About 2.0 mg of this reaction mixture was dissolved in 10 ml of ether and placed in a 15-ml three-necked flask equipped with a gas inlet, a condenser, and a magnetic stirrer. About 2 mg of PtO_2 was added and the solution stirred for 1 hr while H_2 gas was bubbled through. Only a single product was obtained as shown by vlpc on two different columns (column F at 85° and column G at 85°).

Reaction of 1,3-Dimethylbicyclobutane (3) with Dimethyl Acetylenedicarboxylate. A solution of *ca.* 82 mg (1 mmol) of 1,3-dimethylbicyclobutane (**3**) in 400 μl of acetonitrile and 70 μl of dioxane was placed in a 2-ml centrifuge tube equipped with a condenser. To this solution was added 135 mg (0.95 mmol) of dimethyl acetylenedicarboxylate. The solution turned yellow on standing at room temperature for 24 hr. Vlpc analysis (column E at 105°) showed the presence of only one peak in 30% yield. Preparative vlpc gave pure dimethyl (*Z*)-2-(1,3-dimethyl-2-cyclobutenyl)butendioate (**24**) identified as indicated in the text.

Thermal Rearrangement of 24. **24** (18 μl) was heated in a sealed ampoule (0.15 ml) at 120° for 1.5 hr. Vlpc analysis (column E at 105°) showed a single major peak in addition to one for unrearranged starting material. Preparative vlpc afforded 1,3-dimethyl-4,5-dicarbomethoxy-1,3-cyclohexadiene (**26**), identified as indicated in the text.

When 1.5 μl of **26** was heated with 0.1 g of chloranil in refluxing benzene for 3 hr, it was converted to dimethyl 3,5-dimethylphthlalate as shown by vlpc analysis (column H at 140°) and infrared spectroscopy.

Reaction of 1,3-Dimethylbicyclobutane (3) with Acrylonitrile. A solution of 125 mg (1.5 mmol) of **3** and 64 mg (1.2 mmol) of acrylonitrile in 190 μl of acetonitrile and 100 μl of dioxane was kept at room temperature for 24 hr in a 2-ml centrifuge tube equipped with a condenser. Vlpc (column I at 100°) indicated *ca.* 27% yield and gave pure 3-(1,3-dimethyl-2-cyclobutenyl)propanenitrile (**25**) whose spectra are given in the text.

Acknowledgement. We wish to thank the donors of the Petroleum Research Fund administered by the American Chemical Society (Grant 271 G) and the National Science Foundation (Grant GP-7859) for partial support of this work.

1-Azabicyclobutanes. Synthesis and Reactions[1]

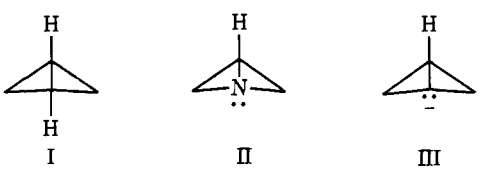
Alfred G. Hortmann* and David A. Robertson[2]

Contribution from the Department of Chemistry, Washington University, St. Louis, Missouri 63130. *Received July 27, 1971*

Abstract: Treatment of 2-phenylazirine with dimethylsulfonium methylide affords a 68% yield of 2-phenyl-1-azabicyclobutane (**2a**), the first authentic example of a heterocyclic bicyclobutane to be isolated and characterized. Extension of the synthesis to the preparation of **2b**, **2c**, **4a**, and **4b** is also described. Acid-catalyzed ring-opening reactions leading predominantly to products of 1,3 addition of water and methanol are described and discussed in detail for several of the azabicyclobutanes. Addition of hydrogen chloride to **2a–c** yields the 3-chloro-3-phenylazetidine hydrochlorides **7a–c** exclusively. The free amines liberated from **7a–c** rapidly and quantitatively recyclize to **2a–c** at 0°.

Since the first synthesis of a substituted bicyclobutane was reported by Wiberg and Cuila in 1959, a number of routes to this carbocyclic ring system have been developed.[3] More recently interest has been focused on the nature of the bonding in bicyclobutane (I).[4] Of particular interest is its high dipole moment (0.675 ± 0.01 *D*),[5] its unexpectedly large strain energy (64 kcal/mol),[3a] and the uv spectra of 1-carboxyl- and 1,3-diphenyl-substituted derivatives which suggest that conjugative interactions of these substituents with the bicyclic ring system can occur.[3a]

The acidity of the bridgehead protons and the ^{13}C–H coupling constant (205 Hz)[6] associated with these hydrogens suggest that the bridgehead C–H bonds have appreciable s character. When considered with the uv data and the ability of bicyclobutanes to undergo facile 1,3 addition of water, methanol, halogens, amines, and olefins,[3a,e,f,7] these data have led a number of workers to regard the central bond of bicyclobutanes as having ethylenic or even acetylenic character;[8] the extent of the latter has been estimated from the value of the bridgehead ^{13}C–H coupling constant,[3a,9] although the application of this parameter to strained ring systems has been questioned.[10]



It was felt, at the outset of this program, that since amines are highly sensitive to electronic effects, an

(1) For earlier reports in this series, see (a) A. G. Hortmann and D. A. Robertson, *J. Amer. Chem. Soc.*, **89**, 5974 (1967); (b) J. L. Kurz, B. K. Gillard, D. A. Robertson, and A. G. Hortmann, *ibid.*, **92**, 5008 (1970); (c) A. G. Hortmann and J. E. Martinelli, *Tetrahedron Lett.*, 6205 (1968).

(2) (a) Abstracted in part from the Ph.D. dissertation of D. A. Robertson, Washington University, 1970; (b) National Science Foundation Trainee, 1968–1969.

(3) (a) K. B. Wiberg, *Advan. Alicyclic Chem.*, 2, 185 (1968), and references cited; (b) M. R. Rifi, *J. Amer. Chem. Soc.*, **89**, 4442 (1967); (c) D. P. G. Hamon, *ibid.*, **90**, 4513 (1968); (d) W. G. Dauben and J. S. Ritscher, *ibid.*, **92**, 2925 (1970); (e) L. Skattebøl, *Tetrahedron Lett.*, 2361 (1970); (f) W. R. Moore, K. G. Taylor, P. Müller, S. S. Hall, and Z. L. F. Gaibel, *ibid.*, 2365 (1970).

(4) J. M. Schulman and G. J. Fisanick, *J. Amer. Chem. Soc.*, **92**, 6653 (1970), and references cited.

(5) M. D. Harmony and K. W. Cox, *ibid.*, **88**, 5049 (1966); K. W. Cox M. D. Harmony, G. Nelson, and K. B. Wiberg, *J. Chem. Phys.*, 50, 1976 (1969).

(6) K. Wuthrich, S. Meiboom, and L. C. Snyder, *ibid.*, **52**, 230 (1970).

(7) (a) E. P. Blanchard, Jr., and A. Cairncross, *J. Amer. Chem. Soc.*, **88**, 487, 496 (1966); (b) K. B. Wiberg and G. Szeimies, *ibid.*, **92**, 571 (1970); (c) W. G. Dauben and C. D. Poulter, *Tetrahedron Lett.*, 3021 (1967).

(8) M. Pomerantz and E. W. Abrahamson, *J. Amer. Chem. Soc.*, **88**, 3970 (1966).

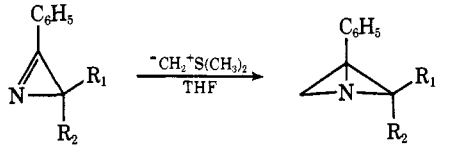
(9) N. Muller and E. Pritchard, *J. Chem. Phys.*, **31**, 768, 1471 (1959).

(10) See discussion in K. B. Wiberg, G. M. Lampman, R. P. Cuila, D. S. Connor, P. Schertler, and J. Lavanish, *Tetrahedron*, **21**, 2749 (1965).

alternate estimate of the hybridization of the bridgehead atoms of bicyclobutanes could be derived from a determination of the pK_a of the conjugate acid of the unknown 1-azabicyclobutane system (II). The pK_a of this system might be expected to lie somewhere in the large range between the pK_a values for, *e.g.*, pyridine (pK_a = 5.3 sp^2 hybridized N) and acetonitrile (pK_a = −10.1, sp-hybridized N).[11] Thus, the synthesis, characterization, and determination of the basicity of a substituted 1-azabicyclobutane became the primary goal of this work.[12,13]

Synthesis and Characterization

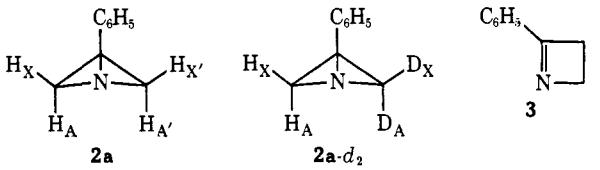
The first approach tried was based in the known reactivity of dimethylsulfonium methylide and dimethyloxosulfonium methylide[14] toward imines to yield aziridines.[14,15] Slow addition of 2-phenylazirine (**1a**)[16] to a slight excess of dimethylsulfonium methylide in tetrahydrofuran maintained under N_2 at −20° consistently produced 3-phenyl-1-azabicyclobutane (**2a**) as a colorless liquid in 60–70% yield after a normal work-up procedure followed by distillation.[17]



1a, $R_1 = R_2 = H$ — **2a**, $R_1 = R_2 = H$
b, $R_1 = CH_3$, $R_2 = H$ — **b**, $R_1 = CH_3$, $R_2 = H$
c, $R_1 = R_2 = CH_3$ — c, $R_1 = R_2 = CH_3$

The structural assignment for **2a** was supported by its nmr spectrum: peaks at δ 1.33, 2.64 (2 H each, identical multiplets, AA'XX' pattern) and 7.1–7.5 (5 H, multiplet). Analysis of the ^{13}C satellites[18] of the 2 H multiplets showed the high-field satellite ($J_{^{13}C-H_A}$ = 175 Hz) of the δ 1.33 multiplet to be a doublet of doublets ($J_{H_AH_X}$ = 2.75 Hz, $J_{H_AH_{A'}}$ = 0.65 Hz); the low-field satellite ($J_{^{13}C-H_X}$ = 166 Hz) of the δ 2.64 multiplet also appeared as a doublet of doublets ($J_{H_XH_X'}$ = 6.25 Hz, $J_{H_XH_A}$ = 2.75 Hz).[19] Using the coupling constants obtained from the ^{13}C satellite spectra it was possible to calculate[20] a theoretical AA'XX' line spectrum which was in agreement with that observed for **2a**.[21]

Additional support for structure **2a** and for the assignments of the above coupling constants was drawn from the nmr spectrum of **2a**-d_2 prepared by treatment of **1a** with the ylide derived from trimethylsulfonium-d_9 iodide:[22] signals at δ 1.33 (1 H, doublet, $J_{H_AH_X}$ = 2.7 Hz), 2.64 (1 H, partially resolved multiplet, six lines of approximately equal intensity, $J_{H_XH_A}$ = 2.7 Hz, $J_{H_XD_X}$ = ~1.0 Hz), and 7.1–7.5 (5 H). These data also serve to eliminate the isomeric 2-phenylazetine (**3**) as a possible structure which could logically arise[23] as a product of reaction of **1a** with dimethylsulfonium methylide.[24]



2a **2a**-d_2 **3**

Interestingly, attempts to form **2a** using a dimethyl sulfoxide–tetrahydrofuran (~4:1) solvent mixture resulted in reduced yields of **2a** (*ca.* 20%) and formation of comparable amounts of 1-phenylcyclopropanecarboxaldehyde along with minor amounts of other products. The aldehyde results from reaction of 2 mol of dimethylsulfonium methylide with **1a**. A possible route (Scheme I) might involve formation of the zwitterionic addition product **a** which may collapse *via* **b** to yield **c**; base-catalyzed tautomerization of **c** to the enamine **d**, fcllowed by loss of dimethyl sulfide would yield the aldimine **e**; conjugate addition of the second mole of ylide to **e** might then result in formation of the aldimine **g** by loss of $(CH_3)_2S$ from **f** (*cf.* formation of cyclopropyl ketones from conjugated ketones and dimethyloxosulfonium methylide).[14] Hydrolysis of **g** during the work-up procedure would yield the observed aldehydic product.

Attempts to prepare **2a** by treatment of **1a** with dimethyloxosulfonium methylide[14] in DMSO also led to 1-phenylcyclopropanecarboxaldehyde in 10–20% yield; the yield of **2a**, if formed, was less than

(11) E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 345 (1963).

(12) *A priori*, there did not seem to be any strong reason why II could not exist since it is isoelectronic with the stable carbanion III, and since no appreciable destabilization appears to be introduced in terms of average bond energies by the replacement of the 1-carbon in I with nitrogen, assuming that C=C and C≡C bonds can be taken as adequate models for the C–C bonds of I (see ref 8). Average bond energies (in kcal/mol) are C=C (146.4), C=N (145); C≡C (199.8), C≡N (213): D. J. Royer, "Bonding Theory," McGraw-Hill, New York, N. Y., 1968, p 184.

(13) Azabicyclobutanes had been suggested previously as possible intermediates in several reactions: N. C. Castellucci, M. Kato, H. Zenda, and S. Masamune, *Chem. Commun.*, 473 (1967); F. Lahmani and N. Ivanoff, *Tetrahedron Lett.*, 3913 (1967); R. K. Armstrong, *J. Org. Chem.*, **31**, 618 (1966). See also A. Padwa and D. Eastman, *ibid.*, **34**, 2738 (1969); V. R. Gaertner, *ibid.*, **35**, 3952 (1970); J. A. Deyrup and C. L. Moyer, *Tetrahedron Lett.*, 6179 (1968); J. A. Deyrup and S. C. Clough, *J. Amer. Chem. Soc.*, **91**, 4590 (1969); A. Hassner, J. O. Currie, Jr., A. S. Steinfeld, and R. F. Atkinson, *Angew. Chem.*, **82**, 772 (1970); D. R. Fagerburg, Ph.D. Dissertation, University of Washington, 1970; J. N. Labows, Jr., and D. Swern, *Tetrahedron Lett.*, 4523 (1971). Similar structures have been described in the earlier literature but are of doubtful validity. For a summary see W. L. Mosby, "Chemistry of Heterocyclic Compounds Series," Vol. 15, A. Weissberger, Ed., Interscience, New York, N. Y., 1961, pp 7–9.

(14) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).

(15) V. Franzen and H.-E. Driesen, *Chem. Ber.*, **96**, 1881 (1963); H. Metzger and K. Seelert, *Z. Naturforsch. B*, **18**, 335, 336 (1963); H. König, H. Metzger, and K. Seelert, *Chem. Ber.*, **98**, 3724 (1965).

(16) G. Smolinsky, *J. Org. Chem.*, **27**, 3557 (1962); see also ref 33.

(17) Since our original communication describing the preparation of **2a** (ref 1a) and its formation in low yield by irradiation of 2-phenylallyl azide (ref 1c), a synthesis of the parent 1-azabicyclobutane (II) and its 3-methyl and 3-ethyl analogs by a double Gabriel-type synthesis has been reported: W. Funke, *Angew. Chem.*, **81**, 35 (1969); *Chem. Ber.*, **102**, 3148 (1969).

(18) Signal-to-noise ratios were improved using a Varian Associates C-1024 time-averaging computer. Estimated accuracies are ±0.10 Hz for J_{H-H} and ±2 Hz for $J_{^{13}C-H}$ values.

(19) The assignment of the δ 2.64 multiplet to the exo protons H_X, H_X') of **2a** is arbitrary and is made on the assumption that the magnitudes of the ^{13}C–H coupling constants (exo *vs.* endo) and of the long-range H_XH_X' coupling constant (6.25 Hz) would be unexceptional when compared to those observed in the carbocyclic bicyclobutane series (see ref 3a, 7a).

(20) J. A. Pople, W. G. Schneider, and H. J. Bernstein, *Can. J. Chem.*, **35**, 1060 (1957).

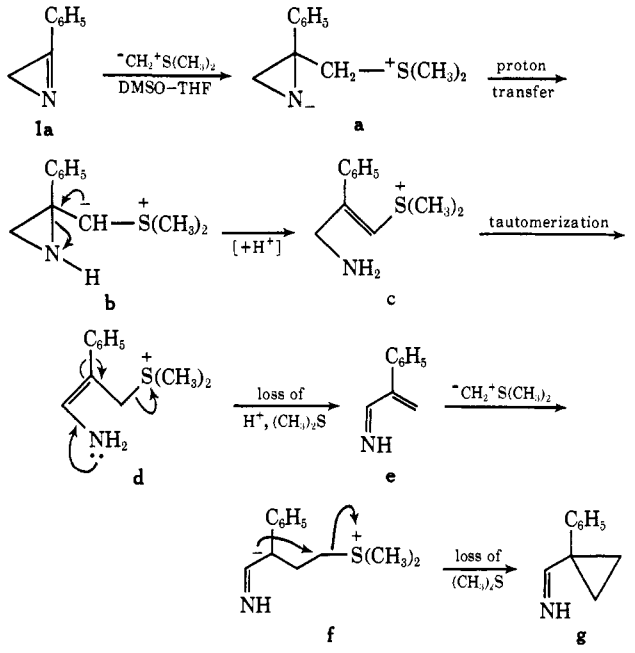
(21) Calculated and observed spectra for H_A, H_A' are recorded in ref 1a.

(22) W. von E. Doering and A. K. Hoffmann, *J. Amer. Chem. Soc.*, 77, 521 (1955).

(23) See footnote 14 in ref 1a.

(24) Several examples of the azetine ring system are now known: A. B. Levy and A. Hassner, *ibid.*, **93**, 2051 (1971), and references cited.

Scheme I



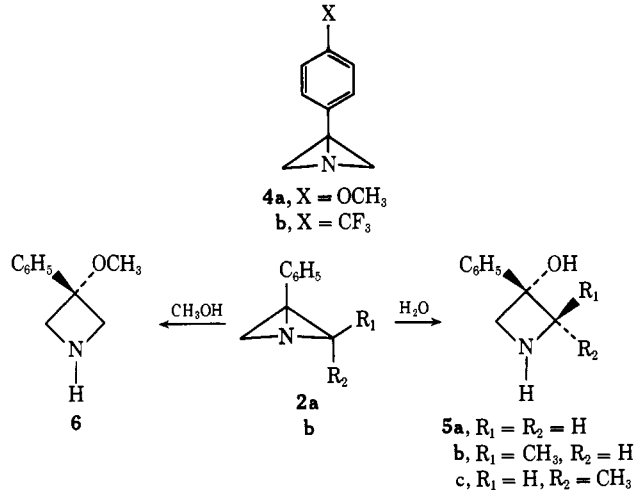
5%.[25] Treatment of **2a** with dimethyloxosulfonium methylide yielded unchanged **2a**, thus establishing that **2a** is not an intermediate in the formation of the aldehyde.

The procedure for the preparation of **2a** could be extended without complication to produce *exo*-2-methyl-3-phenyl-1-azabicyclobutane (**2b**) from 3-methyl-2-phenylazirine (**1b**) in 41% yield. The assigned stereostructure follows from the nmr spectrum of **2b** in which no additional splittings due to the long-range coupling expected of a pair of exo protons at C-2,4 (in the structure epimeric to **2b**) were evident: signals at δ 1.10 (d, 3 H, J = 4.7 Hz; $J_{^{13}C-H}$ = 126 Hz), 1.36 (d, 1 H, J = 2.8 Hz; $J_{^{13}C-H}$ = 172 Hz; 4-*endo*-H), 1.54 (q, 1 H, J = 4.7 Hz; $J_{^{13}C-H}$ = 170 Hz; 2-*endo*-H), 2.36 (d, 1 H, J = 2.8 Hz; $J_{^{13}C-H}$ = 163 Hz; 4-*exo*-H), and 7.3 (m, 5 H); the splitting patterns in the satellite spectra are each identical with the pattern of the corresponding principal peaks. The exclusive formation of the *exo*-methyl stereoisomer indicates that addition of the ylide proceeds entirely from the least hindered side of the azirine. Similar stereospecificity has already been observed in the addition of hydride[26] and of Grignard reagents[27] to azirines.

In a more severe test of the generality of the ylide route to azabicyclobutanes, addition of dimethylsulfonium methylide to **1c** was attempted. The reaction resulted in a 47% yield of 2,2-dimethyl-3-phenyl-1-azabicyclobutane (**2c**): nmr signals at δ 1.07 (s, 3 H), 1.12 (s, 3 H), 2.36 (d, 1 H, J = 1.7 Hz; $J_{^{13}C-H}$ = 173 Hz; 4-*endo*-H), 2.51 (d, 1 H, J = 1.7 Hz; $J_{^{13}C-H}$ = 160 Hz; 4-*exo*-H), and 7.28 (m, 5 H).[28] Of particular interest is the lower field chemical shift of the endo methylene proton in **2c** (δ 2.36) when compared with the chemical shifts of the endo protons in **2a** (δ 1.33) and **2b** (δ 1.36, 1.54). One possible explanation for this lower field shift of the endo proton in **2c** is that it may result, in part, from deshielding due to van der Waals dispersion interactions with the protons of the endo 2-methyl group.[29] An alternate explanation is that any shielding of protons arising from ring-current effects in the bicyclobutanes is probably more intense in the region of the endo methylene protons as a consequence of the folded geometry of the bicyclic ring system; hence, a flattening of the bicyclic structure due to the probable severe interaction of an endo 2-methyl group with the endo C-4 proton in **2c** might reduce the intensity of shielding of the endo proton by altering the position of this proton relative to that of the shielding field. Also, changes in bonding caused by changes in molecular geometry should result in altered ring currents which may contribute positively (or negatively) to the net observed effect.

The azabicyclobutane **2c** was also formed when 2-phenylazirine (**1a**) was treated with diphenylsulfonium isopropylide.[30] However, distillation of the crude product failed to achieve separation of **2c** from numerous other components of the reaction mixture. The yield of **2c** by this route was less than 10% as determined by nmr assay of the distilled product.

Finally, the synthesis of **2a** has been extended to the preparation of the *p*-methoxyl and *p*-trifluoromethyl compounds **4a** and **4b**[31] and, more recently,[32] to the *p*-chloro, *p*-fluoro and *p*-methyl analogs of **2a** in *ca.* 50% yields.[33]



The azabicyclobutane system readily undergoes proton-initiated addition of water. The only detec-

(25) The crude products obtained from several reactions showed an absorption peak at δ 2.60 which indicated possible formation of **2a** in yields of $\leq$5%; no attempts were made at the time to isolate **2a** or confirm its presence.

(26) A. Hassner and F. W. Fowler, *J. Amer. Chem. Soc.*, 90, 2869 (1968).

(27) R. M. Carlson and S. Y. Lee, *Tetrahedron Lett.*, 4001 (1969).

(28) Because of the similarity of chemical shift values in this case, the assignments of peaks due to the exo and endo protons in 2c are based on the $J_{^{13}C-H}$ values.

(29) S. J. Brois, *J. Amer. Chem. Soc.*, 89, 4242 (1967); *Tetrahedron*, 26, 227 (1970).

(30) E. J. Corey, M. Jautelat, and W. Oppolzer, *Tetrahedron Lett.*, 2325 (1967).

(31) The nmr spectrum of **4b** is similar to that of **2a**: δ 1.45, 2.57 (2 H each, identical multiplets, AA'XX' pattern), and 7.52 (m, 4 H). The upfield satellite of the δ 1.45 multiplet ($J_{^{13}C-H}$ = 179 Hz) consists of a doublet of doublets $J_{H_AH_X}$ = 2.40 Hz, $J_{H_AH_{A'}}$ = 0.58 Hz); the downfield satellite of the δ 2.57 multiplet ($J_{^{13}C-H}$ = 166 Hz) also appears as a doublet of doublets ($J_{H_XH_{X'}}$ = 6.40 Hz, $J_{H_XH_A}$ = 2.40 Hz).

(32) B. K. Gillard, unpublished results.

(33) The required 2-(4-substituted)phenylazirines were prepared on a large scale by a modification of the original preparation (ref 16) of **1a**: A. G. Hortmann, D. A. Robertson, and B. K. Gillard, *J. Org. Chem.*, 37, 322 (1972).

table product of hydrolysis of **2a** is 3-phenylazetidin-3-ol (**5a**)[34,35] as evidenced by the following: addition of **2a** (1.00 g) in dioxane (90 ml) to H_2O (1 l.) followed, after 12 hr, by evaporation of the solvent *in vacuo* gave a quantitative yield of crude **5a** which had ir and nmr spectra which were essentially identical with those of analytically pure **5a**. Isotope dilution analysis of the product from **2a** was carried out by adding weighed amounts of both **2a** and **5a**-*2,2-d*$_2$[36] to borax buffer (pH ~9.4) and determining the deuterium content of the carefully purified **5a** product; the yield of **5a** from **2a** was calculated to be 91 ± 5%. The half-life of **2a** at 25° and pH 7 is *ca.* 2 sec.[1b]

Hydrolysis of **2b** in borax buffer provided **5b**, the isomer of 2-methyl-3-phenylazetidin-3-ol having a highly shielded methyl group (δ 0.68; d, 3 H, J = 7.0 Hz) cis to phenyl, as the major product. Two other minor products (overlapping doublets at δ ~1.2, J = ~7.0 Hz) amounting to about 2–3% each of the amount of **5b** formed were also in evidence, one of which is probably the epimeric azetidinol **5b**[37,38] (see below). The result indicates that the addition of water occurs predominantly from the concave face of the protonated azabicyclobutane and supports the structure proposed[1b] for the rate-determining activated complex in the hydrolysis of **2a**.

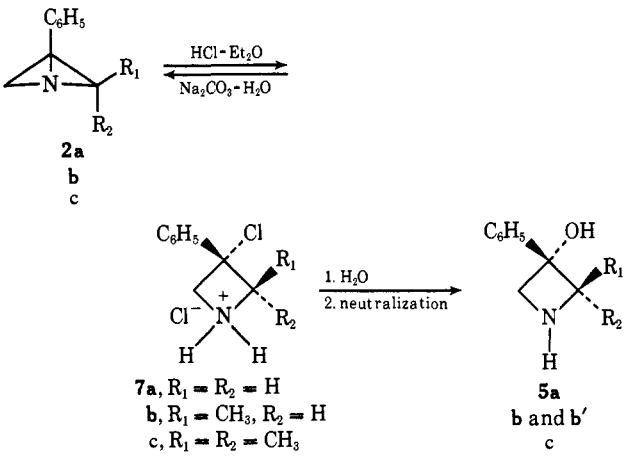
Treatment of a solution of **2a** in anhydrous methanol with a trace of $HClO_4$ afforded 3-methoxy-3-phenylazetidine (**6**) as the only detectable product in 95% yield.

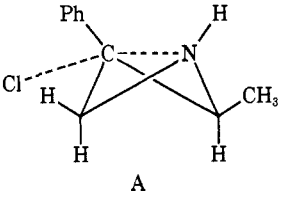
Exposure of the azabicyclobutanes **2a–c** to dry hydrogen chloride in diethyl ether or CH_2Cl_2 led exclusively to formation of the 3-chloro-3-phenylazetidine hydrochlorides **7a–c**; that the addition of chloride to **2b** afforded only one of the two possible stereoisomeric 1,3 addition products is also of interest.

The strong preference for 1,3-bond cleavage in the HCl additions (as well as in the hydrolysis and methanolysis reactions described above) may reflect the ability of the phenyl substituent to stabilize a developing positive charge on C-3, although it is worth noting that Funke[17] has reported the formation of 3-chloro-3-methylazetidine hydrochloride in 85% yield from the addition of hydrogen chloride to 3-methyl-1-azabicyclobutane.

Attempts to liberate the free amines by addition of the hydrochlorides **7a–c** to aqueous Na_2CO_3 solutions at 0–5° led to a surprising observation: in each case the corresponding pure azabicyclobutane **2a–c** was rapidly regenerated in essentially quantitative yield.

Although the formation of 1-azabicyclobutanes from 3-chloroazetidines is related to Funke's[17] double Gabriel-type synthesis of 1-azabicyclobutanes, the 1,3-ring closure of the 3-chloroazetidines apparently takes place under much milder conditions. Since the ring closure is rapid[1b] and the yields of the 1-azabicyclobutanes **2a–c** are high, the mechanism of the ring closure probably involves an internal displacement of the chloride ion by the nitrogen atom of the unprotonated amine. The assumption that an internal displacement mechanism (as depicted by the transition state structure A) is operative can also be inferred from the existence of a trans relationship of the chloro and methyl groups in **7b** which is supported by the presence in **7b** of a methyl group (δ 1.35) shielded by a cis phenyl substituent (*cf.* spectrum of **7c** which has its methyls at δ 1.43 and 2.02).[37,38]





A

When an aqueous solution of **7a** was allowed to stand for several days, the hydrochloride salt of **5a** was formed; similarly, **7c** yielded **5c** after neutralization. Two routes are possible: one involving ring closure of the free amine which is in equilibrium with **7a** to yield **2a** followed by acid-catalyzed hydrolysis of **2a** to yield **5a**[1b] or, alternatively, simple solvolytic replacement of the benzylic chloride by hydroxyl *via* a 1,3-bis-cationic intermediate. The latter route seems more likely in view of the observed formation of a *mixture* (~1:1) of **5b** and **5b'** when the hydrolysis of **7b** was run; it has already been established that **2b**, if formed as an intermediate by the former route, would yield **5b** nearly exclusively.

Attempted hydrogenation of **2a** led to poisoning of the catalysts (Pd–C, Pd–$SrCO_3$) employed after uptake of 0.05–0.15 mol equiv of hydrogen; the **2a** used apparently underwent polymerization. Under homogeneous conditions using tris(triphenylphosphine)-chlororhodium as catalyst, no hydrogen was consumed and **2a** was recovered unchanged. Attempted reduction of **2a** with sodium borohydride in 2-propanol afforded only recovered starting material after 12 hr at room temperature.

The direct measurement of the pK_a of the conjugate acids of **2a–c** was not feasible because of their reactivity;[1b] an indirect determination[11] may be possible.

(34) E. Testa and L. Fontanella, *Justus Liebigs Ann. Chem.*, **671**, 106 (1964).

(35) E. Gold, *J. Amer. Chem. Soc.*, **93**, 2793 (1971).

(36) The deuterated azetidinol **5a**-*2,2-d*$_2$ was obtained by an independent hydrolysis of **2a**-*2,2-d*$_2$ in dioxane–water. The nmr spectrum of the ring protons of **5a**-*2,2-d*$_2$ was a sharp, symmetrical AB pattern (J_{AB} = 8 Hz; $\Delta\nu_{AB}$ = 12 Hz) indicating that the hydrogens do not migrate during the course of the hydrolysis.

(37) The configurational assignments for the methyls in **5b**, **5b'**, and **7b** follow from a comparison of the nmr δ values observed for these methyls with δ values for the methyl signals in **5c** and **7c** (*vide infra*). In each compound, **5c** and **7c**, one of the methyls is strongly shielded by the *cis*-phenyl group (see ref 38). The configurational assignments for **5b** and **5b'** are also consistent with those suggested on similar grounds for *N*-ethyl-**5b** and *N*-ethyl-**5b'** in ref 35.

(38) R. B. LaCount and C. E. Griffin, *Tetrahedron Lett.*, 1549 (1965).

Experimental Section[39]

Trimethylsulfonium-d_9 Iodide.[22] Trimethylsulfonium iodide (89.6 g) recovered from previous deuterium-exchange reactions (incomplete) and containing approximately 35 atom % excess deuterium was dissolved in 145 g of 93% deuterium oxide containing 2.0 g of NaOH. The solution was kept at 60–70° for 5 hr. The solvent was removed *in vacuo*, and the process was repeated with 123 g of 98.5% deuterium oxide containing 1.6 g of additional NaOH. After a third exchange using 224 g of 99.8% deuterium oxide, the solution was acidified with 47% HI, the pH was adjusted to 4–5 with Na_2CO_3, and the solvent was evaporated *in vacuo*. The resulting residue was washed with three 10-ml portions of acetone and dried, yielding 65 g of crude product. Recrystallization from anhydrous EtOH afforded 55 g of trimethylsulfonium-d_9 iodide which had an isotopic purity of 99.1% by nmr analysis.

3-Phenyl-1-azabicyclobutane (2a). Method A. A 500-ml flask fitted with a serum cap was charged with 11.2 g (0.055 mol) of trimethylsulfonium iodide and 200 ml of anhydrous THF. A slight positive pressure of nitrogen was maintained in the flask while the suspension was cooled to −40° and 0.055 mol of *n*-butyllithium in hexane (15.6 g of a 22% solution obtained from Alfa Inorganics) was added dropwise from a syringe. During the addition, the solution was stirred and the temperature was maintained at −20 to −40°. After the addition was complete, the resulting solution of dimethylsulfonium methylide[14] was stirred for 10 min and the temperature was adjusted to −20°. A solution of 5.85 g (0.050 mol) of 2-phenylazirine (**1a**) in 15 ml of anhydrous THF was added dropwise over a period of 50 min. During the addition and for 30 min afterward, the solution was stirred and maintained at −20 ± 2°. The reaction solution was poured into 1 l. of cold H_2O and extracted with four 250-ml portions of CH_2Cl_2 which were combined and dried over anhydrous K_2CO_3. Evaporation of the solvent *in vacuo* left 5.7 g of red oil. Distillation of the crude product *in vacuo* yielded 4.45 g (68%) of 3-phenyl-1-azabicyclobutane (**2a**) which was pure enough for most purposes. Analytically pure **2a** was obtained after four recrystallizations from petroleum ether (bp 35–40°) at low temperature followed by vacuum distillation: bp 50–55° (0.3–0.5 mm); mp 13–15°; nmr (CCl_4) δ 1.33 (m, 2), 2.60 (m, 2), and 7.3 ppm (m, 5); ir (CCl_4) 3050, 2940, 1610, 1584, 1485, 1450, 1400, 1145, 1070, 1025, 820, and 695 cm^{-1}; uv max (cyclohexane) 224.5 nm (ε 9520) and 260 (240, shoulder).

Anal. Calcd for C_9H_9N: C, 82.41; H, 6.92; N, 10.68; mol wt 131.2. Found: C, 82.15; H, 7.05; N, 10.91; mol wt, 131 (mass spectrum), 140 (osmometer).

Method B. A solution of 103 mg (0.51 mmol) of 3-chloro-3-phenylazetidine hydrochloride (**7a**) in 10 ml of EtOH was added with stirring to 10 ml of 5% aqueous Na_2CO_3 solution at 0°. EtOH (5 ml) was used to assure complete transfer of the azetidine hydrochloride. After 1.5 hr at 0°, the solution was diluted with 60 ml of H_2O and thoroughly extracted with CH_2Cl_2. The extracts were combined, dried (K_2CO_3), and evaporated *in vacuo*. The residue was taken up in CCl_4 and transferred to an nmr sample tube containing a weighed amount of 4-nitrotoluene. The nmr spectrum of the product showed only resonance peaks due to the azabicyclobutane **2a** and 4-nitrotoluene; the yield of **2a** (calculated from the integrated spectrum using 4-nitrotoluene as the standard) was 67.5 mg (102%).

2,2-Dideuterio-3-phenyl-1-azabicyclobutane (2a-d_2). 2,2-Dideuterio-3-phenyl-1-azabicyclobutane (**2a-d_2**) was prepared from 2-phenylazirine (**1a**) and trimethylsulfonium-d_9 iodide as described (method A) for **2a**. The nmr spectrum of **2a-d_2** in CCl_4 consists of peaks at δ 1.34 (d, 1, J = 2.7 Hz), 2.60 (m, 1), and 7.3 ppm (m, 5).

2-*exo*-Methyl-3-phenyl-1-azabicyclobutane (2b). Method A. 3-Methyl-2-phenylazirine (**1b**) was prepared as described by Nair.[40] A solution of 6.0 g (0.046 mol) of **1b** in 10 ml of anhydrous THF was added dropwise during *ca.* 30 min to a stirred solution of 0.055 mol of dimethylsulfonium methylide in anhydrous THF at −20°. After 30 min at −20° and 30 min at room temperature, the solution was poured onto 50 g of ice in a separatory funnel. Petroleum ether (200 ml, bp 35–40°) was added, and the organic layer was washed until the wash solutions were colorless, dried (K_2CO_3), and evaporated *in vacuo*. Distillation of the residue yielded 2.76 g (41%) of nearly pure **2b** having bp 36–40° (0.5 mm). A sample of **2b** was recrystallized four times from petroleum ether (bp 35–40°) at −40°. Distillation of the recrystallized material in a short-path still yielded analytically pure **2b**: nmr (CCl_4) δ 1.10 (d, 3, J = 4.7 Hz), 1.36 (d, 1, J = 2.8 Hz), 1.54 (q, 1, J = 4.7 Hz), 2.36 (d, 1, J = 2.8 Hz), and 7.3 ppm (m, 5); ir (CCl_4) 1610, 1480, 1450, 1395, 1170, 1150, 1075, 1030, 995, 870, and 700 cm^{-1}; uv max (cyclohexane) 217.5 nm (ε 8170) and 255 (190, shoulder).

Anal. Calcd for $C_{10}H_{11}N$: C, 82.72; H, 7.64; N, 9.65 Found: C, 82.45; H, 7.49; N, 9.67.

Method B. A solution of 184 mg (8.4 mmol) of 2-methyl-3-chloro-3-phenylazetidine hydrochloride (**7b**) in 20 ml of ethanol was added to 20 ml of 5% Na_2CO_3 solution at 0° with stirring. After 40 min at 0°, the reaction solution was diluted with H_2O and extracted with CH_2Cl_2. The extracts were combined, dried (K_2CO_3), and evaporated *in vacuo* to yield 102 mg (83%) of 2-*exo*-methyl-3-phenyl-1-azabicyclobutane (**2b**) which was pure by nmr analysis.

2,2-Dimethyl-3-phenyl-1-azabicyclobutane (2c). Method A. 3,3-Dimethyl-2-phenylazirine (**1c**) was prepared as described previously.[41] A solution of **1c** (4.83 g, 0.033 mol) in 15 ml of anhydrous THF was added slowly to a solution of 0.036 mol of dimethylsulfonium methylide in anhydrous THF. The reaction temperature was maintained at −12 to −18° during the addition and for 20 min afterward. After the cooling bath was removed and the mixture stirred for 1 hr at ambient temperature, most of the THF was removed *in vacuo* at room temperature and 9 ml of 5% Na_2CO_3 solution was added. The product was extracted with small portions of pentane, and the combined extracts were washed with brine, dried (Na_2SO_4), and concentrated *in vacuo*. Distillation of the remaining oil afforded 2.42 g (46.5%) of pure **2c**, bp 57° (5 mm). An analytical sample was obtained after an additional distillation: bp 69.5–70° (12 mm); nmr (CCl_4) δ 1.07 (s, 3), 1.12 (s, 3), 2.36 (d, 1, J = 1.7 Hz), 2.51 (d, 1, J = 1.7 Hz), and 7.28 ppm (m, 5); ir (CCl_4) 1610, 1450, 1390, 1380, 1305, 1240, 1100, 1090, 1030, 880, and 705 cm^{-1}; uv max (cyclohexane) 217 nm (ε 7920) and 260 (250) (both are shoulders).

Anal. Calcd for $C_{11}H_{13}N$: C, 82.96; H, 8.23; N, 8.81. Found: C, 82.72; H, 8.21; N, 8.81.

Method B. A cylindrical flask was charged with 1.04 g (0.0033 mol) of diphenylisopropylsulfonium tetrafluoroborate[30] and 40 ml of anhydrous THF and immersed in a Dry Ice–acetone bath. Dropwise addition of 0.0033 mol of *tert*-butyllithium (2.66 ml of 1.24 *M* solution in pentane; Alfa Inorganics) was begun. During the addition (1 hr) and for 2 hr afterward the solution was stirred under N_2 and kept at −76°. A solution of 0.35 g (0.003 mol) of 2-phenylazirine (**1a**) in 5 ml of anhydrous THF was added over a period of 1 hr. After an additional 3 hr at −76° the solution was allowed to warm to room temperature. The solution was washed with saturated NaCl solution and the organic layer was dried (Na_2SO_4) and evaporated *in vacuo*. The residue was distilled using a short-path still; yield 0.25 g. The distribution of the products in the distillate was not appreciably different from that of the crude product (nmr analysis). An nmr spectrum showed peaks at 1.07, 1.12, 2.34, and 2.51 ppm which correspond to those of 2,2-dimethyl-3-phenyl-1-azabicyclobutane (**2c**). The area beneath the peaks at δ 2.51 and 2.34 in the integrated spectrum was compared to the total area of the aromatic proton absorption peaks and indicated that about 13 mol % of **2c** was present. No further attempts were made to resolve the mixture of products.

Method C. A solution of 91.4 mg (0.394 mmol) of 2,2-dimethyl-3-chloro-3-phenylazetidine hydrochloride (**7c**) in 20 ml of EtOH was added to 20 ml of 5% Na_2CO_3 solution at 0°. After stirring for 20 min at 0°, the reaction solution was diluted with H_2O and extracted with CH_2Cl_2. The extracts were combined, dried (K_2CO_3), and evaporated *in vacuo* in a tared flask leaving 61.5 mg (98.5%) of 2,2-dimethyl-3-phenyl-1-azabicyclobutane (**2c**) which was pure by nmr analysis.

(39) Melting points and boiling points are uncorrected. Infrared spectra were recorded on Perkin-Elmer Model 21 (prism) or Model 457 (grating) spectrophotometers. Nuclear magnetic resonance spectra were recorded at 60 and 100 MHz using a Varian Associates A-60A or HA-100 instrument. A Varian V-6058A spin decoupler was used for decoupling studies at 60 MHz. Chemical shifts are reported with tetramethylsilane (δ 0.00) or sodium trimethylsilylpropanesulfonate (δ 0.00 in D_2O) as internal standards. Ultraviolet spectra were recorded on a Cary Model 14 instrument. Mass spectra were obtained using a Varian Model M-66 spectrometer. Elemental analyses were provided by Galbraith Laboratories, Knoxvile, Tenn., and by the Microanalytical Laboratory at the Institute for Physical Chemistry, Vienna, Austria. Analyses for deuterium content were performed by Dr. Josef Nemeth, University of Illinois (Urbana), using the falling drop method. Reproductions of the complete infrared and nmr spectra of all compounds described appear in the Ph.D. thesis of D. A. R. (ref 2).

(40) V. Nair, *J. Org. Chem.*, **33**, 2121 (1968).

(41) N. J. Leonard and B. Zwanenburg, *J. Amer. Chem. Soc.*, **89**, 4456 (1967).

3-(4′-Methoxyphenyl)-1-azabicyclobutane (4a). A solution of 1.0 g (0.0069 mol) of 2-(4′-methoxyphenylazirine[33] in 5 ml of anhydrous THF was added to a solution of 0.0082 mol of dimethylsulfonium methylide in anhydrous THF. During the addition and for 30 min afterward the solution was stirred and maintained at about −15°. The solution was allowed to warm to room temperature during about 30 min and was poured into a solution of 2 *N* NaOH saturated with NaCl at 0°. The organic layer was washed with three additional portions of cold NaOH–NaCl solution. The combined washes were thoroughly extracted with CH_2Cl_2. The THF and CH_2Cl_2 solutions were combined, dried (Na_2SO_4), and evaporated *in vacuo* leaving 1 g of viscous red oil which yielded 0.080 g (7.3%) of **4a** after sublimation *in vacuo*. A second sublimation (60° bath temperature, 0.3 mm) gave analytically pure 3-(4′-methoxyphenyl)-1-azabicyclobutane (**4a**): mp 68.5–70.5°; nmr (CCl_4) δ 1.30 (m, 2), 2.57 (m, 2), 3.70 (s, 3), and 6.65–7.35 ppm (m, A_2B_2 pattern, 4); uv max (H_2O) 235 nm (ε 13,300) and 280 (1460).[42]

Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69; mol wt, 161.2. Found: C, 74.30; H, 6.76; N, 8.50; mol wt, 161 (mass spectrum).

In subsequent experiments on a larger scale,[32] yields of 50–60% of **4a** were obtained when the crude product was rapidly distilled (*in vacuo*) at ~50° prior to sublimation.

3-(4′-Trifluoromethylphenyl)-1-azabicyclobutane (4b). 2-(4′-Trifluoromethylphenyl)azirine[33] (1.00 g, 0.0054 mol) in 5 ml of anhydrous THF was added to a solution of 0.0065 mol of dimethylsulfonium methylide in 50 ml of THF. During the addition, which required 20 min, and for 30 min afterward the solution was stirred and maintained at about −20°. After allowing the solution to warm to room temperature over a period of 30 min, the reaction mixture was poured into cold H_2O and extracted with CH_2Cl_2. The extracts were combined, dried (K_2CO_3), and evaporated *in vacuo*. The residue was sublimed at 0.5 mm (50° bath temperature) yielding 0.52 g (48%) of 3-(4′-trifluoromethylphenyl)-1-azabicyclobutane (**4b**), mp 55–58°. The sublimates from several preparations were combined, recrystallized twice from petroleum ether (bp 35–40°), and resublimed yielding analytically pure **4b**: mp 58.5–59.7°; nmr (CCl_4) δ 1.45 (m, 2), 2.67 (m, 2), and 7.52 ppm (m, 4); ir (CCl_4) 1625, 1415, 1330, 1175, 1135, 1070, 1020, 850, 830, 680, and 605 cm^{-1}; uv max (cyclohexane) 230 nm (ε 10,400) and 270 (240, shoulder).

Anal. Calcd for $C_{10}H_8NF_3$: C, 60.30; H, 4.04; N, 7.02. Found: C, 60.18; H, 3.90; N, 6.97.

3-Phenylazetidin-3-ol (5a). Method A. A solution of 1.00 g (0.0076 mol) of 3-phenyl-1-azabicyclobutane (**2a**) in 90 ml of dioxane was added to 1.0 l. of water with stirring. The aqueous solution was allowed to stand for 12 hr. The water was evaporated *in vacuo* at 10–20° leaving 0.98 g (86%) of crude azetidinol **5a**. The water that had been condensed during the evaporation of the reaction solution was reevaporated in the same manner, yielding an additional 0.17 g (15%) of **5a**. The nmr spectra of the residues contained only peaks which were found in the spectra of the finally purified azetidinol **5a**. The residue from the first evaporation was dissolved in CH_2Cl_2 and recrystallized at low temperature yielding pure 3-phenylazetidin-3-ol (**5a**). Analytically pure **5a** was obtained by sublimation (95°, 0.3 mm): mp 150–154° dec (lit.[34] mp 160–162°); nmr (DMSO-d_6) δ 3.72 (m, broad sym A_2B_2 pattern, 4), 4.12 (s, 2, peak width at half-height = 10 Hz), and 7.2–7.8 ppm (m, 5): ir ($CHCl_3$) 3600, 3350, 1420–1450, 1320, 1150, 1065, 1030, 980, 910, and 890 cm^{-1}.

Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39; mol wt, 149.2. Found: C, 72.71; H, 7.40; N, 9.43; mol wt, 149 (mass spectrum).

Method B. A solution of 200 mg (0.98 mmol) of 3-chloro-3-phenylazetidine hydrochloride (**7a**) in 5 ml of H_2O was allowed to stand at ambient temperature for 5 days. The solution was neutralized with Na_2CO_3 and evaporated *in vacuo* at 10–20°. The residue was triturated with CH_2Cl_2. The extract was filtered and evaporated *in vacuo* leaving 120 mg (93%) of white solid. An nmr spectrum of the product showed only absorption peaks due to **5a**.

2,2-Dideuterio-3-phenylazetidin-3-ol (5a-d_2). A sample of 2,2-dideuterio-3-phenyl-1-azabicyclobutane (**2a-d_2**) was hydrolyzed (in D_2O) as described for **2a**. The 2,2-dideuterio-3-phenylazetidin-3-ol obtained was recrystallized from CH_2Cl_2. Mixtures of **5a** and **5a-d_2** exhibited no depression of melting point and **5a-d_2** was identical with **5a** in its nmr spectrum with the exception of the differences due to deuterium substitution which are described in footnote 36.

Anal. Calcd for $C_9H_9D_2NO$: 18.40 atom % excess D. Found: 17.80 ± 0.20 atom % excess D.

Absolute Yield of 5a in Method A as Determined by Isotopic Dilution Assay. A 62.8-mg (0.479 mmol) sample of 3-phenyl-1-azabicyclobutane (**2a**) dissolved in 3 ml of anhydrous dioxane was added to 100 ml of 0.122 *N* NaOH. Additional dioxane (1 ml) was used to assure complete transfer of the azabicyclobutane. The solution was diluted with 100 ml of 0.025 *M* borax solution. A solution of 70.1 mg (0.464 mmol) of 2,2-dideuterio-3-phenylazetidin-3-ol (**5a-d_2**, 17.80 ± 0.20 atom % excess deuterium) in 2 ml of anhydrous dioxane was transferred quantitatively to the aqueous solution. After standing for 18 hr at ambient temperature the solution was evaporated *in vacuo* at 10–20°. The residue was extracted with CH_2Cl_2. Evaporation of the combined and filtered extracts yielded 130 mg (92%) of crude 3-phenylazetidin-3-ol (**5a** and **5a-d_2**). The residue was recrystallized from CH_2Cl_2 yielding 80 mg of pure 3-phenylazetidin-3-ol which contained 9.20 ± 0.15 atom % excess deuterium indicating a yield of 91 ± 5% of **5a** in the hydrolysis of 3-phenyl-1-azabicyclobutane (**2a**).

2-Methyl-3-phenylazetidin-3-ol (5b). A 260-mg (1.8 mmol) sample of 2-*exo*-methyl-3-phenyl-1-azabicyclobutane (**2b**) was dissolved in 2 ml of dioxane and added to a solution of 4 g of borax in 250 ml of water. After 18 hr the solution was evaporated *in vacuo* (10–20°) and the residue was extracted with CH_2Cl_2. The extract was filtered and evaporated leaving 400 mg of residue. The predominant product was 2-methyl-3-phenylazetidin-3-ol (**5b**) (nmr analysis); there were two minor doublets (nmr in $CDCl_3$) at about δ 1.22 (J = 6.5 and 7.0 Hz). The total integrated area of the doublets at δ 1.22 was about 5% of the area beneath the doublet at δ 0.68 due to the azetidinol **5b**. Analytically pure **5b** was obtained by recrystallization and sublimation (50–70°, 0.3 mm): mp 113.5–115° dec; nmr ($CDCl_3$) δ 0.74 (d, 3, J = 7.0 Hz), 3.6–4.4 (m, 5), and 7.4 ppm (m, 5); ir ($CHCl_3$) 3600, 3340, 1415–1450, 1380, 1320, 1140, 1075, 995, and 925 cm^{-1}.

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.71; H, 7.93; N, 8.65.

Mixture of Epimeric 2-Methyl-3-phenylazetidin-3-ols (5b and 5b′) from Hydrolysis of 7b. A solution of 200 mg (0.92 mmol) of 2-methyl-3-chloro-3-phenylazetidine hydrochloride (**7b**) in 5 ml of H_2O was allowed to stand for 11 days at room temperature. The solution was neutralized with NaOH and evaporated *in vacuo* at 10–20°. The residue was extracted with CH_2Cl_2. The extract was filtered and evaporated leaving 150 mg (100%) of an amorphous solid: nmr ($CDCl_3$) δ 0.70 (d, 0.28, J = 6.5 Hz), 1.27 (d, 0.32, J = 6.5 Hz), 3.3–4.4 (m, 1.0), and 7.35 ppm (m, 1.0).[43] The residue was recrystallized from $CHCl_3$–CCl_4–petroleum ether (bp 63–69°) yielding 35 mg of material having a poorly defined crystal structure, mp 100–118°. Sublimation (60° bath, 0.3 mm) yielded material which analyzed satisfactorily for a mixture of **5b** and **5b′**: mp 110–118°; nmr (DMSO-d_6) δ 0.58 (d, 0.13, J = 6.5 Hz), 1.23 (d, 0.34, J = 6.5 Hz), 3.3–4.7 (m, 1.0), and 7.0–7.7 ppm (m, 0.93).[43]

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.57; H, 7.82; N, 8.39.

2,2-Dimethyl-3-phenylazetidin-3-ol (5c). A solution of 200 mg (0.86 mol) of 2,2-dimethyl-3-chloro-3-phenylazetidine hydrochloride (**7c**) in 5 ml of water was allowed to stand at ambient temperatuure for 11 days. The solution was neutralized with 10% NaOH solution and evaporated *in vacuo* at 10–20°. The residue was extracted with CH_2Cl_2. Evaporation of the extracts *in vacuo* afforded 150 mg (98%) of crude product. The nmr spectrum of the crude product contained only absorption peaks due to the azetidinol **5c**. Sublimation (60° bath temperature, 0.3 mm) and recrystallization from petroleum ether (bp 63–69°) gave analytically pure **5c**: mp 83–85°; nmr ($CDCl_3$) δ 0.75 (s, 3), 1.35 (s, 3), 3.2–4.2 (m, 4), and 7.27 ppm (s, 5); ir ($CHCl_3$) 3600, 3250, 1600–1640, 1380–1450, 1150, 1070, and 900 cm^{-1}.

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.72; H, 8.63; N, 7.89.

3-Methoxy-3-phenylazetidine (6). A solution of 260 mg (2 mmol) of 3-phenyl-1-azabicyclobtane (**2a**) in 75 ml of anhydrous CH_3OH was acidified with 5 drops of concentrated $HClO_4$. The solution was allowed to stand for 3 hr and Na_2CO_3 was added. The solution was filtered and evaporated *in vacuo*. The residue was extracted

(42) The uv spectrum was measured by injecting standard solutions of **4a** in dioxane (20 μl) into aqueous NaOH solutions at pH >11 (*cf.* ref 1b).

(43) Since the product is a mixture, the peak areas do not correspond to a ratio of whole numbers.

with CH_2Cl_2. The extract was dried (K_2CO_3) and evaporated yielding 310 mg (95%) of 3-methoxy-3-phenylazetidine (**6**) as the only detectable reaction product (nmr). Short-path distillation yielded 180 mg (55%) of pure **6**: bp 30–35° (0.3 mm); nmr (CCl_4) δ 2.00 (s, 1), 3.00 (s, 3), 3.78 (m, A_2B_2 pattern, 4), and 7.1–7.6 ppm (m, 5); ir (CCl_4) 3355, 1500, 1450, 1330, 1320, 1280, 1205, 1160, 1085, 1045, 1030, 995, 825, and 700 cm^{-1}.

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 72.57; H, 7.81; N, 8.77.

In another experiment the crude product was dissolved in benzene–pyridine and the *p-nitrobenzamide derivative of* **6** was prepared[44] and recrystallized from ethanol: mp 119–120°; nmr ($CDCl_3$) δ 3.06 (s, 3), 4.48 (s, 4, $W_{1/2}$ = 2.5 Hz), 7.34 (s, 5), and 7.65–8.25 ppm (m, A_2B_2 pattern, 4).

Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.61; H, 5.36; N, 9.01.

3-Chloro-3-phenylazetidine Hydrochloride (7a). A solution of 1.0 g (0.0076 mol) of 3-phenyl-1-azabicyclobutane (**2a**) in 50 ml of anhydrous Et_2O was saturated with anhydrous HCl. The precipitate, which formed immediately, was removed by filtration and dried *in vacuo* (0.3 mm, 1 hr, 25°) yielding 1.50 g (96%) of the azetidine hydrochloride (**7a**). Recrystallization from anhydrous EtOH yielded 0.86 g (55%) of pure **7a**: mp 162–163° dec;[45] nmr (D_2O) δ 4.67 (s, 4, HOD), 4.90 (m, A_2B_2 pattern, 4), and 7.53 ppm (s, 5); ir (Nujol mull) 2760–2960, 1575, 1455, 1430, 1365, 1275, 1250, 1110, 790, 710, and 615 cm^{-1}.

Anal. Calcd for $C_9H_{11}NCl_2$: C, 52.96; H, 5.43; N, 6.86. Found: C, 53.15; H, 5.36; N, 6.88.

2-Methyl-3-chloro-3-phenylazetidine Hydrochloride (7b). A solution of 1.0 g (0.0069 mol) of 2-*exo*-methyl-3-phenyl-1-azabicyclobutane (**2b**) in 50 ml of anhydrous Et_2O was saturated with anhydrous HCl gas. The precipitate was removed by filtration and dried *in vacuo* (0.3 mm, 1 hr, 25°) yielding 1.48 g (99%) of the azetidine hydrochloride **7b**. The nmr spectrum (methyl proton resonance) of the crude product indicated that only one product was formed. Recrystallization from EtOH–petroleum ether (bp 63–69°) afforded 1.21 g (80%) of pure **7b**: mp 167° dec; nmr ($CDCl_3$) δ 1.35 (d, 3, J = 7 Hz), 4.5–5.4 (m, 3), 7.3–7.7 (m, 5), and 9.3 ppm (s [br], $W_{1/2}$ = 25 Hz, 2); nmr (CD_3CO_2D) 1.36 (d, 3, J = 7.0 Hz), 4.62 (dd, 1, J = 12.5, 2 Hz), 5.32 (d, 1, J = 12.5 Hz), 5.21 (q [br], 1, $J \sim 7$), and 7.5 ppm (m, 5); ir ($CHCl_3$) 2980, 2620, 2450, 1580, 1500, 1455, 1390, 1355, 1270, 1210–1240, 1070, 1040, 975, and 695 cm^{-1}.

Anal. Calcd for $C_{10}H_{15}NCl_2$: C, 55.06; H, 6.01; N, 6.42. Found: C, 55.25; H, 6.11; N, 6.41.

2,2-Dimethyl-3-chloro-3-phenylazetidine Hydrochloride (7c). A solution of 1.0 g (0.0063 mol) of 2,2-dimethyl-3-phenyl-1-azabicyclobutane (**2c**) in 50 ml of CH_2Cl_2 was saturated with anhydrous HCl. Evaporation of the CH_2Cl_2 *in vacuo* left 1.24 g (85%) of a colorless oil. The nmr spectrum of the crude product indicated that it consisted of only one compound. Crystallization from EtOH–petroleum ether (bp 63–69°) gave 0.91 g (60%) of **7c**. Recrystallization yielded an analytically pure sample: mp 197° dec; nmr (DMSO-d_6) δ 1.32 (s, 3), 1.87 (s, 3), 4.20 (d, 1, J = 12.5 Hz), 5.08 (d, 1, J = 12.5 Hz), 7.42 (s, 5), and 12.1 ppm (s [br], 2, $W_{1/2}$ = 17 Hz); nmr ($CDCl_3$) δ 1.43 (s, 3), 2.02 (s, 3), 4.40 (m [br], 2), 5.00 (m [br], 2), 7.38 (s, 5), and 9.6–11.4 (broad peak, 2); ir ($CHCl_3$) 2980, 2640, 2460, 1580, 1500, 1465, 1450, 1385, 1355, 1205–1240, 1150, and 695 cm^{-1}.

Anal. Calcd for $C_{11}H_{15}NCl_2$: C, 56.91; H, 6.55; N, 6.03. Found: C, 56.86; H, 6.63; N, 5.97.

Treatment of 3-Phenyl-1-azabicyclobutane (2a) with Sodium Borohydride. A solution of 180 mg (1.37 mmol) of 3-phenyl-1-azabicyclobutane (**2a**) and 45 mg (1.4 mmol) of sodium borohydride in 2-propanol (distilled from sodium) was stirred overnight at ambient temperature. Nmr analysis of the product obtained by diluting the reaction solution with H_2O and extracting with CH_2Cl_2 indicated that it was nearly pure **2a**.

Attempted Hydrogenation of 3-Phenyl-1-azabicyclobutane (2a). A side-arm flask was charged with 220 mg of palladium-on-strontium carbonate (2% palladium) in 5 ml of anhydrous EtOH. The catalyst was prereduced and the azabicyclobutane **2a** was added through a serum cap (200 mg, 1.5 mmol, in 11 ml of EtOH). After 1 hr, 2.1 ml of hydrogen had been consumed; after 21 hr a total of 2.5 ml was consumed (0.11 mmol, 7.5%). The reaction solution was filtered and diluted with 20 ml of H_2O. The aqueous solution was extracted with CH_2Cl_2 and the extracts were washed with H_2O and dried. Evaporation of the CH_2Cl_2 left about 180 mg of a gummy material. An nmr spectrum of the residue indicated that no **2a** was present; the spectrum showed only a broad absorption band between 2.5 and 4.5 ppm (maximum at about 4 ppm) and absorption at 7.0–7.5 ppm for the aromatic protons. Short-path distillation yielded about 20 mg of material which gave an nmr spectrum which was similar to that of the crude product. The hydrogenation was repeated as above with addition of fresh catalyst after 4 hr; the result was substantially the same as above.

In another experiment, the flask was charged with 40 mg of tris(triphenylphosphine)chlororhodium and 14 ml of benzene. The solution was stirred under hydrogen for 15 min. 3-Phenyl-1-azabicyclobutane (**2a**) (500 mg in 3 ml of benzene) was added. There was no hydrogen consumed as the solution was stirred for 4 hr. Removal of the benzene *in vacuo* and distillation of the residue at 1 mm yielded 320 mg (64%) of recovered **2a**.

Treatment of 2-Phenylazirine with Dimethylsulfonium Methylide in Dimethyl Sulfoxide–Tetrahydrofuran. Formation of 1-Phenylcyclopropanecarboxaldehyde. A 4.67-g (0.040 mol) sample of 2-phenylazirine (**1a**) was added neat over a period of 30 min to a stirred solution of 0.060 mol of dimethylsulfonium methylide[14] in DMSO–THF (4:1) at −5°. After 2 hr at −5°, the solution was diluted with cold H_2O and extracted with CH_2Cl_2. The extracts were dried (Na_2SO_4) and evaporated *in vacuo*. The residue was distilled under vacuum. The first fraction was nearly entirely 3-phenyl-1-azabicyclobutane (**2a**, 1.26 g); the second fraction was mostly 1-phenylcyclopropanecarboxaldehyde (0.08 g, bp 90–100° (0.5 mm); only a small fraction of the amount formed appeared to be recovered; 2.0 g of residue remained after distillation. The fractions containing 1-phenylcyclopropanecarboxaldehyde from several reactions were combined and chromatographed on Florisil with $CHCl_3$–petroleum ether (bp 63–69°) as eluent. The fraction containing the aldehyde was distilled using a short-path still to yield pure 1-phenylcyclopropanecarboxaldehyde: bp 40° (bath temperature, 0.1 mm); nmr ($CDCl_3$) δ 1.0–1.6 (m, A_2B_2 pattern, 4), 7.18 (s, 5), and 9.30 ppm (s, 1); ir (CCl_4) 1710, 1610, 1500, 1445, 1255, 1065, 1040, 1030, 970, 910, 890, 865, 715, and 700 cm^{-1}; the 2,4-dinitrophenylhydrazone had mp 188–189° (lit.[46] 189°).

When the aldehyde was distilled, some droplets which remained on the condenser solidified after standing overnight. The solid was recrystallized from water and dried over phosphorus pentoxide. The melting point (86–87°) and nmr spectrum indicate that it is 1-phenylcyclopropanecarboxylic acid. A sample of the acid obtained by treatment of the aldehyde with alkaline potassium permanganate had mp 85–86° (H_2O) (lit.[47] 86–87°) and was identical with the material apparently obtained on air oxidation of the aldehyde; nmr[48] (CCl_4) δ 1.00–1.75 (m, A_2B_2 pattern, 4), 7.20 (m, 5), and 12.40 ppm (s, 1); ir[49] (CCl_4) 1685, 1600, 1500, and 695 cm^{-1}.

Reaction of 2-Phenylazirine (1a) with Dimethyloxosulfonium Methylide in Dimethyl Sulfoxide. A 1.2-g (10 mmol) sample of 2-phenylazirine (**1a**) in 5 ml of anhydrous DMSO was added slowly to a stirred solution of 12 mmol of dimethyloxosulfonium methylide[14] in 50 ml of DMSO. After stirring for 15 min at 30° the reaction solution was diluted with H_2O and extracted with CH_2Cl_2. The combined extracts were washed with H_2O, dried (K_2CO_3), and evaporated yielding 330 mg of red oil. The reaction was repeated several times with variations in the ratio of azirine (**1a**) to ylide, the reaction time, and the reaction temperature. The effects of these variations were evaluated by nmr analysis of the crude products. There appeared to be no major variation in total yield or composition of the crude product when the reaction time (15 min to 30 hr) or temperature (0–30°) was varied. The crude products from several reactions were combined and chromatographed on Woelm neutral alumina (activity grade 1) using CCl_4 as eluent. 1-Phenylcyclopropanecarboxaldehyde was the only pure product obtained.

Treatment of 3-Phenyl-1-azabicyclobutane (2a) with Dimethyloxosulfonium Methylide in Dimethyl Sulfoxide. A 500-mg (3.8 mmol) sample of 3-phenyl-1-azabicyclobutane (**2a**) in 3 ml of anhydrous

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(45) A sample that had been aged for 3 months and showed no signs of deterioration had mp 177–178°.

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DMSO was added to a solution of 4.5 mmol of dimethyloxosulfonium methylide in DMSO.[14] After 45 min at 20–25° the reaction solution was diluted with H_2O and extracted with CH_2Cl_2. The extracts were washed with H_2O, dried, and evaporated leaving 310 mg of pure **2a** (nmr analysis). No 1-phenylcyclopropylcarboxaldehyde was detected.

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A Search for the α Effect among Heteroaromatic Nitrogen Nucleophiles[1a]

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Abstract: Relative rates of methylation of heteroaromatic compounds by methyl iodide in DMSO at 23° were obtained using an nmr method. Nucleophiles examined include pyridines, diazines, and their benzologs. Cinnoline, pyridazine, and phthalazine are about three times more reactive than predicted by a Brønsted relationship established by the pyridines. Cinnoline gives a 9:1 mixture of N-2:N-1 methylated products. Rates of acetylation of pyridazine, phthalazine, and three pyridines by *p*-nitrophenyl acetate at 25° in water were obtained. Pyridazine and phthalazine acetylated 20 and 30 times faster, respectively, than predicted by a Brønsted plot established by the pyridine nucleophiles. Rate accelerations for the α-diaza nucleophiles are discussed in terms of pair–pair electron repulsion and the α effect.

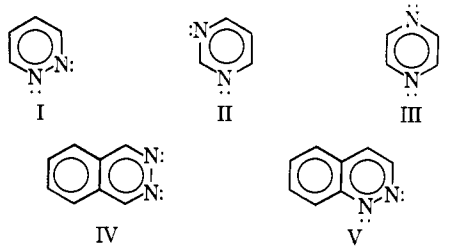
The term α effect was first applied in 1962 to nucleophiles which had an enhanced reactivity toward *p*-nitrophenyl acetate (PNPA).[2] The abnormal reactivity was evidenced by positive deviations from a Brønsted plot established by other nucleophiles.[3] These "supernucleophiles,"[4] *e.g.*, $RONH_2$, H_2NNH_2, ClO^-, and ROO^-, have an unshared electron pair α to the nucleophilic center.

In the ensuing years additional examples of the α effect were found.[5] Many explanations for the enhanced reactivity have been advanced and rejected.[5,6] Current opinion favors the view that no one factor can account for the enhanced reactivity of the entire class of α-effect nucleophiles.[7]

Electron pair–electron pair repulsions were suggested to be a dominant cause of the α effect for certain nucleophiles.[4,8] More recently, it has been suggested that conformational factors may be important in influencing the magnitude of pair–pair repulsion. Thus, ClO^- and ROO^- were said to show the effects of pair–pair repulsion but $HONH_2$ and H_2NNH_2 were said to have conformations which minimize this interaction.[9]

Spectroscopy[10,11] and molecular orbital calculations[12] indicate that the electron pairs on the annular nitrogen atoms in heteroaromatic diazines I–III interact repulsively. Such interactions are not limited to pyridazine (I) where the electron pairs are on adjacent atoms but are also found in pyrimidine (II) and pyrazine (III) where the heteroatoms are more widely separated.

We have employed the diazines and benzologs of I, phthalazine (IV), and cinnoline (V) as nucleophiles in a



I II III IV V

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