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AN UNEXPECTED β-ELIMINATION FROM 3,3-DIFLUOROCYCLOBUTANECARBONITRILE.[1]

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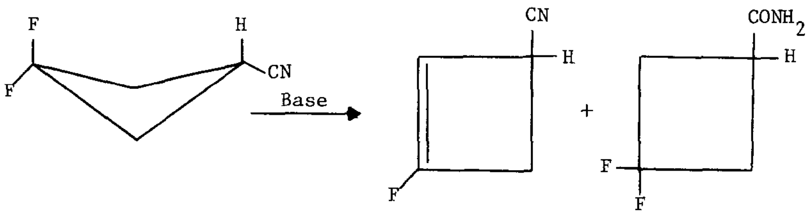
Abstract: 3,3-Difluorocyclobutanecarbonitrile (2) reacts with bases to give β rather than γ-elimination, the latter being the prevailing reaction mode in similar systems.

As compared to β elimination reactions, γ-eliminations are only seldomly encountered. The probability for γ-elimination to occur improves as the distance between carbons 1 and 3 is shortened relative to the distance prevailing in the corresponding open chain compounds. Thus, cyclobutane in which carbons 1 and 3 are separated by ca. 2.1Å [2], may be a suitable candidate for facile γ-elimination reactions. The short distance between the two non-bonded carbons enables them to interact efficiently with each other. It is therefore not surprising that γ-elimination is one of the most frequently employed methods for the synthesis of bicyclobutanes.[3] In the course of our studies of the cyclobutane-bicyclobutane system we attempted to prepare the 3-fluorobicyclobutanecarbonitrile (1) by γ-eliminating HF from 3,3-difluorocyclobutanecarbonitrile (2, prepared by treating 3-oxobicyclobutanecarbonitrile with SF_4 in moist CH_2Cl_2 for 24 hr. ^1H NMR; δ ($CDCl_3$) 2.95 (m,5H), IR: 2280 cm^{-1}, Mass Spect, CI, 118). The elimination reaction itself was performed under various conditions (t-BuO$^-$, ether; t-BuO$^-$, t-BuOH; NaH, THF. Temperature ranges -10 to 30°C) which had been used previously in other cases for the preparation of several bicyclobutanes.[3] Yet, instead of the expected bicyclic compound 1, 3-fluoro-cyclobuta-2-enecarbonitrile (3), the product of a β-elimination reaction was obtained.[4] (^1H NMR δ ($CDCl_3$) 4.9 (d,1H), 3.2 (m,3H). Mass Spect, CI, 98. This was sometimes accompanied by the carboxamido compound 4, ^1H NMR δ ($CDCl_3$) 7.2 (d,2H), 2.7 (m,5H)).



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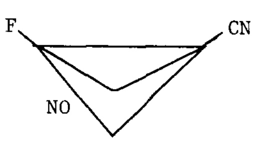

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Since a variety of other bicyclobutanes do not rearrange under these conditions to cyclobutenes, there is no reason to assume that 1 is first formed and then rearranges to the olefinic product 3.

In order to show that the failure of the system to undergo a γ-elimination reaction does not result from a low acidity of the proton on C-1 (α to the cyano group) we have carried out the reaction in deuterated solvent (17% t-BuOD in ether v/v with t-BuO$^-$ 0.13 M). After 10% conversion, the reaction mixture was mass spectrometrically analyzed for deuterium incorporation. It was found that the unreacted starting material incorporated only a single deuterium atom (*ca*. 70% incorporation) indicating that *only* the proton α to the cyano group was exchanged. Thus, although the anion at C-1 was formed, it failed to expel a fluoride anion from the gem-difluoride at C-3, and yet, this system which successfully resisted γ-elimination was rather highly susceptible to β-elimination (probably E2).

It should be pointed out that the facile β-elimination reaction can not be attributed to the simple inductive effect which is exerted by the gem-difluoride group on carbons 2 and 4. This is evident from inspection of the σ* values[5] of various substitutents on C-3 of cyclobutanecarbonitrile: 0.75 (CH_3,I); 1.05 (H,Cl); 1.21 (Ph,Cl); 1.94 (Cl,Cl); 2.35 (CN,Cl). In all these systems, only γ-elimination was observed.[3] Yet although the σ* values of the difluoride is within this range (2.05), it undergoes β rather than γ-elimination. It is thus clearly demonstrated that neighboring proton acidification by simple inductive effects is not the major (if at all) factor governing the energetics of elimination reactions.

Another conclusion which should be inferred is that nucleofugality (leaving group rank as defined by Stirling[6]) is not an absolute feature of the nucleofuge but depends on the course of the reaction and might also show some dependency on the specific molecular system investitated. This conclusion is highly supported by results recently reported by Stirling et.al.[7]

References and Notes

1) This is part 4 in the series: Cyclobutane-Bicyclobutane System. For part 3 see: Hoz, S.; Aurbach, D. J. Am. Chem. Soc. 1980, 102, 2340.

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4) Products were obtained by preparative gas chromatography with a 10% XE60 on Chromosorb W, acid washed 60-80 mesh.

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