Pergamon

Tetrahedron Letters, Vol. 35, No. 9, pp. 1405-1408, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0064-5

Diastereospecific Hydroxyiodination of 1-Acetoxycyclohex-2-ene via Intramolecular Delivery of Oxygen

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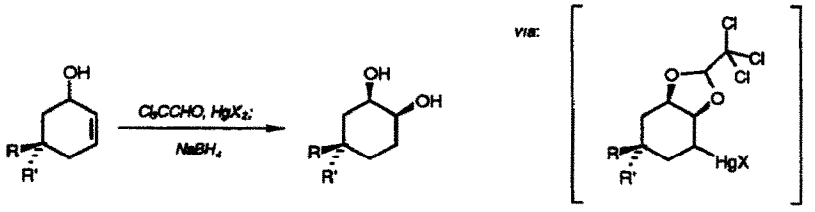
Keywords: cyclohexene, hydroxyiodination, epoxide.

Abstract: *The previously unreported reaction of N-iodosuccinimide with acetoxycyclohex-2-ene to give monoacetates of 3-iodocyclohexane-1,2-diols is diastereospecific.*

The reaction of 3-oxygenated olefins with electrophiles is well-documented[1] and is a valuable synthetic method in the preparation of contiguously trifunctionalized compounds. In some cases a neighbouring group effect can be exploited to provide high selectivity. As an example, cyclohex-2-en-1-ol reacts with mercuric cations in the

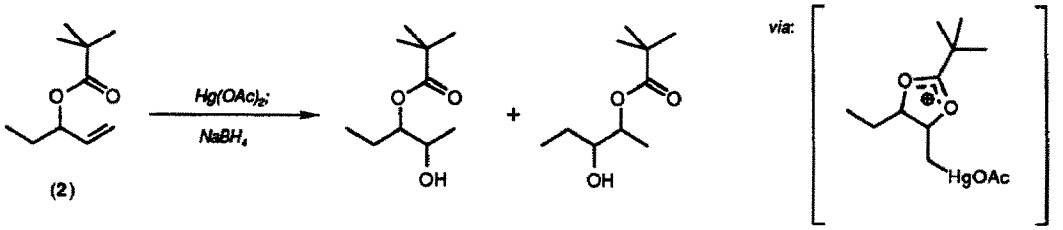


(1)

SCHEME 1

presence of 2,2,2-trichloroacetaldehyde *via* the cyclohex-2-enyl hemiacetal to deliver (after reductive demercuration) 1,2-*cis*-cyclohexane 1,2-diols (1) (scheme 1).[2]

The use of acylated allylic alcohols has not been widely investigated; Giese has shown that mercuration of acetylated and pivaloylated allylic alcohols (2) proceeds *via* a



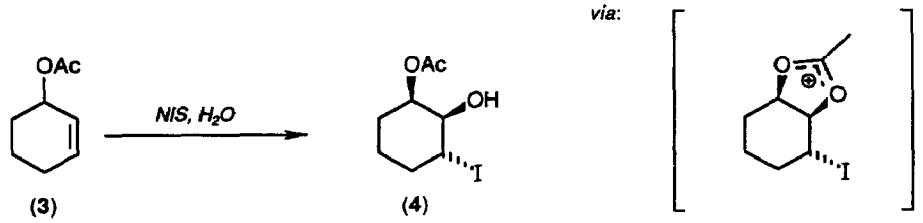
(2)

SCHEME 2

neighbouring group effect (scheme 2),[3] but few other such reactions have been disclosed.

We have studied the previously unreported reaction of imide-based electrophiles with 1-acetoxycyclohex-2-ene (3) in the hope of exerting a stereo- and regioselective functionalization of this cycloalkene; we here report the preliminary results of our studies. The reaction of N-chloro-[4] and N-bromosuccinimide[5] with 1-methoxycyclohex-2-enes is reported to be non-selective, both in terms of regiochemistry and diasterochemistry. Few reports have described the reaction of halosuccinimides with carboxycyclohexenes.

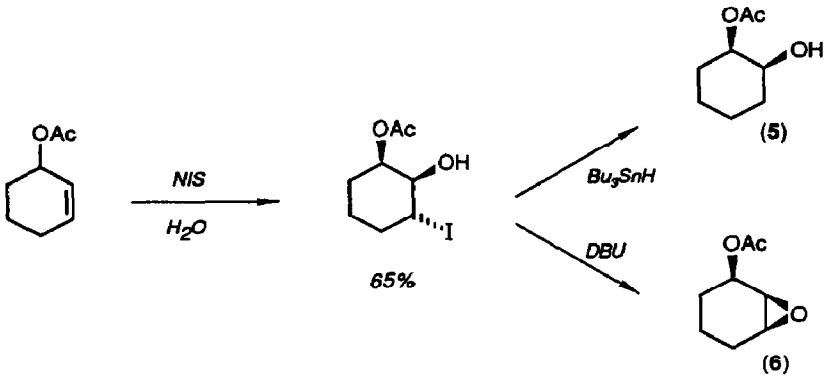
In the presence of water, N-iodosuccinimide reacts at room temperature with acetoxycyclohexene to give a single product, isolated as a colourless crystalline solid in 65% yield after column chromatography. Mass spectra encouraged the suspicion that hydroxyiodination had occurred; the ^{1}H nmr spectrum of this material suggested a 1,2-arrangement of C-O bonds, while ^{13}C nmr spectra indicated the presence of only one diastereomer.[6] Given the previous work showing intramolecular nucleophilic attack of an acyl group and bearing in mind the requirement for *trans*-diaxial ring-opening of iodonium ion, we, therefore, concluded that 1,2-*trans*-2,3-*cis*-3-acetoxy-2-hydroxycyclohexenyl iodide, (4) (scheme 3) had been produced in the reaction, as a single diastereoisomer.



(3) (4)

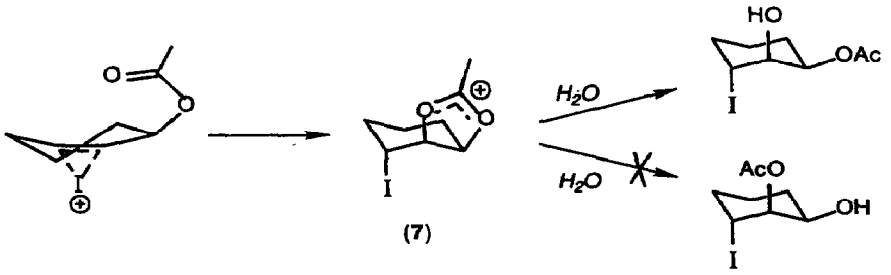
SCHEME 3

The stereochemical arrangement of substituents in (4) was unambiguously established by conversion to previously reported compounds. Thus, tributylstannane reduction of



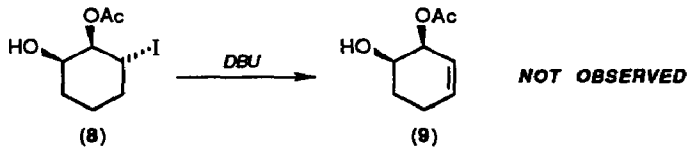
SCHEME 4

(4) gave *cis*-2-hydroxy acetoxycyclohexane (5), whose spectral data concurred exactly with that reported[7,8] while treatment of(4) with DBU gave a quantitative yield of *cis*-3-acetoxycyclohexene oxide (6)[9] (scheme 4). These reactions confirmed the surmise that (4) had been produced as a single stereoisomer. The complete regio- and diastereocontrol observed in the reaction can be rationalized as arising from intramolecular attack by a pseudoequatorially-oriented acetate on the iodonium ion of lesser hindrance as shown in scheme 5, in an analogous fashion to the process detailed by Giese. Oxonium ion (7) reacts with water to give only that product in which there is an equatorially-disposed acetate group and thus there is apparently no acetate migration; the product of the reaction is undoubtedly (4), because *cis*-1-acetoxycyclohexene oxide is formed cleanly when treated with base.



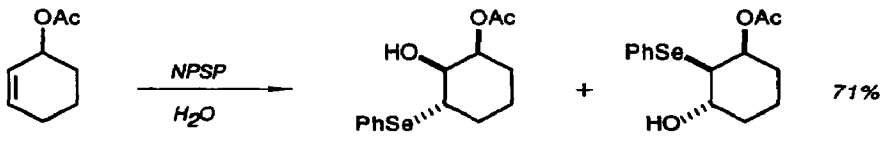
SCHEME 5

The presence of 1,2-*trans*-2,3-*cis*-2-acetoxy-3-hydroxycyclohexenyl iodide, (8) would lead to the formation of 1,6-*cis*-1-acetoxy-6-hydroxycyclohex-2-ene (9) by an eliminative process (scheme 7); no trace of such a product is observed. It is unlikely that (8) would react *via* an sequential acetate migration/ring-closure process to produce (6) because this would invoke the intermediacy of an axial acetate.



SCHEME 6

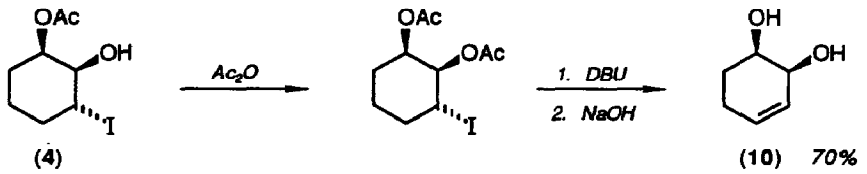
In contrast to the complete selectivity of the reaction of N-iodosuccinimide, N-phenylselenophthalimide exhibits no selectivity in its reaction with (4) (scheme 7).



SCHEME 7

Thus treatment of (4) with NPSP[10] in the presence of water[11] gave in good yield a mixture of equal portions of regiomeric hydroxyselenides. This means that in this reaction there is no face selectivity in the formation of selenonium ion, which is more in accord with other reactions of electrophiles with acetoxycyclohexene.[9] The structural elucidation of the products of this reaction and a fuller discussion of the factors leading to lack of control in this reaction will be reported elsewhere.[12]

Compound (4) is a useful synthetic intermediate in the preparation of cyclitols; for instance, acetylation and elimination of HI from (4) gives *cis*-1,2-diacetoxycyclohex-3-ene in excellent yield (scheme 8). Hydrolysis of this compound gives (±)-3,4-dideoxyconduritol D (10). Since most cyclitol synthesis commences with modification



(4) (10) 70%

SCHEME 8

of *cis*-diols obtained from microbial hydroxylation reactions, the sequence shown above represents a novel entry into such compounds. Extension of the methods shown above to allow preparation of other hydroxylated natural products is a focus of our research at this time.

Acknowledgement

We gratefully acknowledge the financial support of the SERC and the Nuffield Foundation.

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6. Data for (4): ν_{max} (CCl_4)/cm^{-1} 3600 (OH), 1742 (CO); δ_H (270MHz; $CDCl_3$) 1.38-2.45 (6H, m, 3 x CH_2), 2.08 (3H, s, Me), 2.48 (1H, brs, OH), 3.74-3.83 (1H, m, CHI), 4.25-4.37 (1H, m, CHOH), 5.22-5.30 (1H, m, CHOC(O)Me); δ_C (67.5MHz; $CDCl_3$) 170.61 (C), 75.38 (CH), 71.59 (CH), 36.52 (CH_2), 34.08 (CH), 28.30 (CH_2), 21.89 (CH_2), 21.16 (CH_3); m/z 284 (M^+, 0.7%), 266 (1.9), 157 (27.8), 97 (79.0), 79 (24.1), 43 (100).
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(*Received in UK* 20 *December* 1993; *accepted* 7 *January* 1994)