amples of strikingly similar structural effects between classically conjugating groups such as carbonyl or phenyl and various sulfur functionalities.[1c,11] The data in Table I on the *m*-trifluoromethyl substituent effects also indicate efficient transmission of negative charge by sulfur and selenium. The two point Hammet ρ values ($\sigma_{m\text{-}CF_3} = 0.43$) are 3.14 (kinetic) for $ArSCH_3$,[1a] 2.48 (kinetic) for ArSe–allyl, 2.83 (kinetic) and 4.75 (thermodynamic) for ArS–vinyl, and 2.73 (kinetic) and 4.20 (thermodynamic) for ArSe–vinyl. These values are quite comparable to those for kinetic acidities (ρ = 1.2–4[12]) in systems where the carbanion formed is directly conjugated with the aryl ring. They are smaller than the equilibrium ρ value of 7.4 estimated by Bordwell and co-workers[13] for toluenes in the highly dissociating solvent Me_2SO. The high ρ values observed for our vinyl systems suggest that the transmission coefficient for S and Se may be considerably higher here than the value (0.4) found for acidities of $ArYCH_2CO_2H$.[14] It is interesting to note that the introduction of a CF_3 group five bonds away introduces in each case we have studied a much larger perturbation than exchange of directly bonded sulfur by selenium.

The present results are limited by two factors: lithium reagents are being compared under conditions that do not promote ion pair separation, and kinetic acidities are used as a probe of carbanion stability. However, these approximate techniques are still the only ones that can be used for systems which are weakly acidic and for which the carbanions have limited stability.

Acknowledgment. We thank Dr. S. K. Shah and P. D. Clark for carrying out exploratory experiments on the deprotonation of vinyl selenides and the National Science Foundation and the National Institutes of Health for financial support.

Registry No. Phenyl allyl sulfide, 5296-64-0; phenyl allyl selenide, 14370-82-2; phenyl vinyl sulfide, 1822-73-7; *m*-(trifluoromethyl)-phenyl vinyl sulfide, 75599-82-5; phenyl vinyl selenide, 35167-28-3; *m*-(trifluoromethyl)phenyl vinyl selenide, 75599-83-6.

(11) F. G. Bordwell, J. E. Bares, J. E. Bartmess, G. J. McCollum, M. Van Der Puy, N. R. Vanier, and W. S. Matthews, *J. Org. Chem.*, **42**, 321 (1977).

(12) (a) Isotopic exchange of toluenes (lithium cyclohexylamide in cyclohexylamine), ρ = 4.0 [A. Streitwieser and H. F. Koch, *J. Am. Chem. Soc.*, **86**, 404 (1964)]. (b) Rate of deprotonation of diphenylaryl methanes (PhLi, THF), ρ = 2.2 [P. West, R. Waack and J. I. Purmort, *J. Organomet. Chem.*, **19**, 267 (1969)]. (c) Rate of deprotonation of 1-arylpropynes (*n*-BuLi/Et_2O), ρ = 1.3 [J. Y. Becker, *ibid.*, **118**, 247 (1976)].

(13) F. G. Bordwell, D. Algrim, and N. R. Vanier, *J. Org. Chem.*, **42**, 1817 (1977); D. Algrim, J. E. Bares, J. C. Branca, and F. G. Bordwell, *ibid.*, **43**, 5024 (1978). Note that acetophenones show a ρ of 3.55 in Me_2SO: F. G. Bordwell and F. J. Cornforth, *ibid.*, **43**, 1763 (1978).

(14) O. Exner in "Advances in Linear Free Energy Relationships", N. B. Chapman and J. Shorter, Eds., Plenum Press, New York, 1972, p 25.

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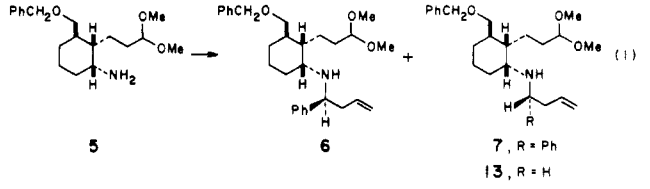
A New Method for Stereoselective Piperidine Annulation. Directing the 2-Azonia-[3,3]-Sigmatropic Rearrangement by Irreversible Hydrolysis[1]

Summary: A new method for stereoselective piperidine annulation is described involving the cyclization and subsequent [3,3]-sigmatropic rearrangement of (5,5-dimethoxypentyl)-3-butenylamines.

Sir: New strategies for forming carbon–carbon bonds under mild conditions, which exploit the facile 2-azonia-[3,3]-sigmatropic rearrangement (e.g., **2** ⇄ **3**), have been described recently from this laboratory.[1-3] One of our central objectives in this area is the development of new procedures for "directing" the 2-azonia-[3,3]-sigmatropic rearrangement such that it is irreversible (e.g., **2** → **3**) in the desired direction. A possible method for achieving this control is outlined in Scheme I. The basic strategy is to conduct the iminium ion rearrangement in the presence of sufficient H_2O such that the amine salts, rather than the iminium ions, are the major components of the mixture and to design the system such that hydrolysis of the starting iminium ion **2** is more readily reversible (via intramolecularity) than that of the desired product iminium ion **3**.[4] In this communication we demonstrate the viability of this strategy and illustrate its preparative value for stereoselective piperidine annulation.

The reaction was first explored with phenylbutenylamines **6**[5] and **7**, which were prepared in a 2:1 ratio and 65% yield by sequential treatment of primary amine **5**[1] with benzaldehyde and allylmagnesium bromide, followed by chromatographic separation on silica gel (eq 1). When



a benzene solution (0.02 M) of the major amine acetal **6** was heated at reflux for 12 h in the presence of 0.95 equiv of *d*-10-camphorsulfonic acid monohydrate and ~3 equiv of H_2O, and the reaction was quenched at 5 °C with $NaBH_4$ and methanol, the 2-allyl-*cis*-decahydroquinolines **8** and **9** were formed in a ratio of 20:1[6] (crude yield ~65%) together with small amounts of unrearranged materials[7]

(1) Part 4 in the series "Synthesis Applications of Directed 2-Azonia-[3,3]-Sigmatropic Rearrangements". For Part 3 see: Overman, L. E.; Fukaya, C. *J. Am. Chem. Soc.* **1980**, *102*, 1454.

(2) Overman, L. E.; Kakimoto, M. *J. Am. Chem. Soc.* **1979**, *101*, 1310. Overman, L. E.; Kakimoto, M.; Okawara, M. *Tetrahedron Lett.* **1979**, 4041.

(3) For a recent review of [3,3]-sigmatropic rearrangements of iminium ions see: Heimgartner, H.; Hansen, H.-J.; Schmid, H. In "Iminium Salts in Organic Chemistry", Part 2; Böhme, H., Viehe, H. G., Eds.; Wiley: New York, 1979; pp 655–732.

(4) That such an approach would be possible was apparent in the original report by Geissman of the 2-azonia-[3,3]-sigmatropic rearrangement: Horowitz, R. M.; Geissman, T. A. *J. Am. Chem. Soc.* **1950**, *72*, 1518.

(5) **6**: IR (film) 3400, 1670, 1425, 1120, 990, 910 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 7.3 (apparent s, Ph), 7.27 (apparent s, Ph), 6.0–5.4 (m, CH_2=CH), 5.4–4.8 (m, CH_2=CH), 4.5–4.3 (m, $CH(OR)_2$), 4.35 (s, $PhCH_2O$), 3.65 t, J = 6 Hz, PhCHN), 3.35 (s, OCH_3), 3.27 (d, J = 7 Hz, CH_2O), 2.5–2.8 (m, CHN), 2.37 (apparent t, J = 7 Hz, CH_2CH=CH_2); ^{13}C NMR (23 MHz, $CDCl_3$) 145.2, 138.9, 135.9, 128.3, 128.2, 127.5, 127.2, 126.9, 117.3, 105.0, 73.7, 73.1, 58.9, 52.6, 50.3, 43.6, 42.7, 37.1, 30.2, 29.0, 27.8, 22.8, 19.9; mass spectrum, m/z (isobutane CI, relative %) 452 (33), 420 (100), 378 (15), 131 (11), 91 (23). **8**: IR (film) 1645, 1455, 995, 915 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.1–7.5 (m, Ph), 5.60–5.82 (m, CH=CH_2), 5.08 (d, J = 17.3 Hz, (Z) =CH_2), 5.05 (d, J = 9.9 Hz, (E) =CH_2), 4.50 (AB q, $\Delta\nu_{AB}$ = 18.9 Hz, J_{AB} = 12.1 Hz, $PhCH_2O$), 3.47 (d, J = 7.0 Hz, CH_2O), 3.02 (m, $w_{h/2}$ = 17 Hz, CHN), 2.82 (m, $w_{h/2}$ = 20 Hz, CHN); ^{13}C NMR (63 MHz, $CDCl_3$) δ 138.6 (s, ipso Ph), 135.8 (d, CH=CH_2), 128.3 (d, *o*-Ph), 127.6 (d, *m*-Ph), 127.4 (d, *p*-Ph), 117.0 (t, CH=CH_2), 73.1 (t, OCH_2Ph), 72.6 (t, CH_2O), 51.0 (d, C-2), 49.1 (d, C-8a), 41.1 (t, CH_2CH=), 39.1 (d, C-4a), 37.1 (d, C-5), 31.8 (t), 27.8 (t), 25.4 (t), 23.6 (t), 21.1 (t); mass spectrum, m/z (isobutane CI, relative %) 300 (100), 258 (49), 107 (20), 91 (25).

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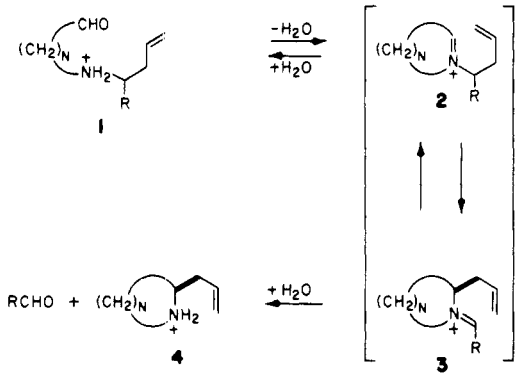
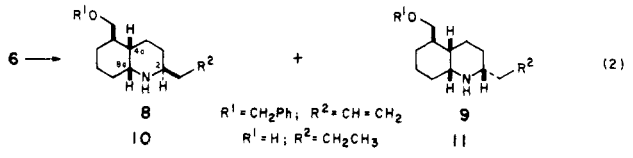
Scheme I. Direction by Irreversible Hydrolysis

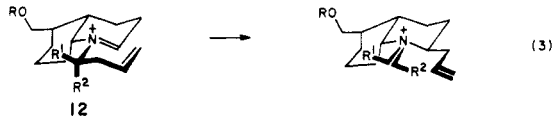


(eq 2). The *N*-benzyl derivatives of 8 and 9 were not



detected. Purification of this mixture by chromatography on silica gel afforded isomerically pure 8[5] in 48% yield. The structure of decahydroquinoline 8 followed from ^{13}C NMR spectra[5] which showed characteristic[8-10] doublet signals in the off-resonance spectrum at 51.0 (C-2), 49.1 (C-8a), and 39.1 ppm (C-4a). This structural assignment was confirmed by conversion of 8, upon catalytic hydrogenation, to *cis*-decahydroquinoline **10** (mp 115–117 °C), which was clearly different from the known[1,11] *cis*-decahydroquinoline **11** (mp 102–104 °C) which was produced by similar treatment of the minor allyl isomer **9**. The **6** → **8** conversion was less stereoselective (10:1 ratio of 8 and 9)[6] in the absence of added H_2O and somewhat slower and considerably less stereoselective (7:3 ratio of 8 and 9)[6] when acetic acid was the solvent.[12] The overall transformation was not reversible, since the formation of 8 was not inhibited by added benzaldehyde, and 8 was not converted to 9[13] (in either benzene or acetic acid) when it was resubmitted to the reaction conditions.

Identical rearrangement of the minor amine acetal stereoisomer **7** in the presence of 0.95 equiv of the sulfonic acid catalyst proceeded more slowly and nonstereoselectively in either benzene or acetic acid as solvent to give a 1:1 mixture[6] of decahydroquinolines 8 and 9 in moderate yield. We have used the quite different behavior of **6** and **7** under these conditions as the basis for our structural assignments to these materials. Rearrangement of iminium ion **12**[14] across the convex face to give ultimately 8 should be considerably more favorable with R^1 (rather than R^2) as the bulky phenyl group, since developing $A^{(1,3)}$ interactions[15] would be minimized (eq 3).



The α-phenyl group is not necessary for the success of this piperidine annulation reaction. Thus treatment of butenylamine acetal **13** (from **5** and 1-bromo-3-butene) with 0.95 equiv of *d*-10-camphorsulfonic acid for 12 h in refluxing benzene gave the 2-allyl-*cis*-decahydroquinolines 8 and 9 in a ratio of >10:1 (~40% yield).[6,16] In this case, the overall transformation could have been partially reversible, since treatment of 8 for 48 h in refluxing benzene with 10 equiv of paraformaldehyde and 0.95 equiv of *d*-10-camphorsulfonic acid monohydrate resulted in the formation of small amounts (~4%) of 9 together with other uncharacterized materials. Preparative-scale conversion of butenylamine acetal **13** to 8 was thus carried out (0.95 equiv of RSO_3H, PhH, 80 °C, 24 h) in the presence of 1.5 equiv of dimedone (5,5-dimethylcyclohexane-1,3-dione, a formaldehyde trap[17]) and afforded isomerically pure 2-allyl-*cis*-decahydroquinoline 8 in 51% yield after chromatographic purification.[18]

The simple and highly stereoselective transformation of cyclohexylamine acetals **6** and **13** to the 2-allyl-*cis*-decahydroquinoline 8 illustrates a new and potentially general method for azacyclic annulation. The application of this chemistry to total synthesis objectives in the gephyrotoxin alkaloid area[1,19] will be described in future publications from this laboratory.

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Registry No. **5**, 75444-01-8; **6**, 75494-55-2; **7**, 75420-93-8; **8**, 75420-94-9; **9**, 75420-95-0; **10**, 75420-96-1; **11**, 75420-97-2; **13**, 75420-98-3; benzaldehyde, 100-52-7; allyl bromide, 106-95-6; 1-bromo-3-butene, 5162-44-7.

(6) Isomer ratios were determined by GLC analysis using a glass capillary column (12 m, SP2100). They were time invariant (±5%) for reaction times up to 24 h.

(7) Minor products having molecular weights of 389 and 421 were detected by GC–MS analyses. Fragmentation patterns were consistent with these materials still retaining the phenylbutenyl fragment.

(8) These carbons of the 2-propyldecahydroquinoline **10** were observed at 51.0 (C-2), 49.4 (C-8a), and 41.8 (C-4a) ppm, while those of the known[1] stereoisomer **11** were observed at 57.8 (C-2), 56.1 (C-8a), and 39.7 (C-4a) ppm. These carbon signals are quite diagnostic for *cis*-decahydroquinolines of the pumiliotoxin C[9] and gephyrotoxin[1] stereochemistries.

(9) Cf.: Overman, L. E.; Jessup, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 5179.

(10) Booth, H.; Griffiths, D. V.; Jozefowicz, M. L. *J. Chem. Soc., Perkin Trans. 2* **1976**, 751. Vierhapper, F. W.; Eliel, E. L. *J. Org. Chem.* **1977**, *42*, 51.

(11) Unpublished results of C. Fukaya, see ref 1.

(12) The temperature (80 °C) and the concentration of **6** (0.020 M) and *d*-10-camphorsulfonic acid (0.019 M) were identical for all experiments.

(13) *cis*-Decahydroquinoline **9** should be thermodynamically more stable than **8**, since both side chains may be equatorial in isomer **9**.

(14) The preferred *cis*-decalin conformation for the bicyclic iminium ion intermediate should be as represented in structure **12**, because of severe $A^{(1,2)}$ interactions[15] in the alternate conformer.[1]

(15) Cf.: Johnson, F. *Chem. Rev.* **1968**, *68*, 375.

(16) We were unable by capillary GLC to cleanly resolve 8 from a small impurity formed in this reaction. The stereoselectivity quoted is a minimum estimate which is consistent with preparative-scale isolation experiments.

(17) Cf.: Horning, E. C.; Horning, M. G. *J. Org. Chem.* **1946**, *11*, 95.

(18) *cis*-Decahydroquinolines 8 and 9 were formed in a ratio of >10:1[16] before chromatographic purification.

(19) Daly, J. W.; Witkop, B.; Tokuyama, T.; Nishikawa, T.; Karle, I. L. *Helv. Chim. Acta* **1977**, *60*, 1128.

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