2 half-lives. The wavelengths used were in the range of 230–236 nm for all amines except for diethyl- and di-*n*-propylamines for which a wavelength of 253 nm was used. Kinetic runs were carried out in duplicate. Solutions in acetonitrile were prepared in a glovebag with a dry nitrogen atmosphere.

The pseudo-first-order rate constants were calculated from the absorbance–time data by the method of Swinbourne.[4]

Amides. 2-Naphthoyl azide (0.500 g, 2.54×10^{-3} mol) dissolved in 20 mL of the appropriate solvent was mixed with 5.08×10^{-2} mol of the amine dissolved in 20 mL of the same solvent. The mixture was allowed to stand at room temperature for a period of 1 h to overnight. The solvent was removed under reduced pressure and the residue was dissolved in 25 mL of 1:1 methylene chloride–ethyl ether. The solution was washed twice with 5% hydrochloric acid, then water, 5% sodium bicarbonate, and water, respectively, and dried over anhydrous magnesium sulfate. The mixture was filtered and the solvent removed from the filtrate under reduced pressure. Solid products were purified by recrystallization from 1:1 ethyl ether–petroleum ether (30–60 °C). Liquid products were purified by column chromatography with acid-washed alumina as absorbent and with petroleum ether (30–60 °C), 1:1 petroleum ether–methylene chloride, and methylene chloride in that order as eluents. All amides gave satisfactory C, H, N analyses (Midwest Microlab, Ltd., Indianapolis, IN), NMR spectra, and the correct molecular ion in the mass spectrum.

Determination of Yield by GC. One-half milliliter of a 0.3200 M solution of 2-naphthoyl azide in the appropriate solvent was mixed with approximately 4×10^{-3} mol of the amine and the mixture allowed to stand overnight at room temperature. One-half milliliter of a 0.3200 M solution of an internal standard (triphenylmethane or phenanthrene) was added and the resulting mixture was analyzed by GC with an SE-30 column. Authentic samples of the amines were used for calibration of the GC procedure.

Registry No. 1, 82740-57-6; 2, 82740-58-7; 3, 82740-59-8; 4, 82740-60-1; 5, 82408-27-3; 6, 82740-61-2; 7, 82740-62-3; 8, 13577-84-9; 9, 53463-19-7; 10, 13797-71-2; 11, 82740-63-4; butylamine, 109-73-9; *tert*-butylamine, 75-64-9; 2-methylbutylamine, 96-15-1; cyclohexylamine, 108-91-8; 2-methoxyethylamine, 109-85-3; phenethylamine, 64-04-0; 3-phenylpropylamine, 2038-57-5; diethylamine, 109-89-7; dipropylamine, 142-84-7; dibutylamine, 111-92-2; pyrrolidine, 123-75-1; 2-naphthalenecarbonyl azide, 1208-11-3.

(4) Swinbourne, E. S. *J. Chem. Soc.* **1960**, 2371.

Communications

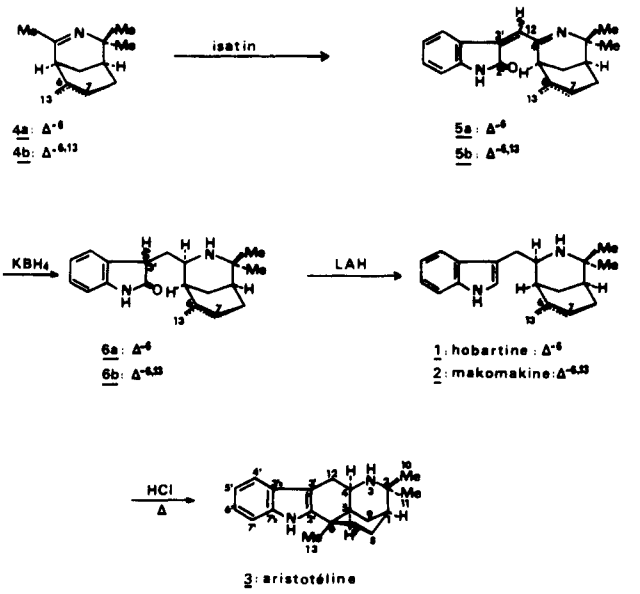
A Synthetic Entry in the *Aristotelia* Alkaloids

Summary: (±)-Hobartine (1) and (±)-aristoteline (3) were prepared from (−)-α-pinene in four and five steps, respectively. In an analogous fashion, (+)-makomakine (2) and (+)-aristoteline (3) were obtained from (−)-β-pinene.

Sir: The *Aristotelia* alkaloids are an emerging class of indole alkaloids that arise from tryptophan and a non-loganin-derived monoterpene unit.[1] Whereas the stepwise assembly of the terpenic part of the molecule would necessarily be lengthy, the recently described mercury-mediated Ritter reactions of acetonitrile with pinenes[2] provide a shortcut to the problem. On the basis of these reactions, we herein describe an expeditious synthesis of hobartine 1,[3] makomakine 2,[4] and aristoteline 3.[5]

Starting material, (±)-**4a**, available in a single step from (−)-α-pinene,[2a,b] was condensed with isatin (EtOH, piperidine, reflux, 30 min) to yield oxindole **5a**[6] (86%; Scheme I), *which contains all the requisite carbon atoms of the target molecules.* The next step in the synthesis demands an adjustment of the oxidation levels at C-2′, C-3′, C-12, and C-4 and a ring closure between C-2′ and C-6. Simultaneous reduction of the unsaturated imine bonds to

Scheme I



6a[7] was achieved with KBH_4; as expected,[2a] reduction of the imine proceeded stereospecifically although a mixture was obtained at C-3′ (46%). This stereospecificity is the result of an axial attack on a six-membered ring and parallels the reduction of similar bicyclic systems.[2] The next step in the synthesis called for conversion of a 3-monosubstituted oxindole to an indole, a reaction that is known to be difficult as a result of the possible enolization to 2-hydroxyindoles.[8] The presence of the terpenic double

(1) Bick, I. R. C.; Hai, M. A.; Preston, N. W. *Heterocycles* **1979**, *12*, 1563–1565.

(2) (a) Delpech, B. Thèse de Doctorat ès Sciences Physiques, Université de Paris-Sud, 1977. (b) Delpech, B.; Khuong-Huu, Q. *J. Org. Chem.* **1978**, *43*, 4898–4900. (c) Pancrazi, A.; Kabore, I.; Delpech, B.; Khuong-Huu, Q. *Tetrahedron Lett.* **1979**, 3729–3730.

(3) Kyburz, R.; Schöpp, E.; Bick, I. R. C.; Hesse, M. *Helv. Chim. Acta* **1979**, *62*, 2539–2546.

(4) Bick, I. R. C.; Hai, M. A. *Heterocycles* **1981**, *16*, 1301–1302.

(5) (a) Anderson, B. F.; Robertson, G. B.; Avey, H. P.; Donovan, W. F.; Bick, I. R. C.; Bremner, J. B.; Finney, A. J. T.; Preston, N. W.; Gallagher, R. T.; Russel, G. B. *J. Chem. Soc., Chem. Commun.* **1975**, 511–512. (b) Bhakuni, D. S.; Silva, M.; Matlin, S. A.; Sammes, P. G. *Phytochemistry* **1976**, *15*, 574–575.

(6) **5a**: UV (EtOH) λ_{max} 207 nm, 258, 313; IR ($CHCl_3$) 1610, 1625, 1710, 3220 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.40 (s, 6 H), 1.75 (s, 3 H), 2.85 (m, 1 H), 5.42 (m, 1 H), 6.70–7.50 (m, 4 H), 8.40 (m, 1 H), 8.85 (s, 1 H); MS, *m/z* 92, 93 (100), 136, 171, 172, 306 (M^+, 26), 307, 308.

(7) **6a**: UV (EtOH) λ_{max} 211 nm, 250, 281; IR ($CHCl_3$) 1620, 1710, 3220 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.90, 1.02, 1.15, 1.30 (4 s, 6 H), 1.75 (m, 3 H), 5.65 (m, 1 H), 6.70–7.50 (m, 4 H); MS, *m/z* 83, 85, 93, 121, 132, 158, 164, 175, 178, 215, 217, 295, 310 (M^+, 27).

(8) Sundberg, R. J. "The Chemistry of Indoles"; Academic Press: New York, 1973; p 357.

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bond prevented the use of the 2-chloroindole reduction route[9] and finally the partial reduction of the lactam **6a** to (±)-hobartine (**1**)[10] was achieved with LAH in ethereal solution. An insoluble derivative precipitated in each run and the reaction had to be completed by submitting the extracted products to repeated reductions (45–55%). Final transformation of hobartine into aristoteline was envisaged as a cationic cyclization of the terpene trisubstituted double bond and the indole nucleus. In the event refluxing of (±)-**1** in concentrated HCl solution for 8 h resulted in cyclization (62%) to (±)-aristoteline (**3**).[11]

In an analogous fashion (+)-**4b**, prepared from (−)-β-pinene,[2a] was condensed with isatin to yield **5b**[12] (98%), which was reduced with KBH_4 to **6b**[13] (56%) and then with LAH to give (+)-makomakine (**2**)[14] (40%). Bick et al.[4] recently cyclized (+)-makomakine (**2**) to (+)-aristoteline (**3**) under aqueous HBr treatment (10%); in boiling concentrated HCl (3 h), synthetic (+)-**2** was converted into (+)-aristoteline (**3**)[15] in 50% yield. The optical purity of synthetic aristoteline (**3**) and makomakine (**2**) was 90% since the optical purity of the commercially available (−)-β-pinene was only 90%.

These two route provide a short approach (four and five steps) to the heretofore rare *Aristotelia* alkaloids. We are currently investigating modifications of this scheme to improve both its yield and flexibility.

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Registry No. (±)-**1**, 82769-16-2; (+)-**2**, 79559-56-1; (+)-**3**, 57103-59-0; (±)-**4a**, 68036-85-1; (+)-**4b**, 82731-94-0; (±)-**5a**, 82731-95-1; **5b**, 82731-96-2; **6a**, 82731-97-3; **6b**, 82731-98-4; isatin, 91-56-5; (−)-α-pinene, 7785-26-4; (−)-β-pinene, 18172-67-3.

Supplementary Material Available: Experimental data for compounds (3 pages). Ordering information is given on any current masthead page.

(9) Kubo, A.; Nakai, T. *Synthesis* **1980**, 365–366.
(10) (±)-**1**: mp 166–167 °C; UV, ^1H NMR, and mass spectra were identical with those of natural (−)-hobartine.
(11) (±)-**3**: mp 173–175 °C; UV, ^1H NMR, and mass spectra were identical with those of natural (+)-aristoteline; the IR spectrum (KBr) of the racemic compound was slightly different from that of (+)-**3**.
(12) **5b**: UV (EtOH) λ_{max} 209 nm, 257, 315; IR ($CHCl_3$) 1615, 1635, 1705, 3200 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.42, 1.52 (2 s, 6 H), 3.15 (m, 1 H), 4.80 (m, 1 H), 4.92 (m, 1 H), 8.65 (br s, 1 H), 8.72 (m, 1 H); MS, *m/z* 93 (100), 136, 143, 170, 171, 306 (M^+, 10), 307, 308.
(13) **6b**: UV (EtOH) λ_{max} 213 nm, 252, 282; IR ($CHCl_3$) 1620, 1705, 3220 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.10, 1.25 (2 s, 6 H), 4.60 (m, 1 H), 4.78 (m, 1 H), 6.80–7.50 (m, 4 H), 8.00 (br s, 1 H); MS, *m/z* 93, 130, 132, 158, 164, 174, 178, 215, 217, 295, 310 (M^+, 100).
(14) (+)-**2**: amorphous; $[\alpha]_D$ +107° (*c* 1.01, $CHCl_3$) (lit.[4] $[\alpha]_D$ +131.2°); the spectral data are identical with those described in ref 4; the 400-MHz ^1H NMR spectrum is in full agreement with structure **2**.
(15) (+)-**3**: $[\alpha]_D$ +13° (*c* 0.71, MeOH) (lit.[5a] $[\alpha]_D$ +16°).

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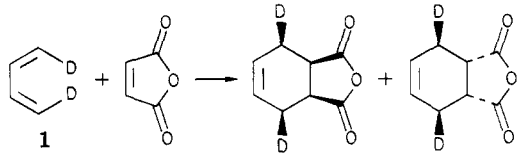
Endo Preference in the Diels–Alder Cycloaddition of Butadiene and Maleic Anhydride

Summary: The reaction of deuterium-labeled 1,3-butadiene with maleic anhydride reveals an 85/15 preference for endo adducts at 80 °C in benzene ($\delta\Delta G^{\ddagger} \sim 1.2$ kcal/mol). Since the endo transition state is sterically disfavored here, this represents a particularly simple measurement of the minimum energy advantage associated with electronic explanations of the Alder endo rule.

Sir: The general observation of endo selectivity in the Diels–Alder synthesis is an important aspect of the usefulness of this reaction. The selectivity, referred to as the Alder endo rule,[1] has been noted for dienophile substituents that are both saturated and unsaturated, that range from moderately electron donating to powerfully electron withdrawing, and that range from sterically simple to complex.[2] In this paper we present our determination of the endo selectivity in a parent system, perhaps the least complex measured to date, that between butadiene and maleic anhydride.

A number of experiments and theoretical arguments have been presented that support several explanations for the endo rule. Endo orientation is argued to be stabilized by inductive[3] or charge-transfer[4] interactions for both unsaturated and saturated groups and by stabilizing secondary orbital overlap[1,5] for unsaturated dienophile substituents. Steric factors, particularly those of the type exemplified by the interactions between the methylene protons of cyclopentadiene and exo oriented dienophiles, have been argued to disfavor the exo transition state by either crowding[6] or by forcing poor alignment of the interacting orbitals.[7]

In the reaction of butadiene with maleic anhydride the ratio of endo to exo transition states can be determined by proper deuterium labeling. We have previously described the synthesis[8] and mechanistic usefulness[9] of *cis,cis*-1,4-dideuterio-1,3-butadiene (**1**). We report here that **1** leads to a mixture of 85% endo and 15% exo in its reaction with maleic anhydride.



1 *exo*-**2** (15%) *endo*-**3** (85%)

Reaction of **1** with maleic anhydride can be conveniently accomplished at 80 °C, in benzene solution (sealed tube). Under these conditions the reaction product is completely stable and the ratio of products **2** and **3** directly reflects the ratios of exo and endo transition states. The assignment of structure derives from two separate chemical shift studies. In both the ene anhydride **4** and *cis*-epoxy anhydride **5**, the H_aH_b methylene protons appear as well-resolved separate resonances. In both cases the lower field of the two signals also shows the strongest response to $Eu(fod)_3$; for example $\Delta\delta$/equivalent of $Eu(fod)_3$ = 280 Hz vs. 165 Hz, for **4**, in benzene [**4**] = 0.26 M. This strongly

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(2) Martin, J. G.; Hill, R. K. *Chem. Rev.* **1961**, *61*, 537–562. This is a comprehensive review of stereochemical features of the Diels–Alder reaction.
(3) Wassermann, A. *J. Chem. Soc.* **1935**, 825, 1511; **1936**, 432; *Trans. Faraday Soc.* **1939**, *35*, 841; and "Diels–Alder Reactions"; Elsevier: New York, 1965.
(4) Woodward, R. B.; Baer, H. *J. Am. Chem. Soc.* **1944**, *66*, 645.
(5) (a) Woodward, R. B.; Katz, T. J. *Tetrahedron* **1959**, *5*, 70. (b) Hoffmann, R.; Woodward, R. B. *J. Am. Chem. Soc.* **1965**, 87, 4388. Woodward, R. B.; Hoffmann, R. *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 781.
(6) This feature was first summarized forcefully by Martin and Hill in ref 2.
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(8) Stephenson, L. M.; Gemmer, R. V.; Current, S. P. *J. Org. Chem.* **1977**, *42*, 212.
(9) (a) Stephenson, L. M.; Gemmer, R. V.; Current, S. *J. Am. Chem. Soc.* **1975**, *97*, 5909. (b) Graham, C. R.; Stephenson, L. M. *Ibid.* **1977**, *99*, 7098.

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