1-Azabicyclo[4.4.4]tetradec-5-ene

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1-Azabicyclo[4.4.4]tetradec-5-ene, synthesized by a ring cleavage route, shows evidence of transannular alkene–amine interaction in its photoelectron spectrum and in its rapid reaction with acids to form the 1-azoniatricyclo[4.4.4.0]tetradecane ion.

Bridgehead alkenes in certain bicyclic medium-ring systems may be *less* strained than their parent alkanes,[1‡] and the first compound of this type, bicyclo[4.4.2]dodec-1-ene, has recently been reported.[2] We report the preparation of 1-azabicyclo[4.4.4]tetradec-5-ene, (1), which also lies in this category according to calculations, but whose chemistry is dominated by transannular interaction between the amino and alkene functionalities.

The synthesis (Scheme 1) follows the strategy used to make *out*-6H-1-azabicyclo[4.4.4]tetradecane, (2).[3] The new preparation of (3) represents a marked improvement on previous routes to this useful intermediate or its equivalent.[4,5] Semi-hydrogenation of the acetylenic amine only proceeded well in acid solution and in the *absence* of catalyst poisons. Reduction of the unsaturated propellane (4)§ with sodium in pure ammonia sometimes yielded (1) but was irreproducible, giving a mixture of 10-(but-1-enyl)- and 10-(but-2-enyl)-quinolizidines as the major product on most occasions. The desired product (1) can be reproducibly obtained free of

quinolizidines by adding a small excess of Bu^{t}OH to a suspension of (4) in NH$_3$ *before* the addition of sodium. We presume that the quinolizidines arise by NaNH$_2$-promoted elimination to give 10-(buta-1,3-dienyl)quinolizidine, followed by reduction of that diene, and that, in contrast with NaNH$_2$, Bu^{t}ONa is not a sufficiently strong base to cause elimination to compete with the direct reduction of (4). Reduction of (4) presumably gives (5), which protonates (kinetic-control) to give (1); we see no evidence for the isomeric 1-azabicyclo[4.4.4]tetradec-4-ene: that alkene is calculated (MM2, see below) to be 17.7 kcal mol^{-1} (1 kcal = 4.186 kJ) less stable than (1).

Preferred conformations according to MM2 calculations[6] for (1) and (2) are shown in Figure 1. Conformations for (1) with the nitrogen atom pyramidal outwards are >10 kcal mol^{-1} less stable than the conformation shown. The calculated heats of formation of (1) and (2) mean that the predicted heat of hydrogenation of (1) to (2) is only 7.6 kcal mol^{-1}. The properties of (1) are in excellent agreement with those expected from the calculated structure. 1-Azabicyclo[4.4.4]tetradec-5-ene melts at 116—122 °C in a sealed tube with decomposition; it decomposes slowly in air. Its ^{1}H and ^{13}C n.m.r. shifts are quite normal and its u.v. spectrum is similar to that of (2) with ϵ_{220} 5400 in 2,2,4-trimethylpentane. In cyclic voltammetry (25 °C, Pt, MeCN, Bu$_4^n$NBF$_4$), both (1) and (2) show only irreversible oxidation at scan rates of up to 1 V/s, but the oxidation wave for (1) is 0.4 V less anodic (0.4 V *vs.* 0.8 V against a standard calomel electrode). The easier oxidation of (1) is in line with its He(Iα) photoelectron (PE) spectrum (Figure 2). The PE band maxima are at $I_1^m = 7.3_0$ eV and $I_2^m = 8.6_0$ eV, compared with $I_1^m = 7.8_5$ eV for (2).[7] Since the MM2 calculations indicate similar geometry at nitrogen for

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‡ Maier and Schleyer took the *out, out*-bicycloalkane as their reference structure. Although this is realistic in terms of actual hydrogenations, it is an arbitrary choice. In the case of their most dramatically hyperstable alkene, bicyclo[4.4.4]tetradec-1-ene, we have already pointed out[3] that the *in, out*-alkane is much more stable (ΔH_f −21.9 kcal mol^{-1}) than the *out, out*-isomer (ΔH_f −9.6) (MM1 calculations).

§ All new compounds gave satisfactory analytical and spectroscopic data.
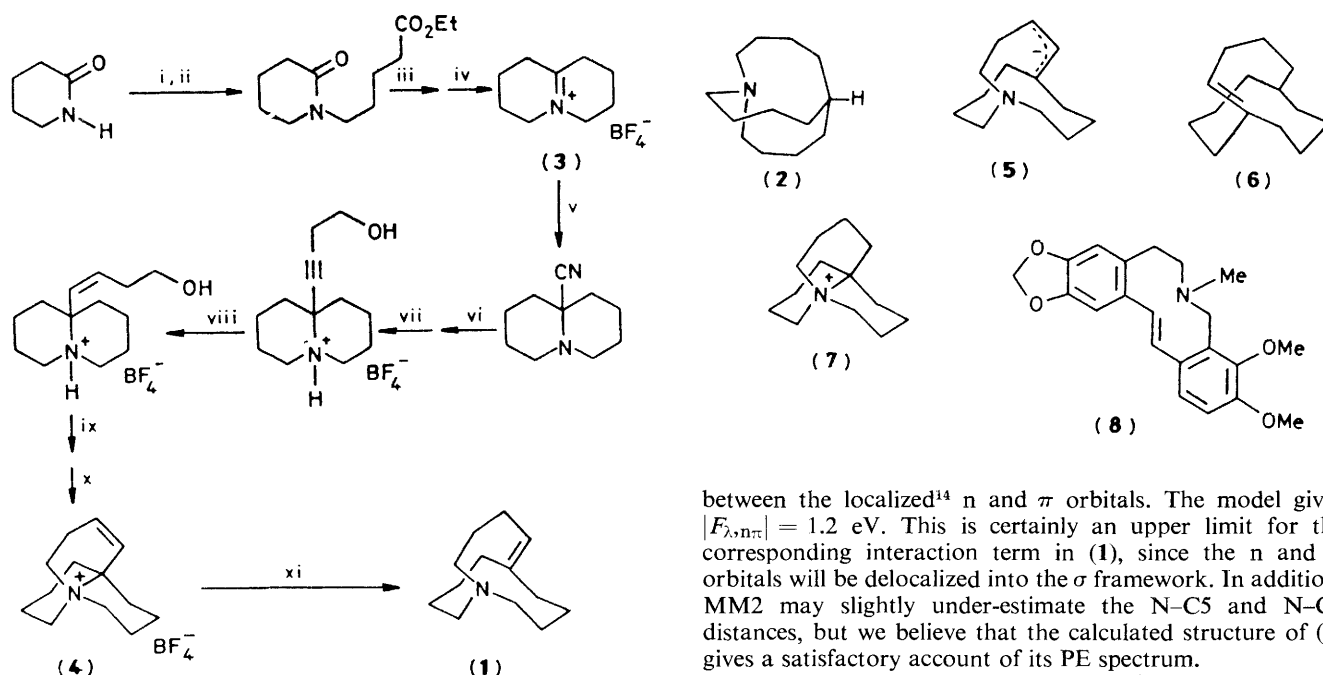
Scheme 1. i, KH,DME; ii, Br[CH$_2$]$_4$CO$_2$Et; yield from i and ii 71%; iii, soda lime distillation; iv, HBF$_4$,Et$_2$O; yield from iii and iv 82%; v, aqueous KCN, 82% yield; vi, 4-(2-tetrahydropyranyl-oxy)butynylmagnesium bromide; vii, aqueous HBF$_4$, yield from vi and vii 81%; viii, H$_2$, Pd–C, MeOH, 83% yield; ix, p-MeC$_6$H$_4$-SO$_2$Cl, Et$_3$N, CH$_2$Cl$_2$; x, aqueous HBF$_4$, yield from ix and x 60%; xi, Na–NH$_3$, Bu^{t}OH, 58% yield.

(1) and (2), $-I_1^m$ (2) $= 7.8$ eV can be taken as A_n, the basis energy for the lone pair in (1) before interaction with the π-orbital. Bicyclo[4.4.4]tetradec-1-ene (6) is unknown, so A_π must be estimated, but this can be done with some confidence in two ways.¶ Both methods leads to $A_\pi = -8.1$ eV.

If the π and n orbitals in (1) only interact by 'through space interaction,' then from elementary algebra and Koopmans' theorem, the relationship $A_\pi + A_n = -(I_1^m + I_2^m)$ should be obeyed. Within the limits of error this is true, i.e. $A_\pi + A_n = -15.95$ eV, $-(I_1^m + I_2^m) = -15.9_0$ eV. Therefore 'through-bond interaction' appears to be negligible and the through-space interaction term $|B_{n\pi}| = |<n|\hat{H}|\pi>| = 0.64$ eV. In order to see if a through-space coupling of this magnitude is reasonable for (1) in the MM2 calculated geometry, an STO-3G *ab initio* calculation[13] has been performed on an ensemble of ethene and ammonia oriented as in (1). The interaction term $F_{\lambda,n\pi}$ from the Fock matrix F_λ is the interaction

¶ I_1^m for the following anti-Bredt alkenes are known: bicyclo-[3.3.1]non-1-ene, 8.3$_5$,[8] bicyclo[4.2.1]non-1(8)-ene, 8.3$_7$, and bicyclo[4.2.1]non-1-ene, 8.4$_5$ eV.[9] These hydrocarbons contain the bridgehead double bond embedded in a 6-, 5-, and 7-membered ring, respectively, in contrast to (6) where it is contained in a 10-membered ring. However it is easy to correct for the influence of the increased σ-frame by removing formally the saturated bridgehead and by applying the necessary corrections for the increased size of the resulting double bond substituents in the 1,1-dibutyl-2-propylethylene derived from (6). From this, one predicts that I_1^m of (6) should be somewhere in the range of 8.0 eV to 8.1 eV. One may also compute the expected ionization energy from a linear-free-energy type of rule as first described by Cocksey, Eland, and Danby.[10] Using the modified formula (39) given in ref. 11 with $\mu_H^{II} = -1.18$ eV, $\mu_{Bu}^{II} = -1.20$ eV (*cf.* Table 3 of ref. 11), $X_{CH_2 CH_2} = 2/3$, and $I_\pi(CH_2-CH_2) = 10.52$ eV, one obtains for 1,1-dibutyl-2-propylethylene a predicted ionization energy of 8.1 eV. It should be noted that deviations from coplanarity of the double bond moiety will not lead to significant shifts.[8,9,12]
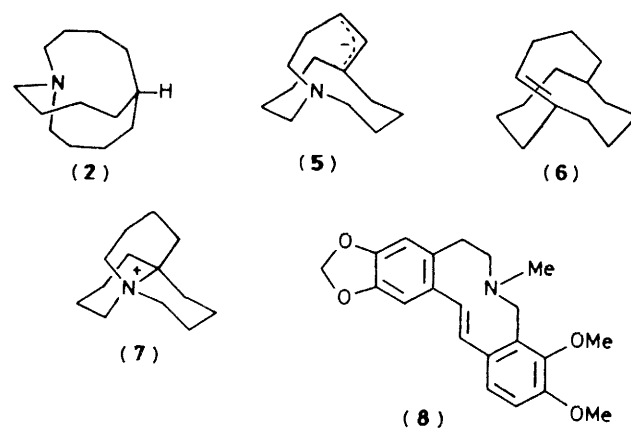
between the localized[14] n and π orbitals. The model gives $|F_{\lambda,n\pi}| = 1.2$ eV. This is certainly an upper limit for the corresponding interaction term in (1), since the n and π orbitals will be delocalized into the σ framework. In addition, MM2 may slightly under-estimate the N–C5 and N–C6 distances, but we believe that the calculated structure of (1) gives a satisfactory account of its PE spectrum.

The amino-alkene (1) reacts rapidly with acid to give the saturated propellane salt (7). Even ethanol is a strong enough acid, with $t_\frac{1}{2} = 9$ min at 25 °C for the disappearance of (1). This extraordinary reactivity indicates that C-protonation of (1) involves simultaneous N-participation *i.e.* a *retro*-Hofmann E2 elimination. Behaviour of this type has been recorded before, the most thorough and recent investigation being the study by Kirby and Logan[15] of the protonation of N-methyl-tetrahydroberberine (8). We find that the half-life of this compound in EtOH at 25 °C is *ca.* 2 min. In aqueous dioxan, the rate of C-protonation of (8) decreases with increasing acidity ($t_\frac{1}{2}$ *ca.* 100 h at 25 °C in 1M HCl)[15] as the compound is converted into the unreactive N-protonated form. What makes compound (1) unique is that C-protonation is fast at all acidities; conversion into (7) is complete within the time of mixing with CF$_3$CO$_2$H. We have earlier shown[3,7] that the saturated amine (2) is a very weak base (pK_a 0.6) towards outside protonation. In view of the MM2 calculations that outside pyramidalised (1) is much more strained than the inside conformation shown in Figure 1, it is probable that N-protonation of (1) is simply not competitive with C-protona-
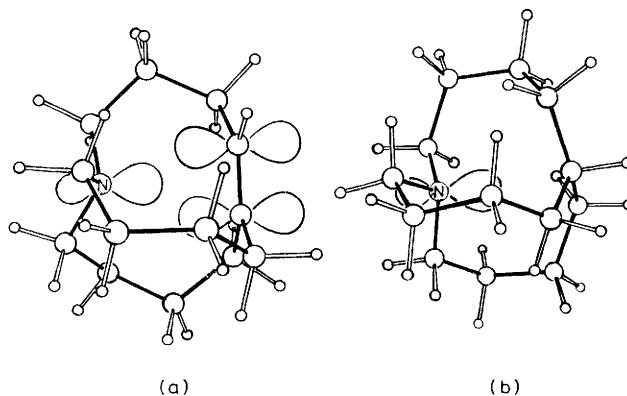

Figure 1. (a) Structure of 1-azabicyclo[4.4.4]tetradec-5-ene (1) as calculated by MM2.[6] $\Delta H_f + 1.81$ kcal mol^{-1}, average C–N–C angle 112.5°, N–C5 distance 2.73 Å, and N–C6 distance 2.74 Å. (b) Structure of *out*-6H-1-azabicyclo[4.4.4]tetradecane, (2) according to MM2; the molecule adopts C$_3$ symmetry. $\Delta H_f -5.83$ kcal mol^{-1}, C–N–C angle 111.8°, and C5–C6–C7 angle 117.3°.
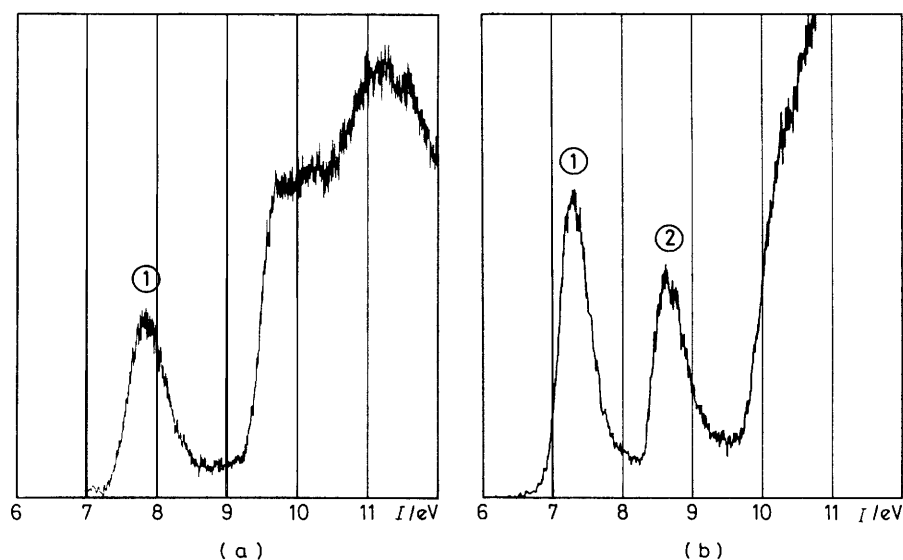
Figure 2. (a) He(Iα) photoelectron spectrum of (2). The band maximum $I_1^m = 7.8_5$ eV. (b) He(Iα) photoelectron spectrum of (1). The band maxima are I_1^m 7.3_0 and I_2^m 8.6_0 eV.

tion.** The contrasting behaviour of (1) and (8) is another example of the interesting differences between transannular and intra-bridgehead chemistry.[16,17] In summary, one can see the unusual properties of (1) as a consequence of the extreme reluctance for outside pyramidalisation of the bridgehead atoms in these medium-ring bicyclic structures and the strong driving force for intra-bridgehead bond formation.

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** Hofmann elimination from (7) does not regenerate (1), but gives 10-(but-3-enyl)quinolizidine exclusively.

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