Tetrahedron Letters,Vol.23,No.23,pp 2339-2342,1982 0040-4039/82/232339-04$03.00/0
Printed in Great Britain

AZIRINYL AND DIAZIRINYL (CHLORIDE) ION PAIRS AS INTERMEDIATES

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Summary. Both ab initio calculations and experimental observations support the intermediacy of diazirinyl or azirinyl cation-chloride anion pairs in transformations (1), (2), and (4).

The final step in the proposed mechanism of Graham's chlorodiazirine synthesis[1,2] features isomerization of isodiazirine 1 to diazirine 2; eq. (1). In an isoelectronic process, isomeric azirines 5(d,e) and 5'(d,e) interconvert;[3] eq. (2). These transformations have been suggested to involve either "bridged polar transition states" 3 (or 6) or diazirinyl (azirinyl) cation-chloride anion pairs 4 (or 7).[1,3] More recently, azirinium ion 7c was suggested as an intermediate in reactions of 5c,[4] although the free cation should be highly energetic.[5]

The uncertainty[1,3a,b] over the best formulation for transformations (1) and (2)[1,2,4] led us to calculate transition states and activation energies for these reactions. The results favor ion pair intermediacy, and are reported here together with new experimental observations.

We carried out ab initio molecular orbital calculations with the GAUSSIAN 80 series of programs[6] in the restricted Hartree-Fock approximation utilizing a split valence 3-21G basis set.[7] No symmetry constraints were imposed in geometry optimizations of reactants 1a,b, 5a,b, products 2a,b, 5(5')a,b, or transition states (and the corresponding free cations), except that the methyl groups were kept locally tetrahedral with fixed C-H bond lengths (1.09Å). Transition states were rigorously located as stationary points with only one negative eigenvalue of the force constant matrix, and it was ensured that the associated eigenvector did lead towards the product.[8]

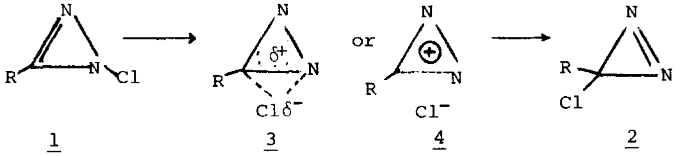
The conversion 1a → 2a was calculated to be exothermic by 24.0 kcal/mol, and a transition state was located 32.6 kcal/mol above 1a; 1b → 2b was exothermic by 18.2 kcal/mol, with a transition state 29.5 kcal/mol above 1b. Geometrical parameters for the parent and methylated structures were similar, and essential values for the latter appear in Figure 1. Importantly, the geometry of the ring in the transition state resembles that of the free methyldiazirinium ion, where N-N = 1.345Å and C-N = 1.337Å. In accord with this structural change is the significant charge separation, relative to reactant or product, reflected in the increased net charge on Cl (-0.65 vs. -0.04 in 1b or 0.08 in 2b) and in the dipole moment (8.47D vs. 5.29D in 1b or 2.72D in 2b). Most significantly, Mulliken population analysis[9] reveals virtually no residual bonding between Cl and C or N atoms in the transition state; the C-Cl overlap population is ~0.05, and for Cl-N it is ~-0.03.

The parent azirine interconversion, 5a ⇄ 5'a, has a calculated activation energy of 36.1 kcal/mol, but methylation (i.e., 5b ⇄ 5'b) lowers the barrier considerably to 22.8 kcal/mol. The transition states possess C_s symmetry and essential parameters for the methylated species are shown in Figure 2. Again, transition state bond lengths are very similar to those of the free dimethylazirinyl cation (C-N = 1.344Å, C-C = 1.360Å) and the Cl acquires close to a full unit of negative charge (-0.82 vs. -0.05 in 5b). The dipole moment of the transition state is very large (9.25D vs. 4.3D in 5b) and the overlap population[9] between C and Cl is essentially nil (~0.01).

Briefly, compared to the methylated species, the transition states for the parents exhibit smaller (~0.05-0.15Å) C-Cl and N-Cl distances, less net charge (~0.1) on Cl, smaller dipole moments (~1.4D), and ring geometries less closely resembling the corresponding free cations. Overlap populations are very similar in both cases.

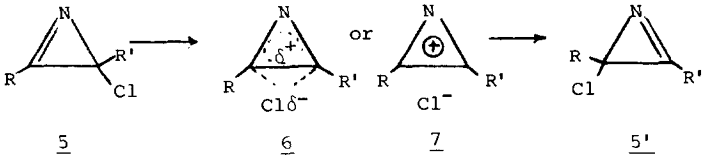
We cannot definitively distinguish between polar bridged transition states 3 or 6 or transition states which closely resemble intimate ion pairs, but the described properties of our calculated transition states clearly conform to those usually associated with ion pairs. It follows that if reactions (1) and (2) involve intimate ion pairs as intermediates, then these ion pairs must closely resemble structures 4 and 7. In the following discussion, we will use 4 and 7 as the simplest representations of either transition states or intimate ion pairs.

Thus, the degree of "intimacy" gradually decreases as cation stability increases;[5] azirinyl ion pairs are less intimate than diazirinyl ion pairs, methylated species are less intimate than their parents. This is reflected in increasing charge separation and dipole moment. Also, the energy separation of the ion pair from the most stable isomer (2, 5') decreases as the stability of the cation increases. In this vein, the degenerate isomerization of 3-chlorocyclopropene (8 $\rightleftarrows$ 8') is believed to transit a more fully developed ion pair (9); eq. (3).[3a,10] Preliminary calculations indicate an activation energy of 22.6 kcal/mol. The C-Cl distance in 9 is 2.70Å; charge transfer is essentially complete (-0.82; μ = 10.6D), and there is no evidence of C-Cl bonding. The smaller rate sensitivity to solvent polarity and the considerably slower isomerization of 5d, relative to 8,[3a,10] are consistent with a more intimate, higher energy ion pair structure for 7a, relative to 9.



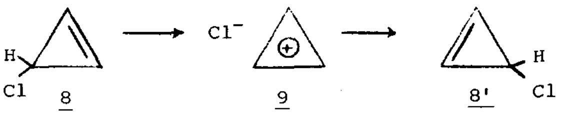
(1)

(a, R=H; b, R=CH$_3$)

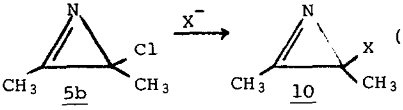


a, R=R'=H
b, R=R'=CH$_3$
c, R=R'=C$_6$H$_5$
d, R=CH$_3$, R'=C$_2$H$_5$
e, R=CH$_3$, R'=C$_6$H$_5$

(2)



(3)

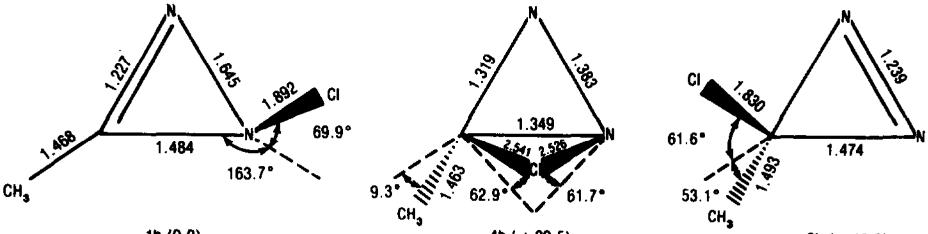


(4)

Our calculations refer to idealized gas phase situations. Obviously, polar solvents will strongly influence the energetics of reactions (1)-(3); transition states should be preferentially stabilized. Crudely estimated from a continuum model,[11] we find preferential transition state solvation stabilizations of 7-15 kcal/mol. This correction would lower activation energy barriers for 1b → 2b, 5b $\rightleftarrows$ 5'b and 8 $\rightleftarrows$ 8' to about 23, 16, and 7 kcal/mol, respectively.

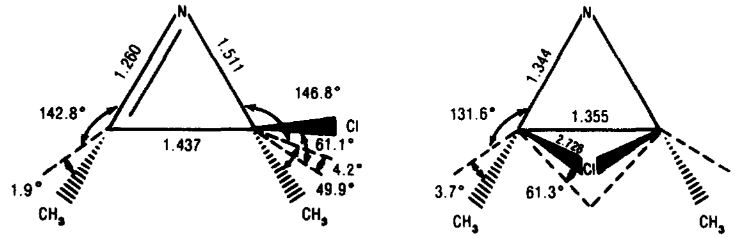
A preliminary experimental study[12] of the chemistry of azirine 5b is consistent with the intermediacy of ion pair 7b. Thus, although 5b decomposes rapidly to uncharacterized products in liquid SO_2,[4] it is stable at 25° in CH_3NO_2. Variable temperature nmr spectroscopy reveals substantial broadening ($W_{\frac{1}{2}}$ ~ 7Hz) of the Me signals ($\delta^{CH_3NO_2}$ 2.55, 1.85) by 89°.[13] Standard procedures applied to the 89° nmr data permit estimates of k ~ 17 sec^{-1} and $\Delta G^{\ddagger}$ ~ 19 kcal/mol for 5b $\rightleftarrows$ 5'b in CH_3NO_2. From the data of Ciabattoni,[3a] the interconversion of 5d and 5'd has $\Delta G^{\ddagger}$ ~ 18 kcal/mol in CH_2Cl_2 at -15°. Additionally, 5e $\rightleftarrows$ 5'e occurs readily in the nmr probe.[3b] Our calculated activation barrier for 5b $\rightleftarrows$ 5'b is in surprisingly good agreement with these experimental barriers. In contrast to the CH_3NO_2 result, and in accord with the significant solvent polarity-rate dependence of eq. (2),[3a] nmr studies of 5b in chlorobenzene revealed insignificant (0.5 Hz) Me resonance broadening up to 98° (k ~0.16 sec^{-1}, maximum).

Next, we surveyed the ability of various nucleophiles to convert 5b into 10 in CD_3CN at ~35° (nmr probe); eq. (4). KOAc (with dibenzo-18-crown-6, 3h, 25°-35°) cleanly transformed 5b (δ^{CD_3CN} 2.47, 1.80) to 10, X = OAc (δ^{CD_3CN} 2.42, 1.87, 1.50; δ^{CDCl_3} 2.53, 1.97, 1.58; ir, 1750 cm^{-1}), purified by gc on SF-96 at 125°. An analogous transformation occurred with LiOAc in CD_3CN, but not as cleanly. Reaction of 5b with CH_3OH in $CH_2Cl_2/CDCl_3$ or pyridine/CD_3CN very rapidly afforded 10, X = OCH_3 (δ^{CDCl_3} 3.37, 2.62, 1.53), as expected.[3a] Reaction with CH_3SLi (dibenzo-18-crown-6, CD_3CN) gave evidence for 10, X = SCH_3 (δ^{CD_3CN} 2.38, 1.93, 1.47), but the reaction was not quantitative and the product decomposed during isolation.



1b (0.0) 4b (+29.5) 2b (−18.2)

Fig. 1*



5b (0.0) 7b (+22.8)

Fig. 2*

*Optimized (HF/3-21G) geometries; values in ( ) are relative energies in Kcal/mol.

When 5b reacted with LiN_3 in CD_3CN, nmr Me signals at $\delta 2.47$ and 1.80 were rapidly replaced by bands at 2.42 and 1.45, which we attribute to 10, $X = N_3$. The latter, however, decomposed completely to CH_3CN ($\delta 1.93$) after ~2h. An analogous reaction has been reported for diphenyl and di-p-tolyl derivatives of 10, $X = N_3$, and was suggested to involve "loss of nitrogen in concert with chelotropic extrusion of the nitrile from the azirine."[4]

No evidence could be obtained for conversion of 5b into 10, X = Br, with LiBr in CH_3NO_2 or CD_3CN, or with KBr in dibenzo-18-crown-6/CD_3CN; slow decomposition to a complex product mixture occurred. With KCN or KF (dibenzo-18-crown-6/CD_3CN) or Et_4N^+ CN^- (CD_3CN) decomposition was also observed, this time with the formation of biacetyl (δ^{CD_3CN} 2.23). Biacetyl formation required ~4 days for completion with KCN, but was already 30% complete in only 40 min with KF. Biacetyl is the presumed hydrolysis product of 5b;[3a] acyloins have also been obtained upon hydrolysis of other derivatives of 5.[3b,4] It may be that CN^- or F^-, strong bases in relatively anhydrous media, catalyze the hydrolysis of 5b by adventitious water.

In summary, 5b undergoes rapid chloride scrambling in warm CH_3NO_2 and can be converted to derivatives of 10 with CH_3OH, SCH_3^-, N_3^-, or OAc^-. It fails to undergo substitution reactions with Br^-, CN^-, or F^-, although, in the two latter cases, it appears to be diverted by reaction with H_2O (OH^-). Its reactivity toward anions is consistent with their nucleophilicities in CH_3CN.[14] The chemistry of 5b, as observed here, and in previous studies,[3,4] is most consistent with the intermediacy of intimate ion pair 7b, which can revert to 5b, be intercepted by a sufficiently nucleophilic X^- to give 10, or react with 5b to give complex products derived from two molecules of azirine.[4] The rate of disappearance of 5b appears to depend on the identity of X^-, so that the rate determining step in reaction (4) is the destruction of ion pair 7b, not its formation.

Acknowledgments. We thank Professors P. A. Chaloner and D. B. Denney for helpful discussions. We are grateful to the National Science Foundation for financial support, and to the Rutgers University Center for Computer and Information Services for a generous grant of computing time on the DEC VAX 11/780. C.M.Y. thanks the Graduate School of Rutgers University for a Special Fellowship.

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(12) This work was in progress when ref. 4 appeared.
(13) Decomposition begins ~90°, but the normal spectrum is largely restored upon cooling.
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(Received in USA 17 February 1982)