3.45 (2 H, d), 3.88 (6 H, m), 5.2 (1 H, m), 6.8–8.0 (13 H, m).

Anal. Calcd for $C_{23}H_{23}NO_3$: C, 76.43; H, 6.41; N, 3.88. Found: C, 76.21; H, 6.43; N, 3.83.

General Procedure for Diborane Reduction of 2-Oxazolines (4). The 2-oxazolines 4 listed in Table I were treated with 2–3 equiv of B_2H_6 in THF at reflux for the specified time. At the end of that time, the solvent was removed and the residue dissolved in 10% HCl. The acidic aqueous solution was washed with ether, basified with K_2CO_3(aq), and extracted several times with chloroform. The combined and dried ($MgSO_4$) organic solution was concentrated to yield alcohols 5.

***N*-(2-Phenylethyl)(3,4-dimethoxyphenyl)acetamide (18).** 5-Phenyl-2-(3,4-dimethoxyphenyl)-2-oxazoline (16; 0.5 g, 1.7 mmol) was dissolved in 100 mL of ethanol and the solution acidified with 4 mL of concentrated hydrochloric acid. To this solution was added 200 mg of 10% palladium on carbon, and the solution was kept under 50-psi hydrogen pressure in a Parr apparatus for 13 h. At the end of this time, the suspension was filtered and concentrated to yield 0.5 g (1.67 mmol, 98%) of amide 18: mp 108 °C; mass spectrum, *m/e* 299 (M^+); IR (KBr) 1640 (s), 1250 (s) cm^{-1}; ^1H NMR ($CDCl_3$) 2.70 (2 H, t), 3.43 (4 H, m), 3.78 (3 H, s), 3.84 (3 H, s), 6.5–7.3 (8 H, m).

Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.67. Found: C, 71.81; H, 7.13; N, 4.62.

***N*-(2-Cyclohexylethyl)(3,4-dimethoxyphenyl)acetamide (19).** 5-Phenyl-2-(3,4-dimethoxyphenyl)-2-oxazoline (16; 0.5 g, 1.7 mmol) was dissolved in 100 mL of ethanol and the solution acidified with 4 mL of concentrated hydrochloric acid. Platinum oxide (50 mg) was added, and the suspension was kept under hydrogen pressure (50 psi) for 13 h and then filtered. The filtrate was concentrated to yield an oil which was basified with 10% NaOH and extracted with methylene chloride. The combined and dried organic layer was concentrated to yield a white solid: 0.4 g (1.31 mmol, 77%); mp 100–102 °C; mass spectrum, *m/e* 305 (M^+); IR (KBr) 3200 (s), 1230 (s), 1260 (s), 1030 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.5–2.0 (13 H, m), 2.5–3.5 (4 H, m), 3.75 (6 H, s), 6.9 (3 H, m), 7.8 (1 H, t, NH).

Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.71; H, 8.34; N, 4.23.

4-Phenyl-6-methoxy-1,2,3,4-tetrahydroisoquinoline (30). *N*-[(β-Hydroxy-2-phenyl)ethyl]-(4-methoxyphenyl)methylamine (28; 0.4 g, 1.55 mmol) was suspended in a mixture of trifluoroacetic acid (1 mL), sulfuric acid (1 mL), and methylene chloride (10 mL). The suspension was heated under reflux 0.5 h and then concentrated to yield an oil that was basified with K_2CO_3(aq) and extracted with chloroform several times. The combined and dried ($MgSO_4$) organic solution was concentrated to yield 0.45 g of crude product. This material was dissolved in ethanolic hydrogen chloride and recrystallized from ethanol–ether to yield product: 0.35 g (1.27 mmol, 82%); mp (hydrochloride) 238–239 °C; mass spectrum, *m/e* 239 (M^+); IR (KBr) 1600 (s), 1500 (s), 1280, 1250, 700; ^1H NMR (Me_2SO-d_6) δ 3.40 (2 H, m), 3.55 (3 H, s), 4.35 (2 H, s), 4.45 (1 H, dd), 6.20 (1 H, d), 6.75 (1 H, dd), 7.2 (6 H, m).

Anal. Calcd for $C_{16}H_{18}ClNO$: C, 69.69; H, 6.58; N, 5.08. Found: C, 69.31; H, 6.63; N, 4.98.

4-Phenyl-1,2,3,4-tetrahydroisoquinoline (29). *N*-(β-Hydroxy-2-phenylethyl)benzylamine (15; 0.35 g, 154 mmol) was treated as above to yield the desired product 29: 78% yield (0.25 g, 1.2 mmol); mp (hydrochloride 224–225 °C; IR (KBr) 1575, 750 (d), 705; ^1H NMR (Me_2SO-d_6) δ 3.5 (2 H, m), 4.3 (3 H, m), 6.7 (1 H, m), 7.25 (8 H, m).

Anal. Calcd for $C_{15}H_{16}ClN$: C, 73.31; H, 6.56; N, 5.70. Found: C, 73.31; H, 6.60; N, 5.67.

Acknowledgment. We are grateful to Dr. Harry Yale for his helpful discussion on reduction of cyclic imidates with diborane.

Registry No. 9, 3433-15-6; 10, 81316-48-5; 12, 22020-69-5; 13, 81316-49-6; 15, 27159-30-4; 16, 81316-50-9; 17, 20011-97-6; 18, 3972-81-4; 19, 81316-51-0; 20, 7127-19-7; 21, 104-63-2; 22, 81316-52-1; 23, 81316-53-2; 24, 81316-54-3; 25, 67287-37-0; 26, 81316-55-4; 27, 71636-38-9; 28, 81316-56-5; 29, 75626-12-9; 29 HCl, 6109-35-9; 30, 81316-57-6; 30·HCl, 81316-58-7; 32, 67287-53-0; 33, 81316-59-8; 34, 81316-60-1; 35, 81316-61-2; 2,3-dichlorobenzonitrile, 6574-97-6; ethanolamine, 141-43-5; ethyl(3,4-dimethoxyphenyl)acetimidate hydrochloride, 81316-62-3; 1-phenylethanolamine, 7568-93-6; ethyl(2-chloro-3,4-dimethoxyphenyl)acetimidate hydrochloride, 81316-63-4; 1-(4-methoxyphenyl)ethanolamine, 55275-61-1.

Supplementary Material Available: Continuation of Table I with IR, NMR, and mass spectral data (1 page). Ordering information is given on any current masthead page.

Reexamination of Stereochemical Issues Concerning 2-Phenyl-1,2-dihydropyridine–Maleimide Cycloadditions

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The reaction of *N*-acetyl- and *N*-(carbomethoxy)-2-phenyl-1,2-dihydropyridines **1d–e** with maleimides **5a–c** has been shown by chemical correlation and X-ray analysis to proceed with only *endo*-maleimide, *anti*-phenyl stereoselectivity, rather than via stereoselectivity favoring a *syn*-phenyl configuration as previously described.[6] The X-ray crystal structure indicates a planar s-cis conformation for the *N*-carbomethoxy function of 2-(carbomethoxy)-3-*endo*-phenyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboxylic acid *N*-phenylimide (**7d**), not tetrahedral configuration about nitrogen as earlier proposed.[6]

Diels–Alder cycloaddition reactions utilizing *N*-acyl-1,2-dihydropyridines **1** offer a convenient pathway to isoquinuclidines **3**, substituted at the 7- and/or 3,7-positions. A number of 7-substituted[1a–f] and 3-substituted[1g] iso-

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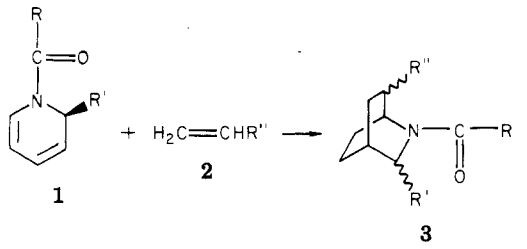


1 2 3

quinuclidines **3** have been found recently to be useful as intermediates in natural product syntheses. As part of our own desire to use isoquinuclidines **3** as natural product synthons, we became concerned about the exo/endo stereochemical orientation of groups R′ at the 3-position of heterocycles **3** resulting from cycloaddition sequences.[2]

On the basis of mechanistic considerations governing the stereochemical outcome of a Diels–Alder [4 + 2] π cycloaddition subject to kinetic control of product formation, a preferential endo configuration for the 3-R′ substituent of **3** is expected to result.[3] Attack by dienophile on the hindered face of the diene to give a 3-*exo*-R′ substituent in **3** would be less favorable due to expected repulsive interactions between the dienophile **2** and the dihydropyridine **1**. Nevertheless, it would be possible for attractive effects between the dienophile and the R′ group to lead to formation of 3-*exo*-R′ stereochemistry in adducts **3**.[4]

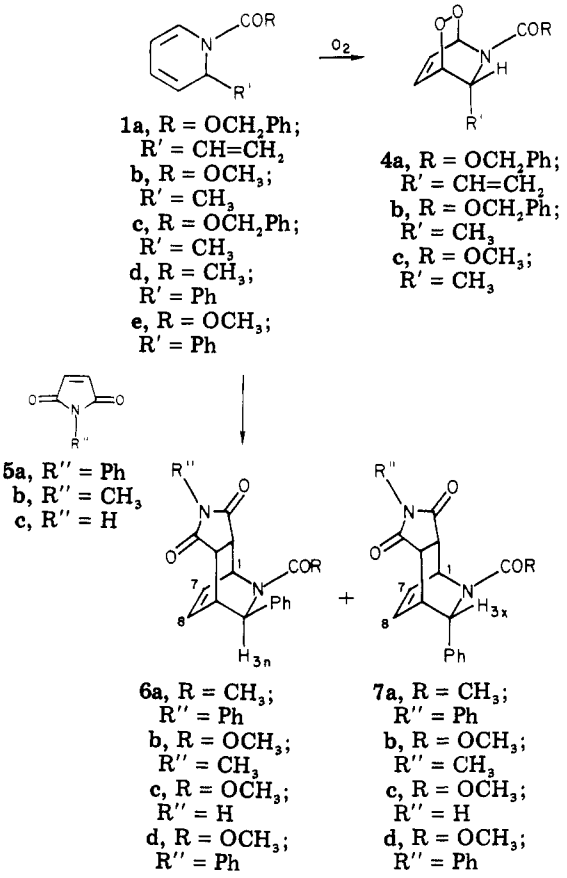
Natsume et al.[5] have reported photosensitized singlet oxygen cycloadditions for *N*-carbalkoxy-1,2-dihydropyridines **1a–c** and have shown by chemical correlation methods that 3-*endo*-R′ stereochemistry obtains in the adducts **4a–c**. By contrast, Knaus et al.[6] reported the major or exclusive formation of 3-*exo*-phenyl adducts **6a–c** in reactions of *N*-carbalkoxy and *N*-acetyl-1,2-dihydropyridines **1d–e** with maleimides **5**. Because the stereochemical assignments to **6a–c** rest only upon H^1 NMR anisotropy effects, we undertook the reexamination of these structures.

Background

Reaction of *N*-acetyl-2-phenyl-1,2-dihydropyridine **1d** with *N*-phenylmaleimide **5a** in refluxing methylene chloride afforded a solid (see Scheme I), reported to be a mixture, which could not be separated by fractional crystallization or thin-layer chromatography, of 3-*exo*-phenyl adduct **6a** (75%) and 3-*endo*-phenyl adduct **7a** (25%), with the maleimide moiety assigned an endo orientation in both cases.[6] The *N*-acetyl substituent was assigned an orientation trans to the 3-phenyl group in both adducts, an endo orientation in **6a** and an exo orientation in **7a**. The structural assgnments rested upon the following data. The ^{1}H NMR spectrum of the hypothetical mixture exhibited an absorption at δ 4.80, assigned as H_{3n} in the *exo*-phenyl adduct **6a**, and one at δ 5.09, attributed to H_{3x} in the *endo*-phenyl adduct **7a**. The acetyl methyl peaks at δ 1.77 and 2.30 were assigned to **6a** and **7a**, respectively. The 7,8-double bond was proposed to shield H_{3n} (δ 4.80) and an *endo*-acetyl group (δ 1.77) in the major isomer **6a**. Aluminum chloride catalysis gave rise to a mixture of the same two cycloaddition products from **1d** and **5a**; a ratio of **6a** (69%) to **7a** (31%) was determined by ^{1}H NMR analysis. Coupling constants $J_{1,6}$ = 4 Hz and $J_{4,5}$ = 3 Hz were deemed consistent with the endo configuration for the maleimide moiety in both **6a** and **7a**.[6]

The *N*-methyl and N-H maleimide **5b–c** reactions with *N*-(carbomethoxy)dihydropyridine **1e** afforded cycloaddition adducts having a single ^{1}H NMR absorption for H_3 at δ 4.75 in each case. The cycloadducts were assigned the 3-*exo*-phenyl stereochemistry of structures **6b–c** by comparing the chemical shift for H_3 with the peak for H_3 at δ 4.80 in the adduct **6a**. The absence of the 3-*endo*-phenyl stereoisomers **7b–c** was presumed to be the result of greater steric hindrance to approach of the maleimides **5b–c** to the dihydropyridine **1e** from the side syn to the *N*-methoxycarbonyl substituent. A transition state for cycloaddition having dihydropyridine **1e** with a syn-oriented phenyl group and an anti-oriented methoxycarbonyl

Scheme I



1a, R = OCH_2Ph; R′ = $CH{=}CH_2$
b, R = OCH_3; R′ = CH_3
c, R = OCH_2Ph; R′ = CH_3
d, R = CH_3; R′ = Ph
e, R = OCH_3; R′ = Ph

4a, R = OCH_2Ph; R′ = $CH{=}CH_2$
b, R = OCH_2Ph; R′ = CH_3
c, R = OCH_3; R′ = CH_3

5a, R″ = Ph
b, R″ = CH_3
c, R″ = H

6a, R = CH_3; R″ = Ph
b, R = OCH_3; R″ = CH_3
c, R = OCH_3; R″ = H
d, R = OCH_3; R″ = Ph

7a, R = CH_3; R″ = Ph
b, R = OCH_3; R″ = CH_3
c, R = OCH_3; R″ = H
d, R = OCH_3; R″ = Ph

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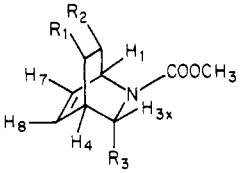
(6) Knaus, E. E.; Pasutto, F. M.; Giam, C. S.; Swinyard, E. A. *J. Heterocycl. Chem.* **1976**, *13*, 481–486.

Table I. Chemical Shift Values[a] for *N*-(Carbomethoxy)-3-*endo*-phenyl-2-azabicyclo[2.2.2]oct-7-enes



compd	R_1	R_2	R_3	shift, δ H_1	H_{3x}	H_4	H_8	H_7
7b	CO-NCH$_3$-CO		Ph	5.44	4.80	3.45[b]	5.90	6.49
7c	CO-NH-CO		Ph	5.40	4.77	3.47	5.97	6.53
7d	CO-NPh-CO		Ph	5.50	4.81	3.55[c]	6.04	6.62
7e	CO-O-CO		Ph	5.42	4.73	3.52	6.00	6.59
10[d]	H	H	Ph	4.88	4.70	2.90	5.88[e]	6.44[e]
11	CO-NPh-CO		H	5.30	3.34[f]	3.34	6.46	6.46
12	H	H	H	5.67	3.26[f]	2.70	6.32	6.32

[a] 90 MHz ($CDCl_3$). [b] Overlaps the resonance for H_5 (H_6). [c] At 360 MHz H_4 separates from H_5 and H_6. [d] Acetone-d_6 (see ref 2a). [e] For structure **10**, the numbering system is altered so that $H_8 = H_5$ and $H_7 = H_6$; compare for the *exo*-phenyl isomer δ 4.38 (H_{3n}) and 6.50 (olefinic H_5, H_6). [f] H_{3n} at δ 3.04. Compare the *N*-triphenylmethyl analogue [NMR δ 5.61, 5.28 (HC=CH), 3.4, 2.43 (H_{3x}, H_{3n})] in ref 13c.

substituent was presumed.[6] Such a transition state presupposes a tetrahedral arrangement around the nitrogen atom of **1e** for substituents and the electron lone pair.

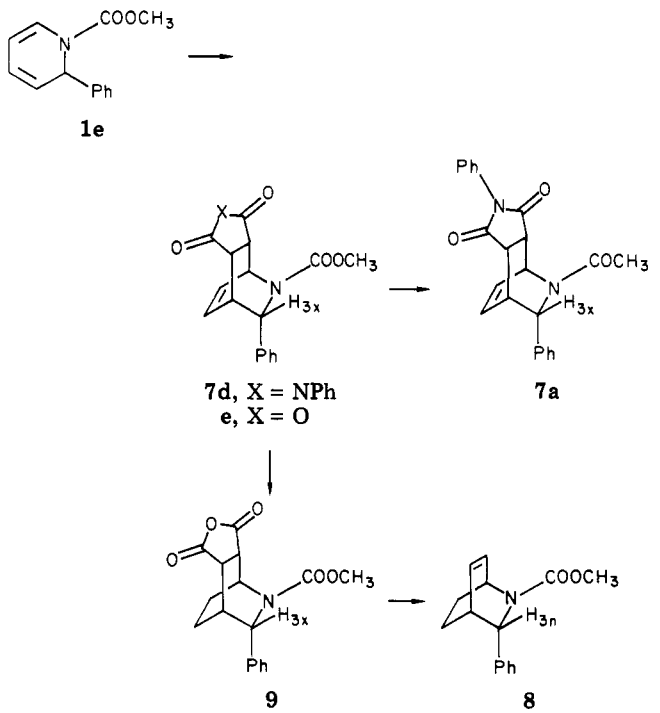
A tetrahedral *N*-acetyl or *N*-methoxycarbonyl functionality in dihydropyridine **1e** and the adducts **6a–c** and **7a** did not appear likely to us on the basis of the principles of amide resonance.[7] Additionally, the ^1H NMR analysis[6] overlooked amide conformational possibilities. We therefore were led to reexamine the structures of the adducts of dihydropyridines **1d–e** with maleimides **5a–c**.

Chemical Correlation of 3-Phenyl Stereochemistry

A chemical correlation of *N*-(carbomethoxy)-3-*exo*-phenyl-2-azabicyclo[2.2.2]oct-5-ene[2a] (**8**) with adduct **7d**, formed upon reaction of *N*-phenylmaleimide (**5a**) with *N*-(carbomethoxy)-2-phenyl-1,2-dihydropyridine (**1e**), was effected as shown in Scheme II. The chemical correlations indicate a single stereoisomer with a C-3 *endo*-phenyl as in structure **7a**, not the previously assigned mixture of **6a** and **7a** with **7a** as a minor component.[6]

Cycloaddition of the 2-phenyl-1,2-dihydropyridine **1e** to maleic anhydride[8] in refluxing chloroform gave in 90% yield bright yellow oil **7e**, homogeneous by TLC, whose 90-MHz NMR ($CDCl_3$) spectrum showed H_3 at δ 4.73 and two separate olefinic resonances at δ 6.59 (H_7) and 6.00 (H_8). Next, **7e** was hydrogenated over 5% platinum on carbon in methanol to give in 91% yield isoquinuclidine **9**. Oxidative decarboxylation of **9** by electrolysis in aqueous pyridine with added triethylamine[9] gave the known *N*-(carbomethoxy)-3-*exo*-phenyl-2-azabicyclo-[2.2.2]oct-5-ene[2a] (**8**): NMR ($CDCl_3$) δ 4.38 (H_{3n}), 6.44 (olefinic H_5, H_6).[10] With the *endo*-phenyl stereochemical assignment for **7e** secure, this anhydride was converted by reaction with aniline in ether to the *N*-phenyl imide **7d**, also formed thermally from *N*-(carbomethoxy)-2-phenyl-1,2-dihydropyridine (**1e**) and *N*-phenylmaleimide (**5a**).[6] Cycloadduct **7d** showed a single NMR absorption for H_3 at δ 4.80 of characteristic shift for H_{3x} and two sets of

Scheme II. Correlation of Phenyl Stereochemistry at C-3 for Cycloadduct 7a with That of Known Heterocycle 8



olefinic absorptions at δ 5.97 (H_8) and 6.53 (H_7), also previously noted for the olefinic peaks of 3-endo-substituted *N*-(carboalkoxy)-2-azabicyclo[2.2.2]oct-5-enes[2a–e] (see Table I).

The *N*-(carbomethoxy)-3-*endo*-phenyl adduct **7d** was next converted to its *N*-acetyl isomer **7a** [NMR ($CDCl_3$) δ 4.78 and 5.05 (H_3), 1.73 and 2.20 (CH_3CO)] in 57% yield by trimethylsilyliodide cleavage[11] of the carbamate moiety to the free amine and immediate reaction with acetyl chloride. The single adduct **7a** formed from **7d** had a 90-MHz NMR spectrum and an IR spectrum identical with those of the **7d** formed by direct cycloaddition of *N*-phenylmaleimide (**5a**) with *N*-acetyl-2-phenyl-1,2-dihydropyridine (**1d**).[6]

At 360 MHz the NMR ($Cl_2CHCHCl_2$) downfield resonance for H_{3x} of **7a** resolved into multiple resonances at

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(10) No evidence for the 3-*endo*-phenyl stereoisomer **10** [NMR ($CDCl_3$) δ 4.75 (H_{3x}), 6.53, 5.95 (olefinic H_5, H_6)[2a]] was found.
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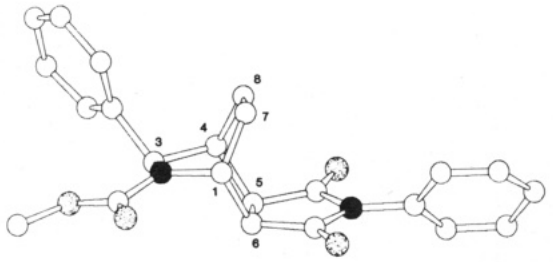

Figure 1. 2-(Carbomethoxy)-3-*endo*-phenyl-2-azabicyclo-[2.2.2]oct-7-ene-5,6-dicarboxylic acid *N*-phenylimide (**7d**).

δ 5.13 (overlapping doublets, $J_{3,4}$ = 3.6 Hz, 0.1 H each), 5.07 (s, 0.2 H), and 4.82 (s, 0.6H), while the acetyl methyl peaks remained as a pair of singlets at δ 2.30 (0.6 H) and 1.78 (2.4 H).[12] When the sample was heated to 115 °C the NMR spectrum simplified to a single peak for H_{3x} at δ 4.87 and a singlet for acetyl methyl at δ 1.89. The four resonances for H_{3x} we attribute to conformational minima associated with amide and phenyl rotamers. The observance of $J_{3,4}$ in two cases and not in two others we propose is related to a substituent enhancement of the coupling value in some conformations and not others; however, we cannot cite precedent for this suggestion (See paragraph at the end of the paper about supplementary material.)

Cycloadducts **7b,c** were prepared also from *N*-(carbomethoxy)-2-phenyl-1,2-dihydropyridine (**1e**) and the appropriate maleimide **5b,c** by using aluminum trichloride catalysis.[6] Relevant absorptions in the NMR spectra of **7b,c** are tabulated in Table I along with those of related molecules. The chemical shift values of **7b–e** are seen to be consistent with only 3-*endo*-phenyl stereochemistry in each case. Chemical shift values for H_{3x} are affected little by the endo-oriented maleimide or anhydride linkages at C_5–C_6 as seen in the similar shifts δ 4.73–4.81 for H_{3x} in **7b–e** and δ 4.70 in the C_5–C_6-unsubstituted analogue **10**. Similarly, 3-*endo*-phenyl substituents can be seen to shield H_8 δ 0.56–0.59 upfield relative to H_7 by comparing the chemical shifts for H_7 and H_8 of **7b–e** and **10**. For adducts **11** and **12**, which lack an *endo*-phenyl substituent, resonances for H_7 and H_8 overlap. It has been noted previously[2a] that for the *exo*-phenyl compound **8** there is also an overlap of resonances for the olefinic hydrogens.

X-ray Analysis of 7d

The chemical correlation of Scheme II does not enable us to assign configurations to the imide and anhydride moieties of the cycloadducts **7a–e**. We initially assigned endo orientations to the imide entities utilizing mechanistic considerations and the Alder endo rule.[3,13] X-ray structure analysis[14] of **7d** confirms this *endo*-imide assignment, as well as the *endo*-phenyl configuration of **7d** as determined by chemical correlation.

Additionally, the X-ray structure of Figure 1 clearly indicates for the crystalline state a favored s-cis conformation for the *N*-methoxycarbonyl substituent of **7d** with the carbonyl oxygen oriented away from the 3-*endo*-phenyl ring. The *N*-methoxycarbonyl function is planar in configuration rather than tetrahedral as postulated by Knaus et al.[6,15]

In conclusion, the arrangement of substituents in 3-*endo*-phenyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-*endo*-dicarboxylic acid imides **7a–d** is that expected for attack by an endo-oriented dienophile on the sterically less hindered face of a 2-phenyl-1,2-dihydropyridine (1d,e) opposite the 2-phenyl substituent.[16,17] We favor a kinetic explanation for observation of the 3-*endo*-phenyl configuration in adducts **7a–e**, since equilibration studies of the 3-acetyl-2-azabicyclo[2.2.2]oct-5-ene (**3**; R″ = H, R = OEt, R′ = $COCH_3$) led to a mixture of 3-*endo*/*exo*-acetyl isomers rather than to a single *endo*-acetyl isomer.[2a]

Experimental Section

Infrared spectra were measured with Perkin-Elmer 137 sodium chloride spectrophotometer. Elemental analyses were performed by Micro Analysis, Inc., Wilmington, DE. Proton NMR spectra were obtained in $CDCl_3$ solutions with tetramethylsilane as an internal standard by using a Perkin-Elmer R-32 90-MHz spectrometer and a Varian XL-100-15 spectrometer fitted with a Nicolet FT computer. High-resolution (360 MHz) NMR spectra were recorded at the University of Pennsylvania Middle Atlantic NMR facility, G. McDonald, director. Exact mass measurements were taken on an RMH-2 Hitachi Perkin-Elmer mass spectrometer at an ionization energy of 70 eV at the University of Pennsylvania Mass Spectrometry Center, D. T. Terwilliger, director. Routine mass spectra were obtained by R. Dumphy on a Perkin-Elmer mass RMU-6H spectrometer. Dry-column chromatography was performed by using Woelm dry column silica gel (activity III) with a fluorescent indicator. Thin-layer chromatography was conducted by using Analtech silica gel GF plates containing a fluorescent indicator.

N-Acetyl- and *N*-(carbomethoxy)-2-phenyl-1,2-dihydropyridines **1e** and **1f** were prepared according to published procedures.[6,18] *N*-Phenyl-, *N*-methyl, and *N*-protiomaleimides **5a–c** were obtained from Aldrich Chemical Co. Adducts **7a** (99%, mp 271–272 °C), **7b** (26%, yellow oil), and **7c** (40%, yellow oil) were prepared according to the procedure of Knaus et al.[6]

2-(Methoxycarbonyl)-3-*endo*-phenyl-2-azabicyclo[2.2.2]-oct-7-ene-5,6-*endo*-dicarboxylic Acid *N*-Phenylimide (7d). To a stirred solution of *N*-(methoxycarbonyl)-2-phenyl-1,2-dihydropyridine (**1e**; 0.20 g, 0.93 mmol) in dry dichloromethane (3 mL) was added a solution of *N*-phenylmaleimide (**5a**; 0.161 g, 0.93 mmol) in dry dichloromethane (2 mL) at room temperature. The resulting mixture was refluxed for 60 h under an argon blanket and cooled to room temperature, and the solvent was removed in vacuo to yield 0.352 g of a crude yellow oil. The oil was chromatographed on a preparative thin-layer plate with diethyl ether to yield 0.093 g of a mixture of **1e** and **5a** (R_f 0.61–0.79) and 0.244 g (91%) of adduct **7d**: R_f 0.43; mp 220–221 °C; low-resolution mass spectrum, m/e 388 (M^+); IR ($CHCl_3$) 1770, 1720, 1440, 1375 cm^{-1}; NMR ($CDCl_3$) δ 7.10–7.40 (m, 10 H), 3.75–3.15 (br, OCH_3, H_5, H_6, H_4); see Table I. Anal. Calcd for $C_{23}H_{20}N_{24}$: C, 71.12; H, 5.19; N, 7.21. Found: C, 71.49; H, 5.28; N, 6.81.

Crystals for X-ray analysis were obtained by slow growth in a sealed chamber saturated with ether with **7d** dissolved in methylene chloride in a small beaker inside the chamber.

***N*-(Methoxycarbonyl)-3-*endo*-phenyl-2-azabicyclo-[2.2.2]oct-7-ene-5,6-*endo*-dicarboxylic Anhydride (7e).** A solution of *N*-(methoxycarbonyl)-2-phenyl-1,2-dihydropyridine

(12) Our observed ratio of 20:80 for the acetyl methyl peaks at δ 2.30 and 1.78 compares with ratios of 25:75 and 31:69 reported by Knaus in Table IV of ref 6. The difference in values for the same compound **7a** we attribute to the range of experimental error in comparing NMR integrals and/or small variations in conformational preferences due to differences in NMR solvent or temperature parameters.

(13) (a) Williamson, K. L.; Hsu, Y. F. L. *J. Am. Chem. Soc.* **1970**, *95*, 7385–7389. (b) Several reports of exo adducts from *N*-phenylmaleimide involve heterocyclic dienes. See: Eckroth, D. R. *J. Org. Chem.* **1976**, *41*, 394–395. (c) Lyle, R. E.; Boyce, C. B. *Ibid.* **1974**, *39*, 3708–3711.

(14) Complete details of the crystallographic study will be published separately: Zacharias, David E.; Krow, Grant R., manuscript in preparation.

(15) Knaus, E. E.; Avasthi, K.; Giam, C. S. *Can. J. Chem.* **1980**, *58*, 2447–2451. In this paper the authors investigated azabicyclic amides and urethanes formed from **1d** and **1e** with nitrosobenzene. They found both the NCOOMe and NCOMe groups to exist as a mixture of rotamers.

(16) The above is not to say that the conformational analysis of dihydropyridines 1 is securely understood (see ref 1).

(17) The adduct of **1d** and *N*-phenyl-1,2,4-triazoline-3,5-dione[6] also has a 3-*endo*-phenyl orientation.[14]

(18) (a) Giam, C. S.; Stout, J. L. *J. Chem. Soc., Chem. Commun.* **1969**, 142. (b) Giam, C. S.; Knaus, E. E.; Pasutto, F. M. *J. Org. Chem.* **1974**, *39*, 3565–3568.

(1e; 0.87 g, 4.1 mmol) in chloroform (1.5 mL) was added dropwise to a refluxing solution of maleic anhydride (0.397 g, 4.1 mmol) in chloroform (2 mL). Heating was continued for 67 h. The solution was cooled to room temperature, and the solvent was removed in vacuo to give 1.41 g of a crude dark brown oil. The oil was chromatographed (10 methylene chloride/ether) to give 1.14 g (90%) of 7e: bright yellow oil; mass spectrum, m/E 313.0941 (calcd for $C_{17}H_{15}NO_5$, 313.0950); IR ($CHCl_3$) 1790, 1730–1690 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (s, 5 H), 3.8–3.35 (br, OCH_3, H_4, H_5, H_6); see Table I.

Reduction of 7e. *N*-(Methoxycarbonyl)-3-*endo*-phenyl-2-azabicyclo[2.2.2]octane-5,6-*endo*-dicarboxylic Anhydride (9). A solution of anhydride 7e (0.87 g, 2.78 mmol) in methanol (40 mL) was shaken with 5% platinum on carbon (0.1 g) in a Parr apparatus for 3 days at an initial hydrogen pressure of 52 psi. After the pressure had dropped to 47 psi, the reaction was stopped, the mixture was filtered through Celite, and the solvent was removed in vacuo to give 0.792 g (91%) of 9: Colorless solid; mp 139–141 °C; NMR ($CDCl_3$) δ 7.30 (s, 5 H), 4.82 (br, 1 H), 4.60 (br, 1 H), 3.8–3.1 (br, 6 H), 2.60 (br, 1 H), 1.81 (br, 2 H), 1.22 (br, 1 H); IR ($CHCl_3$) 1780, 1720–1690 cm^{-1}; high-resolution mass spectrum, m/e 315.1081 (calcd for $C_{17}H_{17}NO_5$, 315.1107).

Electrochemical Oxidation of 9. *N*-(Methoxycarbonyl)-3-*exo*-phenyl-2-azabicyclo[2.2.2]oct-5-ene (8). A solution of anhydride 9 (0.30 g, 0.95 mmol), water (11 mL), and triethylamine (0.35 mL) in pyridine (110 mL) was placed in a tall-wall 300-mL beaker with two Pt wire baskets as electrodes and stirred by a Sargent synchronous stirrer wired to an exteral power supply.[9] The electrolysis was started at 125 mA and 50 V. After 4 h there was noted a color change form a slight yellow to a transparent brown and the current dropped to 45 mA and the voltage to 20 V, where it was held constant for 30 min. After removal of the electrodes, water (100 mL) was added, and the solution was extracted three times with pentane. Drying (magnesium sulfate) and removal of the organic solvent in vacuo afforded 0.065 g (28%) of 8, NMR identical with that of independently prepared 8.[2c] The NMR spectrum did not indicate the presence of any *N*-(methoxycarbonyl)-3-*endo*-phenyl-2-azabicyclo[2.2.2]oct-5-ene (10).[2c]

Conversion of Carbamate 7d to Amide 7a. *N*-Acetyl-3-*endo*-phenyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-dicarboxylic Acid *N*-Phenylimide. To carbamate 7d (0.118 g, 0.3 mmol) in chloroform (1 mL) at room temperature under an argon atmosphere was added slowly (dropwise) trimethylsilyl iodide (0.128 g, 0.64 mmol).[11] The mixture was heated to 45 °C for 11 h, after which methanol (3 mL) was added. The solution was taken to dryness and dissolved in methanol (3 mL), and sodium methoxide (0.04 g) was added. After stirring for 5 min and removal of solvent in vacuo, the dark red oil was stirred vigorously with 5% potassium hydroxide (3 mL) and dichloromethane (3 mL) while acetyl chloride (0.024 g, 0.3 mmol) was added dropwise. After 2 h, the layers were separated, the aqueous layer was extracted with dichloromethane, and the combined organic layers were dried (sodium sulfate). Filtration and removal of solvent in vacuo afforded 0.076 g (57%) of 7a [mp 269–270 °C lit.[6] mp 269–271 °C)] as an off-white solid. The NMR and IR spectra were identical with those of 7a prepared by cycloaddition of *N*-acetyl-2-phenyl-1,2-dihydropyridine (1d) and *N*-phenylmaleimide (5a).[6]

Conversion of Anhydride 7e to Imide 7d. To anhydride 7e (0.25 g, 0.799 mmol) in diethyl ether (5 mL) at 0 °C was added aniline (0.074 g, 0.799 mmol) in diethyl ether (2 mL) dropwise over a 3-min period.[19] The mixture was brought to room temperature and stirred for 1.5 h. Solvent was removed under reduced pressure to yield 0.281 g of a crude dark red oil, which was recrystallized twice from dichloromethane and diethyl ether to afford 0.157 g (49%) of pure 7d: mp 220–221 °C; NMR, IR, and mass spectra were identical with those of 7d synthesized from *N*-(methoxycarbonyl)-2-phenyl-1,2-dihydropyridine (1e) and *N*-phenylmaleimide (5a).

***N*-(Methoxycarbonyl)-2-azabicyclo[2.2.2]oct-7-ene-5,6-dicarboxylic Acid *N*-Phenylimide (11).** A solution of *N*-(methoxycarbonyl)-1,2-dihydropyridine[8] (1.0 g, 7.24 mmol) and *N*-phenylmaleimide (5a; 1.25 g, 7.24 mmol) in dichloromethane (35 mL) was refluxed for 65 h. After the mixture cooled to room temperature the solvent was removed in vacuo to yield 1.61 g of crude material. Chromatography (10% methylene chloride in ethanol) afforded 0.368 g of 5a (R_f 0.73) and 0.713 g of 11 (R_f 0.61) in 45% yield as a pink amorphous solid: IR ($CHCl_3$) 1770, 1700 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (br, 5 H), 3.70 (s, 3 H), 3.34 (m, H_6, H_4, H_{3x}, $J_{3x,3n}$ = 12 Hz), 3.04 (m, H_5, H_{3n}); see Table I; mass spectrum, m/e 312 (M^+); high-resolution mass spectrum, m/e 312.1106 (calcd for $C_{17}H_{16}N_2O_4$, 312.1110).

Crystallographic Experimental Data.[14] Crystals of 2-(methoxycarbonyl)-3-*endo*-phenyl-2-azabicyclo[2.2.2]oct-7-ene-5,6-dicarboxylic acid *N*-phenylimide (7d) were obtained from methylene chloride/ether as monoclinic prisms, space group $P2_1/n$, with a = 17.920 (11) Å, b = 6.177 (3) Å, c = 17.915 (9) Å, β = 90.48 (4)°, V = 1983 (2) Å^3, and d_{calcd} = 1.30 g cm^{-3} for Z = 4 ($C_{23}H_{20}N_2O_4$, = 388.43). Intensity data were collected with graphite-monochromated Cu Kα radiation on a four-circle automated diffractometer by using θ–2θ scans in the θ range 0–55° on a crystal of 0.15 × 0.07 × 0.35 mm dimensions. A total of 2590 reflections was measured of which 1770 were considered to be above the observation threshold: $I \geq 0\ \sigma(I)$. The structure was solved by a multiple-solution method[20] and refined by a full-matrix least-squares procedure. The final refinement cycle of the nonhydrogen atoms using anisotropic thermal parameters gave a residual R = 0.163. Positions were calculated for all hydrogen atoms. They were assigned temperature factors equivalent to those of the atoms to which they are attached and were included in the structure factor calculations, but their parameters were not refined. The final residuals are R = 0.149 and R_w = 0.138 for 1770 observable reflections.

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Supplementary Material Available: Figures 2–4 containing proton magnetic resonance spectra showing H_{3x} of 7a before and after irradiation of H_4 and after averaging of conformations and also showing H_1 and H_{3x} of 7d before and after conformational averaging, an atomic parameter table, and a discussion of the R values for the X-ray structure of 7d shown in Figure 1 (6 pages). Ordering information is given on any current masthead page.

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