Theoretical Prediction and Experimental Confirmation of Relative Stabilities of Isomeric Allyl Anions from Enamines and Vinyl Ethers

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Relative stabilities of isomeric allyl anions from enamines and vinyl ethers are predicted in terms of the continuity–discontinuity of the orbital phase. The predictions are supported by *ab initio* molecular orbital calculations and confirmed by experiments on model compounds.

Carbanions from enamines have been used as synthetic reagents for carbon–carbon bond formation.[1] Enamines can give rise to 1- and 2-aminoallyl anions. The relative stabilities of these isomeric species should determine the regioselectivity of subsequent alkylation reactions. Recently, cyclic orbital interaction was found to be involved in acyclic conjugation.[2] Acyclic delocalization of electrons is under the control of the orbital phase properties, as is cyclic delocalization.

In this paper we predict the stabilities in terms of orbital phase, carry out geometry optimization by *ab initio* molecular orbital calculations, and examine the prediction by experiments.

Results

Orbital Phase Prediction.—Aminoallyl anions are considered to be composed of a double bond and lone pairs of electrons on an anionic centre and a nitrogen atom. The mechanism of electron delocalization among the three systems is illustrated in Figure 1. Electron shifts from both lone pairs to the double bond involve the interactions between the nonbonding orbitals (n_C and n_N) and the antibonding orbital (π^*). The resulting electron holes in the anionic centre and in nitrogen can be supplied with an electron from the double bond through the interactions of the nonbonding orbitals with the bonding orbital (π) [Figure 1(*a*)]. As a result, the delocalization process contains cyclic orbital interaction between the n_C, π^*, n_N, and π orbitals [Figure 1(*b*)]. The orbital phase conditions for delocalization[2] are: (1) electron-donating orbitals out of phase, (2) electron-accepting orbitals in phase, and (3) donating and accepting orbitals in phase. The cyclic orbital interaction that simultaneously satisfies these three requirements promotes delocalization. The systems that contain such an orbital interaction are electron delocalizing or stable. The others are electron localizing or unstable. Application of these conditions leads to the prediction that the 2-aminoallyl anion is electron delocalizing [Figure 1(*c*)] whereas the 1-aminoallyl anion is electron localizing [Figure 1(*d*)].

Geometry Optimization.—Molecular geometries of aminoallyl anions were optimized by *ab initio* molecular orbital calculations with an STO-3G basis set. The first of the constrained geometries subjected to the optimization was the π-planar model with all atoms in the same plane (Figure 2). Under the constraint the 1-aminoallyl anion belongs to the C_s point group and the 2-aminoallyl anion to the C_{2v}. In the second geometry, the constraint is partially relaxed: the pyramidization at the nitrogen is allowed. Interaction between the allyl anion and the nitrogen lone-pair electrons is weakened but still remains to an appreciable extent. In this π-pyramidal model the 1-aminoallyl anion has no symmetry constraint, and the the 2-aminoallyl anion belongs to the C_s point group. In the last model, the nonbonding orbital lies in the σ-plane, and the pyramidization is allowed. There is no overlap interaction between the lone-pair electrons and the allyl π-systems. Both anions belong to the C_s point group in this σ-pyramidal model.

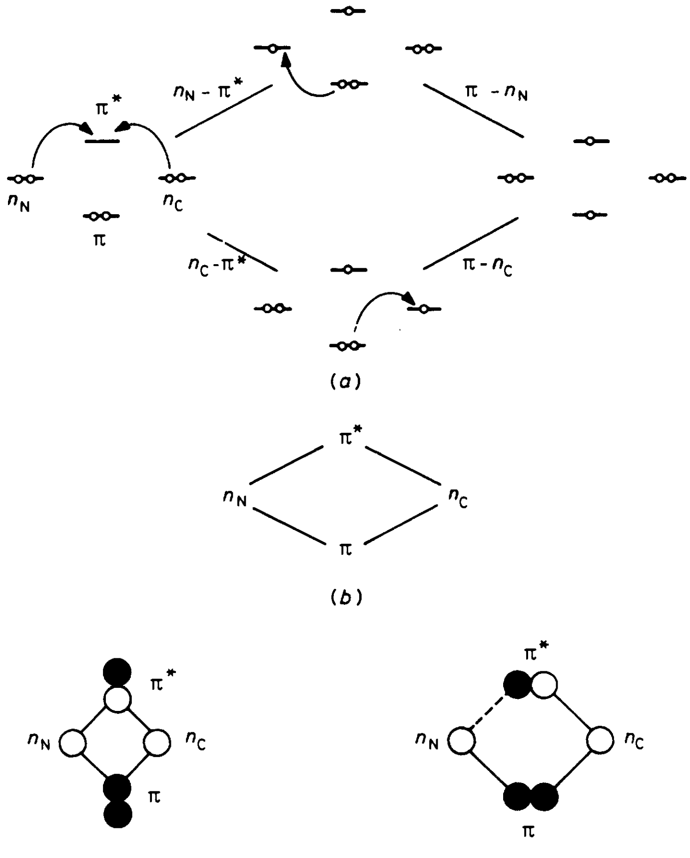
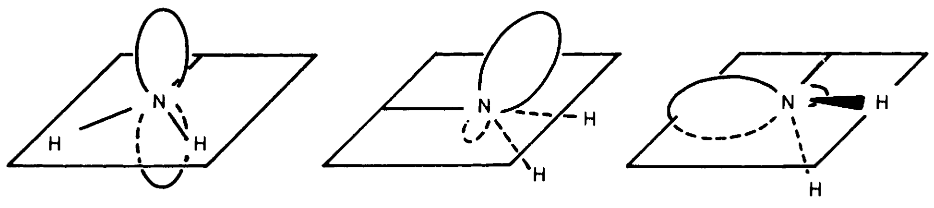


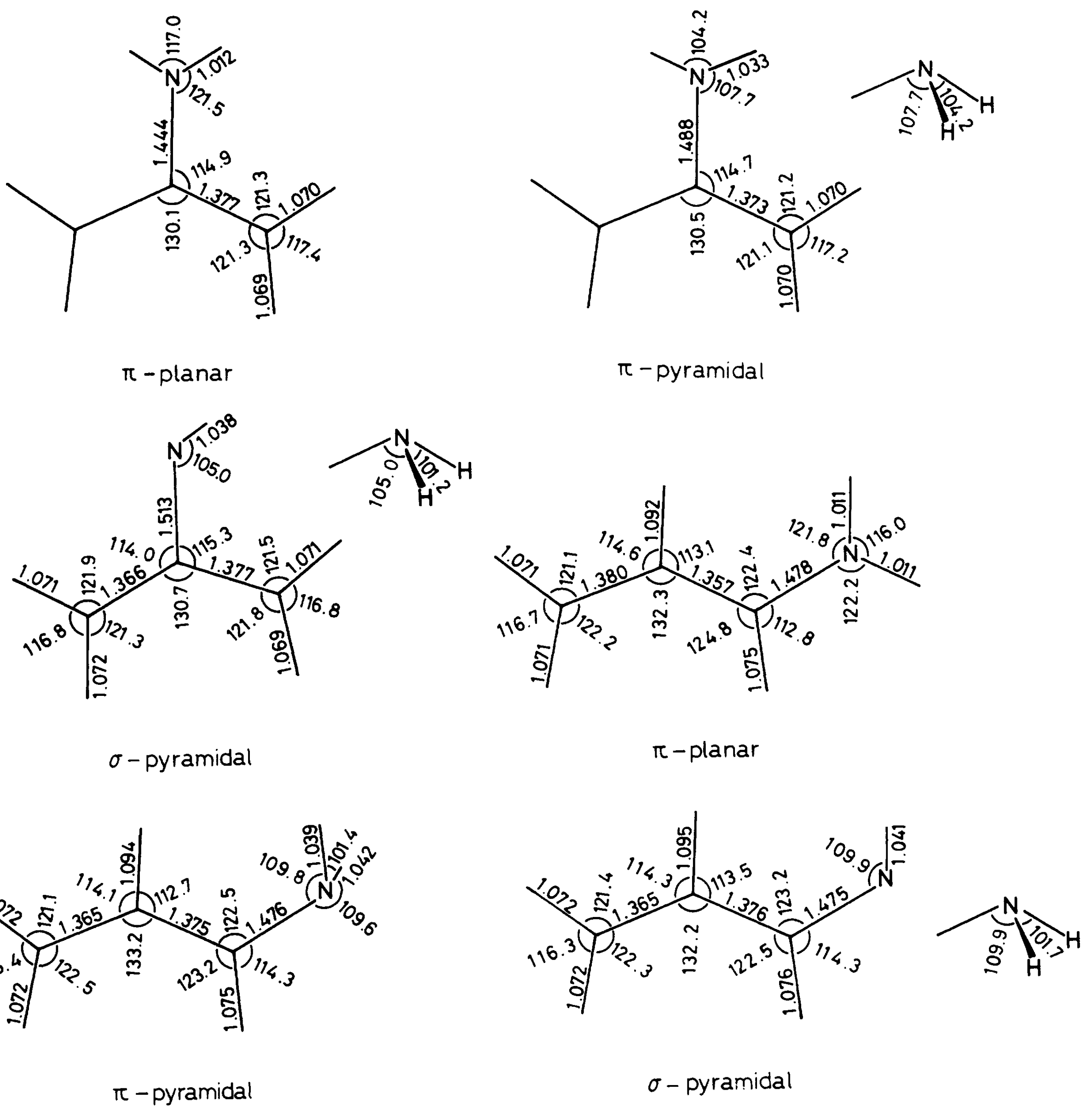
Figure 1. Electron delocalization in aminoallyl anions. (*a*) Mechanism; (*b*) cyclic orbital interaction; (*c*) orbital phase continuity in cross conjugation; and (*d*) discontinuity in linear conjugation

The orbital phase prediction of the relative stabilities was born out by *ab initio* molecular orbital calculations (Table 1). The 2-aminoallyl anion was found to be more stable than the 1-aminoallyl anion as far as the overlap interaction between the nonbonding orbital on nitrogen and the π-orbitals was concerned (π-models). The calculations with the 4-31G basis set on STO-3G optimized geometries also confirmed the relative stabilities. The most stable model of the 2-aminoallyl anion is a π-model (planar or pyramidal). This is also consistent with the prediction that the 2-aminoallyl anion with the π-type interaction between the allyl and amino moieties is electron delocalizing. It is worth noting that the most stable conformer



π - planar π - pyramidal σ - pyramidal

Figure 2. Models for geometry optimization



π - planar π - pyramidal

σ - pyramidal π - planar

π - pyramidal σ - pyramidal

Figure 3. Optimized geometries

of the 1-aminoallyl anion is σ-pyramidal. This result could be expected from the prediction that the conjugation that includes the lone-pairs of electrons in the 1-aminoallyl anion is electron localizing.

The optimized geometries also support the orbital phase prediction. In the π-planar models the C–N bond length is shorter in the 2-aminoallyl anion than in the 1-aminoallyl (Figure 3). This is interpreted as being the result of electron delocalization between allyl and amino moieties. The lone pairs of electrons can delocalize to a greater extent in the electron-delocalizing 2-aminoallyl anion. The significant bond alternation in the 1-aminoallyl anion may be due to the localization.

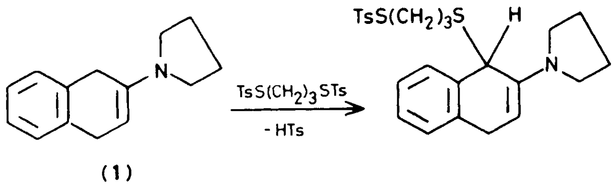
Table 1. Relative energies of aminoallyl anions (kcal mol^{-1})

Anion	Model		Relative energy[a]	
			STO-3G/STO-3G	4-31G/STO-3G
2-Aminoallyl	π-planar	(C_{2v})	+9.08	0
	π-pyramidal	(C_s)	0	+1.45
	σ-pyramidal	(C_s)	+4.56	+6.43
1-Aminoallyl	π-planar	(C_s)	+24.38	+19.77
	π-pyramidal	(C_1)	+3.45	+9.25
	σ-pyramidal	(C_s)	+3.28	+8.80

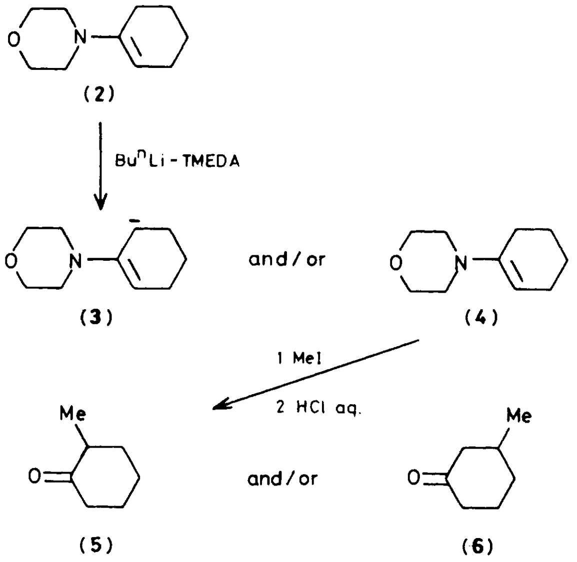
[a] The reference is the total energy of the most stable model.

Table 2. Yields of methylcyclohexanones

Substrate	Equivalents of Bu^nLi–TMEDA	Reaction time (h)	Yield (%)	
			(**5**)	(**6**)
1-Morpholinocyclohex-1-ene	1	1.0	26	0
	1	2.0	35	0
	5	2.0	58	0
	10	2.0	64	0
	20	2.0	76	0
	3	1.0	45	0
	3	72	63	0
Methyl cyclohexenyl ether	1	2.5	26	0
	2	2.0	58	0
	5	2.0	65	0



(1)



(2)

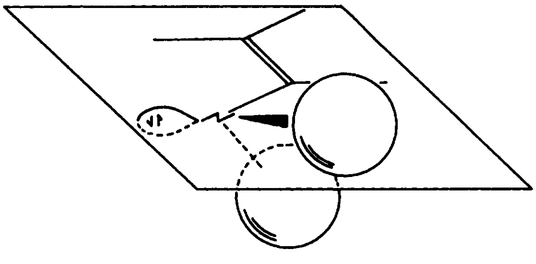
The π-pyramidal model of the 1-aminoallyl anion, which has no symmetry constraint, is optimized to have almost the same geometry as the σ-pyramidal model. This is a result of the reluctance of the nitrogen lone pair of electrons to conjugate with the allyl systems in the localization.

Experimental Confirmation.—In order to test our prediction, enamines are required to have aliphatic substituents with abstractable hydrogens at both the α and β positions in chemically comparable environments. The number of experiments on these enamines reported so far is extremely limited. Woodward *et al.*[3] showed that 2-pyrrolidino-1,4-dihydronaphthalene (**1**) undergoes deprotonation of the α substituents [equation (1)]. In our experiments a less perturbed enamine, 1-morpholinocyclohex-1-ene (**2**), was used to confirm and generalise the theoretical prediction. The results of deprotonation by Bu^nLi–TMEDA followed by methyl iodide quenching [equation (2)] are listed in Table 2. No trace of 3-methylcyclohexanone was detected irrespective of the reaction time (1—72 h) and the molar ratio of Bu^nLi–TMEDA to the substrate (1—20). The results strongly suggest that the 2-aminoallyl anion (**3**) is more stable than the 1-aminoallyl anion (**4**).

A similar orbital phase argument is applicable to the relative stabilities of 1- and 2-alkoxyallyl anions. Methyl cyclohexenyl ether was employed as a model compound. The results of deprotonation followed by methyl iodide quenching are listed in Table 2. The sole product is 2-methylcyclohexanone. The predicted stability of the 2-alkoxyallyl anion relative to the 1-isomer was found to be overwhelming.

Discussion

The relative stability of allyl anions with 1- and 2-substituents that have a lone pair of electrons can be predicted by the frontier orbital interaction between the allyl anion moiety and the substituents. The LUMO of the allyl anion has greater extension at the central carbon. The HOMO of the substituent is the nonbonding orbital. The HOMO–LUMO interaction is then expected to lead to more stabilization in the 2- than the 1-



(7)

substituted anions. It is interesting that the same conclusion can be drawn from the continuity–discontinuity of the orbital phase in acyclic conjugation and from the frontier orbital amplitude. At present, the generality of the parallelism of both approaches remains open to question.

Recently, the trimethylenemethane dianion was observed[4] to be thermodynamically more stable than the butadiene dianion. The dianions are isoelectronic with 2- and 1-aminoallyl anions, respectively. The relative stability can be explained in a similar manner.[2]

As regards organic synthesis, there seems to be no superiority of the enamine anion routes for introducing substituents into ketones, as long as the lone pair of electrons on nitrogen is allowed to conjugate. The enamine routes lead to α-substituted ketones, and do not alter the regioselectivity of the reactions *via* enolate anions. The *ab initio* molecular orbital calculations of the σ-models is noteworthy in this respect. The STO-3G/STO-3G and 4-31G/STO-3G results show an opposite thermodynamic preference of the isomeric aminoallyl anions. The relative stability deserves further investigation in more detail, since some enamines may undergo deprotonation from the γ-position to give 1-aminoallyl anions according to the STO-3G/STO-3G result. The process could provide a short route to β-substituted ketones. In other words, the enamine anions of the σ-models can serve as homo-enolate anion equivalents. The lone pair of electrons must be forced to lie on the σ-plane by some constraints for this purpose. A promising strategy is to attach bulky substituents to the heteroatoms to prevent the lone pair from π-conjugation (7).

Experimental

A mixture of 1-morpholinocyclohex-1-ene or methyl cyclohexenyl ether with an n-butyl-lithium–tetramethylethylenediamine complex (Bu^nLi–TMEDA) was stirred under an atmosphere of argon at room temperature, and was then quenched by methyl iodide at −20 °C. After hydrolysis with hydrochloric acid followed by extraction with ether the reaction mixture was subjected to g.l.c. analysis on dioctyl phthalate (DOP).

Acknowledgements

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