%) derived from unreacted (**7**) by hydrolytic workup. At no stage of this reaction were aldehydes (**8**) detected by n.m.r or t.l.c. of the crude reaction mixture. The formation of a trimethylsiloxychlorohydrin possessing a *tertiary*-alkyl chloride would therefore appear to be a *sine qua non* for zinc induced reductive elimination to alkene. The viability of path B, proceeding by direct deoxygenation of the carbonyl compound *via* an organozinc carbenoid,[6] was then separately tested by treatment of a mixture of aldehydes (**8**) (3α:3β; 1:7.3) with chlorotrimethylsilane and zinc to give alkenes (**10**) and (**11**) (75%, (**10**):(**11**); 14:1). A similar pattern of behaviour was confirmed using the sterically more accessible stereoisomer (**12**) which reacted at a faster rate to afford alkenes (**10**) and (**11**) (62%, (**10**):(**11**); 9:1) after 22 hours. Once again, after a shorter reaction time (4 hours), chlorohydrins (**13**) and (**14**) (70%, (**13**):(**14**); 8:1) and aldehydes (**8**) (12%, 3α:3β; 11:1) were isolable intermediates.



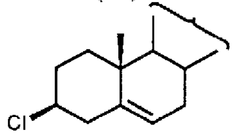
(**15**)



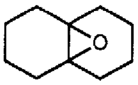
(**16**)



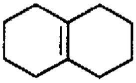
(**17**)



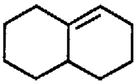
(**18**)



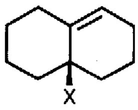
(**19**)



(**20**)



(**21**)



(**22**) X= $OSiMe_3$
(**23**) X= Cl

The results of the above study then allowed us to rationalise the behaviour of some of our earlier screening experiments using trisubstituted epoxides. Thus, epoxides (**15**) and (**16**) could be efficiently recovered ((**15**) 70%, (**16**) 90%) from attempted deoxygenation reactions by using a work up procedure involving reclosure of unreactive trimethylsiloxychlorohydrins with *tetra*butylammonium fluoride. Alkene formation was not detected in these reactions. Contrastingly, a competition experiment using a mixture of (**16**) and the stereoisomeric β-epoxide (**17**) ((**16**):(**17**); 87:13) led, after fluoride anion work-up, to recovery of (**16**) (81%), absence of (**17**) in the crude reaction mixture and alkene (**18**) (77% based on (**17**)). Consideration of these three epoxides in terms of trans diaxial ring opening reveals, once again, that only (**17**) is capable of forming a tertiary chloride and hence reinforces the argument that this substructure is necessary for efficient insertion of zinc in the subsequent reductive elimination to an alkene. Finally, we also note in the case of the tetrasubstituted example (**19**) that formation of volatile alkenes (**20**) and (**21**) is possible (33%, (**20**):(**21**); 43:57; recovered (**19**) (28%)), although under somewhat more vigorous conditions (diethyl ether reflux 3.5 days, F^- workup). Interestingly, in this particular case, isomerisation of tetrasubstituted alkene (**20**) to trisubstituted alkene (**21**) was not possible using *para*-toluenesulphonic acid, boron trifluoride etherate or zinc chloride and chlorotrimethylsilane. Formation of (**21**) may therefore involve epoxide ring opening with concomitant proton loss to give (**22**) followed by conversion to the *tertiary*-allylic chloride (**23**) and reductive dehalogenation by zinc.

In view of the above results, it is surprising to note that the reaction of epoxides with chlorotrimethylsilane and zinc in dichloromethane at room temperature is reported to give the corresponding alcohols.[7] In our hands, however, using the experimental conditions described and a range of variously activated forms of zinc, cyclohexene oxide consistently afforded the corresponding chlorohydrin and no traces of cyclohexanol were detected by g.l.c. analysis.

While a wide range of reagents are now available for the deoxygenation of epoxides to olefins,[8] the present study has indicated that opportunities for highly selective processes exist using chlorotrimethylsilane and zinc. Thus the reaction pathway may be channelled, either *via* prior isomerisation to a carbonyl compound or, in certain cases, by conversion to an appropriately substituted trimethylsiloxychlorohydrin.

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5. A control experiment established that the observed ratio of Δ^2 and Δ^3 olefins results from isomerisation of the less stable *exo* isomer in the presence of both zinc chloride and chlorotrimethylsilane. This isomerisation has also been studied recently using boron trichloride-hydrogen chloride solutions. Hawkins, J.M.; Loren, S.D.; Kim, Y.-K. *Tetrahedron Lett.*, **1991**, *32*, 1635.
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