QUINUCLIDIN-4-YL ANION. GENERATION AND STABILITY COMPARISON BY RADICAL ANION REDUCTION

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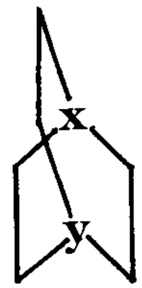
Abstract - Radical anion reduction of 4-bromoquinuclidine and 1-bromobicyclo-[2.2.2]octane leads to similar product distributions. The lone pair of electrons on the nitrogen atom in the heterocyclic compound do not affect the anion stability.

The bridgehead positions in a bicyclo [2.2.2]octyl system provide a valuable framework for studies of long-range orbital interaction in saturated systems.[1] These interactions can be either stabilizing or destabilizing depending upon the number of electrons and the various effects can be classified as occurring via "through space" or "through bonds" mechanisms.[2] A particular excellent example of the latter involves the lone pairs on the two nitrogen atoms in diazabicylooctane [DABCO] (3c) which interact very strongly and lead to a structure with extensive delocalization as indicated by both experimental[3] and theoretical evidence.[4]



X	Y	Compound
N	C	1
CH	C	2
N	N	3

a = 2 electrons
b = 3 electrons
c = 4 electrons
d = Br

The quinuclidin-4-yl (1) system with a nitrogen and carbon atom offers intersting possibilities for testing interactions. The consequences of differing orbital energies bears directly on the various models to account for interaction. Accordingly by suitable selection of reaction and comparison with the model system the effects of the nitrogen lone pair on the chemical reactivity and stability of the carbon bearing orbitals can be studied for the full range of chemical intermediates.

For the cationic system with 2 electrons, (1a) solvolyses studies reveal a large rate factor (~10^4) for the heterocyclic compound (1d) relative to the carbocyclic (2d).[5] Additionally, the sole product is that arising from fragmentation reaction. There is little doubt that the nitrogen interacts appreciably. Surprisingly chemical and EPR studies reveal that radical stabilization and/or electron interaction is comparatively unimportant for the radical species (1b) (3 electrons).[6] In this communication we describe experiments which demonstrate that the anion (1c) (4 electron system) is not destabilized by the heteroatom and that there is essentially no interaction between the nitrogen lone pair and the lone pair of the carbanion.

We have used a novel competitive radical anion technique for comparing the stability of the quinuclidin-4-yl anion (1c) and the structurally related bicyclooctyl anion (2c). *This method* avoids the manifold difficulties of equilibration studies of organometallics in this range of hydrocarbon *acidity*. *Equilibration methods are limited* by the aggregation of organolithium compounds in ether which vary with structure in often unknwon ways leading to problems.[7] Our *methods* derives from the well studied reduction of alkyl halides to monomeric and essentially uncompleted anions by aromatic radical anions.[8]

$$RX + Naph^{\ominus} \rightarrow R\cdot + X^{\ominus} + Naph \qquad (1)$$

$$R\cdot + Naph^{\ominus} \left\{ \begin{array}{l} \xrightarrow{a} R^{\ominus} \rightarrow RH \\ \xrightarrow{b} R\text{-}Naph^{\ominus} \rightarrow R\text{-}Naph\text{-}H \end{array} \right. \qquad (2)$$

Reaction of sodium naphthalene radical anion for example with alkyl halides leads to two major products, a hydrocarbon reduction product and alkylated adduct. Radical formation (equation 1) is *rate determining and partitioning occurs in the subsequent* competitive steps.[9] Discrimination occurs at steps 2a and 2b. Electron transfer reaction (equation 2a) from a second molecule of *radical anion* produces a carbanion which subsequently abstracts a proton yielding the reduction product. Radical-radical anion coupling (eq. 2b) with a second molecule of radical anion leads to the alkylated dihydronaphthalene adduct. Often the partitioning is about equal and reactivity factors can be conveniently studied. This partitioning forms the basis of this carbanion stability study.

The extent of reduction relative to coupling has been varied by increasing the stability of anions and by increasing the steric effects of the aromatic radical anion. Thus, for example benzyl and allyl systems lead to predominant (~95%) reductions.[10] In the present use of this partitioning we note that the relative amounts of reduction for the 4-quinuclidinyl and bicyclooctyl radicals reflects the anion stabilities since the radicals are known to have comparable stabilities[6] and the steric effects to coupling are essentially the same.

The 4-quinuclidinyl and 1-bicyclooctyl bromides (1d and 2d) were prepared according to literature *procedures*[11,12] *and a representative reduction was run* as follows. A weighed amount of 4-bromoquinuclidine (9.7 mg, 0.051 mmol) hexadecane (10.0 mg, 0.044 mmol) and 0.5 ml of dry benzene in a small vial was sealed with a septum and degassed with Argon. A tetrahydrofuran solution of sodium naphthalene (0.4 ml, 0.22M, .088 mmol) was added by syringe until the green color just persisted. After five minutes the solution was a clear light yellow. The solution was then analysed by gas liquid chromatography for the reduction product, quinuclidine. The extent of coupling can be obtained by subtraction from 100% since it is known that the only products are alkylation and reduction.[9] In select instances alkylated products were isolated by column chromatography and characterized by spectroscopic methods (MS and NMR).

Table. Product Distribution from Sodium Naphthalene Reduction of Select Tertiary Halides[a]

Halide (RX)	% RH[b]	% R-Naph-H[c]
1-Adamantyl Bromide	41	59
1-Bicyclo[2.2.2]octyl Bromide	42	58
4-Bromoquinuclidine	50	50
<u>Tert</u>. Pentyl Iodide	39[d]	61[d]

a) In tetrahydrofuran-benzene at 20°C.

b) Analysed by glpc and the values given are averages of replicate reductions.

c) Determined from reduction yield and subtraction from 100% since dimerization does not occur.

d) G. D. Sargent and G. A. Lux., J. Am. Chem. Soc. 1968, 90, 7160.

The table records the results for the relevant bridgehead halides along with others for comparison. Most importantly reaction of sodium naphthalene with 4-bromoquinuclidine afforded nearly equal amounts of adduct and reduction product. In actual fact slightly more adduct was formed with the model system 1-bromobicyclooctane. Significantly, the product distribution which is dependent upon anion stability is the same for the heteroatomic and carbocyclic system. Accordingly it is unlikely that the quinuclidin-4-yl anion is destabilized as is demanded by interaction of the nitrogen lone pair orbital and the carbon anion orbital. Additionally, this contrasts with the known destabilization of carbanions by β hetero nitrogen atoms[13] and clearly points to an absence of any long range electron interaction.

Another interesting feature that emerges upon inspection of the table concerns the parallel amount of reduction for tertiary acyclic and tertiary bridgehead systems. Clearly the alkylation step can not have strong stereochemical demands. Among other implications an SN 2 process is ruled out by this result.

There is value in comparing the results of orbital interaction for the heterocyclic systems with one and two nitrogen atoms at the bridgehead positions. For the DABCO system there is large interaction for the radical cation (3b) (3 electrons) and for the neutral amine (3c) (4 electrons). Delocalization and long range interaction in this system likely derives much (if not most) from the orbital degeneracy. In the quinuclidin-4-yl system the 3 electron radical and 4 electron anion show no evidence of the respective stabilization and destabilization expected from orbital interaction. The disparate energies of the interacting orbitals renders the interaction small or non-existent.

For this system only the cation (2 electrons) shows any interaction terms and the cation likely derives stabilization via a mode other than delocalization. On the one hand there is a concomitant fragmentation with strain relief. On the other hand Professor Brown has investigated a related isoelectronic species with a nitrogen atom and a boron at the bridgehead positions and concludes that the species has the strong nitrogen lone pair interaction giving rise to the "triptych" structure.[14] Were such forms to contribute to the quinuclidine cation stabilization would be expected.

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