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ANIONIC FRAGMENTATION OF A PERCHLORINATED CAGE AMINE - A REMARKABLE REARRANGEMENT[1]

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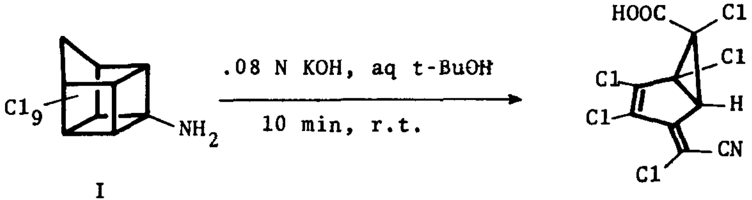
I report here the fascinating result depicted in equation 1, and propose a mechanism rationalizing the novel and deep-seated rearrangement taking place.

Eq. 1)

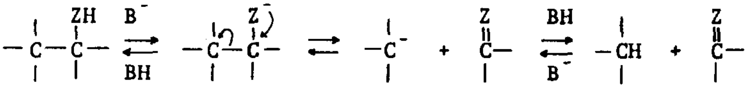


I

III

Although the anionic fragmentation of alcohols in the sense of equation 2a, exemplified by the retrograde aldol reaction and the base-catalyzed cleavage of cyclopropanols,[2a] cyclobutanols[2b,c] and even unstrained alkanols[3] is well-documented, the analogous fragmentation of amines is much less familiar.

Eq. 2)



a) Z = O, b), Z = NH Or NR

Presumably the major factor in the greater stability of amines is the lower carbon-nitrogen π-bond strength in imines - 68 kcal/mole[4a]--compared to 90-93 kcal/mole for the carbon-oxygen π-bond of aldehydes and ketones,[4b] though the lower acidity of amines would play a role also. To make up for the relative weakness of the developing π-bond in process 2b, the carbon-carbon σ-bond being broken must be especially labilized by strain or by stabilization of the incipient carbanion. Aside from some instances of the retro-Mannich reaction, I am aware of but one prior example of reaction 2b in which the starting material and product are well-characterized,[5] and several others in which the reaction is probable,[6] but it is likely that the process will become recognized as a common source of instability as the chemistry of small-ring amines develops further.[7]

Early in our studies of highly-chlorinated cage compounds, we observed that amine I and the related 4-amino-9,9-ethylenedioxyheptachlorohomocubane (II) were labile to base;[8] the initial observation was that attempts to prepare II by basic hydrolysis of its urethan or sym-urea derivatives led to complete decomposition and evolution of ammonia,[8c] but further study showed that even very mild base treatment converted I to a mixture of products.[8b] In one particular case a crystalline degradation product was easily isolated in pure form: 2.00 g of I was dissolved in 50 ml of t-butanol and the solution mixed with 50 ml of 0.16 M aqueous potassium hydroxide. After ten minutes at room temperature the homogeneous reaction mixture was poured into 1 N sulfuric acid and worked up by ether extraction; from acidification of the subsequent bicarbonate extract I isolated 343 mg (26%) of a crystalline carboxylic acid, (III) which was not purified but converted with diazomethane into its methyl ester IV for characterization. The ester, after recrystallization from hexane and vacuum sublimation, proved to have composition $C_{10}H_4O_2Cl_5N$, (**found:** C, 34.37; H, 1.22; Cl, 50.18; N, 4.23) m.p. 86-88°, and the following significant spectroscopic properties: ir, (CCl_4) 3060 (w), 2957 (w); (C_2Cl_4), 2220 (w), 1756 (s), 1600 (w), and 1540 (m) cm^{-1}; uv, λ_{max}^{hexane} 302 (17,500); nmr (CCl_4) δ 3.78 (s, 3H) and δ 3.33 (s, 1H).

The 2957 cm^{-1}, 1756 cm^{-1} and δ 3.78 absorptions may be attributed to the carboxymethyl group, the 2220 cm^{-1} absorption to a cyano group, the 1600 cm^{-1}, 1540 cm^{-1} and 302 nm bands to a conjugated diene system, and the 3060 cm^{-1} and δ 3.33 absorptions to a hydrogen bound to a cyclopropane ring.[9] Unable to reconcile these data with a unique structure derivable in a rational manner from Ia, I submitted crystals of the compound grown by vacuum sublimation to Professor R. Bau of this department for an x-ray crystallographic study.[10] Ester IV turned out to have the novel homofulvene structure shown, methyl 4-Z-(chlorocyanomethylene)-1,2,3,6-tetrachlorobicyclo[3.1.0]hex-2-ene-6-syn-carboxylate.

In hindsight, the mechanism shown in Chart I may be postulated for this remarkable rearrangement; except for the novel but plausible fragmentation iii→iv, all steps have good analogy: ionization of a 7-chlorine, ordinarily unreactive in a norbornene so heavily substituted with electron-withdrawing substitutents,[11a] would be much more ready in the enolate-like species vi;[11b] ready base cleavage of the ketone-hydrate vii is well known for polyhalo-norbornenones;[12] and the formation of the cyclopropane ring, viii→III resembles in geometry the familiar norbornene-nortricyclene rearrangement. Several steps are written as concerted for economy of intermediates rather than out of conviction, though loss of chloride concerted with scission of the last cyclobutane ring accounts nicely for the stereochemistry about the exocyclic double bond.

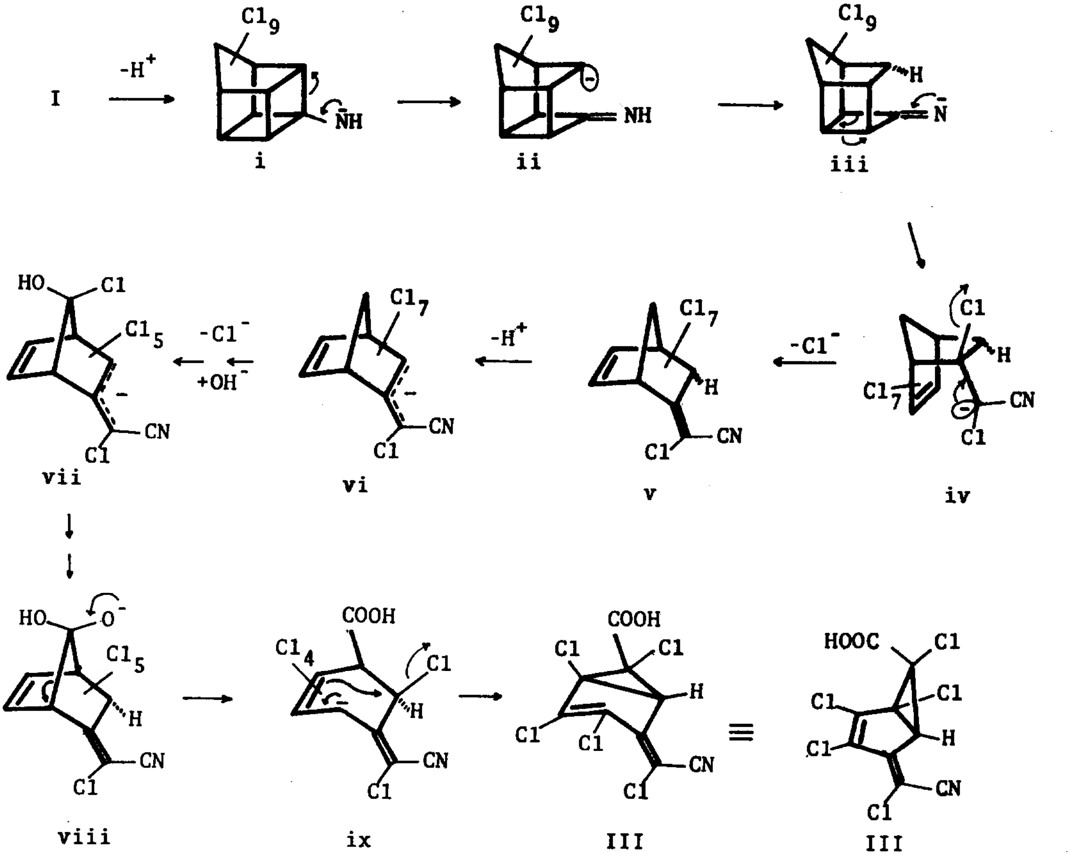


Chart I

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