(1.5 mL). The mixture was vigorously refluxed for 2.5 h in an oil bath heated at 110 °C. After being cooled, the mixture was passed through a short silica gel column (hexane/EtOAc 5:1). The product obtained was further purified by preparative LC on silica gel (hexane/EtOAc 20:1), giving 0.047 g (66%) of the tetraene **7** as a faintly yellow oil. The analytical sample was obtained by distilling in vacuo: bp 35–45 °C (0.067 kPa); ^{1}H NMR (100 MHz, CDCl$_3$) δ 0.81 (3 H, s, CH$_3$), 3.55 (3 H, s, OCH$_3$), 4.43 (1 H, br s, 1-H), 5.78 (1 H, br d, J = 10.0 Hz, 8-H), 5.96–6.40 (6 H, m); [α]$_D$ +393.3° (c 0.11798, hexane); UV (EtOH) λ_{max} 324.3 nm (ϵ 6000), 223.2 (23700); CD (EtOH) λ_{ext} 321.0 nm ($\Delta\epsilon$ +5.7), 249.2 (0.0), 221.3 (−24.5). High resolution mass spectrum calcd for C$_{12}$H$_{14}$O: 174.1044. Found: 174.1044.

(1S,6ξ,8aS)-1,2,6,8a-Tetrahydro-1-methoxy-6,8a-dimethyl-6-azulenol (19). To a solution of the trienone **17** (0.267 g, 1.40 mmol) in dry ether (30 mL) was added dropwise an ethereal solution of CH$_3$Li (2.2 mL, 1.25 M, 2.81 mmol) at −55 °C. The reaction mixture was stirred at −55 °C for 1.5 h, poured into ice–water, and extracted with ether. The organic layer was washed with brine and evaporated, giving 0.290 g (100%) of the alcohol **19**: ^{1}H NMR (60 MHz, CDCl$_3$) δ 1.07 and 1.12 (3 H, s each, 8a-CH$_3$), 1.37 and 1.43 (3 H, s each, 6-CH$_3$), 3.41 (3 H, s, OCH$_3$), 3.79 (1 H, dd, J = 8, 8 Hz, 1-H), 5.3–6.2 (5 H, m, 3,4,5,7,8-H).

(1S,8aS)-(+)-1,8a-Dihydro-1-methoxy-6,8a-dimethylazulene (8). To a solution of the alcohol **19** (0.290 g, 1.40 mmol) in dry benzene (40 mL) was added a solution of iodine (0.003 g, 0.012 mmol) in dry benzene (2 mL). The mixture was vigorously refluxed for 1 h in an oil bath heated

at 110 °C. After being cooled to room temperature, the mixture was passed through a short silica gel column (hexane/EtOAc 5:1). The crude product obtained was purified by preparative LC on silica gel (hexane/EtOAc 20:1), affording 0.139 g (52.5%) of the tetraene **8** as a faintly yellow liquid. The analytical sample was obtained by distilling in vacuo: bp 60–70 °C (0.029 kPa); ^{1}H NMR (360 MHz, CDCl$_3$) δ 0.780 (3 H, s, 8a-CH$_3$), 2.013 (3 H, s, 6-CH$_3$), 3.514 (3 H, s, OCH$_3$), 4.356 (1 H, br s, 1-H), 5.746 (1 H, d, $J_{7,8}$ = 10.9 Hz, 8-H), 5.957 (1 H, dd, $J_{2,3}$ = 5.8, $J_{1,2}$ = 2.1 Hz, 2-H), 5.961 (1 H, d, $J_{7,8}$ = 10.9 Hz, 7-H), 5.986 (1 H, d, $J_{4,5}$ = 7.0 Hz, 4-H), 6.143 (1 H, dq, $J_{4,5}$ = 7.0, $J_{5,6-Me}$ = 1.1 Hz, 5-H), 6.197 (1 H, dd, $J_{2,3}$ = 5.8 Hz, $J_{1,3}$ = 1.9 Hz, 3-H); NOE correlation, +8.93% between 6-CH$_3$ and 7-H, +12.13%, 6-CH$_3$ and 5-H, +8.81%, OCH$_3$ and 1-H, +8.71% ~ 11.29%, 1-H and 8-H; [α]$_D$ +323.8° (c 0.20723, hexane); UV (EtOH) λ_{max} 324.5 nm (ϵ 7200), 226.2 (24300); CD (EtOH) λ_{ext} 318.6 nm ($\Delta\epsilon$ +4.3), 240.2 (+1.6), 237.0 (0.0), 220.7 (−18.1). High resolution mass spectrum calcd for C$_{13}$H$_{16}$O: 188.1201. Found: 188.1200.

Conjugative Interaction in the Orthogonal Enamine, 1-Azabicyclo[3.2.2]non-2-ene

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Abstract: Synthesis of 1-azabicyclo[3.2.2]non-3-ene and establishment of equilibrium with 1-azabicyclo[3.2.2]non-2-ene by catalysis either with potassium *tert*-butyloxide or hydridonitrosotris(triphenylphosphine)ruthenium reveals no free energy difference between the allyl amine and the orthogonal enamine. In unrestricted examples, the enamine is favored by ~4 kcal/mol. Thus, conjugative interaction in enamines requires parallel overlap of the orbitals containing the non-bonded nitrogen pair and the π-olefinic pair of electrons.

Structure and thermochemistry of enamines derive their importance from the extraordinary versatility of the various Stork reactions in synthesis[1] and from their bearing on the theory of conjugation between an olefinic π-bond and the unshared electron pair of nitrogen.[2]

In this work, an orthogonal enamine is prepared, set into equilibrium with an (equally orthogonal) allylamine, and compared in free energy with configurationally unrestricted enamines. Although much structural and thermochemical information already exists in the literature, there is no direct examination of the influence of orthogonality.

An authoritative crystallographic study of enamines has brought to light a spectrum of structures ranging from the nearly coplanar expected from an sp^2 configuration and 2p$_z$ disposition of the lone pair through the pyramidal, in varying degrees, to an eclipsed, nearly tetrahedral associated with sp^3 hybridization about nitrogen.[3]

Scheme I
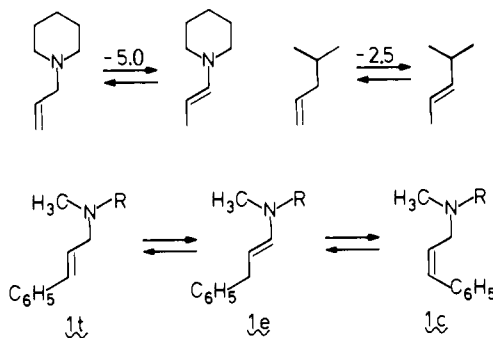
The thermochemistry of the n,π-interaction has been probed by hydrogenation and by equilibration in the allyl–propenyl system (see Scheme I). Comparison of the heats of hydrogenation of N-allyl- and N-*trans*-propenylpiperidine has revealed a heat of isomerization of -5.0 kcal/mol.[4] Given that the heat of isomerization of 4-methylpentene-1 to *trans*-4-methylpentene-2 is −2.5 kcal/mol, and that of pentene-1 to *trans*-pentene-2 is −2.6
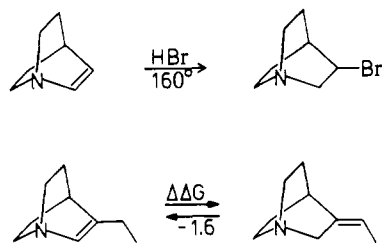
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Scheme II

Scheme III

a) CH_2N_2 / CH_3OH b) $C_7H_7SO_2NHNH_2$

c) $LiCH_3$ d) $LiN(CH_3)_2 / HMPA$

e) $[(C_6H_5)_3P]_3RuH(NO)$ f) KOD / H_2O

kcal/mol, the enthalpy of conjugative interaction of the enamine (relative to that of methyl as standard) is −2.5 kcal/mol.

Experiments designed to establish equilibria by means of strongly basic catalysts such as potassium *tert*-butyloxide in dimethyl sulfoxide originate in studies of Price and Snyder[5] of the isomerization of allyl tertiary amines to *trans*-propenylamines. Qualitatively, this and other works referred to by Martinez and Joule,[6] have shown that thermodynamics favors the enamine.

Quantitatively reliable information has been elusive, however, owing to the sensitivity of enamines to oxygen and to traces of acid. For example, acid-catalyzed rearrangement of the thermodynamically less stable cis isomer to the more stable trans isomer of the enamine can be so rapid that, without special precaution,[7] kinetic favoring of the cis isomer under catalysis by strong bases may be obscured[5] during workup.

In a work devoted primarily to rates of deuterium exchange, Coates and Johnson[8] pit phenyl against *N*-methylanilino in the widely studied[2] 1,3-disubstituted propene system and report a ratio of trans enamine (**1e**, R = C_6H_5) to the sum of cis and trans allylamines (**1t** and **1c**, R = C_6H_5) of at least 10:1. In the closely related dimethylamino system, Hine et al.[9] report the ratio of **1e** to **1t** (R = CH_3) to be 40 ± 15. From these experiments (see Scheme I), the enamine emerges as more strongly conjugating than phenyl by 1.5–2.5 kcal/mol, while phenyl is itself more strongly conjugating than methyl by 1.8 kcal/mol.[10]

A similarly strong favoring of enamine in the necessarily cis system of *N*-methyltetrahydropyridine has been observed by Coates and Johnson[8] (equilibrium ratio at least 16:1) and Fowler and Beeken[11] ($\Delta\Delta G$ = 4.1 kcal/mol).

Correlation between ^{15}N NMR shifts and experimentally accessible barriers to internal rotation in substituted enamines, elaborated by Schwotzer and von Philipsborn,[12] is remarkably good. Extrapolation to simple enamines points to a basic barrier of 4–5 kcal/mol, a result in excellent agreement with the theoretical prediction of Dixon et al.[2b] that the coplanar vinylamine have a barrier to rotation of 6.1 kcal/mol.

The conformation of nitrogen in coplanar enamines is predicted by the same authors to prefer pyramidal over planar by 1.5 kcal/mol.[2b] The results of Brown et al.[3] point to a softness in respect to sp² planarity or sp³ pyramidality and suggest that avoidance of eclipsing is of comparable energetic importance.

That the reactivity of enamines toward electrophilic reagents depends on the production of coplanar iminium ions as intermediates seems well established. A striking demonstration of this requirement has been given by Grob, Kaiser, and Renk[13] in a study of dehydroquinuclidine. In an example in which the resulting iminium ion would seriously violate Bredt's rule, 1-azabicyclo[2.2.2]oct-2-ene reacts with hydrogen bromide at 160°, not to give 2-bromoquinuclidine or its decomposition product but rather 3-bromoquinuclidine. In a second example, 3-phenyl-1-azabicyclo[2.2.2]oct-2-ene reacts with nitric acid in acetic anhydride not
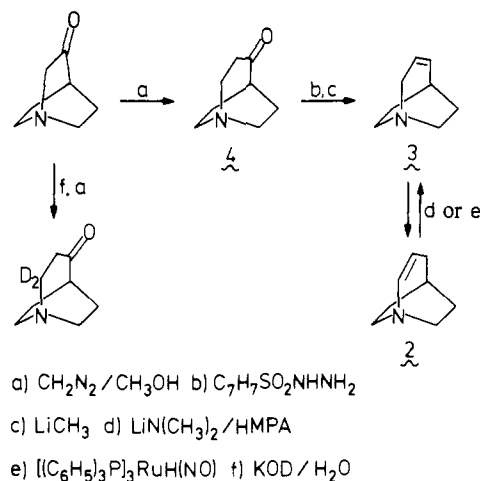
to give the ring-opened products to be expected of an iminium ion but a mixture of 3-phenyl- and 3-*p*-nitrophenyl-2-nitro-1-azabicyclo[2.2.2]oct-2-ene. Of the conventional chemistry of enamines not a vestige remains.

However clear the dependence of enamine reactivity may be on the ability to attain coplanarity in the iminium ion, the question whether the substantial energy of conjugation in enamines requires a coplanar or nearly coplanar relation between the π-orbital of ethylene and the nonbonded orbital of the sp² or sp³ nitrogen atom remains experimentally uncertain.

Observations of Van Binst and colleagues[14,15] indicate that much of the conjugation may be lost if coplanarity is not attainable. Building on the work of Ernest,[16] they have prepared a mixture of 3-ethyl-1-azabicyclo[2.2.2]oct-2-ene (25%) and its exocyclic isomer, (Z)-3-ethylidene-1-azabicyclo[2.2.2]octane (75%), by dehydration of a common tertiary alcohol under conditions (P_2O_5 in toluene at 110 °C) that might have been expected to establish equilibrium. Under different conditions (sodium on alumina at 23 °C), only 6% of the endo isomer is present at equilibrium. The change from ca. 5 kcal/mol of conjugative interaction to a deconjugative interaction ($\Delta\Delta G$) of 1.6 kcal/mol may be blamed on the orthogonal arrangement of the nonbonded pair at the bridgehead nitrogen, even though part of the shift may be ascribed to the same factors that make ethylidenebicyclo[2.2.2]octane (configuration unspecified) more stable than 2-ethylbicyclo-[2.2.2]oct-2-ene by 1.3 kcal/mol.[17]

Estimation of the dependence of conjugative interaction on geometry is approached in this work through Δ^2- and Δ^3-1-azabicyclo[3.2.2]nonenes (**2** and **3**) in which the nitrogen atom is constrained to remain pyramidal or tetrahedral and eschew a planar, trigonal configuration and, more importantly, to have its nonbonded electron-pair disposed nearly perpendicular to the hybridized 2p orbitals of the π-bond. In this sense, **2** represents a frozen approximation to the transition state that might be assumed for rotation of the amino group about the double bond in a simple acyclic enamine. Its isomer, **3**, retains much of the perpendicularity and may serve as an unconjugated model. The amount of strain in each isomer should be about equal, and any difference in entropy should be close to zero.

From the position of equilibrium between **2** and **3**, any significant thermodynamic contribution arising from a difference in σ-bond strengths should be discernible. In terms of the Dewar–Schmeising analysis,[18] the question concerns a possible

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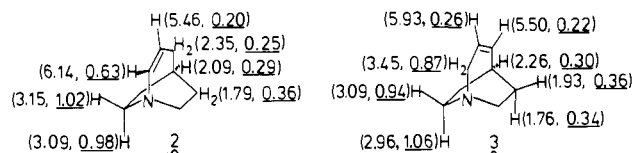(13) Grob, C. A.; Kaiser, A.; Renk, E. *Helv. Chim. Acta* **1957**, *40*, 2170–2185.

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Figure 1. The ^{1}H NMR spectra (chemical shifts in ppm (δ)) and *relative responses to Eu(fod)$_3$* of 1-azabicyclo[3.2.2]non-2-ene (3), respectively. Chemical shifts are obtained by extrapolation to zero concentration of Eu(fod)$_3$.

non-zero difference in the strength of the sp^3-nitrogen–sp^3-carbon bond and that of the sp^3-nitrogen–sp^2-carbon bond. A strong favoring of **2** over **3** would constitute support for this suggestion.

The preparation of 1-azabicyclo[3.2.2]non-3-ene (3) begins with the reaction of the readily available azabicyclo[2.2.2]octan-3-one[19] with diazomethane to generate azabicyclo[3.2.2]nonan-4-one (4). Distinction from the alternative nonan-3-one structure was made by repeating the synthesis with 1-azabicyclo[2.2.2]octan-3-one-2,2-d_2 and comparing the NMR spectra of deuterated and non-deuterated product (see Experimental Section).

Conversion of the methylene ketone function to the olefin **3** is accomplished by the two-step procedure of Shapiro and Duncan.[20] The resulting **3** can be set into equilibrium with **2** by treatment with lithium dimethylamide in hexamethylphosphoric triamide. An enriched sample of **2** can be separated by fractional crystallization of the hydrogen iodides.

Assignment of position to the double bonds is based on NMR. Both isomers are well-suited to analysis by lanthanide-induced shift (LIS) owing to the relatively rigidly fixed position of the coordinating unshared electrons in the bicyclic amines. As revealed in Figure 1, not all the pairs of exo and endo hydrogen atoms at C_6 and C_9 and at C_7 and C_8, respectively, are resolved, but their assignment is not critical to fixing the positions of the double bonds.

The structurally definitive comparison involves the responses (relative to the average of the pair at C_7 and C_8) of the allylic methylene groups and the α- and β-vinyl hydrogen atoms. In one isomer, these three types have the following properties (chemical shift and *relative LIS*): 2.35 (2 H) *0.25*; 5.46 (1 H) *0.20*; 6.14 (1 H) *0.63*; in the other: 3.45 (2 H), *0.87*; 5.93 (1 H) *0.26*; 5.50 (1 H) *0.22*.

In the former, the less strongly chemically shifted methylene group is the less responsive to LIS, whereas one vinyl hydrogen is strongly responsive; in the latter, the more strongly chemically shifted methylene group is the more responsive to LIS, but none of the vinyl hydrogen atoms is markedly responsive. This ordering correlates well with an estimate of the relative slopes based on distances taken from Dreiding models (the average of the two twist conformations; Eu–N taken as 2.60 Å) and the McConnell expression for pseudo-contact shift ($[3 \cos \theta^2 - 1]/r^3$): in **2** (same order of hydrogen types as above), 0.40, 0.38, and 0.96 are the relative responses to LIS; in **3** 1.08, 0.38, and 0.35.

Similarities in ^{13}C resonances in *N*-methyl-Δ^3-piperidine[21] and **3** are sufficiently clear not to warrant comment. Models for **2** include *N*-cyclohexenylpiperidine and pyrrolidine in both of which the β-carbon of the enamine is far upfield from the α-carbon: 100.0 and 93.8 ppm vs. 146.3 and 142.6 ppm, respectively.[22] Much the same spread is found in several of the relatively unhindered enamines examined by Achmed and Hickmott:[23] *N*-(Z)-propenylpyrrolidine (βC, 97.1; αC, 137.6) and *N*-[(E)-4-methylpent-3-enyl]pyrrolidine (βC, 95.4; αC, 151.5). However, this spread is narrowed significantly by a downfield shift of the β-carbon atom in two *cis*-propenyl derivatives of piperidine: *N*-[2-methylpropenyl]piperidine (βC, 123.5; αC, 135.9) and *N*-[2,4-dimethylpent-3-enyl]piperidine (βC, 125.2; αC, 147.2).[23]

Their similarity to **2** (βC, 128.6; αC, 143.3) lends some support to the speculation that these, too, have twisted, non-overlapping systems of π-bonded and nonbonded orbitals.

Equilibrium between **2** and **3** is established in two ways. The first involves catalysis by lithium diisopropylamide in hexamethylphosphoric amide. In four runs with **3** at room temperature for times ranging from 0.4 to 144 h (recovery droping with time from 100% to 45%), the composition was 51.5 ± 0.6% **3** corresponding to an equilibrium constant $K = 2/3 = 0.94$ ($\Delta\Delta G = +35$ cal/mol). In one run starting with **2** (11% **3**), the equilibrium composition was 51.6% **3**.

In light of the discovery by Ahlbrecht and Rauchschwalbe[24] that enamines can be lithiated by butyllithium, it needed to be established that 4-lithio-1-azabicyclo[3.2.2]non-2-ene had not been formed quantitatively and given rise to **2** and **3** under the kinetic control of protonation. Deuterium oxide was therefore added instead of water at the conclusion of the equilibration. Examination of the ^{2}H NMR spectrum of the resulting mixture limited the maximum amount of incorporation of deuterium to 3%.

Another catalytic system for migrating double bonds and therefore potentially for establishing equilibrium among unsaturated isomers is the ruthenium hydridonitrosotris(triphenylphosphine) catalyst of Osborn and Wilson.[25,26] It has been applied to several systems[27] and is successful with amino olefins in contrast to the strongly basic catalysts, which often effect extensive elimination to dienes where structurally possible.

In the hope of refining our thermochemical understanding of the enamine system, the ruthenium catalyst was applied to the (dimethylamino)phenyl three-carbon system, **1t**, **1c**, and **1e** (R = CH$_3$, Scheme I). As described in greater detail elsewhere,[27] the analytical problems connected with the enamines can only be resolved imperfectly, so that the level of accuracy remains insufficient to the task of extracting reliable values for ΔH and ΔS. From equilibrium values (**1e/1t**, R = CH$_3$) of 12.3 ± 2 at 80.6 °C, 5.2 ± 2 at 97.5 °C, 6.3 ± 2 at 110.7 °C and 4.9 ± 2 at 126.1 °C, little can be concluded about ΔH, although ΔG (80.6 °C) with a value of 1.8 kcal/mol falls within the same range as that determined by previous workers.[8,9]

When applied to the bicyclic amines **2** and **3** the catalyst works well and establishes equilibrium at 97.5 °C corresponding to a value of K (**2/3**) of 1.0 ± 0.1. Although this value does not, for analytical reasons, have the hoped-for accuracy, it also points to a difference in free energy near zero.

The conclusion seems clear: the considerable conjugative interaction (ΔG) in an enamine (1.8 kcal/mol greater than phenyl; in turn 1.8 kcal/mol greater than methyl; itself 2.3 kcal/mol greater than hydrogen) vanishes when the nonbonded electrons of nitrogen are restricted to an orbital obligatorily nearly orthogonal to the π-orbital of the olefin. In full agreement with theoretical calculations and the inference of Schwotzer and von Philipsborn,[12] maximum conjugative interaction in enamines requires a parallel orientation of the n-pair of the nitrogen atom and the π-pair of the olefinic bond. Whether the n-pair prefers an sp^3 pyramidal to a p trigonal conformation cannot be differentiated in this work, although theoretical work gives an affirmative answer.[2b]

There appears to be no acceptable way of transferring this experience with enamines to enol ethers; but an extension to the analogous phosphine system is easily imaginable.

Experimental Section

NMR spectra are measured in CDCl$_3$ solution on Varian T-60, JEOL FX-270, and Bruker WM 300 spectrophotometers and are reported in ppm (δ) from Me$_4$Si. IR spectra are measured on a Perkin-Elmer 337 grating spectrophotometer and calibrated against the 1601-cm^{-1} ab-

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Conjugative Interaction in 1-Azabicyclo[3.2.2]non-2-ene

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sorption of polystyrene. GLC analyses are performed on a Perkin-Elmer Model 990 gas chromatograph with flame ionization detector and a Hewlett-Packard Model 3380S recording digital integrator. Preparative GLC and approximate analyses are effected with an Aerograph A90-P3 instrument. The following columns are used in analytical or preparative work—column A, 2 m × $^1/_4$ in. 10% XF 11–50 on 50/60 mesh Anakrom ABS; column B, 3 m × $^3/_8$ in. 10% Carbowax 20M on 50/60 mesh Anakrom ABS; column C, 1 m × $^1/_4$ in. 15% Carbowax 20M on 50/60 mesh Anakrom ABS; column D, Perkin-Elmer Carbowax capillary column K20M 300 ft × 0.010 in.

Melting points (uncorrected) are determined on a Hershberg apparatus. Mass spectra are recorded on an AEI Model MS-9 double-focussing mass spectrometer.

1-Azabicyclo[3.2.2]nonan-4-one (4). A stirred suspension of 3-quinuclidone hydrochloride (Aldrich) (20 g, 0.124 mol) in methanol (120 mL) is treated with sodium carbonate (24 g, 0.23 mol) at room temperature. Stirring is continued for 2 h. The filtered solution of the free amine is added dropwise at −15 °C to a stirred solution of diazomethane prepared from *N*-nitroso-*N*-methylurea (34 g, 0.33 mol) in ether (480 mL). Stirring is continued at room temperature for 20 h, when a test with acetic acid shows complete disappearance of diazomethane. The yellow reaction mixture is filtered from inorganic salts and concentrated in vacuo. The residue is treated with ether (200 mL) and kept at ca −10 °C for 3 h, when some tar is deposited. Filtration through a short column of neutral alumina (Woelm) and removal of the solvent in vacuo gives 15.6 g (90%) of pale-yellow oil, shown by GLC (Aerograph, column A, 129 °C, He 60 mL/min) to consist of unreacted 3-quinuclidone (20%, retention time 12 min), 4 (75%, 67.5% of the yield, retention time 25 min), and two higher homologues (5%, retention time 35 and 38 min) not further investigated. The crude reaction mixture is conveniently used in the subsequent step without further purification. For analytical purposes a pure sample of 4 is obtained by preparative GLC: IR 1725 (C=O) cm⁻¹; NMR (60 MHz) 1.87 (m, 4), 2.40 (q, 1), 2.56 (t, 2), 2.90 (m, 6); mp 120–121 °C; methiodide mp 160–161 °C dec. Anal. Calcd for $C_9H_{16}NOI$: C, 38.5; H, 5.7; N, 5.0. Found: C, 38.4; H, 5.9; N, 4.7.

1-Azabicyclo[3.2.2]nonan-4-one-2,2-d_2. A solution of 3-quinuclidone hydrochloride (10 g, 0.062 mol) in 40% KOD (50 mL) is allowed to stand in the dark at room temperature for 2 weeks. The aqueous solution is extracted with ether (4 40-mL portions), and the ether extract is dried (MgSO₄), filtered, and concentrated by distillation through a 30-cm vacuum-jacketed Vigreaux column to yield a yellow, waxy solid, sublimation of which (in vacuo) gives 3-quinuclidone-d_2 (0.37 g): NMR (60 MHz) 1.96 (m, 4), 2.33 (q, 1), 2.93 (m, 4), no signal at 3.1 (s, 2) as seen in 3-quinuclidone.

A solution of 3-quinuclidone-d_2 (0.198 g, 0.0016 mol) in methanol (2 mL) is treated with a 0.3 M solution of diazomethane in ether (6.4 mL, 0.002 mol CH₂N₂) and allowed to stand in an ice bath for ca. 24 h. The solvent is removed in vacuo, giving a yellow, oily residue, which is dissolved in methanol and purified by preparative GLC (column B, 120 °C, He 50 mL/min, retention time 2.5 min). The NMR spectrum (60 MHz) reveals two changes: the triplet at 2.56 in undeuterated material is now a singlet, while the multiplet at 2.90 is reduced from 6 H to 4 H.

1-Azabicyclo[3.2.2]non-3-ene (3). A solution of crude 4 (15.6 g, 0.112 mol) and tosylhydrazine (22.9 g, 0.124 mol) in dry THF (100 mL) is refluxed with stirring under nitrogen for 24 h. The cooled reaction mixture is filtered and the precipitate is washed with ether, leaving 17.1 g (50%) crude tosylhydrazone, mp 169–170 °C dec, which is conveniently used in the next step without further purification. An analytical sample is obtained by recrystallization from methanol: mp 172–173 °C. Anal. Calcd for $C_{15}H_{21}N_3SO_2$: C, 58.6; H, 6.9; N, 13.7; S, 10.4. Found: C, 58.9; H, 6.8; N, 12.6; S, 10.8.

In the procedure of Shapiro and Duncan,[20] a 1.65 M ethereal solution of methyllithium (68 mL) is added to a stirred suspension of dry, powdered tosylhydrazone (9.3 g, 0.03 mol) in ether (150 mL) at 21–24 °C over a period of 40 min under nitrogen. Stirring is continued for 3.5 h, and the yellow suspension is quenched with water (80 mL). The water layer is extracted with pentane, the combined organic layers are dried (MgSO₄), and the solvent is removed with a 30-cm Vigreaux column, giving 2.1 g of crude product shown by GLC analysis (column C, 100 °C, He 40 mL/min) to consist of 7% 1-azabicyclo[2.2.2]octene (identified by its NMR spectrum and co-injection with an authentic sample; retention time 4 min), 90% 3 (retention time 7 min), and 3% higher homologues. Pure 3 (1.8 g, 48% of the yield) is collected by GLC as colorless hygroscopic crystals: ¹H NMR (270 MHz) 1.86 (m, 4), 2.25 (m, 1), 2.92 (t, 4), 3.47 (s, 2), 5.50 (d, 1, J = 10 Hz), 5.93 (dd, 1, J = 10.5 Hz); ¹³C NMR 135.3, 131.2, 60.6, 47.0, 30.8, 26.5; *m/e* 123.1054 (calcd for $C_8H_{13}N$ 123.1048).

General Procedure for Isomerization of 1-Azabicyclo[3.2.2]nonenes. Amine is treated with a 1 M solution of lithium dimethylamide (Ventron Corp.) in hexamethylphosphoric amide, freshly distilled from LiAlH₄.

Table I. Isomerization of Δ²- and Δ³-1-Azabicyclo[3.2.2]nonenes with 1 M LiNMe₂ in HMPA at Room Temperature

amine, g	base, mL	time, min	recovery, %	composition, %	
				3	2
3, 0.618	5.4	120	87.5	52.2	47.8
(aliquot		25		51.7	48.3)
3, 0.421	3.5	1440	69.3	50.9	49.1
3, 0.040	0.5	8640	45.0	51.2	48.8
2, 0.040^a	0.14	120		51.6	48.4

^{a} 90% **2**; 10% **3**.

(All operations are performed in a plastic bag under argon.) The resulting dark red solution is allowed to stand at room temperature for various lengths of time. The reaction mixture is then diluted with pentane, quenched with ice water, and extracted continuously with pentane for 24 h. The organic layer is washed with water, dried (MgSO₄), and concentrated by distillation with a Vigreaux column (water bath). The residual product is analyzed by GLC (Perkin-Elmer 990; column D, 65 °C; He 32 lb): retention times of **3** and **2** are 14 and 13 min, respectively. The results are given in Table I.

1-Azabicyclo[3.2.2]non-2-ene (2). A mixture of isomerized amines (44% **2** and 56% **3** by GLC, column D) (0.172 g) is dissolved in 0.5 mL of absolute ethanol and treated at 0 °C with 47% HI (0.450 mL). Solvent and excess HI are removed in vacuo at 0 °C to give a residue which is dissolved in 4 mL of absolute EtOH. Left overnight in the refrigerator, the solution deposits crystals which are suspended in ether and treated at 0 °C with 1 N NaOH. The ether layer is separated, the aqueous layer is extracted three times with ether, and the combined ether layers are dried (MgSO₄). Removal of solvent by distillation with a Vigreaux column (water bath) gives a mixture consisting of 66% **3** and 34% **2**.

The dark yellow mother liquor is treated with charcoal and concentrated in vacuo at 0 °C to a residue which is recrystallized twice from absolute ethanol. Decomposition with NaOH as above yields 0.027 g (36%) of enriched **2** (89.2% **2**, 10.8% **3**) of sufficient purity to furnish good NMR spectra: ¹H NMR (270 MHz) 1.67 (m, 4), 1.96 (m, 1), 2.23 (m, 2), 2.06 (m, 4), 5.38 (m, 1), 6.07 (m, 1); ¹³C NMR 143.3, 128.6, 50.2, 39.1, 38.4, 27.4 (derived from the spectrum of an ca. 1:1 mixture of **2** and **3**); *m/e* 123.1050 (calcd for $C_8H_{13}N$ 123.1048).

The magnitude of the shifts induced by the lanthanide, Eu(fod)₃, was determined at 270 MHz, examination at 60 MHz having failed to separate completely the hydrogen atoms in **3** 1.71, 2.02, and 2.21 ppm. In the usual manner, both CHCl₃ and Me₄Si were included as internal standards in order to fix the chemical shifts extrapolated to zero concentration of LIS reagent. The results are indicated in Figure 1.

Quenching of the Isomerized Mixture of 2 and 3 with D₂O. Isomerization of **3** is performed as above: the dark-red solution is kept at room temperature for 2 h and quenched with D₂O from a vial freshly opened under argon. The isolated mixture of **2** and **3** (>95%) is analyzed by ¹H NMR (270 MHz) by using the base-line-separated allylic protons of **3** and the sum of the vinyl hydrogen atoms of **2** and **3**. The ratio [3 (allylic)/[2 + 3](vinylic)] is 0.46 ± 0.06.

A solution of the mixture in 2.5 mL of CCl₄ is treated with 10 μL each of 10% solutions of CHCl₃ and CDCl₃ in CCl₄. These serve as quantitative references. The ²H NMR (Bruker 300 MHz) at a spectral frequency of 46.07 MHz shows only the peak for CDCl₃ at 7.25 ppm. The ratio of noise to this signal is 0.021. On the basis of the solution containing 0.0123 mmol of DCCl₃, an estimate of the maximum amount of deuterium in the mixture of **2** and **3** is 2.6 × 10⁻⁴ mmol. From the amount of CHCl₃ as reference in the ¹H NMR and an observed ratio of vinylic H to HCCl₃ of 1.38, it is calculated that 8.5 × 10⁻³ mmol of bicyclic amines are present in the solution. A reasonable value for maximum incorporation of deuterium is then 3%.

The equilibrium constant, $K = 2/3$, estimated from the results of the ¹H NMR above, has the value 1.2 ± 0.3.

Ruthenium-Catalyzed Isomerization of 3. A solution of **3** (0.012 g) in benzene-d_6 (0.5 mL) containing RuH(NO)(Ph₃P)₃ (0.005 g) and toluene (1 mL) as internal standard is apportioned between two Pyrex ampules (previously soaked in aqueous NH₃, washed with water and acetone, and dried at 250 °C for 24 h), degassed under vacuum by 4 "freeze-thaw" cycles, and sealed. The sealed ampules are suspended in vapors of 1-propanol (bp 97.5 °C) boiling under reflux in a long-necked (46 × 5 cm) 1-L round-bottomed flask insulated with asbestos tape. Temperature is monitored by an iron–constantan thermocouple (Leeds and Northrup millivolt potentiometer, Model 8686). After being heated for 48 and 24 h, respectively, the ampules are introduced into liquid nitrogen and opened under argon. Volatile material is separated from

the catalyst by two trap-to-trap distillations (recovery ca. 100%) and analyzed by GLC (column D). Quantitative estimation of the composition of the reaction mixture from the ampule heated at 97.5 °C is accomplished by "cut and weigh" of enlarged traces from 10 copies of the chromatogram ($K = 1.1 \pm 0.1$).
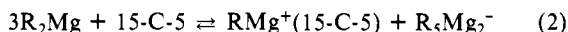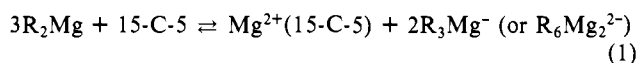
Magnesiate Ions in Solutions and Solids Prepared from Dialkylmagnesium Compounds and Cryptands

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Abstract: Addition of 2,1,1-cryptand to diethylmagnesium solutions greatly speeds reactions with pyridine and leads to formation of significant amounts of a 1,4- as well as a 1,2-addition product, observations attributed to formation of magnesiate species. In crystalline [EtMg$^+$(2,2,1-cryptand)]$_2$ Et$_6$Mg$_2$$^{2-}$, the magnesiums of the dianion are identical and have essentially a tetrahedral bonding geometry. They share two bridging ethyl groups, and each is bonded to two terminal ethyl groups. The magnesium of the cation is bonded to five of the heteroatoms of the cryptand and to the ethyl group. In crystalline NpMg$^+$(2,1,1-cryptand) Np$_3$Mg$^-$, the magnesium of the anion has a trigonal planar bonding geometry. The coordination geometry of the magnesium of the cation is essentially that of a pentagonal bipyramid with bonds to all six of the heteroatoms of the cryptand and a bond to the neopentyl group. The ^{1}H NMR spectrum of a benzene solution of this solid is consistent with the presence of the same ions in the solution.

Earlier work on the consequences of adding 15-crown-5 to diethyl ether or tetrahydrofuran solutions of dialkylmagnesium compounds led to the proposal that striking chemical properties of the resulting solutions were due to low concentrations of magnesium "ate" species, such as R$_3$Mg$^-$, formed by equilibria such as those in eq 1 and 2.[2] In this paper we report much stronger evidence for the formation of such anions.

$$3R_2Mg + 15\text{-}C\text{-}5 \rightleftharpoons Mg^{2+}(15\text{-}C\text{-}5) + 2R_3Mg^- \text{ (or } R_6Mg_2^{2-}) \quad (1)$$

$$3R_2Mg + 15\text{-}C\text{-}5 \rightleftharpoons RMg^+(15\text{-}C\text{-}5) + R_5Mg_2^- \quad (2)$$

It was reasonable that an appropriate cryptand might coordinate Mg^{2+} or RMg$^+$ more effectively than does 15-crown-5, and models indicated 2,1,1-cryptand to be a particularly attractive possibility. The models were constructed[3] both (1) by considering magnesium to be an ion (Mg^{2+}) with a radius of 0.7–0.8 Å and the atoms bonded to it to have conventional van der Walls radii and (2) by considering magnesium to be covalently bonded and the Mg–C, Mg–N, and Mg–O bonds to have typical lengths observed in crystal structures. Models of both sorts indicated that all heteroatoms of the cryptand could potentially bond to magnesium, enveloping it so effectively that no more than one bond to any other group would be possible.

Addition of 2,1,1-cryptand to diethyl ether solutions of Et$_2$Mg resulted in immediate formation of precipitates. Such suspensions exhibited reactivity toward added pyridine similar to that of solutions[2] formed by adding 15-crown-5 to Et$_2$Mg. In the absence of an additive, addition of Et$_2$Mg is very slow and produces exclusively **1**. Addition of 15-crown-5 leads to much more rapid additions that also produce significant amounts of **2**. As indicated by the results summarized in Table I, even relatively small amounts

Table I. Product Compositions from Reactions of Diethylmagnesium, Cryptands, and Pyridine in Diethyl Ether at 25 °C^a

relative molar amounts^b			additive	**1**,^{c} %	**2**,^{c} %
Et$_2$Mg	: cryptand	: pyridine			
1	0	2		0.6	<0.01
1	0.03	1.5	2,1,1-cryptand	2	8
1	0.05	2	2,1,1-cryptand	6	12
1	0.2	0.75	2,1,1-cryptand	4	22
1	1	0.5	2,1,1-cryptand	13	24
1	1	1	2,1,1-cryptand	14	31
1	1	2	2,1,1-cryptand	15	15
3	1	1	2,1,1-cryptand	10	24
1	0.05	1	2,2,1-cryptand	0.5	2
1	1	2	2,2,1-cryptand	15	10
2	1	1	2,2,1-cryptand	20	25
3	1	1	2,2,1-cryptand	10	28
1	1	1	2,2,2-cryptand	5	2
2	1	1	2,2,2-cryptand	4	10

^{a} Reaction times are ~24 h. ^{b} The concentration of pyridine generally was ~0.1 M. ^{c} Yields are based on mol of **1** and **2** per mol of Et$_2$Mg or pyridine, whichever was in lesser amount.

of 2,1,1-cryptand produced the same effects.[4] Suspensions formed by adding 2,2,1-cryptand or 2,2,2-cryptand to Et$_2$Mg showed similar reactivity.
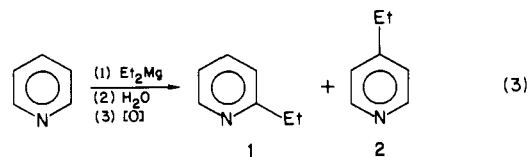
We have not succeeded in obtaining crystals suitable for single-crystal X-ray analysis from solids prepared from Et$_2$Mg and

(1) Most of this material is taken from: Squiller, E. P. Ph.D. Dissertation, The Pennsylvania State University, University Park, PA, 1984.

(2) Richey, H. G., Jr.; King, B. A. *J. Am. Chem. Soc.* **1982**, *104*, 4672.

(3) The cryptand was constructed by using CPK space-filling molecular models (Ealing Corp.).

(4) The yields of **1** and **2** do not increase greatly with longer reaction times. Metalation of pyridine, a significant competing reaction, is at least one limitation to these yields.