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THE STEREOCHEMISTRY OF THE CLEAVAGE OF CYCLOPROPANES BY MERCURIC ACETATE[1]

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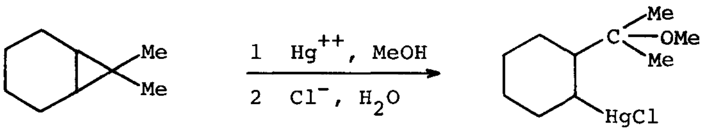
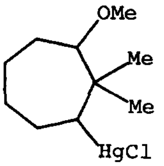
Because of the current interest[2] in the stereochemistry of electrophilic aliphatic substitution, we with to report the results of reaction of 7,7-dimethylnorcarane, 1, and norcarane with mercuric acetate. Cleavage of 1 in methanol (30 hrs, 25°) after filtration to remove mercurous acetate (10%) and addition of chloride ion yielded 90 ± 2% crude chloromercurial. On the basis of the evidence presented herein, the isolated organomercurial is a mixture of 83% trans- and 17% cis-2(1-methoxy-1-methylethyl)-1-chloromercuricyclohexane, 2, the Markownikov cleavage product of 1 (eq 1).



1

2a trans 83%
2b cis 17%

(1)



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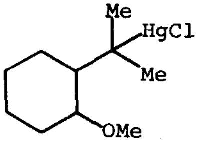

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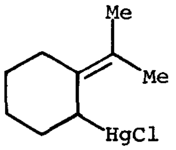


5

Nmr spectra of the isolated mercurial and of its reduction product, as well as glpc analysis of the latter, showed no indication of compound 3, which probably would have survived the cleavage conditions if formed. The acetoxymercurial corresponding to 4, the formation of which would require a particularly unlikely anti-Markownikov cleavage, should undergo rapid solvolytic demercuration[3] under the cleavage conditions (eq 2).

$$RHg^{+} \longrightarrow R^{+} + Hg^{0} \tag{2}$$

$$Hg^{O} + HgOAc_2 \longrightarrow Hg_2OAc_2 \qquad (3)$$

This could account for the observed mercurous acetate but a more likely candidate is the allylic mercurial 5, the corresponding acetoxymercurial of which would also demercurate rapidly under the cleavage conditions.[3,4]

The major compound, 2a, can be readily isolated from the cleavage mixture by recrystallization from acetone, mp 82-85°.[5] The minor compound, 2b, was obtained (15-30% yield) by epimerization[6] of 2a by heating with benzoyl peroxide in pyridine. Separation and purification of the mercurials was accomplished by extraction into aqueous thiosulfate and precipitation with iodide ion followed by column chromatography on alumina. Conversion of the iodo- to the chloromercurials by, (1), AgOAc and (2), NaCl gave 2a as described above and 2b, mp 115-116°.[5]

The nmr spectra in CCl_4 of both 2a and 2b showed downfield singlets at δ 3.21 due to the methoxyl protons. Upfield, however, the Me_2C groups of each compound, with magnetically inequivalent methyls, produce separate doublets: 2a (δ 1.12, 1.06), 2b (δ 1.23, 1.17). The nmr spectrum of the cleavage products is fully accounted for by the spectra of 2a and 2b. In pyridine solution, the methoxyl singlets are resolved (2a, δ 3.15, 2b, δ 3.09) and give, by integration, a 2a:2b ratio of 83:17 in the cleavage reaction.

The proton α to mercury, H_α, appears in the nmr spectrum of 2a as a broad doublet centered at δ 2.28 (CCl_4) with a total half-height width (W_H) of ca. 20 Hz. H_α of 2b is a single peak at δ 2.97 with a W_H of 8 Hz. The broader splitting pattern and upfield chemical shift of H_α in 2a indicate that it is an axial proton and thus that 2a is trans whereas the nmr parameters of H_α in 2b are consistent with its being an equatorial proton, i.e., that 2b is cis.

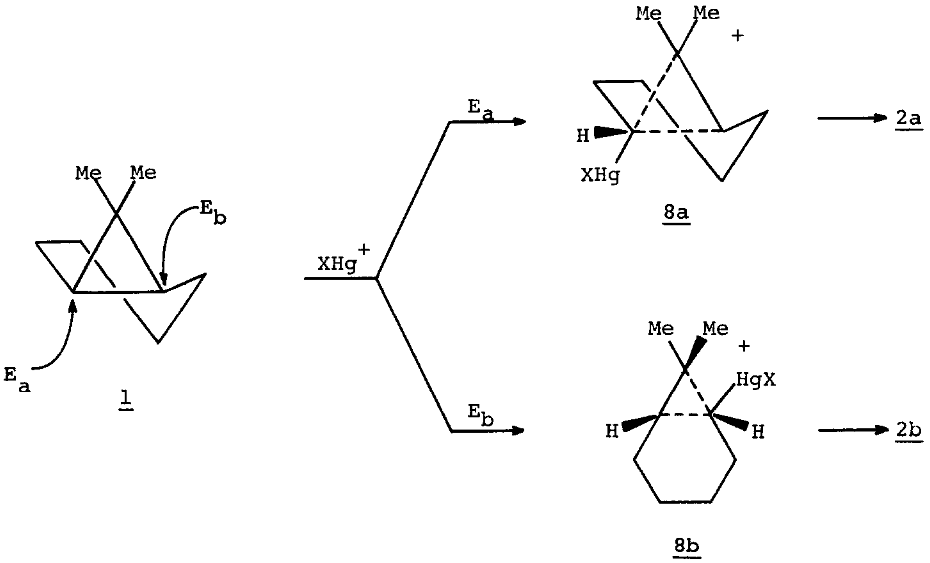
Chlorodemercuration of 2a in pyridine yields a single alkyl chloride, 6a. The resonance of H_α occurs as a sextet centered at δ 3.98 (CCl_4) produced by a coupling of 8.2 Hz to two protons plus coupling to a third with a constant of 4.0 Hz. This splitting pattern corresponds uniquely to an axial proton in the expected position. The alkyl chloride 6a is thus trans and therefore, since the chlorodemercuration is stereoretentive,[6b,7] 2a is the trans-chloromercurial.

Chlorodemercuration of 2b under the same conditions, however, yields a 1:1 mixture of 6a and its cis isomer, 6b. The nmr spectrum of the product shows, in addition to H_α of 6a, H_α of 6b as an unresolved band centered at δ 4.55 (CCl_4) with a W_H of 7 Hz and resembling H_α of 2b itself. Halodemercuration of oxymercurials in special situations sometimes gives some product with inverted stereochemistry.[6b] It has been postulated that this is due to prior complexation of electrophilic halogen with the oxygen atom followed by internal cleavage of the carbon-mercury bond, either frontside or backside.[6b] In the case of 2a, backside cleavage should be facile only with the very unfavorable diaxial conformer and thus no inverted product is observed. For 2b, on the other hand, the favored conformer, with mercury axial, appears well suited to backside attack.

Further evidence for the assignment of 2a as trans was obtained by the stereoretentive replacement of mercury by deuterium from the reduction of 2a with sodium amalgam in deuterium oxide and the stereoconvergent reduction by sodium borodeuteride.[8] Based on the generalizations of Corey,[9] the C-D stretching frequencies of the stereoretentive reaction product were assigned as equatorial, which indicates that 2a is the trans-chloromercurial.

The stereochemistry of the nucleophilic attack, not ascertainable from the results for 1, was investigated for the hydroxymercuration of norcarane, 7. The mercurial, trans-2-hydroxycyclohexylmethylmercuric chloride, previously characterized by Levina, was obtained in 83% yield. It was shown to be essentially the sole product by careful glpc analysis of the product of the reduction ($NaBH_4$) of the crude cleavage product which showed only trans-2-methylcyclohexanol and a trace (∿0.1%) of cycloheptanol. No cis-2-methylcyclohexanol or cyclohexylmethanol were detected.

Thus, cleavage of 1 with mercuric acetate in methanol proceeds with predominant inversion of configuration for the electrophile and the cleavage of 7 in water proceeds with 100% inversion for the nucleophile. These results can be rationalized by a mechanism involving intermediate corner-mercurated cyclopropanes,[1,2a] for 1, structures 8a and 8b of eq. 4.



(4)

In these representations it is assumed that attack occurs from the least hindered side of the C_6 ring, although other factors may also be important. Thus, E_a attack, which leads to inversion predominates. In the cases of 8a and 8b, the products may be obtained through ring opening to yield a tertiary carbonium ion, RC^+Me_2, which could either undergo nucleophilic trapping by solvent to give 2a and 2b, respectively, or eliminate a proton to give the proposed intermeidate allylic mercurial 5. The analogous intermediate for 7 apparently undergoes direct nucleophilic trapping, resulting in the observed complete inversion for the nucleophile.

In the previous work, both retention and inversion have been observed in different systems for S_E2 substitution at saturated carbon.[2b-d,6b] For the closely related S_E2 cleavage of cyclopropanes, both inversion and retention are observed in the same reaction.[2a] Although the cleavage of cyclopropanes may represent a special class of S_E2 type reactions, the finding here support the general idea that the difference in energy for retention *vs.* inversion is small and the observed stereochemistry may result from peculiarities of a particular system.

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