Insights into Regioselective Oxy (−O−) and Imino (−NH−) Group Insertions of 3-Nortricyclanone

Murray G. Rosenberg,† Ulrike Haslinger, and Udo H. Brinker*

Institut für Organische Chemie, Universität Wien, Währinger Strasse 38, A-1090 Wien, Austria

Udo.Brinker@univie.ac.at

Received July 20, 2001

Lactam 4-azatricyclo[3.2.1.$0^{2,7}$]octan-3-one (**16a**) was proven to be formed in a previously reported reaction that claimed production of lactam 3-azatricyclo[3.2.1.$0^{2,7}$]octan-4-one (**17a**). In a related reaction, bicyclo[3.1.0]hex-2-ene-*endo*-6-carbonitrile (**15**), lactam (**16a**), and novel hydroxycarbonitriles **19**−**21** were selectively formed when 3-nortricyclanone (**1**) was treated with aqueous hydroxylamine-*O*-sulfonic acid (HOSA). Since nitrile **15** neither hydrolyzed nor underwent intramolecular Ritter reaction under these conditions, mechanisms involving Beckmann rearrangement of **3** to nitrilium ion **9** (normal) and Beckmann fragmentation of **3** to cation **8** (abnormal) were investigated using semiempirical calculations. When alkaline HOSA was employed, lactams **16a** and **17a** were formed in a 1:2 ratio, perhaps via oxaziridine **6a**. A similar selectivity was observed using an NH_3/NaOCl reagent solution, which afforded lactone 4-oxatricyclo[3.2.1.$0^{2,7}$]octan-3-one (**16b**) in addition to both lactams. Consequently, the Baeyer−Villiger oxidation of **1** with NaOCl gave **16b** exclusively. Finally, the Schmidt reaction of ketone **1** gave only the lactam **17a**, via cyclopropyl migration, and the same fragmentation products obtained from the acidic HOSA reaction. Migration selectivities are rationalized in terms of nucleofugacity, electronic effects, cyclopropyl regulation, and MO theory.

Introduction

The transformation of a strained cyclic ketone into its corresponding spiroannular diaziridine is plagued by ring expansion when ketimine formation is inefficient.[1] Therefore, the conversion of highly strained 3-nortricyclanone (**1**) into 3-hydrazinortricyclane (**6**) is difficult (eq 1, Scheme 1).[2] Nevertheless, new insights regarding the migration selectivities within ketone **1** have been gained.

Skeletal rearrangements involving migration to an electron-deficient carbon include the homologation of ketones by diazomethane,[3] the Tiffeneau−Demjanov ring expansion,[4] and the pinacol rearrangement.[5] Similarly, migrations to electron-deficient heteroatoms constitute a synthetically useful class of organic reactions worthy of attention.[6] The Beckmann rearrangement, among others, involves migration to an electron-deficient nitrogen,[7] while the Baeyer−Villiger oxidation features migration to an electron-deficient oxygen.[8] The Beckmann rearrangement of oxime derivatives proceeds stereospecifically whereby the neighboring group lying *anti* to the *N*-nucleofuge assists the ionization during its migration.[9] The stereoconfiguration of the migrating group is retained. Retention of configuration is also observed for the Baeyer−Villiger oxidation, for which general migratory aptitudes within unsymmetrical ketones have been ascertained: 3°-alkyl > 2°-alkyl > benzyl > phenyl > 1°-alkyl > cyclopropyl > methyl.[10] The migrating substituent is the electrofuge that can better stabilize a partial positive charge. Thus, cyclopropyl migration is normally observed only with methyl-substituted ketones, giving acetic esters.[11] However, exceptions can be found. Treatment of bicyclo[3.1.0]hexan-2-one with peroxy acid *m*-CPBA led only to the lactone 2-oxabicyclo[4.1.0]heptan-3-one, via cyclopropyl migration.[12] Consequently, experimentation is warranted since other factors like steric effects may be operating.

Cyclopropylmethyl cations are stabilized by conjugation between the cyclopropane ring's π-type Walsh orbitals and the vacant p-orbital on the vicinal carbocation center.[13,14] Thus, 3-nortricyclanone (tricyclo[2.2.1.$0^{2,6}$]-

* Corresponding author. Phone: +43-1-4277-52121. Fax: +43-1-4277-52140.

† Department of Chemistry, State University of New York, Binghamton, NY 13902-6016.

(1) (a) Kupfer, R. Ph.D. Dissertation, State University of New York at Binghamton, Binghamton, New York, 1995; pp 18, 154. (b) Kupfer, R.; Brinker, U. H. Unpublished results.

(2) Rosenberg, M. G.; Brinker, U. H. *J. Org. Chem.* **2001**, *66*, 1517−1522.

(3) Gutsche, C. D. *Org. React. (NY)* **1954**, *8*, 364−429.

(4) Smith, P. A. S.; Baer, D. R. *Org. React. (NY)* **1960**, *11*, 157−188.

(5) Collins, C. J. *Q. Rev., Chem. Soc.* **1960**, *14*, 357−377.

(6) Smith, P. A. S. In *Molecular Rearrangements*; de Mayo, P., Ed.; Wiley: New York, 1963; pp 457−591.

(7) (a) Donaruma, L. G.; Heldt, W. Z. *Org. React. (NY)* **1960**, *11*, 1−156. (b) Gawley, R. E. *Org. React. (NY)* **1988**, *35*, 1−420.

(8) (a) Krow, G. R. *Org. React. (NY)* **1993**, *43*, 251−798. (b) Krow, G. R. *Tetrahedron* **1981**, *37*, 2697−2724. (c) Lee, J. B.; Uff, B. C. *Q. Rev., Chem. Soc.* **1967**, *21*, 429−457. (d) Hassall, C. H. *Org. React. (NY)* **1957**, *9*, 73−106.

(9) Nevertheless, it is the aryl group of alkyl aryl oximes that typically migrates regardless of the initial configuration.

(10) (a) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; pp 321−329. (b) Plesničar, B. In *Oxidation in Organic Chemistry*; Trahanovsky, W. S., Ed.; Academic: New York, 1978; Part C, pp 254−267.

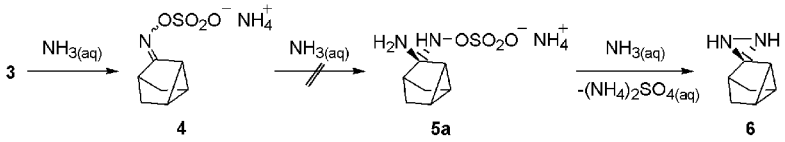
(11) Emmons, W. D.; Lucas, G. B. *J. Am. Chem. Soc.* **1955**, *77*, 2287−2288.

(12) Wiberg, K. B.; Snoonian, J. R. *J. Org. Chem.* **1998**, *63*, 1390−1401.

(13) (a) *Advanced Organic Chemistry*, 4th ed.; March, J., Ed.; Wiley: New York, 1992; pp 152, 169, 323−324. (b) Jorgensen, W. L.; Salem, L. *The Organic Chemist's Book of Orbitals*; Academic: New York, 1973; pp 35−37, 206−209. (c) Wilcox, C. F.; Loew, L. M.; Hoffmann, R. *J. Am. Chem. Soc.* **1973**, *95*, 8192−8193. (d) Macomber, R. S. *J. Chem. Educ.* **1998**, *75*, 1346−1350.

10.1021/jo0159587 CCC: $22.00
Published on Web 12/15/2001

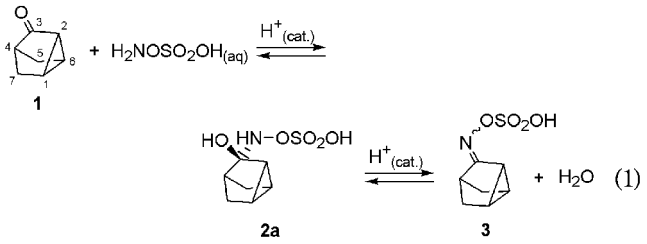
Scheme 1. Diaziridine Formation Was Not Observed When 3 Was Quenched by Ammonia



heptan-3-one)[15] (**1**) is an ideal system with which to study this effect because its three-membered ring is locked in an endocyclic configuration that keeps the C1−C6 bond in **1** parallel to the electrophilic p-orbital on C3 (eq 1).[16] Indeed, this perfect alignment is the main feature responsible for the inexorable cyclopropylcarbene fragmentation of the corresponding singlet carbene, 3-nortricyclanylidene.[2,17] With this in mind, the lactamization of **1**,[18] reportedly giving "3-azatricyclo[3.2.1.0^{2,7}]octan-4-one (**17a**)" in 37.9% yield,[15d] is surprising for two reasons: (1) the yield of **17a** is rather high given the tricyclic system's propensity to relieve strain via fragmentation, and (2) alleged lactam **17a** derives from an unpreferred cyclopropyl migration.[19] So, if imino (−NH−) group insertion is truly permissible for **1**, the migration selectivity is still questionable.

Results and Discussion

Elusive diaziridines are sometimes accessible by the action of ammonia upon oxime-*O*-sulfonic acids or esters.[20] Therefore, 3-nortricyclanone oxime-*O*-sulfonic acid (**3**) was immediately sought for this transformation because such diaziridine precursors are easily formed by the action of H_2NOSO_2OH, hydroxylamine-*O*-sulfonic acid (HOSA), upon cyclic ketones (eq 1).[21]



(1)

It was anticipated that the quenching of in situ **3** with NH_3 would lead to the planned diaziridine, 3-hydrazinotricyclane (**6**) (Scheme 1).[2] However, none was formed.

Historically, oxime-*O*-sulfonic acids are unstable species that, on occasion, have been isolated as their potassium or ammonium salts (e.g., **4** in Scheme 1).[22] Furthermore, a facile way to perform the Beckmann rearrangement directly upon cyclic ketones makes use of HOSA.[21] This eliminates the need for preparing the oxime, e.g., 3-nortricyclanone oxime (**7**),[15d,23] in a separate step because the rearrangement proceeds through oxime-*O*-sulfonic acids.[24]

Thus, when ketone **1** was treated with aqueous HOSA and either subsequently quenched with concentrated aqueous NH_3 or not, the major product formed was bicyclo[3.1.0]hex-2-ene-*endo*-6-carbonitrile (**15**) (Scheme 2).[15d,25] This demonstrates that **3** is truly unstable and ionizes prior to the addition of NH_3. Indeed, in a follow-up experiment employing a different weak base quencher (saturated aqueous K_2CO_3), the potassium salt of **3** (cf. **4**) could not be precipitated from the aqueous solution.[22a]

In addition, three novel "hydrolysis" products of **15** were also formed during the reaction, regardless of quenching (Scheme 3). These were 3-hydroxybicyclo[3.1.0]hexane-*endo*-6-carbonitrile (**19**),[26] 2-hydroxybicyclo[3.1.0]hexane-*endo*-6-carbonitrile epimer 1 (**20**), and 2-hydroxybicyclo[3.1.0]hexane-*endo*-6-carbonitrile epimer 2 (**21**). But control experiments showed that nitrile **15** was unaffected by the original acidic reaction conditions. Thus, hydroxycarbonitriles **19**−**21** were formed contemporaneously with **15**.

(14) For related examples involving the activation of σ-bonds vicinal to cyclopropane rings, see: (a) Xu, L.; Smith, W. B.; Brinker, U. H. *J. Am. Chem. Soc.* **1992**, *114*, 783−784. (b) Banwell, M. G.; Haddad, N.; Huglin, J. A.; MacKay, M. F.; Reum, M. E.; Ryan, J. H.; Turner, K. A. *J. Chem. Soc., Chem. Commun.* **1993**, 954−957. (c) Halton, B.; Battiste, M. A.; Rehberg, R.; Deyrup, C. L.; Brennan, M. E. *J. Am. Chem. Soc.* **1967**, *89*, 5964−5965.

(15) (a) Meinwald, J.; Crandall, J. K. *J. Am. Chem. Soc.* **1966**, *88*, 1292−1301. (b) Meinwald, J.; Crandall, J.; Hymans, W. E. *Org. Synth. Coll.* **1973**, *5*, 866−868. (c) Upadek, H. Ph.D. Dissertation, Ruhr-Universität Bochum, Germany, 1977; pp 156−159. (d) Hall, H. K., Jr. *J. Am. Chem. Soc.* **1960**, *82*, 1209−1215.

(16) The carbonyl carbon of ketone **1** is partially positive (i.e., +0.2558) according to AM1 calculations. See Supporting Information.

(17) Herges, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 255−276.

(18) Via in situ 3-nortricyclanone oxime-*O*-benzensulfonic ester. Bicyclo[3.1.0]hex-2-ene-*endo*-6-carbonitrile (**15**) is also reported, likely formed via δ-elimination (i.e., 1,4-conjugate elimination) of in situ 3-nortricyclanone oxime *O*-benzensulfonic ester with the excess NaOH via the E2′ mechanism.

(19) "Since the structure **50** [i.e., **17a**] was assigned [in ref 15d] on the *assumption* of cyclopropane ring migration, it should be considered *unproven* without confirmatory spectral data." See p 1291 in Krow, G. R. *Tetrahedron* **1981**, *37*, 1283−1307.

(20) (a) Schmitz, E. In *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC Press: Boca Raton, FL, 1987; Vol. 1, pp 57−98. (b) Schmitz, E. In *Methoden der Organischen Chemie (Houben-Weyl)*; Klamann, D., Ed.; Thieme: Stuttgart, 1992; Vol. E16c; pp 678−728. (c) Schmitz, E. *Adv. Heterocycl. Chem.* **1979**, *24*, 63−107. (d) Makhova, N. N.; Petukhova, V. Y.; Khmel'nitskii, L. I. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1982**, *31*, 1858−1862. (e) Mikhailyuk, A. N.; Makhova, N. N.; Bova, A. E.; Khmel'nitskii, L. I.; Novikov, S. S. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1978**, *27*, 1367−1371. (f) Briner, K.; Vasella, A. *Helv. Chim. Acta* **1989**, *72*, 1371−1382. (g) Vasella, A.; Witzig, C.; Waldraff, C.; Uhlmann, P.; Briner, K.; Bernet, B.; Panza, L.; Husi, R. *Helv. Chim. Acta* **1993**, *76*, 2847−2875. (h) Brunner, J.; Senn, H.; Richards, F. M. *J. Biol. Chem.* **1980**, *255*, 3313−3318. (i) Nassal, M. *Liebigs Ann. Chem.* **1983**, 1510−1523. (j) Schustov, G. V.; Tavakalyan, N. B.; Kostyanovsky, R. G. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 200−201.

(21) (a) Sanford, J. K.; Blair, F. T.; Arroya, J.; Sherk, K. W. *J. Am. Chem. Soc.* **1945**, *67*, 1941−1943. (b) Novoselov, E. F.; Isaev, S. D.; Yurchenko, A. G.; Vodichka, L.; Trshiska, Y. *J. Org. Chem. USSR* **1981**, *17*, 2284−2289. (c) Olah, G. A.; Fung, A. P. *Synthesis* **1979**, 537−538. (d) *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 4, pp 2764−2767.

(22) (a) Smith, P. A. S. *J. Am. Chem. Soc.* **1948**, *70*, 323−326. (b) Smith, R. A. G.; Knowles, J. R. *J. Chem. Soc., Perkin Trans. 2* **1975**, 686−694.

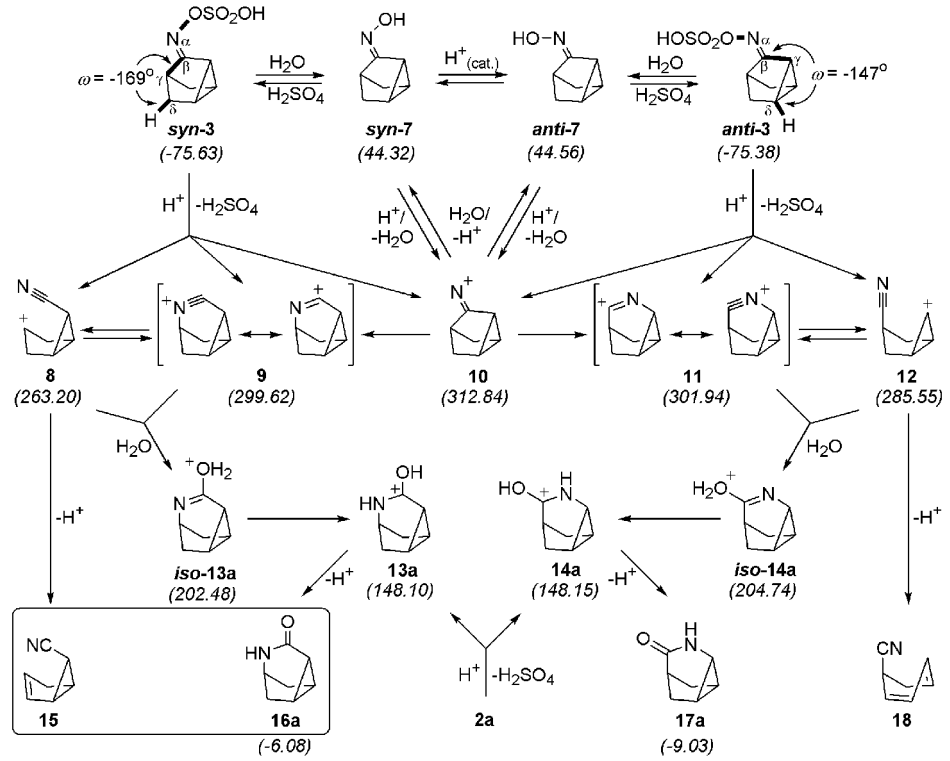
(23) (a) Hawkes, G. E.; Herwig, K.; Roberts, J. D. *J. Org. Chem.* **1974**, *39*, 1017−1028. (b) Botto, R. E.; Westerman, P. W.; Roberts, J. D. *Org. Magn. Reson.* **1978**, *11*, 510−515. (c) Chizhov, A. O.; Zefirov, N. S.; Zyk, N. V. *J. Org. Chem.* **1987**, *52*, 5647−5655.

(24) (a) Gregory, B. J.; Moodie, R. B.; Schofield, K. *J. Chem. Soc., B* **1970**, 338−346. (b) Kim, S.-G.; Kawakami, T.; Ando, T.; Yukawa, Y. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1115−1120. (c) Yukawa, Y.; Ando, T. *J. Chem. Soc., D* **1971**, 1601−1602. (d) Pearson, D. E.; Ball, F. *J. Org. Chem.* **1949**, *14*, 118−131.

(25) Lübbe, F.; Sustmann, R. *Chem. Ber.* **1979**, *112*, 57−70.

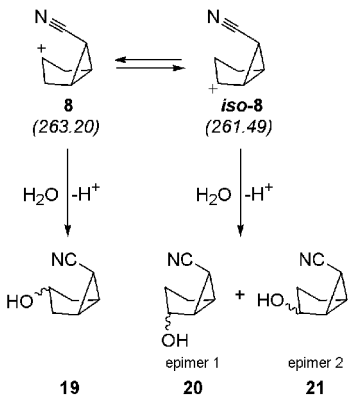
(26) Steric hindrance by the cyano group of cation **8** likely precludes the formation of *endo*-3-hydroxybicyclo[3.1.0]hexane-*endo*-6-carbonitrile.

Scheme 2. Depiction of the *Normal* and *Abnormal* Beckmann Rearrangements from 3, and Shechter−Schmidt-Type Reaction from 2a, Leading to Lactams and Nitriles[a]



[a] AM1 enthalpies are in kcal/mol.

Scheme 3. Formation of Hydroxycarbonitriles 19−21



Finally, the lactam 4-azatricyclo[3.2.1.0^{2,7}]octan-3-one (**16a**) was also formed from **1**, but in low yield (Table 1). In fact, when we repeated a published procedure on a small scale,[15d] we obtained nitrile **15** and lactam **16a**,[18] not **17a** as reported. So, imino group insertion *is* truly permissible for **1** but the usual methylidyne migration preference is observed (vide supra).[7b] Curiously, the ^{13}C NMR spectra for both lactams **16a** and **17a** have been reported but neither preparative details nor allusion to the earlier structural misassignment are mentioned.[27] We herein report both the separation of lactams **16a** and **17a** via column chromatography and their structural verification using heteronuclear correlation (HETCOR) spectroscopy.[28]

Lactam **16a** likely derives from the *normal* Beckmann rearrangement ***syn*-3→9**. But **16a** could also stem from a tandem reaction involving the *abnormal* Beckmann rearrangement ***syn*-3→8**, called Beckmann fragmentation,[29] and the subsequent Ritter reaction **8→9**,[21b,30] even though intramolecular Ritter reactions are rare.[31] Still, lactam **16a** might arise from the path **2a→13a**, a mechanistic variant of the well-known Schmidt reaction for ketones.[32] Therefore, theoretical chemistry was engaged to help elucidate the mechanism. The results of AM1 calculations are also summarized in Scheme 2.[33]

Nitrile **15** results from Beckmann fragmentation. But C−N rupture can occur in either one (***syn*-3→8**) or two (***syn*-3→9→8**) steps. The calculated dihedral angle (ω) depicted for ***syn*-3** is ±169°. Thus, the pertinent C_δ−H σ-orbital is not parallel (i.e., ±180°) to the N_α−O bond. Yet substantial overlap between the filled C_δ−H σ-orbital and the empty C_β−C_γ σ^*-orbital could still develop. It is therefore reasonable that **15** is generated by a concerted heterolytic fragmentation (***syn*-3→8**) because ***syn*-3** essentially meets the rigorous stereoelectronic requirements outlined by Grob's *antiparallelism principle*.[34] But the activation enthalpy ($\Delta H^{\ddagger}$) would be somewhat elevated, making the transformation less rapid.[35]

(27) Barfield, M.; Babaqi, A. S. *Magn. Reson. Chem.* **1987**, *25*, 443−451.

(28) See Experimental Section and Supporting Information.

(29) Ferris, A. F. *J. Org. Chem.* **1960**, *25*, 12−18.

(30) (a) Hill, R. K.; Conley, R. T.; Chortyk, O. T. *J. Am. Chem. Soc.* **1965**, *87*, 5646−5651. (b) Palmere, R. M.; Conley, R. T.; Rabinowitz, J. L. *J. Org. Chem.* **1972**, *37*, 4095−4097. (c) Korsloot, J. G.; Keizer, V. G. *Tetrahedron Lett.* **1969**, 3517−3520.

(31) Van Emelen, K.; De Wit, T.; Hoornaert, G. J.; Compernolle, F. *Org. Lett.* **2000**, *2*, 3083−3086.

(32) Fikes, L. E.; Shechter, H. *J. Org. Chem.* **1979**, *44*, 741−744.

(33) Austin Model 1: Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902−3909.

(34) Grob, C. A. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 535−546.

Table 1. Relative Yields (%) of Heteroatom Insertion Products of Ketone 1

reagent	inserting group(s)	leaving group	**16a**	**17a**	**16b**	**15**, **19**−**21**	other[a]
HOSA	−NH−	$H_2SO_{4(aq)}$	8.1			90.4	1.6
HOSA/NaOH	−NH−	$Na_2SO_{4(aq)}$	18.6	37.3			44.1
NH_3/NaOCl	−NH−, −O−	$NaCl_{(aq)}$	17.3	43.6	27.7		11.4
NaOCl	−O−	$NaCl_{(aq)}$			95.9		4.1
HN_3	−NH−	$N_{2(g)}$		11.2		45.7	43.0

[a] See Experimental Section.

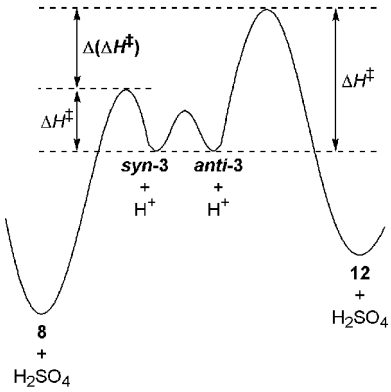


Figure 1. Degree to which Grob fragmentation is allowed is a function of the pertinent torsional angle (ω) and is related to the activation enthalpy ($\Delta H^{\ddagger}$).

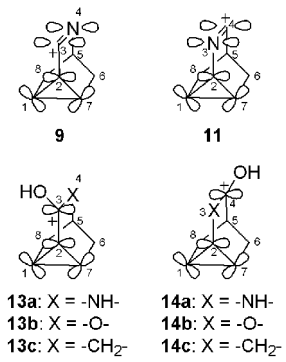


Figure 2. Participation of π-type Walsh orbitals might regulate migration selectivity by either competing against or cooperating with group X.

Regarding ***anti*-3**, concerted heterolytic fragmentation (i.e., ***anti*-3→12**) leading to **18** is truly doubtful because its $\omega = \pm 147°$. This transformation is Grob-forbidden and would have a large $\Delta H^{\ddagger}$ (Figure 1).[36] Besides, **12** is avoided because it has a highly angle-strained cationic sp^2 center on cyclopropyl C6 and is thus more than 20 kcal higher in energy than **8**.[37]

However, it should be emphasized that *both* diastereomers of **3** are expected to be formed, especially under acidic conditions where isomerization occurs readily.[38] So, the concerted *anti* migration/ionization steps from each diastereomer should yield the respective nitrilium ion intermediates **9** and **11**, which differ by ca. 2 kcal. However, since no products deriving from **11** were observed,[39] it is likely that cyclopropyl migration leading to **11** does not take place due to kinetic factors. Stabilization of **9** by the cyclopropane ring's π-type Walsh orbitals could be relevant (Figure 2).

Note that nitrilium ions have linear sp centers, both on carbon and on nitrogen. However, AM1 calculations show that **9** and **11** are bent. Interestingly, imposing a linear constraint on C3 of **9** led to cation **8** after geometry optimization. Thus, the increased ring strain that linearity would incur is simply avoided via C−N rupture. Finally, it must be mentioned that expulsion of the H_2SO_4 nucleofuge from protonated **3** *without* skeletal rearrangement would give nitrenium cation **10**. But **10** is not a real intermediate. Indeed, geometry optimization of **10** also leads to **8**. Hence, this common "intermediate" from ***syn*-3** and ***anti*-3** could explain how ionization of the latter diastereomer also leads to the elimination, substitution, and rearrangement products stemming from cation **8**.

The Shechter−Schmidt-type intermediate,[32] i.e., **2a** (eq 1), can give both **13a** and **14a**, which are *O*-protonated tricyclic lactams.[40] These cations have essentially the same energy, so there would be no thermodynamic origin of selectivity. Remarkably, migratory aptitudes during the Schmidt reaction tend somehow to conflict with those of the Beckmann rearrangement.[41] This could be due to the nature of the *N*-nucleofuge (Table 1; vide infra).

So, to elucidate matters, the *N*-(sulfooxy)carbinolamine intermediate **2a** (eq 1) was again targeted.[42] But now, its formation within an alkaline environment should thwart dehydration to **3** and lend insight into lactam formation. Remarkably, when ketone **1** was introduced into an alkaline solution of HOSA, *both* lactams **16a** and **17a** were formed with a 2-fold preference for **17a** (Scheme 4). However, in contrast to the acidic HOSA reaction, the alkaline HOSA reaction would not go to completion and was also hampered by side reactions.[43]

Schmitz has shown that cyclization of *N*-(sulfooxy)-carbinolamine intermediates, which yields the *oxa*-

(35) Hence, nitrile **15** formation from ***syn*-3** is an example of δ-elimination (i.e., 1,4-conjugate elimination) by the E1′ mechanism. [cf. ref 18].

(36) Also, see Figure S3 in Supporting Information for AM1-calculated energies.

(37) The cyclopentane ring in **8** adopts a flat conformation after geometry optimization regardless of the starting geometry. For a conformational analysis, see Figure S4 in Supporting Information. Cation **12** is more boatlike. However, the large energy difference of 22.4 kcal is mostly due to cation **12** being very strained.

(38) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper & Row: New York, 1987; p 491.

(39) The hypothetical elimination of HCN by nitrile **18** to give benzene was not investigated.

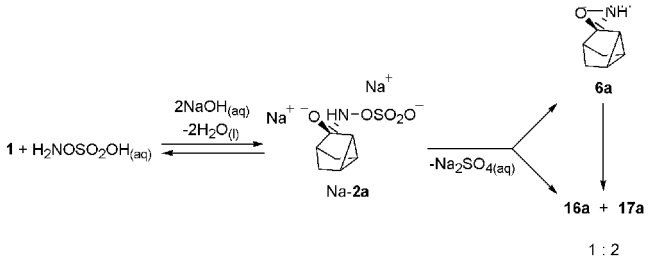
(40) They are also *N*-protonated lactims. Note that strained lactams with pyramidal N atoms, like α-lactams, are normally *N*-protonated in acidic media.

(41) (a) Krow, G. R.; Szczepanski, S. W.; Kim, J. Y.; Liu, N.; Sheikh, A.; Xiao, Y.; Yuan, J. *J. Org. Chem.* **1999**, *64*, 1254−1258. (b) Krow, G. R.; Cheung, O. H.; Hu, Z.; Lee, Y. B. *J. Org. Chem.* **1996**, *61*, 5574−5580. (c) Krow, G. R. *Tetrahedron* **1981**, *37*, 1283−1307. (d) Elderfield, R. C.; Losin, E. T. *J. Org. Chem.* **1961**, *26*, 1703−1710. (e) Potti, N. D.; Nobles, W. L. *J. Pharm. Sci.* **1968**, *57*, 1785−1787. (f) Shechter, H.; Kirk, J. C. *J. Am. Chem. Soc.* **1951**, *73*, 3087−91.

(42) Urbansky, E. T. *J. Chem. Educ.* **2000**, *77*, 1644−1647.

(43) Azine is formed from the side reaction of ketone **1** and in situ hydrazine: (a) $3H_2NOSO_2OH_{(aq)} + 6OH^-_{(aq)} \rightarrow NH_{3(aq)} + N_{2(g)} + 6H_2O_{(l)} + 3SO_4^{2-}{}_{(aq)}$, (b) $H_2NOSO_2OH_{(aq)} + 3NH_{3(aq)} \rightarrow NH_2NH_{2(aq)} + 2NH_4{}_{(aq)} + SO_4^{2-}{}_{(aq)}$ (cf. Raschig hydrazine synthesis: (i) Raschig, F. *Chem. Ber.* **1907**, *40*, 4580−4588. (ii) Adams, R.; Brown, B. K. *Org. Synth. Coll.* **1941**, *1*, 309−310.), and (c) 2(**1**) + $NH_2NH_{2(aq)} \rightarrow$ azine + $2H_2O_{(l)}$.

Scheme 4. Reaction of Ketone 1 with *Alkaline* Aqueous HOSA Leads to Both Lactams 16a and 17a

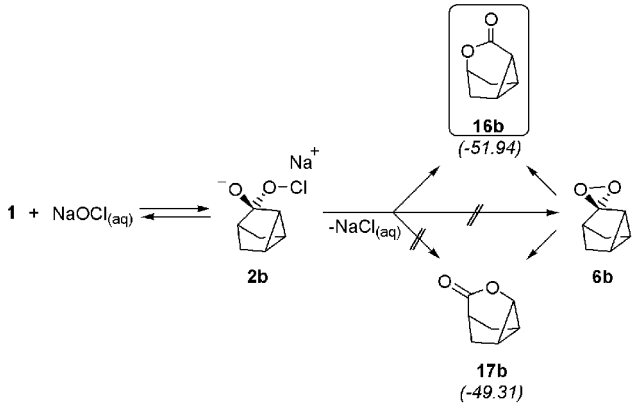


ziridine system (e.g., **6a** in Scheme 4),[44] can occur when ketones are reacted with HOSA under alkaline conditions.[20c,45] Nevertheless, the intermediacy of oxaziridine **6a** can currently only be inferred from the reaction conditions, which give 1-oxa-2-azaspiro[2.5]octane from cyclohexanone.[45a] Yet the direct ring expansion of Na-**2a** to lactams **16** and **17** may be operative. Finally, as suggested by AM1, it is doubtful that protonation and direct rearrangement of *N*-(sulfooxy)carbinolamine **2a** to either cation **13a** or cation **14a** occur during the acidic HOSA reaction (Scheme 2) because no **17a** had been formed.

Next, diaziridine **6** was sought from an *N*-chloro-*gem*-diamine intermediate,[46] which is related to the *N*-(sulfooxy)-*gem*-diamine intermediate **5a** (Scheme 1). But when dilute NaOCl, sodium hypochlorite,[47] was cautiously added to a stirred mixture of ketone **1** and aqueous NH_3, no diaziridine **6** was formed. Instead, *both* lactams **16a** and **17a** were again produced (**16a**:**17a** = 1:2.5), perhaps via the same oxaziridine **6a** (vide supra).[44d,48] In addition, the lactone 4-oxatricyclo[3.2.1.$0^{2,7}$]-octan-3-one (**16b**) was formed.[49,50]

Accordingly, when ketone **1** was treated with just dilute NaOCl, the alkaline Baeyer−Villiger oxidation gave lactone **16b** exclusively, in 52% overall yield (Scheme 5).[51,52] This selective lactonization is in agreement with a previous account of the customary acidic Baeyer−Villiger oxidation of **1**.[49b] Lactone **16b** may arise directly from *O*-chloro-*gem*-diol **2b** or indirectly from dioxirane

Scheme 5. Baeyer−Villiger Oxidation of Ketone 1 with Aqueous Hypochlorite Leads Only to Lactone 16b



6b, but no evidence for the latter was apparent.[53] Nonetheless, both intermediates should, in principle, form both lactones **16b** and **17b**. Hence, the absence of lactone **17b** is intriguing since both lactams **16a** and **17a** were formed under analogous conditions (cf. Scheme 4).

It is noteworthy, when *N*-(sulfooxy)-*gem*-diamine **5a** is compared to *O*-chloro-*gem*-diol **2b**, that our attempt to form the *diaziridine* **6** (Scheme 1) mimicked the classical attempt of Baeyer and Villiger to form the isoelectronic *dioxirane* ring system (e.g., **6b** in Scheme 5).[53] They also observed migration to an electron-deficient heteroatom in lieu of spiroannulation.[54]

Finally, to determine whether the migratory aptitude during the Schmidt reaction of ketone **1** would conflict with that of the Beckmann rearrangement,[41] ketone **1** was reacted with in situ HN_3, hydrazoic acid.[55,56] Surprisingly, in addition to nitrile **15** and hydroxycarbonitriles **19**−**21**, lactam **17a** was formed exclusively. This unexpected result clearly demonstrates that cation **8** is not a precursor of lactam **16a**.

Notwithstanding, the homologation of ketone **1**, either with diazomethane or by the Tiffeneau−Demjanov ring expansion,[3,4] is reported to give mostly tricyclo[3.2.1.$0^{2,7}$]-octan-4-one (**17c**) and only minor amounts of tricyclo-

(44) (a) Aubé, J.; Hammond, M.; Gherardini, E.; Takusagawa, F. *J. Org. Chem.* **1991**, *56*, 499−508, 4086. (b) Smith, B. T.; Gracias, V.; Aubé, J. *J. Org. Chem.* **2000**, *65*, 3771−3774. (c) Oliveros-Desherces, E.; Rivière, M.; Parello, J.; Lattes, A. *Tetrahedron Lett.* **1975**, 851−854. (d) Schmitz, E.; Ohme, R.; Schramm, S.; Striegler, H.; Heyne, H.-U.; Rusche, J. *J. Prakt. Chem.* **1977**, *319*, 195−200. (e) Streith, J.; Fizet, C.; Fritz, H. *Helv. Chim. Acta* **1976**, *59*, 2786−2792.

(45) (a) Schmitz, E.; Ohme, R.; Schramm, S. *Chem. Ber.* **1964**, *97*, 2521−2526. (b) Schmitz, E. *Adv. Heterocycl. Chem.* **1963**, *2*, 83−130. (c) Schmitz, E. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 333−341.

(46) (a) Kuznetsov, V. V.; Makhova, N. N.; Khmel'nitskii, L. I. *Russ. Chem. Bull.* **1997**, *46*, 1354−1356. (b) Kuznetsov, V. V.; Makhova, N. N.; Strelenko, Y. A.; Khmel'nitskii, L. I. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1991**, *40*, 2496−2505. (c) Makhova, N. N.; Petukhova, V. Y.; Kuznetsov, V. V.; Khmel'nitskii, L. I.; Lebedev, V. P.; Pepekin, V. I. *Int. Annu. Conf. ICT* **1998**, *29th* (Energetic Materials), 10.1−10.13; *Chem. Abstr.* **1998**, *129*, 138094.

(47) (a) *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 7, pp 4580−4585. (b) Chakrabartty, S. K. In *Oxidation in Organic Chemistry*; Trahanovsky, W. S., Ed.; Academic: New York, 1978; Part C; pp 359−363.

(48) The potential formation of transient 3-nortricyclanone *N*-chloroimine (cf. **3**) cannot be refuted a priori; see refs 44d and 66.

(49) (a) Sustmann, R.; Lübbe, F. *Chem. Ber.* **1976**, *109*, 444−454. (b) Sauers, R. R. *Tetrahedron Lett.* **1962**, 1015−1017. (c) Olah, G. A.; Prakash, G. K. S.; Rawdah, T. N.; Whittaker, D.; Rees, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 3935−3939.

(50) For details about the parent system, tricyclo[3.2.1.$0^{2,7}$]octan-3-one (**16c**), see: Moore, W. R.; Moser, W. R.; LaPrade, J. E. *J. Org. Chem.* **1963**, *28*, 2200−2205.

(51) Na^+OCl^- is rarely used to conduct the Baeyer−Villiger oxidation. Moreover, Lieben hypohalite oxidation predominates with aryl methyl ketones, giving arenecarboxylates (i.e., haloform reaction): (a) Lieben, A. *Ann. Chem. Pharm. (Suppl.)* **1870**, *7*, 218−236. (b) Lieben, A. *Ann. Chem. Pharm. (Suppl.)* **1870**, *7*, 377−378. (c) Hassner, A.; Stumer, C. *Organic Syntheses Based on Name Reactions and Unnamed Reactions*; Pergamon: Tarrytown, New York, 1994; p 235). Yet the Baeyer−Villiger oxidation can compete, giving methyl esters stemming from unpreferred methyl migration. For an example, see: (d) Kawano, N.; Okigawa, M.; Hasaka, N.; Kouno, I.; Kawahara, Y.; Fujita, Y. *J. Org. Chem.* **1981**, *46*, 389−392.

(52) Compare to Dakin reaction with Na^+OOH^-. See: Hocking, M. B.; Bhandari, K.; Shell, B.; Smyth, T. A. *J. Org. Chem.* **1982**, *47*, 4208−4215.

(53) Murray, R. W.; Singh, M.; Jeyaraman, R. *J. Am. Chem. Soc.* **1992**, *114*, 1346−1351. Note that Murray et al. use the term "Criegee intermediate" when referring to their α-hydroxyperoxysulfuric ester intermediate **6**. But this term is usually reserved for carbonyl-*O*-oxides, though both can form dioxiranes. Since Criegee devised the mechanisms for the *Baeyer−Villiger oxidation* of ketones, the *Criegee rearrangement* of peroxycarboxylic esters and hydroperoxides, and the *ozonolysis* of alkenes, confusion may arise.

(54) Baeyer, A.; Villiger, V. *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 3625−3633.

(55) Wolff, H. *Org. React. (NY)* **1946**, *3*, 307−336.

(56) Notably, HN_3 has also been used to form diaziridines, but from *thio*ketones. See: Middleton, W. J. U.S. Patent 3 226 439, 1965; *Chem. Abstr.* **1966**, *64*, 9597. See ref 20c.

[3.2.1.0^{2,7}]octan-3-one (**16c**).[57] Like lactam **17a**, ketone **17c** also stems from the ostensibly unpreferred cyclopropyl migration.

From AM1 calculations, the 4-azatricyclo[3.2.1.0^{2,7}]oct-3-en-3-yl cation (**9**) and the 3-hydroxy-4-azatricyclo-[3.2.1.0^{2,7}]oct-3-yl cation (**13a**) benefit little thermodynamically from delocalization of their cyclopropane rings with their p-orbitals on C3.[58] This may be due to an overwhelming $+R$ effect of N4 (Figure 2, compounds **9** and **13a**).[59] Conversely, the 3-hydroxy-4-oxatricyclo-[3.2.1.0^{2,7}]oct-3-yl cation (**13b**), which is putatively formed during the acidic Baeyer−Villiger oxidation, is more stable than the 4-hydroxy-3-oxatricyclo[3.2.1.0^{2,7}]oct-4-yl cation (**14b**) by ca. 7 kcal.[58] Perhaps this is due to the $-I$ effect of O4 (Figure 2, compound **13b**).[60] Accordingly, lactone **16b** is exclusively produced. In the same vein, the 3-hydroxytricyclo[3.2.1.0^{2,7}]oct-3-yl cation (**13c**), which is generated during the Tiffeneau−Demjanov ring expansion, is more stable than the 4-hydroxytricyclo[3.2.1.0^{2,7}]-oct-4-yl cation (**14c**) by ca. 5 kcal.[58,61] However, ketone **17c** is preferentially formed. As astutely stated by a reviewer of this report, "It is a puzzle why the Baeyer−Villiger and Demjanov reactions, which are mechanistically similar, give different regiochemistry."

A possible solution to this enigma may depend on the nucleofugacity of the leaving group. Even though the Baeyer−Villiger oxidation is mechanistically similar to the Tiffeneau−Demjanov ring expansion, different leaving groups are expelled (Table 1). In contrast, the Schmidt rearrangement and the Tiffeneau−Demjanov ring expansion both feature cyclopropyl migration via departure of $N_{2(g)}$.

Experimental Section

General Information. 3-Nortricyclanone (**1**) was prepared according to the literature.[15b,62] Hydroxylamine-*O*-sulfonic acid (HOSA, 95%, Fluka) was used as purchased. FT-NMR spectra were recorded on a Bruker Avance DPX-250 spectrometer (B_o = 5.875 T) at the following Larmor frequencies: $\nu_o(^1H) = 250.1$ MHz and $\nu_o(^{13}C) = 62.9$ MHz. NMR coupling constants (J) are given in Hertz. IR absorption spectra were recorded on a Perkin-Elmer 1600 FT-IR spectrometer by applying samples as neat liquids onto a Si wafer or by pressing dilute KBr pellets. Analytical GC analyses were conducted using a Fisons 8000 series GC instrument outfitted with a 30 m poly-(dimethylsiloxane) capillary column (Perkin-Elmer, PE-1, 0.32 mm i.d., and a 0.25 μm film thickness) and a flame-ionization detector. The following conditions and temperature program were used: $T_{oven,i}$ = 50 °C (5 min), ramp = +10 °C/min, $T_{oven,f}$ = 230 °C (7 min), $T_{injector}$ = 185 °C, T_{FID} = 260 °C, and a flow = 2.1 (mL He)/min. GC-MS analyses were conducted using a Hewlett-Packard 6890 series GC instrument outfitted with a 30 m poly(methylphenylsiloxane) capillary column (Hewlett-Packard, HP-5MS (95% dimethyl and 5% diphenyl), 0.25 mm i.d., and a 0.25 μm film thickness) and a Hewlett-Packard 5973 MSD instrument. The following GC conditions and temperature program were used: $T_{oven,i}$ = 80 °C (7 min), ramp = +10 °C/min, $T_{oven,f}$ = 270 °C (5 min), $T_{injector}$ = 200 °C, and an initial flow = 0.8 (mL He)/min. Analytical HPLC was performed using a Hewlett-Packard HP 1090 Liquid Chromatograph, with a Hewlett-Packard 35900E interface, equipped with a Spherisorb S5W 5-μm column (250 × 4 mm). Isocratic elution giving a 70% hexanes and 30% EtOAc mixture was employed at 1.0 mL/min. Product signals were observed using a HP 1047A RI detector.

Reaction of 3-Nortricyclanone (1) with Acidic HOSA. Neat ketone **1** (0.541 g, 5.0 mmol) was injected into a solution of HOSA (0.595 g, 5.0 mmol, 5.0 mL H_2O) whereupon homogenization occurred within 1 min of swirling. A pH measurement of the aqueous solution demonstrated that it was acidic (pH = 1), as expected from the liberation of H_2SO_4.[63] After 1 h, the solution became turbid, and after 24 h, oil globules were observed. Next, the mixture was extracted with $CHCl_3$ (4 × 5 mL). The combined extracts were dried over anhydrous $MgSO_4$, filtered, analyzed by GC and GC-MS, and rotary evaporated to give 0.493 g of a clear, uncolored liquid that turned slightly orange upon standing. The product mixture contained 3.1% of unreacted **1**. Relative yield of products: **15** (43.1%), **16a** (8.1%), **19** (17.7%), **20** (12.4%), **21** (17.2%), and 3-nortricyclanol (1.6%).[64]

Bicyclo[3.1.0]hex-2-ene-*endo*-6-carbonitrile (15): R_f 0.59 (alkaline $KMnO_4$; hexanes/EtOAc, 2:3); ^{1}H NMR ($CDCl_3$) δ 1.68 (1 H, dd, J = 7.4, J = 7.0), 2.08 (1 H, ddm, J = 13.9, J = 7.0), 2.43−2.47 (1 H, m), 2.51 (1 H, dm, J =18.8), 2.74 (1 H, ddm, J = 18.8, J = 6.7), 5.78−5.84 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 10.7 (d, J = 173), 22.2 (d, J = 171), 30.8 (d, J = 177), 33.9 (t, J = 128), 117.6 (s), 128.2 (d, J = 165), 132.4 (d, J = 167); $\bar{\nu}_{max}$/cm^{-1} (neat) 3065, 2911, 2839, 2232, 1677, 802, 764; *m*/*z* (EI) 105 (M$^+$, 67), 104 (100), 79 (14), 78 (74), 77 (42), 66 (5), 65 (31), 52 (16), 51 (16).

4-Azatricyclo[3.2.1.0^{2,7}]octan-3-one (16a): R_f 0.18 (alkaline $KMnO_4$; $CHCl_3$/MeOH, 97:3); mp 173−180 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$)[65] δ 1.52 (2 H, d, J = 11.9), 1.72−1.81 (3 H, m), 1.85 (2 H, d, J = 7.6), 3.52−3.58 (1 H, m), 7.01 (1 H, br s); ^{13}C NMR (100.6 MHz, $CDCl_3$)[65] δ 17.2 (d, J = 174), 21.8 (d, J = 169), 31.7 (t, J = 132), 46.3 (d, J = 151), 171.7 (s); $\bar{\nu}_{max}$/cm^{-1} (KBr) 3162, 3052, 2933, 2858, 1670, 1654, 1625, 1475, 1321, 1272, 1089, 808; *m*/*z* (EI) 123 (M$^+$, 100), 122 (5), 96 (5), 95 (41), 94 (58), 82 (8), 81 (18), 80 (42), 79 (47), 77 (24), 68 (30), 67 (23), 53 (23), (found M$^+$ 123.0687, calcd for C_7H_9NO 123.0684). Found: C, 68.35; H, 7.44; N, 11.33%. Anal. Calcd for C_7H_9NO: C, 68.27; H, 7.37; N, 11.37%.

3-Hydroxybicyclo[3.1.0]hexane-*endo*-6-carbonitrile (19): R_f 0.29 (alkaline $KMnO_4$; hexanes/EtOAc, 1:2); ^{1}H NMR ($CDCl_3$) δ 1.45 (1 H, tm, J = 7.8), 1.85−2.01 (2 H, m), 2.08−2.16 (1 H, m), 1.99 (2 H, ddm, J = 14.4, J = 5.6), 2.26 (2 H, dd, J = 14.4, J = 6.8), 4.38−4.49 (1 H, m); ^{1}H NMR (C_6D_6) δ 0.48 (1 H, tm, J = 7.9), 0.98 (2 H, ddm, J = 7.9, J = 3.5), 1.04−1.08 (1 H, m), 1.52−1.64 (2 H, m), 1.93 (2 H, dd, J = 14.3, J = 6.8), 4.11−4.23 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 10.1 (d, J = 170), 24.2 (d, J = 173), 36.1 (t, J = 131), 73.1 (d, J = 148), 119.3 (s); $\bar{\nu}_{max}$/cm^{-1} (neat) 3418, 3040, 2936, 2233, 1079; *m*/*z* (EI) 123 (M$^+$, 2), 122 (10), 105 (11), 104 (14), 96 (9), 95 (38), 94 (49), 83 (9), 82 (55), 81 (18), 80 (96), 79 (11), 67 (100), 57 (29).

2-Hydroxybicyclo[3.1.0]hexane-*endo*-6-carbonitrile, Epimer 1 (20): R_f 0.27 (alkaline $KMnO_4$; hexanes/EtOAc, 1:2); ^{1}H NMR ($CDCl_3$) δ 1.49 (1 H, tm, J = 7.5), 1.74 (1 H, ddm, J = 13.2, J = 10.8), 1.85−2.11 (4 H, m), 2.15−2.35 (2 H, m), 4.41 (1 H, dm, J = 5.5); ^{1}H NMR (C_6D_6) δ 0.53 (1 H, tm, J = 8.0), 0.92−0.98 (1 H, m), 1.03−1.11 (1 H, m), 1.09−1.16 (1 H, m), 1.33 (1 H, ddm, J = 14.1, J = 9.0), 1.48−1.59 (1 H, m), 1.74−1.88 (1 H, m), 1.85−2.01 (1 H, m), 3.91−3.98 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 6.1 (d, J = 168), 24.0 (t, J = 134), 25.0 (d, J = 176), 31.7 (d, J = 173), 32.9 (t, J = 134), 73.3 (d, J = 151), 119.0 (s); $\bar{\nu}_{max}$/cm^{-1} (neat) 3418, 3040, 2936, 2233, 1079; *m*/*z*

(57) (a) Krow, G. R. *Tetrahedron* **1987**, *43*, 3−38. (b) Lumb, J. T.; Whitham, G. H. *Tetrahedron* **1965**, *21*, 499−501. (c) Sauers, R. R.; Beisler, J. A.; Feilich, H. *J. Org. Chem.* **1967**, *32*, 569−575.

(58) See Supporting Information.

(59) $\bar{\nu}_{CO}$(**16a**) = $\bar{\nu}_{CO}$(**17a**) = 1654 cm^{-1}.

(60) $\bar{\nu}_{CO}$(**16b**) = 1725 cm^{-1}.

(61) $\bar{\nu}_{CO}$(**16c**) = 1710 cm^{-1} (see ref 50); $\bar{\nu}_{CO}$(**17c**) = 1730 cm^{-1} (see ref 57b).

(62) Schmerling, L.; Luvisi, J. P.; Welch, R. W. *J. Am. Chem. Soc.* **1956**, *78*, 2819−2821.

(63) When performed, quenching with concentrated aqueous NH_3 (10.0 mL, ca. 150 mmol) was conducted at this juncture.

(64) Hydroxycarbonitriles **19** and **21** gave a combined signal on both GC columns. However, **19** and **21** gave well-separated signals on the HPLC column, and thus their ratio was determined by HPLC integration.

(65) Bruker Avance DRX-400 spectrometer (B_o = 9.398 T).

(EI) 123 (M^+, 9), 122 (16), 105 (7), 104 (10), 96 (17), 95 (17), 94 (34), 83 (13), 82 (68), 81 (20), 80 (87), 79 (24), 67 (100), 57 (20).

2-Hydroxybicyclo[3.1.0]hexane-*endo*-6-carbonitrile, Epimer 2 (21): R_f 0.23 (alkaline $KMnO_4$; hexanes/EtOAc, 1:2); mp 48−54 °C; ^{1}H NMR ($CDCl_3$) δ 1.48 (1 H, dd, J = 7.8, J = 7.5), 1.60−1.78 (1 H, m), 1.78−1.87 (1 H, m), 1.97−2.16 (1 H, m), 2.09 (2 H, dm, J = 11.5), 2.16−2.30 (1 H, m), 4.80 (1 H, td, J = 8.3, J = 4.8); ^{13}C NMR ($CDCl_3$) δ 5.1 (d, J = 169), 24.2 (t, J = 134), 24.9 (d, J = 172), 30.2 (t, J = 132), 30.7 (d, J = 175), 74.5 (d, J = 141), 120.1 (s); $\bar{\nu}_{max}$/cm^{-1} (neat) 3284, 3035, 2968, 2934, 2233, 1039, 822; *m*/*z* (EI) 123 (M^+, 8), 122 (9), 105 (3), 104 (9), 96 (11), 95 (26), 94 (23), 91 (17), 83 (52), 82 (87), 81 (27), 80 (95), 79 (14), 67 (100), 57 (80), (found [M − H]$^+$ 122.0601, calcd for C_7H_8ON 122.0606).

3-Nortricyclanol: R_f 0.36 (alkaline $KMnO_4$; hexanes/EtOAc, 2:3); mp 97−101 °C; ^{1}H NMR ($CDCl_3$) δ 0.98−1.04 (1 H, m), 1.08−1.18 (3 H, m), 1.21 (1 H, dm, J = 10.6), 1.30 (1 H, dm, J = 10.6), 1.71−1.79 (2 H, m), 2.21−2.27 (1 H, m), 3.74−3.80 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 10.5 (d, J = 177), 13.3 (d, J = 176), 16.0 (d, J = 177), 29.2 (t, J = 133), 30.4 (t, J = 133), 35.4 (d, J = 148), 77.2 (d, J = 150); $\bar{\nu}_{max}$/cm^{-1} (neat) 3330, 3062, 2986, 2940, 2868, 1454, 1307, 1290, 1134, 1077, 1049, 944, 908, 803; *m*/*z* (EI) 110 (M^+, 38), 109 (21), 95 (55), 92 (33), 91 (70), 82 (21), 81 (63), 79 (100), 77 (46), 69 (20), 68 (20), 67 (73), 66 (87), 65 (22), 55 (43), 53 (25), 51 (13), (found M^+ 110.0734, calcd for $C_7H_{10}O$ 110.0732).

Reaction of 3-Nortricyclanone (1) with Acidic HOSA and Saturated K_2CO_3. Neat ketone **1** (0.541 g, 5.0 mmol) was injected into a solution of HOSA (0.595 g, 5.0 mmol, 5.0 mL H_2O) whereupon homogenization occurred within 1 min of swirling. After 2 min, 8.1 *m* K_2CO_3 (1.31 g, 5.0 mmol) was swirled in and the mixture was set in an ice bath. However, crystal formation could not be initiated by scratching the cold inner walls with a glass rod.

Reaction of 3-Nortricyclanone (1) with Alkaline HOSA. HOSA (5.95 g, 50 mmol) was dissolved in ice cold 1.0 M NaOH (100 mL, 100 mmol). Neat ketone **1** (5.41 g, 50 mmol) was immediately stirred into the effervescing solution, which was subsequently stoppered and rapidly stirred in an ice bath. Stirring was continued at room temperature for 48 h. The mixture was subsequently extracted with CH_2Cl_2 (20 × 20 mL). The combined organic extracts were washed with H_2O, dried over anhydrous $MgSO_4$, suction filtered, and analyzed by GC and GC-MS. The product mixture contained 65.9% of unreacted **1**. Relative yield of products: **16a** (18.6%), **17a** (37.3%), 3-nortricyclanol (9.1%), di(3-nortricyclanylidene)hydrazine (19.0%),[43] unknown a (*m*/*z* = 123, 9.3%), and unknown b (*m*/*z* = 124, 6.7%). After rotary evaporation, the residual crystalline solid (1.17 g) was chromatographed (silica gel 60, 230−400 mesh) using a 97:3 mixture of $CHCl_3$ and MeOH to yield lactams **16a** (0.392 g, 6.4%) and **17a** (0.590 g, 9.6%) as separate fractions.

3-Azatricyclo[3.2.1.0^{2,7}]octan-4-one (17a): R_f 0.27 (alkaline $KMnO_4$; $CHCl_3$/MeOH, 97:3); mp 160−161 °C; ^{1}H NMR (400.1 MHz, $CDCl_3$)[65] δ 1.45 (2 H, dm, J = 6.8), 1.54 (2 H, d, J = 12.4), 1.83 (2 H, dd, J = 5.1, J = 12.4), 2.56−2.62 (1 H, m), 2.78 (1 H, dd, J = 6.8, J = 11.8), 7.58 (1 H, br s); ^{13}C NMR (100.6 MHz, $CDCl_3$)[65] δ 14.0 (d, J = 172), 27.0 (t, J = 133), 28.9 (d, J = 178), 40.4 (d, J = 145), 174.5 (s); $\bar{\nu}_{max}$/cm^{-1} (KBr) 3180, 3048, 2938, 2862, 1670, 1654, 1312, 1168, 1128, 846, 790; *m*/*z* (EI) 123 (M^+, 100), 96 (8), 95 (17), 94 (49), 82 (16), 81 (5), 80 (60), 79 (34), 77 (8), 69 (28), 68 (28), 67 (44), 56 (12), 55 (32), (found M^+ 123.0686, calcd for C_7H_9NO 123.0684). Found: C, 68.17; H, 7.32; N, 11.29%. Anal. Calcd for C_7H_9NO: C, 68.27; H, 7.37; N, 11.37%.

Reaction of 3-Nortricyclanone (1) with NH_3 and NaOCl. CAUTION! Neat ketone **1** (0.541 g, 5.0 mmol) was injected into a rapidly stirred 2.33 M NH_3 solution (4.5 mL, 10.5 mmol) that was submerged in an ice bath. The mixture became peach colored (pH = 9).[66] Next, a 0.56 M NaOCl solution (8.9 mL, 5.0 mmol) was slowly dripped in. The ice bath twice needed replenishing. Stirring was continued for 1 h (pH = 11). The mixture was refrigerated overnight (4 °C). The yellow solution was then administered 5 M NaOH (1.0 mL, 5.0 mmol) and refrigerated for another 2 days to destroy any remaining NH_2Cl, chloramine. Since no diaziridine **6** had precipitated, the dark yellow mixture was neutralized with 6 M HCl (ca. 1 mL) to pH = 7, warmed to 30 °C, and diluted with MeOH (40 mL). The mixture was placed in the freezer (−25 °C) for 2 days, but still no precipitate was observed. So, the mixture was rotary evaporated (35 °C) to dryness. The tan residue was triturated with CH_2Cl_2 (3 × 8 mL), and the resulting light yellow filtrate was analyzed by GC and GC-MS. (The residue tested positive for NH_4^+ cation.) Relative yield of products: **16a** (17.3%), **17a** (43.6%), **16b** (27.7%), di(3-nortricyclanylidene)-hydrazine (3.9%),[43] unknown a (*m*/*z* = 123, 3.6%), and unknown b (*m*/*z* = 124, 3.9%). Evaporation of the solvent left 0.200 g of yellow residue.

Reaction of 3-Nortricyclanone (1) with NaOCl. Neat ketone **1** (0.541 g, 5.0 mmol) was injected into a 0.57 M NaOCl solution (27.0 mL, 15.3 mmol) that was submerged in an ice bath. The reaction mixture was stirred for 2 h at 0 °C and then for 46 h at room temperature in the dark. It was then poured into 50 mL of H_2O and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with 45 mL of 0.67 M $Na_2S_2O_3$ (to reduce unreacted hypochlorite) and then with 45 mL of H_2O. The organic layer was dried over anhydrous $MgSO_4$, filtered, and shown via GC and GC-MS to contain **16b** (95.9%) and 3-nortricyclanol (4.1%). After rotary evaporation, the residue was free of 3-nortricyclanol giving pure **16b** (0.320 g, 51.6%) as a white solid: mp 68−69 °C; ^{1}H NMR ($CDCl_3$) δ 1.74−1.88 (5 H, m), 2.00 (2 H, dm, J = 7.5), 4.52−4.58 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 18.5 (d, J = 179), 21.3 (d, J = 173), 30.7 (t, J = 134), 73.5 (d, J = 164), 170.9 (s); $\bar{\nu}_{max}$/cm^{-1} (KBr) 3080, 3019, 2962, 2941, 2862, 1725, 1217, 1196, 1066, 811; *m*/*z* (EI) 124 (M^+, 69), 96 (15), 81 (41), 80 (70), 79 (100), 77 (31), 68 (56), 67 (37), 54 (30), 53 (52), (found M^+ 124.0524, calcd for $C_7H_8O_2$ 124.0524).

Reaction of 3-Nortricyclanone (1) with HN_3. CAUTION! A three-necked round-bottom flask was equipped with a stirbar, thermometer, balloon, and twistable solids addition flask and set in an ice bath. It was charged with a mixture of ketone **1** (0.541 g, 5.0 mmol, 10.0 mL $CHCl_3$) and 50% H_2SO_4 (10.0 mL) at 0 °C. Sodium azide (0.390 g, 6.0 mmol) was slowly "twisted" into the mixture whereupon N_2 evolution was observed. Afterward, stirring was continued for 2 h at at 0 °C and then overnight at room temperature. The reaction mixture was set in an ice bath, slowly neutralized with ca. 100 mL of 3 M NaOH, and then extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were washed with H_2O, dried over anhydrous $MgSO_4$, suction filtered, analyzed by GC and GC-MS, and rotary evaporated to give 0.351 g of a brown oil. Relative yield of products: **15** (13.1%), **17a** (11.2%), **19**+**21** (18.4%), **20** (14.2%), unknown c (*m*/*z* = 123, 3.8%), unknown d (*m*/*z* = 123, 5.3%), and unknowns e−j (*m*/*z* = 228, 33.9%).

Acknowledgment. We thank the Fonds zur Förderung der wissenschaftlichen Forschung in Österreich (Project P12533-CHE) for financial support. We are also grateful to Dr. D. Krois, Mag. W. Knoll, and the late Dr. A. Werner for their assistance. The reviewers of this report were exceptionally helpful.

Supporting Information Available: HETCOR spectra of lactams **16a** and **17a**; reaction paths for **9**→**8**, ***syn*-3**→**8**, and ***anti*-3**→**12**; computed conformational analysis of **8**; and *Z*-matrixes for **1**, ***syn*-3**, ***anti*-3**, ***syn*-7**, ***anti*-7**, **8**, ***iso*-8**, **9**−**12**, **13a**, ***iso*-13a**, **13b**, **13c**, **14a**, ***iso*-14a**, **14b**, **14c**, **16a**−**c**, and **17a**−**c** with computed total energies. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0159587

(66) This might be ascribed to 3-nortricyclanone imine or its trimer (see ref 2, footnote 48).