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THE ROLE OF LONE-PAIR MOBILITY ON THE DIRECTION OF GEOMETRIC ISOMERIZATION IN MODEL ANNULATED AZONINES; AROMATIC STABILIZATION vs. SKELETAL STRAIN

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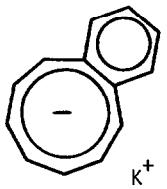
Benzannulated anions 1 and 1' were recently shown here to undergo an unprecedented cis → trans isomerization yielding the mono-trans variants depicted in 2a[1] and 2b.[2] We have since extended our work in the area to the corresponding pyridazino azonines and have also examined the thermal response of all currently available N-substituted mono-trans variants, i.e., 4. In this report we present our findings on the subject with emphasis placed particularly on the fact that the cis → trans process observed earlier[1,2] may be induced to reverse by properly restricting the lone pair mobility of the system's π excessive center.



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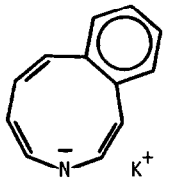
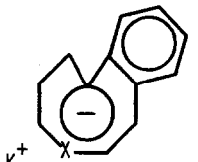


1'

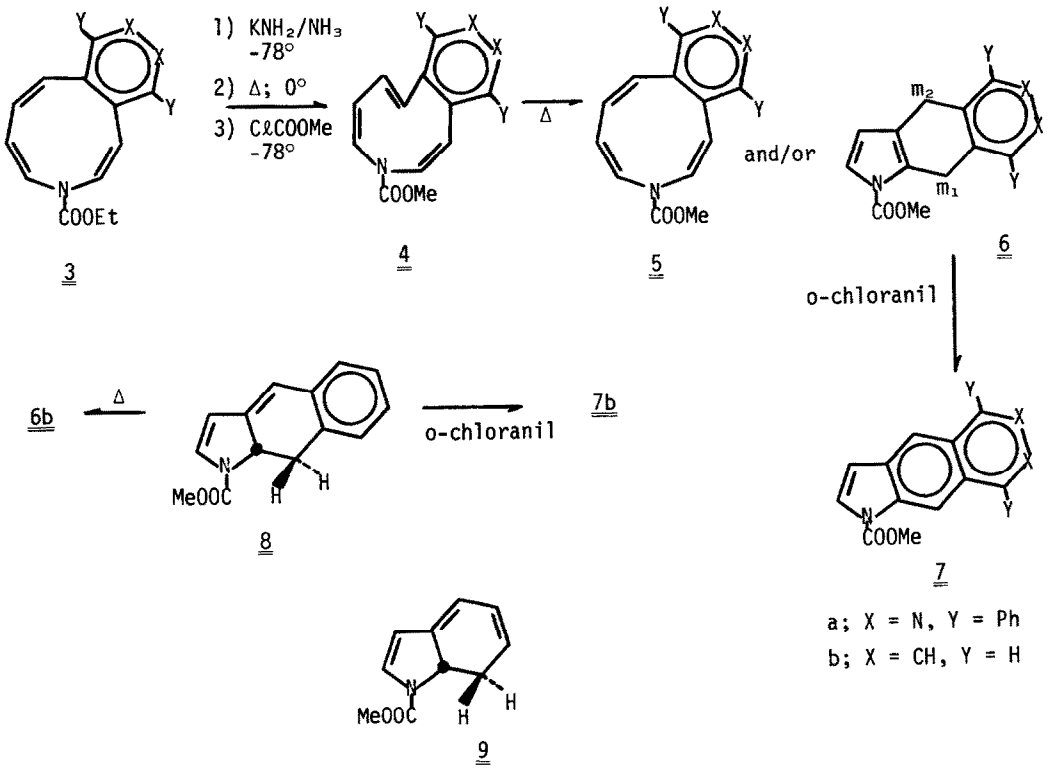


2

a; X = CH
b; X = N

Exposure of the all-cis pyridazino azonine, 3a[3] to potassium amide in liquid ammonia at ca. -78° followed by warming to 0° (~2 hr) then quenching with methyl chloroformate at -78° produced 4a (mp 127-128°; ^{1}H-NMR, UV, IR, MS) in ca. 50% yield. This substance readily isomerizes in hot benzene ($\Delta G^{\ddagger}_{61.3°}$ = 25.5 kcal/mol.)[4] cleanly yielding a two-component mixture shown (^{1}H-NMR) to consist of isomers 5a and 6a in a ratio of ca. 2:1. Separation by column chromatography at ca. -15°, yielded pure samples of the known pyridazino azonine 5a (IR, ^{1}H-NMR)[3] and an air sensitive white solid (mp 160-161°) possessing spectroscopic characteristics (^{1}H- and ^{13}C-NMR, MS, IR) which are clearly indicative of the tricyclic structure depicted in 6a.[5] It is notable that our preference for 6a over its two dihydrophenanthrene-like position isomers (not shown) draws primarily from the

results of ^{1}H-NMR shift studies conducted on 6b[6] (vide infra). Chemically, the presence of a "linearly"-fused skeleton in 6a was confirmed by the molecule's ready oxidation by o-chloranil to produce 7a (mp 154-156°; ^{1}H-NMR, IR, MS) a substance whose anthracene-like frame is clearly indicated by the appearance of the two available "aromatic" protons as sharp singlets in the ^{1}H-NMR spectrum.



The thermolytic response of 4b in benzene at 140° sharply contrasts that of its triaza analog, 4a, insofar as the molecule slowly ($\Delta G^{\ddagger}_{140.°}$= 32.5 kcal/mol.; $t_{½}$ = 224 min.)[4] rearranges to a single air sensitive product shown (^{1}H-NMR) to possess the structure depicted in 8. Particularly revealing in the NMR spectrum of this substance is the appearance of one of the two methylene protons as a strongly coupled dd (J = 17 Hz, 14 Hz), i.e., a situation previously encountered with the molecule's debenzo counterpart 9.[7] Operationally, a notable feature of 8 is that while stable at the temperature (140°) required for its formation it slowly ($t_{½}$ ~ 10 hr.) rearranges at 198° to yield 6b[8] (mp 64-66°; spectroscopically analogous to 6a). Particulary revealing in the structural elucidation of 6b were the results of ^{1}H-NMR shift studies and specifically the finding that the presence of shift reagent [Eu(fod)$_3$-d$_{27}$] induces the low-field methylene unit (m_1) to shift at a significantly faster pace (~4X) than its higher-field counterpart m_2; consistently, the relative shifts

of the various proton functions affected by the reagent were found to be in the order: Me > H^{α} > m_1 > H^{β} > m_2. Chemically, the structures depicted in 6b and 8 were confirmed by their ready conversion to 7b (mp. 71-71.5°; spectroscopically analogous to 7a) on treatment with o-chloranil.

With regards to mechanism, the conversion of 8 to 6b clearly entails 1,3 shift of the reactant's single available methine hydrogen, while the rearrangement of 4b to 8 may be conjectured to obtain via a two-step sequence analogous to that previously advanced to explain the formation of 9 from the de-benzo analog of 4b, i.e., the corresponding cis,[2] trans, cis azonine.[7,9]

Useful mechanistic insight into the nature of the heat-induced response of 4b was gained by effecting its thermal activation in a variety of solvents. Briefly, what we find is that while such basic media as pyridine and triethylamine-contaminated benzene promote slow rearrangement, $t_{1/2}$ (140) ~ 100 min. and 213 min. respectively, exclusively to 8, use of either pure chloroform or benzene contaminated (<10%) with acetic acid rapidly leads, $t_{1/2}$(140°) ~ 5 min., and $t_{1/2}$(80°) ~ 116 min., respectively, in each case to the exclusive formation of the cis isomer 5b![10] Quite obviously the conversion of 4b to 5b is catalyzed by acid, the $\Delta G^{\ddagger}$ term controlling this process in acidified benzene being a striking 5 kcal/mol. lower than that needed to activate the 4b to 8 transformation in the neutral solvent.

In conclusion, we might briefly stress that the trans → cis isomerization described in this report undoubtedly arises as a means of releasing skeletal strain. Further, this interesting reversal in the direction of isomerization previously observed for anions 1[1] and 1'[2] and that derived from pyridazino azonine 3a, i.e., cis → trans, where aromatic stabilization with its requirement for planarity clearly dominates the change, firmly establishes the crucial influence that lone pair mobility has in determining the system's preference for a specific geometric arrangement.

Acknowledgement: We are grateful to the National Science Foundation (CHE76-06462) for support of this work.

Reference and Notes

(1) A. G. Anastassiou and E. Reichmanis, Angew. Chem. 86, 784 (1974).

(2) A. G. Anastassiou and E. Reichmanis, Chem. Commun., 149 (1975).

(3) A. G. Anastassiou and E. Reichmanis, Chem. Commun., 313 (1976).

(4) This value was determined upon monitoring the consumption of reactant by ^{1}H-NMR spectroscopy.

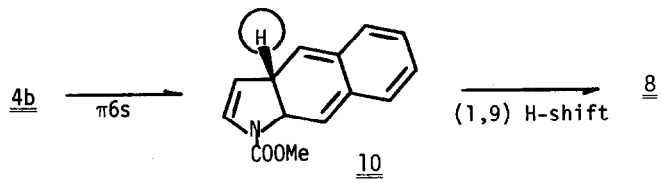
(5) Particularly informative in the structural elucidation of 6a was the combined nmr information which clearly requires that the molecule (i) lack molecular symmetry as indicated by the presence of two mutually coupled 1H doublets in the pmr spectrum attributed to H^{α} and H^{β}, (ii) incorporate a small-size π excessive heterocyclic moiety as required by the small magnitude of $J_{\alpha,\beta}$ (~ 4 Hz) and (iii) possess two distinct CH_2 units as evidenced by the presence of 1. two well separated 2H resonances in the "benzylic" region of the pmr spectrum and 2. two closely shifted triplets (J_{C-H} = 135 Hz) in the "aliphatic" region of the H-coupled cmr spectrm.

(6) The interpretation of the results obtained by conducting the "shift studies" on 6a are complicated by the fact that at low shift-reagent concentration complexation occurs predominantly on the pyridazine moiety of the molecule; the key carbamate function does not appear to participate in complexation until substantial shift reagent proportion is attained.

(7) A. G. Anastassiou, R. L. Elliott, H. Wright and J. Clardy, J. Org. Chem. 38, 1959 (1973).

(8) This transformation occurs at a conveniently faster pace when activated in chloroform; $\Delta G^{\ddagger}_{140.^{\circ}}$ = 30.5 kcal/mol; $t_{\frac{1}{2}}$ ~ 23 min.

(9) In the present instance such a process would entail 6π disrotatory electrocyclization to the trans-fused o-quinodimethane shown in 10 followed by [1,9] shift of this molecule's doubly allylic hydrogen.



(10) A. G. Anastassiou, E. Reichmanis and R. L. Elliott, Tetrahedron Letters, 3805 (1973).

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