A Retro-Diels-Alder Approach to Oxazoles and Imidazoles

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Heating *N*-acyl derivatives **4** of 3-*endo*-aminobicyclo[2.2.1]hept-5-en-2-*endo*-ol (**3**) at 185–195 °C for 4–5 h provides oxazoles **1a–e** in 49–88% yields. The reaction proceeds via initial dehydration to an oxazoline which undergoes retro-Diels–Alder reaction to provide the oxazole. Similarly, imidazoles **7a–f** may be obtained in 40–79% yields by heating imidazolines **6a–f** to effect the cycloreversion.

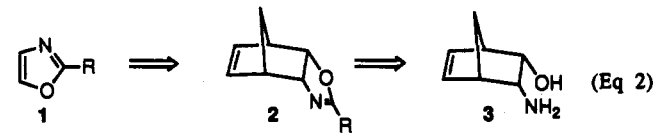
In support of ongoing efforts to identify potent antipicornaviral compounds[1] we required a new method for the synthesis of 5-[5-[2,6-dichloro-4-(2-oxazolyl)phenoxy]-pentyl]-3-methylisoxazole (**1**).[2] Attempts at generating the oxazole subunit by classical condensation approaches or via oxidation of the corresponding oxazoline had failed.[3,4] We decided to develop a new approach to oxazoles in which the C=C bond is generated via a retro-Diels–Alder reaction.[5]

Various workers over the years have studied 1,3-dipolar additions to norbornadiene analogs. Upon heating, the products of such additions undergo retro-Diels–Alder reaction to form 5-membered polyheteroaromatics such as isoxazoles,[6a,b] isothiazoles,[6c] pyrazoles,[6d-f] and triazoles[6d,g-i] (illustrated for isoxazoles in eq 1). Since an

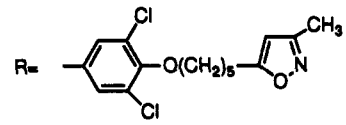
(Eq 1)

aromatic ring is generated, the cycloreversion step proceeds under relatively mild thermal conditions. Both *exo*- and *endo*-adducts have been shown to undergo the retro-Diels–Alder reaction.[6e]

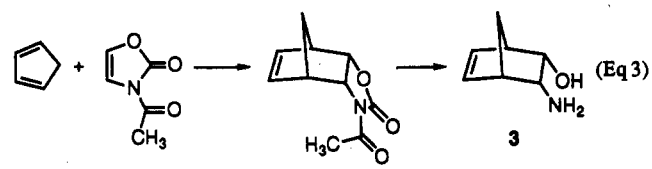
The range of heterocycles which has been synthesized in this way directly reflects the availability of a suitable 1,3-dipolarophile. We felt that it might be possible to use a retro-Diels–Alder protocol to introduce the C=C bond of an oxazole from an appropriate oxazoline **2** (eq 2). However, oxazolines are not amenable to synthesis by dipolar addition. Rather, they are generally synthesized



(Eq 2)



by cyclodehydration of a hydroxyamide which is itself derived from an amino alcohol. Since *endo*-3-aminobicyclo[2.2.1]hept-5-en-*endo*-2-ol (**3**) has been synthesized by Scholz et al. using a Diels–Alder reaction of 3-acetyloxazol-2-one with cyclopentadiene followed by exhaustive base hydrolysis, we decided to use it for our studies[7] (eq 3). By following the Scholz protocol gram



(Eq 3)

quantities of amino alcohol **3** could be synthesized.[8]

Amide formation was achieved by reacting the amino alcohol with a suitable acylating agent under standard conditions. For less reactive R groups the acid chloride or anhydride was used; for the formyl analog (R = H) the ethyl ester was sufficient. However, we were surprised to find that cyclization of the hydroxyamides **4** using standard reagents such as $POCl_3$ or $SOCl_2$ provided only low yields of the oxazolines **2**.[9] It occurred to us that since the hydroxy and amide moieties are held in close proximity by the backbone of the structure, thermolysis of **4** might provide the desired dehydration product under neutral conditions. We were gratified to find that heating hydroxyamides **4a–e** in decalin at 185–195 °C gave dehydration to the oxazolines **2** as the initial product as indicated by TLC comparison (in one case) with a sample prepared as above. Continued heating of the reaction mixture for a total of 4–5 h at this temperature allowed the retro-Diels–Alder reaction to the target oxazoles **1** to proceed (Table I). On the basis of the relative intensity

(1) For previous work in this area see: Diana, G. D.; Cutcliffe, D.; Oglesby, R. C.; Otto, M. J.; Mallamo, J. P.; Akullian, V.; McKinlay, M. A. *J. Med. Chem.* **1989**, *32*, 450–455.

(2) This work was presented in part at the 200th National Meeting of the American Chemical Society, Washington, D.C., Aug 1990; paper ORGN 115.

(3) For a comprehensive review of oxazole chemistry see: Turchi, I. J. *Oxazoles*; Weissburger, A., Taylor, E. C., Eds.; The Chemistry of Heterocyclic Compounds; John Wiley and Sons: New York, 1986; Vol. 45, pp 1–342.

(4) Personal communications from Tom Bailey, John Mallamo, and Phil Carabateas of these laboratories.

(5) For pertinent reviews of the retro-Diels–Alder reaction see: (a) Kwart, H.; King, K. *Chem. Rev.* **1968**, *68*, 415–447. (b) Ripoll, J.-L.; Rouessac, A.; Rouessac, F. *Tetrahedron* **1978**, *34*, 19–40.

(6) (a) Huisgen, R.; Christl, M. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 456–457. (b) Huisgen, R.; Christl, M. *Chem. Ber.* **1973**, *106*, 3291–3311. (c) Mckie, M. C.; Paton, M. R. *J. Chem. Res., Synop.* **1987**, *8*, 245. (d) Reinhoudt, D. N.; Kouwnhoven, C. G. *Tetrahedron Lett.* **1974**, 2163–2166. (e) Tanaka, K.; Masuda, H.; Mitsuhashi, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3901–3904. (f) Huisgen, R.; Seidel, M.; Wallbillich, G.; Knupfer, H. *Tetrahedron* **1962**, *17*, 3–29. (g) Paulissen, R. *J. Chem. Soc., Chem. Commun.* **1976**, 219–220. (h) Alder, K.; Trimborn, W. *Liebigs Ann. Chem.* **1950**, *566*, 58–69. (i) Huisgen, R.; Mobius, L.; Muller, G.; Stangl, H.; Vernon, J. M. *Chem. Ber.* **1965**, *98*, 3992–4013.

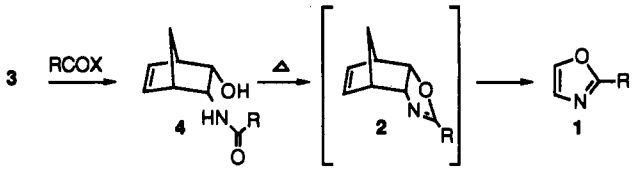
(7) Scholz, K.-H.; Heine, H.-G.; Hartmann, W. *Liebigs Ann. Chem.* **1977**, 2027–2035; *Org. Synth.* **1984**, *62*, 149–157.

(8) Although not stable for long periods on the benchtop, amino alcohol **3** undergoes no appreciable decomposition for at least six months if stored at 0 °C or as its hydrochloride salt at room temperature.

(9) For a review of oxazoline syntheses see: Frump, J. A. *Chem. Rev.* **1971**, *71*, 483–505.

0022-3263/93/1958-3387$04.00/0

Table I. Retro-Diels–Alder Approach to Oxazoles



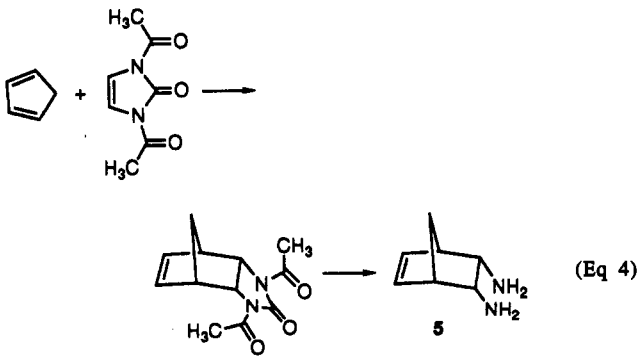
entry	R	X	yield[a] of 4 (%)	yield[b] of 1 (%)
a	H	OEt	88	49
b	Me	O_2CMe	79	63
c	Et	Cl	94	61
d	Bu	Cl	95	88
e	Ph	Cl	83	84[a]

[a] Isolated yield. [b] Calculated by integration of ^1H NMR peaks using *p*-dinitrobenzene internal standard.

of the TLC spots as the reaction proceeds it appears that the cyclodehydration and retro-Diels–Alder steps occur at comparable rates.[10]

Due to the volatility of the lower molecular weight oxazoles they were not purified, and the yields for these compounds were calculated by integration of the oxazole 4- and 5-H of the crude reaction mixture using 1,4-dinitrobenzene as internal standard. The yields for the low molecular weight compounds are somewhat worse than those for the isolable phenyl analogs, in part presumably because of their volatility but also because they may be less stable to the reaction conditions. In particular, the lower molecular weight oxazoles appear to be quite acid sensitive, and the yields were diminished if the glassware was not base-washed prior to use.

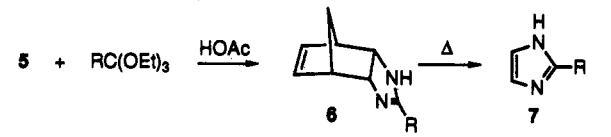
We were encouraged by these results to see whether the retro-Diels–Alder approach could be applied to other 1,3-heteroatomic aromatic systems. To this end we explored its potential application to imidazoles. The required diamine **5** was synthesized in an analogous fashion to that described above for **3**. 1,3-Diacetylimidazol-2-one was reacted with cyclopentadiene to provide the known Diels–Alder adduct in 69% yield.[11] Vigorous base hydrolysis provided **5**[12,13] (eq 4).



(Eq 4)

Unfortunately, our attempts to monacylate **5** in the manner described for **3** were largely unsuccessful. Reaction of **5** with acid chlorides, even at low temperature and with inverse addition, provided mainly *N,N'*-diacylated products. Use of anhydrides under high dilution improved the yield of monoacylated product somewhat, but diacylated material still predominated.[14,15] It occurred to us that an imidazoline, not an amide, was the required intermediate in the retro-Diels–Alder sequence. Methods are well-known for the conversion of diamines into imidazolines directly. Indeed, the required imidazolines **6a–f** could be prepared in 62–87% yield by reacting **5** with appropriate orthoesters in the presence of acetic acid.[16] Heating imidazolines **6a–f** in decalin at 185–195 °C for 3–4 h provided the target imidazoles **7a–f** in 40–79% yield (Table II). The imidazoles are much less volatile than the oxazoles, and thus the yields in Table II are for purified, fully characterized compounds. It is noteworthy that the apparently unknown 2-alkoxy analog **7f** is readily prepared using this approach; the potentially labile ethoxy group does not pose a problem.[17,18]

Table II. Retro-Diels–Alder Approach to Imidazoles



entry	R	yield[a] of 6 (%)	yield[a] of 7 (%)
a	H	74	40
b	Me	62	79
c	H	72	60
d	Bu	79	73
e	Ph	73	54
f	OEt	87	70

[a] Isolated yield.

In conclusion, we have demonstrated that the retro-Diels–Alder reaction of intermediates derived from *endo*-3-aminobicyclo[2.2.1]hept-5-en-*endo*-2-ol (**3**) and bicyclo[2.2.1]hept-5-ene-2-*endo*,3-*endo*-diamine (**5**) provides a variety of oxazoles and imidazoles under relatively mild, neutral, thermal conditions. The reaction should provide a useful, general approach not only to oxazoles and imidazoles but also potentially to other related heteroaromatic systems.[20]

Experimental Section

Melting points are uncorrected. Analytical thin-layer chromatography (TLC) was performed on E. Merck 5 × 20 Kieselgel 60 F-254 plates. Flash chromatography was performed with Kieselgel 60 (230–400 mesh). All reactions were performed under a nitrogen atmosphere. Resealable Pyrex tubes (Ace Glass) were used for the thermolyses. Tubes were washed 3× with 2 N NaOH

(10) The details of the application of this method to the preparation of compound **1** as well as the antiviral activity of this compound have been reported separately: Bailey, T. R.; Diana, G. D.; Kowalczyk, P. J.; Akullian, V.; Eissenstat, M. A.; Cutcliffe, D.; Mallamo, J. P.; Carabateas, P. M.; Pevear, D. C. *J. Med. Chem.* **1992**, *35*, 4628–4633.

(11) (a) Scholz, K.-H.; Heine, H.-G.; Hartmann, W. *Synthesis* **1979**, 579–580. (b) Whitney, R. A. *Tetrahedron Lett.* **1981**, *22*, 2063–2066. (c) Scholz, K.-H.; Hartmann, W.; Heine, H.-G. U.S Patent 4238618, 1980; *Chem. Abstr.* **1979**, *90*, 54937.

(12) (a) Scholz, K.-H.; Hinz, J.; Heine, H.-G.; Hartmann, W. *Liebigs Ann. Chem.* **1981**, 248–255. (b) Burns, E. A.; Jones, R. J. U.S. Patent 3748310, 1973; *Chem. Abstr.* **1973**, *79*, 105838.

(13) The diamine decomposes gradually, but can be stored as the dihydrochloride salt indefinitely.

(14) Jacobson, A. R.; Makris, A. N.; Sayre, L. M. *J. Org. Chem.* **1987**, *52*, 2592–2594.

(15) The monoacylated materials on heating cyclize to the imidazolines and undergo the retro-Diels–Alder reaction to form the corresponding imidazole.

(16) Taylor, E. C.; Ehrhart, W. A. *J. Org. Chem.* **1963**, *28*, 1108–1112.

(17) A single citation for this compound has data consistent for 2-ethoxy-4,5-dihydroimidazole, not 2-ethoxyimidazole: Orlov, S. I.; Khasan'yanova, E. Sh. U.S.S.R. Patent 522185, 1976; *Chem. Abstr.* **1976**, *85*, 192733.

(18) No rearrangement to 1-ethyl-4-imidazolin-2-one[19] is observed.

(19) Wong, O.; Tsuzuki, N.; Richardson, M.; Rytting, H.; Konishi, R.; Higuchi, T. *Heterocycles* **1987**, *26*, 3153–3158.

(20) For example, by replacing the hydroxy by a sulfhydryl group, one should be able to synthesize thiazoles.

and then with distilled H_2O until the washes were no longer basic. A 2-L stirred stainless steel pressure reactor (Parr) was used in the synthesis of diamine **5**. NMR (δ) J values are given in Hz.

Acylations of *endo*-3-Aminobicyclo[2.2.1]hept-5-en-2-*endo*-ol. *N*-(*endo*-2-Hydroxybicyclo[2.2.1]hept-5-en-3-*endo*-yl)propanamide (4c). To a stirred solution of 375 mg (3.0 mmol) of *endo*-3-aminobicyclo[2.2.1]hept-5-en-2-*endo*-ol[7] (**3**) in 40 mL of CH_2Cl_2 at −30 °C was added 637 mg (6.3 mmol) triethylamine. To this mixture was added a solution of 277 mg (3.0 mmol) of propionyl chloride in 15 mL CH_2Cl_2 over 30 min. The reaction was allowed to warm to rt for 1 h. The resulting solution was extracted with 25 mL of 2 N NaOH. The base layer was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic phase dried over $MgSO_4$, filtered, and concd to give a white solid which was triturated with Et_2O to give 480 mg (88%) of amide **4c**. An analytical sample was prepared by recrystallization of this material from EtOAc: mp 124–125 °C; ^{1}H NMR 6.25 (m, 2H), 5.68 (br s, 1H), 4.48 (dd, J = 7.8, 3.9, 1H), 4.21 (ddd, J = 7.6, 7.6, 3.7, 1H), 3.12 (br s, 1H), 3.06 (br s, 1H), 2.19 (q, J = 7.6, 2H), 2.04 (s, 1H), 1.51 (br d, J = 9.5, 1H), 1.32 (d, J = 9.5, 1H), 1.13 (t, J = 7.7, 3H); IR (KBr) 3316, 2970, 1644 cm^{-1}; MS (CI) m/z (relative intensity) 182 (MH^+, 24), 126 (71), 115 (100), 108 (14). Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 65.86; H, 8.41; N, 7.63.

***N*-(*endo*-2-Hydroxybicyclo[2.2.1]hept-5-en-3-*endo*-yl)pentanamide (4d):** mp 85–86 °C (EtOAc); ^{1}H NMR 6.25 (m, 2H), 5.65 (br s, 1H), 4.48 (dd, J = 7.8, 3.9, 1H), 4.22 (ddd, J = 7.6, 7.6, 3.9, 1H), 3.12, (br s, 1H), 3.06 (br s, 1H), 2.15, (t, J = 7.6, 2H), 1.89 (s, 1H), 1.67–1.21 (m, 6H), 0.90 (t, J = 7.3, 3H); IR (KBr) 3310, 2963, 1642 cm^{-1}; MS (CI) m/z (relative intensity) 210 (MH^+, 100), 143 (82), 126 (74), 108 (10). Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.48; H, 9.23; N, 6.65.

***N*-(*endo*-2-Hydroxybicyclo[2.2.1]hept-5-en-3-*endo*-yl)benzamide (4e):** mp 145–146 °C (EtOAc–hexane); ^{1}H NMR 7.72 (d, J = 8.1, 2H), 7.52–7.33 (m, 3H), 6.42 (br s, 1H), 6.29 (s, 2H), 4.55 (m, 1H), 4.40 (m, 1H), 3.24 (m, 1H), 3.10 (m, 1H), 1.57 (m, 2H), 1.38 (d, J = 9.5, 1H); IR (KBr) 3420, 3312, 2980, 1628 cm^{-1}; MS (CI) m/z (relative intensity) 230 (MH^+, 100), 163 (22), 105 (16). Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.15; H, 6.59; N, 6.05.

***N*-(*endo*-2-Hydroxybicyclo[2.2.1]hept-5-en-3-*endo*-yl)acetamide (4b).** Reaction run as for **4c**, but using acetic anhydride at 0 °C: mp 81–82 °C (CH_2Cl_2–hexane); ^{1}H NMR 6.26 (br s, 2H), 5.62 (br s, 1H), 4.47 (dd, J = 7.9, 3.9, 1H), 4.24 (ddd, J = 7.7, 7.7, 3.7, 1H), 3.11 (br s, 1H), 3.06 (br s, 1H), 1.96 (s, 3H), 1.81 (br s, 1H), 1.52 (dt, J = 9.5, 2.0, 1H), 1.32 (d, J = 9.5, 1H); IR (KBr) 3304, 2966, 1644 cm^{-1}; MS (CI) m/z (relative intensity) 168 (MH^+, 41), 126 (23), 101 (100). Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.27; H, 7.94; N, 8.40.

***N*-(*endo*-2-Hydroxybicyclo[2.2.1]hept-5-en-3-*endo*-yl)formamide (4a).** Amino alcohol **3** (200 mg, 1.6 mmol) and 1.2 mL of ethyl formate were combined and heated at reflux for 6 h. The reaction mixture was concd and crystallized from *t*-BuOMe to provide 215 mg (88%) of amide **4a** as a tan solid: mp 125–127 °C; ^{1}H NMR 8.16 (s, 1H), 6.27 (s, 2H), 5.78 (bs, 1 H), 4.51 (dd, J = 8.0, 3.8, 1H), 4.30 (ddd, J = 8.1, 7.7, 4.0, 1H), 3.17 (br s, 1H), 3.08 (br s, 1H), 1.66 (s, 1H), 1.57 (dt, J = 9.7, 2.1, 1H), 1.33 (d, J = 9.5, 1H); IR (KBr) 3320, 3237, 2981, 1651 cm^{-1}; MS (CI) m/z (relative intensity) 154 (MH^+, 100), 126 (78). Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.56; H, 7.23; N, 9.10.

Cyclodehydration Retro-Diels–Alder Reaction of Amides 4a–e. 2-Ethyloxazole (1c).[21] Amide **4c** (181 mg, 1.0 mmol) was dissolved in 4 mL of decalin in a resealable tube. Nitrogen was bubbled through the solution for several minutes to remove oxygen. The tube was then sealed and immersed for 4 h in an oil bath maintained at 195 °C. The reaction mixture was cooled, and three 0.1-mL aliquots were added to NMR tubes each containing 0.4 mL of a 0.0156 M standard solution of 1,4-dinitrobenzene in $CDCl_3$. The final concentration of 1,4-dinitrobenzene in each tube was thus 0.0124 M. The theoretical concentration of product in each tube is 0.050 M. The integration of the two oxazole H's was compared to the integration of the reference standard (4H) for each of the three tubes and the average of the six values taken. In this way the yield was calcd to be 61.0 ± 2.7%. Using an authentic sample of oxazole in this protocol a theoretical value of 92.6 ± 3.1% was measured. Thus, this procedure provides a conservative estimate of the yield in the reaction. The reactions could also be run in the absence of decalin with some sacrifice in yield in order to obtain an NMR spectrum without decalin peaks. In these cases the crude reaction mixture was filtered through Supercel using a small volume of $CDCl_3$: ^{1}H NMR 7.56 (s, 1H), 7.05 (s, 1H), 2.84 (q, J = 7.7, 2H), 1.37 (t, J = 7.7, 3H).

Oxazole (1a):[22] ^{1}H NMR 7.95 (s, 1H), 7.65 (s, 1H), 7.09 (s, 1H).

2-Methyloxazole (1b):[22] ^{1}H NMR 7.49 (s, 1H), 6.94 (s, 1H), 2.40 (s, 3H).

2-Butyloxazole (1d): ^{1}H NMR 7.48 (s, 1H), 6.92 (s, 1H), 2.71 (t, J = 7.9, 2H), 1.68 (m, 2H), 1.31 (m, 2H), 0.87 (t, J = 7.0, 3H).

2-Phenyloxazole (1e).[23] Amide **5e** (169 mg, 0.74 mmol) was dissolved in decalin and heated at 195 °C for 5 h. The reaction mixture was allowed to cool and was then applied directly onto a silica gel column and eluted with $CHCl_3$ to provide after concentration in vacuo 90 mg (84%) of 2-phenyloxazole as an amber oil: ^{1}H NMR 8.06 (m, 2H), 7.71 (s, 1H), 7.46 (m, 3H), 7.23 (s, 1H); IR (neat) 3128, 3062, 1558 cm^{-1}; MS (CI) m/z (relative intensity) 146 (MH^+, 100). Anal. Calcd for C_9H_7NO: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.05; H, 4.72; N, 9.61.

Bicyclo[2.2.1]hept-5-ene-2-*endo*,3-*endo*-diamine (5)[12b] Dihydrochloride. A slurry of 59.4 g (254 mmol) of (3aα,4α,7α,7aα)-1,3-diacetyl-1,3,3a,4,7,7a-hexahydro-4,7-methano-2*H*-benzimidazol-2-one[11] (eq 4) in 200 mL of MeOH and 75 mL of 50% KOH was heated at reflux for 4 h. The resulting slurry was filtered and the solid washed several times with H_2O and dried in a vacuum oven for 24 h at 60 °C to provide 39.2 g of crude (3aα,4α,7α,7aα)-1,3,3a,4,7,7a-hexahydro-4,7-methano-2*H*-benzimidazol-2-one. The filtrate was partially concd, extracted with $CHCl_3$, neutralized with 6 N HCl, and again extracted with $CHCl_3$. The combined organic phase was dried over $MgSO_4$, filtered, and concd to 1.6 g of additional product.

A portion of this crude material (34 g, 212 mmol theoretical) in 300 mL of 50% KOH and 120 mL of MeOH was heated in a stirred pressure reactor at 155 °C for 24 h. The reaction mixture was extracted with 6 × 200 mL of $CHCl_3$[24] and the combined organic phase dried over Na_2SO_4, filtered, and concd to a brown oil. The oil was dissolved in Et_2O and filtered to remove some solid brown impurities. The filtrate was cooled to 0 °C and treated with ethereal HCl to provide 18.8 g (45%) of the dihydrochloride salt of **8** as a tan solid suitable for further use. Recrystallization from MeOH–CH_2Cl_2 provided an analytical sample: mp 275 °C dec; ^{1}H NMR (DMSO-d_6) 8.30 (br s, 6H), 6.31 (s, 2H), 3.92 (s, 2H), 3.12 (s, 2H), 1.52 (m, 2H); IR (KBr) 3200–2500, 1573 cm^{-1}; MS (CI) m/z (relative intensity) 125 (MH^+, 63), 108 (93), 94 (26), 91 (100). Anal. Calcd for $C_7H_{12}N_2$·2HCl: C, 42.66; H, 7.16; N, 14.21; Cl, 35.97. Found: C, 42.76; H, 7.27; N, 13.94; Cl, 35.66.

Preparation of Imidazolines. (3aα,4α,7α,7aα)-2-Butyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-benzimidazole (6d). To 320 mg (1.6 mmol) of **8** dihydrochloride and 200 mg (2.4 mmol) of NaOAc in 5 mL of HOAc was added 728 mg (4.5 mmol) trimethyl orthovalerate. The reaction mixture was allowed to stir overnight. It was then concd and partitioned between 2 N NaOH and EtOAc. The EtOAc phase was dried over $MgSO_4$, filtered, and concd to 250 mg (79%) of a tan solid. Trituration with Et_2O followed by sublimation at 80 °C (0.15 mm) provided an analytical sample as a white solid: mp 82–83 °C; ^{1}H NMR 6.02 (s, 2H), 4.33 (br s, 2H), 3.34 (br s, 1H), 3.11 (br s, 1H), 2.07 (t, J = 7.7, 2H) 1.22–1.58 (m, 6H), 1.12 (d, J = 8.9, 1H), 0.90 (t, J = 7.3, 3H); IR (KBr) 3068, 2964, 2928, 1596 cm^{-1}; MS (CI) m/z (relative intensity) 191 (MH^+, 100), 153 (19), 125 (89). Anal. Calcd for $C_{12}H_{18}N_2$: C, 75.74; H, 9.53; N, 14.72. Found: C, 75.73; H, 9.63; N, 14.54.

(3aα,4α,7α,7aα)-3a,4,7,7a-Tetrahydro-4,7-methano-1*H*-benzimidazole (6a): mp 90–92 °C (sublimed); ^{1}H NMR 6.27 (s, 1H), 6.02 (m, 2H), 4.33 (br s, 2H), 3.14 (br s, 1H), 2.89 (br s, 1H),

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(24) Diamine **8** has significant water solubility.

1.40 (d, J = 8.8, 1H), 1.14 (d, J = 8.8, 1H); IR (KBr) 3129, 2990, 2914, 1664, 1580 cm^{-1}; MS (CI) m/z (relative intensity) 135 (MH^+, 100), 111 (76), 97 (91), 95 (34), 91 (16). Anal. Calcd for $C_8H_{10}N_2$: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.32; H, 7.60; N, 20.64.

(3aα,4α,7α,7aα)-2-Methyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-benzimidazole (6b): mp 132–133 °C (sublimed); ^{1}H NMR 6.03 (m, 2H), 4.31 (br s, 2H), 3.80 (br s, 1H), 3.10 (m, 1H), 1.79 (s, 3H), 1.40 (d, J = 8.9, 1H), 1.11 (d, J = 8.9, 1H); IR (KBr) 3200–2600, 1599 cm^{-1}; MS (CI) m/z (relative intensity) 149 (MH^+, 100), 111 (59). Anal. Calcd for $C_9H_{12}N_2$: C, 72.94; H, 8.16; N, 18.90. Found: C, 72.50; H, 8.24; N, 18.81.

(3aα,4α,7α,7aα)-2-Ethyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-benzimidazole (6c): mp 105–106 °C (sublimed); ^{1}H NMR 6.02 (s, 2H), 4.32 (br s, 2H), 3.58 (br s, 1H), 3.12 (br s, 1H), 2.09 (q, J = 7.6, 2H), 1.39 (d, J = 8.9, 1H), 1.12 (d, J = 8.9, 1H), 1.08 (t, J = 7.6, 3H); IR (KBr) 3200–2600, 1595 cm^{-1}; MS (CI) m/z (relative intensity) 163 (MH^+, 37), 97 (100), 95 (71). Anal. Calcd for $C_{10}H_{14}N_2$: C, 74.03; H, 8.70; N, 17.27. Found: C, 73.62; H, 8.77; N, 17.21.

(3aα,4α,7α,7aα)-2-Phenyl-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-benzimidazole (6e): mp 137–138 °C (sublimed); ^{1}H NMR 7.66 (d, J = 6.6, 2H), 7.37 (m, 3H), 6.05 (s, 2H), 4.52 (br s, 2H), 3.24 (br s, 2H), 1.90 (br s, 1H), 1.47 (d, J = 8.8, 1H), 1.12 (d, J = 8.5, 1H); IR (KBr) 3069, 2972, 1562, 1516 cm^{-1}; MS (CI) m/z (relative intensity) 211 (MH^+, 10), 144 (100). Anal. Calcd for $C_{14}H_{14}N_2$: C, 79.97; H, 6.71; N, 13.32. Found: C, 79.83; H, 6.70; N, 13.40.

(3aα,4α,7α,7aα)-2-Ethoxy-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-benzimidazole (6f): mp 105–106 °C (sublimed); ^{1}H NMR 6.07 (s, 2H), 4.23 (br s, 2H), 4.09 (q, J = 7.1, 2H), 3.08 (m, 2H), 2.68 (br s, 1H), 1.42 (d, J = 8.9, 1H), 1.23 (t, J = 6.9, 3H), 1.10 (d, J = 8.7, 1H); IR (KBr) 3200–2700, 1603 cm^{-1}; MS (CI) m/z (relative intensity) 179 (MH^+, 17), 151 (11), 112 (100). Anal. Calcd for $C_{10}H_{14}N_2$: C, 67.39; H, 7.92; N, 15.72. Found: C, 67.66; H, 8.07; N, 15.63.

Retro-Diels–Alder Reaction of Imidazolines 6 to Imidazoles 7. 2-Butylimidazole (7d). Imidazoline **6d** (210 mg, 1.11 mmol) in 5 mL of decalin was heated at 195 °C for 2 h. The cooled reaction mixture was then applied to a silica column and eluted with 10% MeOH–$CHCl_3$ to give 100 mg (73%) of off-white solid. Sublimation at 70 °C (0.15 mm) provided an analytical sample as a white solid, mp 53–54 °C (lit.[25] mp 52–53.5 °C).

Imidazole (7a): mp 84–85 °C (MeOH–$CHCl_3$) (lit.[26] 90 °C).

2-Methylimidazole (7b): mp 137–139 °C (sublimed) (lit.[26] 139 °C).

2-Ethylimidazole (7c): mp 83–84 °C (sublimed) (lit.[26] 89 °C).

2-Phenylimidazole (7e): mp 148–149 °C (sublimed) (lit.[25] 144–146 °C).

2-Ethoxyimidazole (7f): mp 91–92 °C (sublimed); ^{1}H NMR 8.38 (s, 1H), 6.62 (s, 2H), 4.40 (q, J = 7.1, 2H), 1.40 (t, J = 6.9, 3H); IR (KBr) 3200–2400, 1593 cm^{-1}; MS (CI) m/z (relative intensity) 113 (MH^+, 30), 85 (100). Anal. Calcd for $C_5H_8N_2O$: C, 53.56; H, 7.19; N, 24.98. Found: C, 53.96; H, 7.11; N, 24.66.

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