22252). High-resolution mass spectra were measured at the Bio-organic, Biomedical Mass Spectrometry Resource (A.L. Burlingame, Director), UC, San Francisco, supported by NIH Division of Research Resources Grant RR01614.

Registry No. **7**, 96246-88-7; **8**, 92284-77-0; **9**, 94098-79-0; **10**, 94098-80-3; **11**, 96258-26-3; **12**, 96246-95-6; **13**, 96246-98-9; **14**, 96246-86-5; **15**, 96246-87-6; **16**, 31862-33-6; **18**, 967-38-4; **19**, 83089-91-2; **20**, 51089-83-9; **21** (unlabeled), 965-20-8; **21** (labeled), 96246-74-1; **22** (unlabeled), 1925-61-7; **22** (labeled), 96246-75-2; **23**, 96246-77-4; **24**, 3284-46-6; **25**, 96246-78-5; **26**, 96246-79-6; **27** (unlabeled), 96246-81-0; **27** (labeled), 96246-80-9; **28** (unlabeled), 40236-19-9; **28** (labeled), 96246-82-1; **29a**, 96246-84-3; **29b**, 2199-58-8; **30**, 96246-85-4; **31**, 96246-94-5; **32**, 96246-91-2; **33**, 96246-92-3; **34**, 96246-93-4; **36**, 96246-96-7; **37**, 96246-97-8; **38**, 96246-99-0; **39**, 96247-00-6; **40**, 96247-01-7; $HS(CH_2)_2SH$, 540-63-6; $Cu(OAc)_2$, 142-71-2; $CuCl_2$, 7447-39-4; $CuNH_4Cl_2$, 10534-87-9; $Cu(NO_3)_2$, 3251-23-8; $CuBr_2$, 7789-45-9; $CuSO_4$, 7758-98-7; 4-ethyl-2,5-dimethyl-2-pyrrolecarboxylic-*5-methyl*-^{13}C acid, 96246-76-3; 3,5-dimethyl-2-pyrrolecarboxylic-*5-methyl*-^{13}C acid, 96246-83-2.

Some Regio- and Stereochemical Aspects of the Diels–Alder Reaction of Nitrosocarbonyl Compounds with N-Substituted 1,2-Dihydropyridines

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Received July 19, 1984

The intramolecular cycloaddition reaction of N-substituted 1,2-dihydropyridines **1** with (nitrosocarbonyl)benzene, phenyl nitrosoformate, and benzyl nitrosoformate afforded 2,3,5-oxadiazabicyclo[2.2.2]oct-7-enes **2**, **5**, and **7** and/or 2,3,6-oxadiazabicyclo[2.2.2]oct-7-enes **3**, **6**, and **8**. The regiochemistry of the cycloaddition reaction is dependent upon the electronic effects of substituents present in the dienophile and dienamide. The regiochemistry of the cycloaddition products was determined with ^{13}C NMR spectral data together with an X-ray analysis of **4b**, a product arising from a [3,3]-sigmatropic rearrangement reaction of **2b**.

Various *C*-nitroso compounds are versatile reagents for the preparation of 3,6-dihydro-1,2-oxazines, which have been utilized for the preparation of 1,4-amino alcohol derivatives.[1] Although Kirby[2] has employed nitrosocarbonyl compounds as dienophiles in Diels–Alder reactions, the reaction with heterocyclic dienamines and dienamides has not been reported. N-Substituted 1,2-dihydropyridines (**1**) are useful synthons for use in heterodiene condensation reactions and they have played a significant role in the synthesis of various alkaloids[3] and bicycloheterocycles of pharmacological interest.[4-7] In some earlier studies we reported the reactions of 1,2-dihydropyridines **1** with azides,[4] nitrosobenzene,[5] oxyamination reagents,[6] and phenylsulfonyl cyanide *N*-oxide.[7] We now report the Diels–Alder reaction of 1,2-dihydropyridines **1** with nitrosocarbonyl compounds of varied dienophilicity, the electronic effect of substituents upon regiochemistry, the stereochemistry of the cycloadducts formed, and the structures of rearrangement products.

Chemistry

The reaction of *N*-acetyl-2-*n*-butyl-1,2-dihydropyridine (**1a**) with *N*-benzoylhydroxylamine in the presence of tetraethylammonium periodate at −78 °C in methylene chloride afforded **2a** as the major product (70% yield) and **4a** as a minor product (about 5% yield, Scheme I). The formation of both **2a** and **4a** initially suggested the addition of (nitrosocarbonyl)benzene to the C_3–C_6 diene system as well as the C_3–C_4 olefinic bond of **1a** had occurred. It was subsequently observed that **2a** undergoes a slow conversion into **4a** at room temperature, indicating that **4a** may not be a primary reaction product. Similar reactions of **1b,c** with (nitrosocarbonyl)benzene yielded **2b,c** in 84% and 55% yield, respectively. The regioisomer **2b** also undergoes a slow conversion to **4b** at 25 °C. In contrast **2c** is stable at 25 °C, but heating a solution of **2c** in Me_2SO at 60 °C afforded **4c** in quantitative yield. On the other hand, a similar reaction of the 1,5-bis(methoxycarbonyl)-1,2-dihydropyridine (**1d**) gave both regioisomers **2d** and **3** in a 93% combined yield in a ratio of 4:1. Regioisomer **3** is stable at 25 °C but **2d** slowly converted to **4d** at room temperature.

Reaction of **1a,b** with phenyl nitrosoformate yielded **5a,b** in 24% and 25.5% yield,[8] respectively, whereas reaction with **1c** gave both regioisomers **5c** and **6** in 47% overall yield in a ratio of 4:3, respectively. The related reactions of **1a–c** with benzyl nitrosoformate afforded regioisomers **7a–c** and **8a–c**. The regioisomer **8a** could not be isolated since it was converted to **9** (36.5% yield from **1a**) during silica gel chromatography, presumably due to reaction with water. When a solution of **9** in methanol was heated at reflux, **10** was obtained in near-quantitative yield. Silica gel column purification of **8b** gave rise to **11** and **12** in 13.6% and 6.8% yield, respectively, from **1b**. The ^1H NMR spectrum of the reaction mixture containing **7b** and **8b** exhibited absorptions at δ 6.29 and 6.12 which can be attributed to the H_1 proton of **8b**.

Discussion

The assignment of the regio- and stereochemistry of products **2–12** was based on their ^1H and ^{13}C NMR spectral

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(8) The low yield of products in this series of compounds is attributed to a low formation of the phenyl nitrosoformate. The crude reaction mixture exhibited the smell of phenol and a substantial quantity of unreacted N-substituted 1,2-dihydropyridines was recovered.

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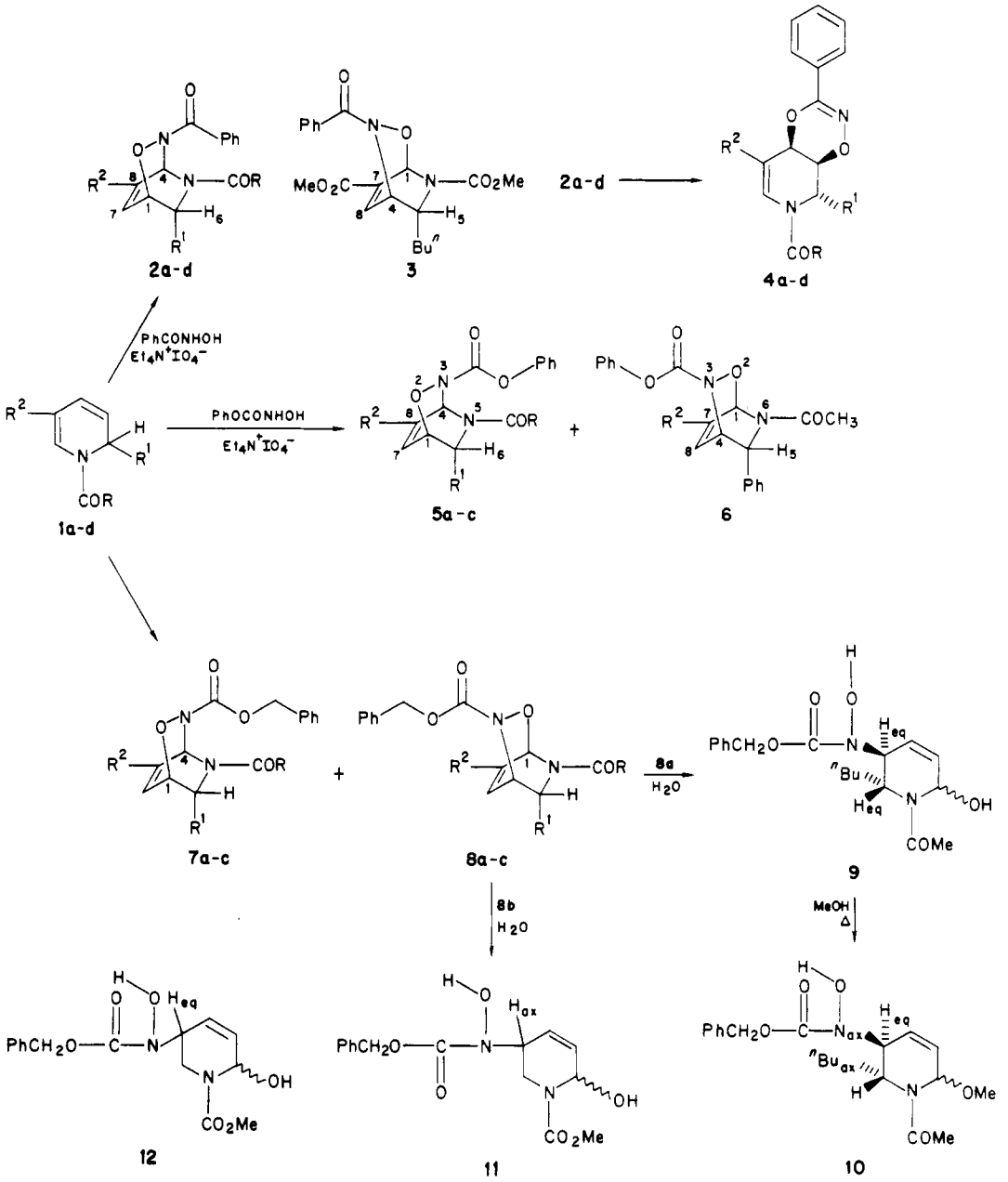
Scheme I[a]



[a] a, R = Me; R^1 = *n*-Bu; R^2 = H. b, R = OMe; R^1 = R^2 = H. c, R = Me; R^1 = Ph; R^2 = H. d, R = OMe; R^1 = *n*-Bu; R^2 = CO_2Me.

data and a single-crystal X-ray analysis for **4b**. Proton resonance assignments rest largely on decoupling experiments, and carbon resonances were confirmed by irradiation of the attached proton. The ^1H NMR spectra for **2–12** showed the presence of rotational conformers due to restricted rotation about the amide bonds[5,9] present in these molecules. Variable-temperature ^1H NMR studies confirm the existence of rotational conformers which coalesced upon heating and returned to the same original ratio after cooling.

A major part of this study was concerned with the assignment of the regiochemistry of the Diels–Alder adducts. Examination of the ^1H NMR spectra indicated some conflicting results as indicated in the following discussion. The dual resonances for H_1 of **5a** at δ 5.04 and 4.98 would suggest that the regiochemistry of **5a** is opposite to that shown in Scheme I. If this were true H_1 would give rise to dual absorptions due to the vicinal NCOOPh moiety and this regiochemistry would be consistent with the regiochemistry observed in an earlier study[5] of the Diels–Alder adducts obtained from the reaction of **1a–c** with nitrosobenzene. However, the spectrum of **5b**, which exhibited a single resonance for H_1, raised the question whether the regiochemistry of **5a** and **5b** is the same or different. Furthermore, reaction of **1c** with phenyl nitrosoformate afforded both regioisomers **5c** and **6**. The single resonances observed for H_1 of **5c** or H_4 of **6** indicate that even when both regioisomers are available, the assignment of regiochemistry based on the dual resonances for H_1 as observed for **5a** is not possible. It has been reported[10] that $Eu(dpm)_3$ binds selectively to the oxygen atom of amides, whereas the fluorinated shift reagent $Eu(fod)_3$ binds to both amide

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Table I. ^{13}C Nuclear Magnetic Resonance Data for 2,3,5-Oxadiazabicyclo[2.2.2]oct-7-enes[a]

compd	C_1	C_4	C_6
2a	74.0, 73.4	60.8	58.7, 57.5
2b	70.6 (br)	60.0, 59.8	46.4
2c	75.9, 75.7	58.74, 59.93	61.5, 61.0
2d	73.2	61.6	57.7
5a	74.0, 73.3	63.3, 58.6	58.3, 57.5
5b	70.4, 70.0	60.8, 60.4	46.0
5c	75.5, 75.3	59.5, 58.5	63.4, 61.1
7a	72.6, 72.0	62.6	57.5, 56.5
7b	70.2 (br)	60.9, 60.6	46.3
7c	75.0	59.1, 58.4	63.4, 61.1

[a] Spectra were obtained in $CDCl_3$ at 25 °C; chemical shifts are in δ units relative to tetramethylsilane.

Table II. ^{13}C Nuclear Magnetic Resonance Data for 2,3,6-Oxadiazabicyclo[2.2.2]octen-7-enes[a]

compd	C_1	C_4	C_6
3	77.8	50.8	56.3
6	74.7, 79.7	56.6	59.3, 57.9
8c	74.3, 79.3	56.5	59.1, 57.8

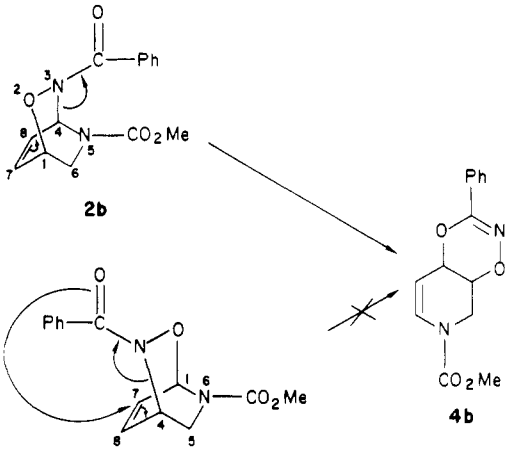
[a] Spectra were obtained in $CDCl_3$ at 25 °C; chemical shifts are in δ units relative to tetramethylsilane.

oxygen and heteroatoms present in *N*-*n*-butyl-*N*-(4-methyloxazol-2-yl)-2-methylpropionamide. When 2 molar equiv of $Eu(dpm)_3$ was added to solutions of **5c** and **6** in deuteriochloroform, H_4 of **5c** was shifted downfield δ 3.4 whereas H_1 (corresponding to H_4 of **5c**) of **6** was only shifted downfield by δ 1.5. This observation would support the assigned regiochemistry for **5c** and **6**.

The ^1H NMR spectra of **2a** and **2c** also exhibited dual resonances for H_1, whereas the H_1 resonance of **2b** appeared as a single broad peak at δ 4.94–5.08. It was observed that compounds **2a–c** underwent a rearrangement reaction to other compounds subsequently shown to have structures **4a–c**. The ^1H NMR spectra for **4a–c** indicated the presence of a 1,2,3,4-tetrahydropyridine ring structure. Since **2a–c** rearranged to the same structural ring system **4**, the regiochemistry of products **2a–c** must be the same, irrespective of the fact that H_1 of **2a** and **2c** exhibits dual resonances while a single peak for H_1 of **2b** is displayed. Regioisomer **2d** also rearranged to **4d** while **3** was stable.

The ^{13}C NMR spectral studies for compounds **2**, **5**, and **7** and **3**, **6**, and **8c** provided a useful technique for assigning the regiochemistry of the products as illustrated by the results in Tables I and II, respectively. The C_1 resonance or regioisomers **2**, **5**, and **7** is downfield relative to their respective C_4 resonances, whereas the C_1 resonance (C_4 equivalent of the other regioisomers **2**, **5**, and **7**) of compounds **3**, **6**, and **8c** is downfield relative to the C_4 resonance (C_1 equivalent of the other regioisomers). It was expected that the oxygen atom would deshield the carbon atom to which it is attached to a greater extent than would the NCO group. It is known[11] that the anisotropic effect of the carbonyl group is much less pronounced in ^{13}C NMR compared to ^1H NMR. The carbon resonances for atoms bonded to oxygen are δ 15–20 further downfield than those of the corresponding carbon resonances for atoms bonded to NCO (see Tables I and II). The anisotropic effect, obtained from the chemical shift values for C_1, C_4, and C_5 or C_6, varies from δ 0.5 to 1. The regiochemistry of compounds **2a–d**, **5a–c**, and **7a–c** and **3**, **6**, and **8c** was thus assigned with the aid of ^{13}C NMR as described above and illustrated in Scheme I.

The final proof for the regiochemical assignments was provided by an X-ray crystal analysis[12] for compound **4b**. The product **4b** could arise via a [3,3]-sigmatropic rearrangement of **2b** only if the regiochemistry of **2b** is as shown in Scheme I. Compounds **3**, **6**, and **8c** having the opposite regiochemistry would not afford this product. Similar rearrangements involving a [3,3]-sigmatropic shift[13] have been reported by Kirby. The failure of compounds **5** and **7** to undergo this rearrangement reaction may be due to the decreased electron-withdrawing effect (due to the mesomeric effect of the oxygen atom attached to the carbonyl in **5** and **7**) of the carbonyl group attached to N_3, which is not sufficient to induce the C_4–N_3 shift necessary for the rearrangement reaction.



Regioisomers **8a,b** are quite labile and undergo a ring-opening reaction upon reaction with water present in the silica gel and/or solvents used for column chromatography. In this way **8a** gave **9** exclusively and **8b** gave rise to **11** and **12**. The product **8c** was less labile than **8a** and **8b** and was isolated from silica gel preparative TLC or column chromatography. However, two other products were also obtained from this latter purification operation which were not identified. The relative stereochemistry of the C_2 and C_3 substituents for **9** can be assigned readily since $J_{2,3}$ = 0 Hz, which is possible only if both protons are equatorial. This assignment is consistent with spectral data for **12**, where $J_{2_{ax},3}$ = 4.95 Hz and $J_{2_{eq},3}$ = 0 Hz. The stereochemistry of the C_6 substituents for **9–12** could not be assigned since the dihedral angles H–C_5–C_6–H pseudoaxial and H–C_5–C_6–H pseudoequatorial are essentially the same. Displacement of the C_6-OH of **9** upon reaction with methanol afforded **10**, which would have the same stereochemistry at C_2 and C_3. Since the coupling constants H–C_5–C_6–H for **9** ($J_{5,6}$ = 3.3 Hz) and H–C_5–C_6–H for **10** ($J_{5,6}$ = 3.6 Hz) are very similar it was not possible to assign the substituent stereochemistry at C_6 on the basis of J values. Nuclear Overhauser enhancement (NOE) difference spectroscopy experiments for **10** did not provide any additional information regarding the stereochemistry of the C_6 hydroxyl group.

The orientation of the C_6 substituent for **2a,c,d**, **5a,c**, and **7a,c** was assigned endo on the basis of ^1H NMR data. Compounds **2b**, **5b**, and **7b** exhibited H–C_1–C_6–H_{endo} and H–C_1–C_6–H_{exo} coupling constants of 0 and 3.5 Hz, re-

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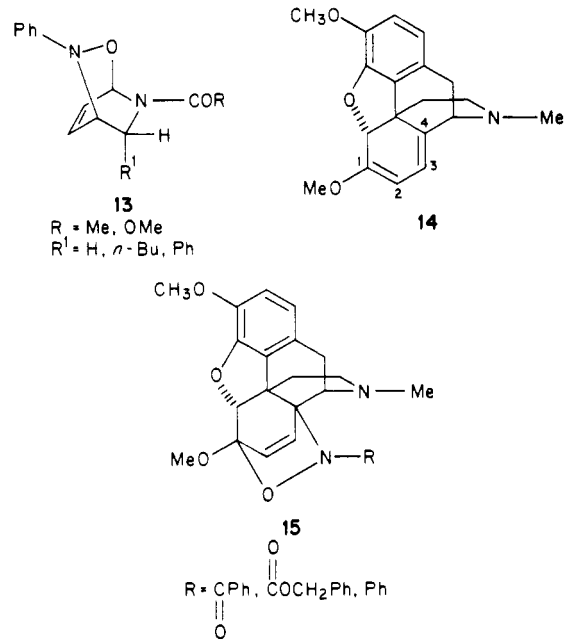
spectively. The $J_{1,6}$ coupling constant for the 6-substituted adducts is about 3.5 Hz. A comparison of the chemical shift values for **2a** and **2c**, **5a** and **5c**, and **7a** and **7c** indicates that the C_6 phenyl group shields H_7 and the acetyl methyl protons appreciably relative to the corresponding analogues having a C_6 butyl substituent. This is possible only if the C_6 phenyl group is endo. The orientation of the C_6 *n*-butyl substituent for **2a**, **5a**, and **7a** was also assigned endo since the $J_{1,6}$ coupling constants are very similar to those for **2c**, **5c**, and **7c**. The same observations were valid for **3**, **6**, and **8c**.

The ^{1}H NMR endo assignment for the C_6 substituent agrees with mechanistic considerations governing the stereochemical outcome of Diels–Alder [4+2]π cycloaddition reactions. Attack by the dienophile occurs at the least hindered face of the 1,2-dihydropyridine opposite the C_2 substituent to give the endo product.[14]

Results

In a previous study we reported that reactions of 1,2-dihydropyridines **1** with nitrosobenzene (PhN=O) resulted in the regiospecific formation of **13**.[5,15] The regiochemistry



of products **13** is the reverse of that for cycloadducts **2a–c** obtained from the reaction of **1a–c** with (nitrosocarbonyl)benzene. Similar reactions of phenyl nitrosoformate with **1a–c** afforded predominantly or exclusively regioisomers **5**, while the reaction of benzyl nitrosoformate with **1a–c** yielded both regioisomers **7a–c** and **8a–c**.

On the other hand, Kirby et al.[16] have reported that (nitrosocarbonyl)benzene, benzyl nitrosoformate, and nitrosobenzene each yielded the same regioisomer **15** upon reaction with thebaine (**14**). Boger and Patel recently reported that reaction of either an electron-rich or electron-deficient 2-substituted 1,3-cyclohexadiene with either (nitrosocarbonyl)benzene or methyl nitrosoformate each gave similar ratios of proximal and distal adducts ($\simeq$3:1 ratio). These results were consistent with the prediction that nitrosocarbonyl compounds behave as well-defined electron-deficient 2π-components in a normal (HOMO diene controlled) Diels–Alder reaction with electron-rich dienes. The reaction with electron-deficient 2-substituted 1,3-cyclohexadienes were consistent with either a normal (HOMO diene controlled) or inverse electron demand (LUMO diene controlled) Diels–Alder reaction.[17]

It has been proposed that Diels–Alder reactions involving unsymmetrical dienes and/or dienophiles are nonsynchronous and proceed via unsymmetrical transition states where one of the forming CC bonds is short and strong and the other is long and weak. The transition state could then be regarded as a weakly perturbed biradical or zwitterion. The regioselectivity of such reactions could then be interpreted in terms of qualitative molecular orbital theory.[18]

The results of our study indicate that the regiospecificity and/or regioselectivity of the Diels–Alder reactions described is highly dependent upon the electronic effects of substituents present in the dienamides **1** and the nitroso dienophile.

The application of regio **2**, **5**, and **7** and **3**, **6**, and **8c** as synthons for the preparation of substituted 1,4-amino alcohols is being investigated.

Experimental Section

Melting points were determined with a Büchi capillary apparatus and are uncorrected. Proton nuclear magnetic resonance spectra were determined for solutions of deuteriochloroform or deuteriodimethyl sulfoxide with a Bruker AM-300 spectrometer. Double-resonance studies were used to confirm assignments. ^{13}C nuclear magnetic resonance spectra were determined for solutions of deuteriochloroform with a Bruker AM-300 spectrometer operating at 75.4 MHz. Infrared spectra were recorded on a Nicolet 5DX FT spectrometer. Mass spectra were measured on an AEI MS-50 mass spectrometer. N-Substituted 1,2-dihydropyridines **1** were prepared by literature procedures.[19] The required substituted carbonylhydroxylamines were prepared according to the procedure of Boyland.[20]

5-Acetyl-3-[(benzyloxy)carbonyl]-6-*n*-butyl-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (7a) and 1-Acetyl-2(*S*(*R*))-*n*-butyl-6-hydroxy-3(*S*(*R*))-[*N*-hydroxy-*N*-((benzyloxy)carbonyl)amino]-1,2,3,6-tetrahydropyridine (9). General Procedure. A solution of tetraethylammonium periodate[21] (6.42 g, 20 mmol) in 20 mL of dry methylene chloride was added dropwise with stirring to a solution of 1-acetyl-2-*n*-butyl-1,2-dihydropyridine (3.1 g, 18 mmol) and *N*-[(benzyloxy)carbonyl]-hydroxylamine[20] (3.34 g, 20 mmol) in 150 mL of dry methylene chloride under a nitrogen atmosphere at –78 °C. The reaction mixture was allowed to warm to 25 °C with continued stirring for 6 h. The solvent was removed in vacuo, and the residue was triturated with ether (50 mL) and then ethyl acetate (200 mL). The solvent from the combined organic extracts was removed in vacuo. The residue was chromatographed on a silica gel column with ether–hexane (7:3 v/v) as eluant to yield **7a** (2.0 g, 32.3%): mp 69–70 °C; IR (KBr) 1739, 1700 (N*CO*$_2$CH$_2$), 1688 (N*CO*Me) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.4 (s, 5 H, Ph), 6.96 and 6.15 (dd and br d (3:7 ratio), $J_{4,8}$ = 5.72 Hz, $J_{4,7}$ = 1.9 Hz, 1 H, H_4), 6.64–6.82 (m, $J_{7,8}$ = 7.65 Hz, 1 H, H_8), 6.4–6.64 (m, 1 H, H_7), 5.1–5.32 (m, $J_{CH_2 gem}$ = 15 Hz, 2 H, OCH_2), 4.98 and 4.92 (2 m (3:7 ratio), $J_{1,7}$ = 5.8 Hz, $J_{1,8}$ = 1.7 Hz, 1 H, H_1), 4.2–4.3 and 3.96–4.04 (2 m (7:3 ratio), $J_{1,6}$ = 3.8 Hz, J_{6,CHH^1} = 3.8 Hz and J_{6,CHH^1} = 10 Hz, 1 H,

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(15) The reaction of *N*-acetyl-2-phenyl-1,2-dihydropyridine (**1c**) with nitrosobenzene was repeated, and the structure of the adduct was found to be correct as reported earlier.[5] ^{13}C NMR spectral data ($CDCl_3$): δ 73.8 and 73.0 (C_1), 63.2 (C_4), 59.7 and 58.5 (C_5). The lithium aluminum hydride reduction of this adduct afforded 1-ethyl-2-phenyl-3-(phenylamino)-1,2,3,6-tetrahydropyridine, confirming the structure of the adduct to be **13** (R^1 = Ph, R = Me).

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(21) Sklarz, B.; Al-Sayyab, A. F. *J. Chem. Soc.* **1964**, 1318.

H_6), 2.2 and 2.16 (2 s (7:3) ratio), 3 H, $COCH_3$), 1.82–1.96 and 1.52–1.7 (2 m (7:3 ratio), 1 H, C_6-$CH^1H^1(CH_2)_2CH_3$), 1.0–1.42 (m, 5 H, $CH^1H^1(CH_2)_2CH_3$), 0.84–0.96 (m, 3 H, $(CH_2)_3CH_3$). Anal. Calcd for $C_{19}H_{24}N_2O_4$: C, 66.27; H, 6.97; N, 8.13. Found: C, 65.96; H, 7.06; N, 7.99.

Continued elution with ethyl acetate afforded **9** as a foam (2.37 g, 36.5%); IR (KBr) 3320 (OH), 1703 (NCO_2CH_3, $NCOCH_3$), 1626 (C=C) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 9.24 and 9.08 (2 s (1:2 ratio), 1 H, NO*H*, exchanges with deuterium oxide), 7.34–7.5 (m, 5 H, Ph), 6.08 (d, $J_{4,5}$ = 10.4 Hz of d, $J_{5,6}$ = 3.3 Hz, 1 H, H_5), 6.0 and 5.9 (d and br s, $J_{6,OH}$ = 5 Hz, 1 H, C_6-O*H*, exchanges with deuterium oxide), 5.68–5.84 (2 d, $J_{4,5}$ = 10.4 Hz of d, $J_{3,4}$ = 6 Hz of d, $J_{2,4}$ < 1 Hz, 1 H, H_4), 5.9 and 5.47 (2 br s, on exchange with deuterium oxide becomes a d, $J_{5,6}$ = 3.3 Hz, 1 H, H_6), 5.08–5.26 (m, 2 H, OCH_2), 4.7 and 3.88 (2 t (2:1) ratio), J_{2,CH_2} = 7.5 Hz, 1 H, H_2), 4.42 (distorted t, becomes a d at +80 °C, $J_{3,4}$ = 6 Hz, 1 H, H_3), 2.12 and 1.95 (2 s, 3 H, $COCH_3$), 1.14–1.76 (m, 6 H, $(CH_2)_3CH_3$), 0.74–0.9 (m, 3 H, $(CH_2)_3CH_3$); high-resolution mass spectrum, exact mass calcd for $C_{19}H_{26}N_2O_5$ 362.1842, found 362.1842.

Products **2a–d**, **3**, **5a–c**, **6**, **7b–c**, and **8a–c** were also prepared by using this general procedure. Some of the chromatographic separation and/or purification procedures used are described below.

Silica gel column chromatography was used to remove traces of **4a,b** present in the reaction products **2a,b**. Regioisomers **2d** and **3** were separated by a combination of column and TLC silica gel chromatography. The reaction mixture was partially separated initially on a silica gel column. Elution with ether–hexane (1:1 v/v) gave a mixture of **2d** and **3** (0.7 g), which was subsequently separated by preparative TLC using 0.75-mm silica gel plates with hexane–ether (1:1 v/v) as development solvent. Extraction of the fractions with R_f 0.35 gave **2d** (106 mg) and R_f 0.5 gave **3** (225 mg). Continued elution of the silica gel column using ether as eluant gave **2d** (1.12 g), which was purified to homogeny by a second elution from a silica gel column as described above to yield **2d** (718 mg).

The products **5a,b** were purified by silica gel column chromatography with ether as eluant.

Regioisomers **5c** and **6** (1.5 g) were separated by silica gel column chromatography. The initial fraction obtained with ether–hexane (7:3 v/v) as eluant exhibited an odor of phenol and was discarded. Further elution with ether gave pure **5c** (205 mg) and then a mixture of **5c** and **6** (625 mg). This latter mixture was separated by preparative silica gel TLC using plates 0.75 mm in thickness with ether as development solvent. Extraction of the fractions having R_f 0.4 gave **6** (300 mg) and R_f 0.5 gave **5c** (250 mg).

Regioisomers **7c** and **8c** (2 g of crude reaction mixture) were separated by preparative silica gel TLC, using plates 0.75 mm in thickness, with ether as a development solvent. Extraction of the fractions having R_f 0.45 yielded **8c** (790 mg, 43.4%) and R_f 0.5 afforded **7c** (245 mg, 26.9%).

Some physical data for 2,3,5-oxadiazabicyclo[2.2.2]oct-7-enes **2a–d**, **5a–c**, and **7b–c** are listed below:

5-Acetyl-3-benzoyl-6-*n*-butyl-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (2a): yield 70%; viscous oil; IR (film) 1663 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 25 °C) δ 7.8 (d, J = 7 Hz, 2 H, ortho phenyl hydrogens), 7.44 (m, 3 H, meta and para phenyl hydrogens), 6.78–7.02 (m, 1 H, H_8), 6.4–6.7 (m, 2 H, H_4, H_7), 5.02–5.1 and 4.8–4.98 (2 m (3:7 ratio), 1 H, H_1), 4.2–4.34 and 4.02–4.14 (2 m (7:3 ratio), $J_{1,6}$ = 3.3 Hz, $J_{6,C(H)H^1}$ = 3.3 Hz, $J_{6,C(H^1)H}$ = 10 Hz, 1 H, H_6), 2.24 and 2.16 (2 s (7:3 ratio), 3 H, $COCH_3$), 1.9 and 1.6 (2 m (7:3 ratio), 1 H, $C_6CH^1H^1(CH_2)_3CH_3$), 1.0–1.5 (m, 5 H, $CH^1H^1(CH_2)_2CH_3$), 0.9 (m, 3 H, $(CH_2)_3CH_3$); high-resolution mass spectrum, exact mass calcd for $C_{18}H_{22}N_2O_3$ 314.1631, found 314.1628.

3-Benzoyl-5-(methoxycarbonyl)-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (2b): yield 84%; viscous oil; IR (film) 1713 (CO_2), 1650 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.72 (d, J = 7 Hz, 2 H, ortho phenyl hydrogens), 7.45 (m, 3 H, meta and para phenyl hydrogens), 6.68–6.88 (m, 2 H, H_4, H_8), 6.56–6.67 (m, 1 H, H_7), 4.94–5.08 (m, 1 H, H_1), 3.92–4.06 (d, $J_{4,6\,exo}$ = 3 Hz of d, $J_{6\,gem}$ = 11.5 Hz, 1 H, $H_{6\,exo}$), 3.76 (s, 3 H, OCH_3), 3.0 and 3.26 (2 d (1:1 ratio), $J_{6\,gem}$ = 11.5 Hz, 1 H, $H_{6\,endo}$); high-resolution mass spectrum, exact mass calcd for $C_{14}H_{14}N_2O_4$ 274.0953, found 274.0950.

5-Acetyl-3-benzoyl-6-phenyl-2,3,5-oxadiazabicyclo[2.2.2]-oct-7-ene (2c): yield 55%; mp 162–163 °C; IR (KBr) 1670, 1657 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.0–7.9 (m, 11 H, phenyl hydrogens, H_4), 6.72–6.9 (m, 1 H, H_8), 6.2–6.36 (m, 1 H, H_7), 5.33 and 5.45 (2 d (3:7 ratio), $J_{1,6}$ = 3.85 Hz, 1 H, H_6), 5.02–5.14 and 4.88–4.96 (2 m (7:3 ratio), 1 H, H_1), 2.4 and 1.9 (2 s (3:7 ratio), 3 H, $COCH_3$); high-resolution mass spectrum, exact mass calcd for $C_{20}H_{18}N_2O_3$ 334.1333, found 334.1325. Anal. Calcd for $C_{20}H_{18}N_2O_3$: C, 71.85; H, 5.38; N, 8.38. Found: C, 71.56; H, 5.41; N, 8.30.

3-Benzoyl-5,8-bis(methoxycarbonyl)-6-*n*-butyl-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (2d): yield 75%; viscous oil; IR (KBr) 1727 (CO_2), 1640 (CO) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 8.02 (d, J = 7 Hz, 2 H, ortho phenyl hydrogens), 7.46–7.7 (m, 5 H, phenyl hydrogens), 7.46–7.7 and 6.6 (2 m (1:3 ratio), 1 H, H_4), 7.5 (m, 1 H, H_7), 5.45 (d, $J_{1,7}$ = 6 Hz of d, $J_{1,6}$ = 3.5 Hz, 1 H, H_1), 4.02–4.12 (m, $J_{1,6}$ = 3.5 Hz, $J_{6,C(H)H^1}$ = 4.4 Hz and $J_{6,C(H^1)H}$ = 9.9 Hz, 1 H, H_6), 3.66 and 3.77 (2 s, 6 H, OMe), 0.9–1.7 (m, 9 H, n-C_4H_9); high-resolution mass spectrum, exact mass calcd for $C_{20}H_{24}N_2O_6$ 388.1640, found 388.1641.

5-Acetyl-3-(phenoxycarbonyl)-6-*n*-butyl-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (5a): yield 24% mp 97–98 °C; IR (KBr) 1756 (CO_2), 1662 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1–7.48 (m, 5 H, phenyl hydrogens), 7.09 and 6.23 (2 d, $J_{4,8}$ = 5.8 Hz of d, $J_{4,7}$ = 1.15 Hz (3:7 ratio), 1 H, H_4), 6.85–6.94 (d, $J_{7,8}$ = 8.1 Hz of d, $J_{4,8}$ = 5.8 Hz, of d, $J_{1,8}$ = 1.8 Hz, 1 H, H_8), 6.67 and 6.01 (2 d, $J_{1,7}$ = 5.4 Hz of d, $J_{7,8}$ = 8.1 Hz of d, $J_{4,7}$ = 1.15 Hz, 1 H, H_7), 5.04 and 4.98 (2 m (3:7 ratio), 1 H, H_1), 4.32 and 4.0–4.1 (2 m (7:3 ratio), $J_{1,6}$ = 4 Hz, $J_{6,C(H)H^1}$ = 4 Hz, $J_{6,C(H^1)H}$ = 10.2 Hz), 1 H, H_6), 2.26 and 2.18 (2 s (ratio 7:3), 3 H, $COCH_3$), 1.86–2.0 and 1.04–1.4 (2 m (7:3 ratio), 1 H, $CH^1H^1(CH_2)_2CH_3$), 1.04–1.4 (m, 5 H, $CH^1H^1(CH_2)_2CH_3$), 0.84–0.96 (m, 3 H, $(CH_2)_3CH_3$). Variable-temperature ^1H NMR studies confirmed the existence of rotational conformers which coalesced upon heating and returned to the same original ratio after cooling: ^1H NMR (Me_2SO-d_6, 25 °C) δ 7.04 and 6.99 (H_8), 6.88 and 6.41 (H_4), 6.74 (H_7), 5.3 and 5.2 (H_1), 4.02–4.14 (H_6). Heating the sample to 80 °C induced coalescence of the rotamers (single resonances) to exhibit the following spectral data: ^1H NMR δ 6.96 (H_8), 6.7 (H_7), 6.2–6.9 (br peak, H_4), 5.13 (H_1), 4.07 (H_6). Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 65.45; H, 6.66; N, 8.48. Found: C, 65.42; H, 6.74; N, 8.38.

5-(Methoxycarbonyl)-3-(phenoxycarbonyl)-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (5b): yield 25.5%; mp 128–129 °C; IR (KBr) 1718 and 1690 (CO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1–7.45 (m 5 H, phenyl hydrogens), 6.8–6.96 (m, 1 H, H_8), 6.6–6.8 (m, 1 H, H_7), 6.6–6.8 and 6.5–6.6 (2 m (1:1 ratio), H_4), 4.94–5.10 (m, 1 H, H_1), 3.94 (d, $J_{6\,gem}$ = 12 Hz of d, $J_{6\,exo,1}$ = 3 Hz, 1 H, $H_{6\,exo}$), 3.76 and 3.78 (2 s (1:1 ratio), 3 H, OCH_3), 3.16 and 3.24 (2 d (1:1 ratio), $J_{6\,gem}$ = 12 Hz, 1 H, $H_{6\,endo}$). Anal. Calcd for $C_{14}H_{14}N_2O_5$: C, 57.93; H, 4.82; N, 9.65. Found: C, 57.75; H, 4.87; N, 9.53.

5-Acetyl-3-(phenoxycarbonyl)-6-phenyl-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (5c): yield 27%; foam; IR (KBr) 1757 and 1724 (CO_2), 1619 and 1610 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.15–7.52 (m, 5 H, phenyl hydrogens), 7.35 and 6.52 (2 br d (4:1 ratio), H_4), 6.98–7.06 (m, $J_{4,8}$ = 6 Hz, $J_{7,8}$ = 8 Hz, 1 H, H_8), 6.3–6.46 (m, $J_{7,8}$ = 8 Hz, $J_{1,7}$ = 5.6 Hz, 1 H, H_7), 5.5 and 5.29 (2 d, $J_{1,6}$ = 3.8 Hz (1:4 ratio), 1 H, H_6), 5.02–5.08 (m, 1 H, H_1), 2.42 and 1.88 (2 s (1:4 ratio), 3 H, $COCH_3$); high-resolution mass spectrum, exact mass calcd for $C_{20}H_{18}N_2O_4$ 350.1266, found 350.1268.

5-(Methoxycarbonyl)-3-[(benzyloxy)carbonyl]-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (7b): yield 41%; viscous oil; IR (film) 1744 and 1714 (CO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4 (m, 5 H, phenyl hydrogens), 6.7–6.78 (m, 1 H, H_8), 6.56–6.7 and 6.44 (m and br d (6.5:3.5 ratio), $J_{4,8}$ = 5 Hz, 1 H, H_4), 6.56–6.7 (m, 1 H, H_7), 5.16–5.3 (m, J_{gem} = 15 Hz, 2 H, OCH_2), 4.92–5.0 (m, 1 H, H_1), 3.9 (d, $J_{6\,exo,1}$ = 3.85 Hz of d, $J_{6\,gem}$ = 11 Hz, 1 H, $H_{6\,exo}$), 3.76 (s, 3 H, OCH_3), 3.18 and 3.14 (2 d, $J_{6\,gem}$ = 11 Hz, 1 H, $H_{6\,endo}$); high-resolution mass spectrum, exact mass calcd for $C_{15}H_{16}N_2O_5$ 304.1056, found 304.1055.

5-Acetyl-3-[(benzyloxy)carbonyl]-6-phenyl-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (7c): yield 26.9%; foam; IR (KBr) 1739, 1711 (CO_2), 1668 (CO) cm^{-1}; $C_{21}H_{20}N_2O_4$ NMR ($CDCl_3$) δ 7.4 (m, 10 H, phenyl hydrogens), 7.2 and 6.4 (2 br d (4:1 ratio), $J_{4,8}$ = 5.5 Hz, $J_{4,7}$ = 2.2 Hz, 1 H, H_4), 6.8–6.94 (m, $J_{7,8}$ = 8 Hz, 1 H, H_8), 6.2–6.38 (m, $J_{1,7}$ = 5.4 Hz, 1 H, H_7), 5.43 and 5.23 (2 d (1:4 ratio), $J_{1,6}$ = 3.75 Hz, 1 H, H_6), 5.14–5.36 (m, J_{gem} = 15 Hz, 2 H, OCH_2), 4.94–5.0 (m, $J_{1,6}$ = 3.75 Hz, $J_{1,7}$ = 5.4 Hz, 1 H, H_1),

2.32 and 1.82 (2 s (1:4 ratio), 3 H, $COCH_3$); high-resolution mass spectrum, exact mass calcd for $C_{20}H_{20}N_2O_4$ 364.1418, found 364.1417.

Some physical data for 2,3,6-oxadiazabicyclo[2.2.2]oct-7-enes **3**, **6**, and **8c** are listed below:

3-Benzoyl-5-*n*-butyl-6,7-bis(methoxycarbonyl)-2,3,6-oxadiazabicyclo[2.2.2]oct-7-ene (3): yield 18%; viscous oil; IR (KBr) 1727 (CO_2), 1660, 1640 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.8 and 7.4–7.5 (m, 5 H, phenyl hydrogens), 7.62 (m, 1 H, H_8), 6.52 (br s, 1 H, H_1), 5.44–5.56 (m, $J_{4,8}$ = 5.6 Hz, $J_{4,5}$ = 2.5 Hz, 1 H, H_4), 4.1–4.2 (m, $J_{4,5}$ = 2.5 Hz, $J_{5,C(H)H^1}$ = 4.5 Hz, $J_{5,C(H^1)H}$ = 9.0 Hz, 1 H, H_5), 3.88 (s, 3 H, OMe), 3.86 (s, 3 H, OMe), 1.85, 1.32, and 0.96 (m, 9 H, $CH_2CH_2CH_2CH_3$); high-resolution mass spectrum, exact mass calcd for $C_{20}H_{24}N_2O_6$ 388.1633, found 388.1633.

6-Acetyl-3-(phenoxycarbonyl)-5-phenyl-2,3,6-oxadiazabicyclo[2.2.2]oct-7-ene (6): yield 20%; foam; IR (KBr) 1754, 1724 (CO_2), 1671 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.12–7.52 (m, 10 H, phenyl hydrogens), 7.0 and 6.19 (2 d, $J_{1,7}$ = 5.5 Hz of d, $J_{1,8}$ = 1.6 Hz (3:1 ratio), 1 H, H_1), 6.84–6.92 (m, $J_{7,8}$ = 8 Hz, $J_{1,7}$ = 5.5 Hz, 1 H, H_7), 6.32–6.52 (m, $J_{4,8}$ = 5.75 Hz, $J_{7,8}$ = 8 Hz, 1 H, H_8), 5.48 and 5.26 (2 d, $J_{4,5}$ = 3.8 Hz (1:3 ratio), 1 H, H_5), 5.16–5.24 (m, 1 H, H_4), 2.38 and 1.88 (2 s, 3 H, $COCH_3$); high-resolution mass spectrum, exact mass calcd for $C_{20}H_{18}N_2O_4$ 350.1267, found 350–1259.

6-Acetyl-3-[(benzyloxy)carbonyl]-5-phenyl-2,3,6-oxadiazabicyclo[2.2.2]oct-7-ene (8c): yield 43.4%; mp 118–120 °C; IR (KBr) 1745, 1713 (CO_2), 1670 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1–7.48 (m, 10 H, phenyl hydrogens), 6.92 and 6.12 (dd and br d, $J_{1,7}$ = 5.5 Hz, $J_{1,8}$ = 1.65 Hz (4:1 ratio), 1 H, H_1), 6.76–6.86 (m, $J_{7,8}$ = 8 Hz, $J_{1,7}$ = 5.5 Hz, 1 H, H_7), 6.2–6.34 (m, $J_{7,8}$ = 8 Hz, 1 H, H_8), 5.38 and 5.16 (br d and d, $J_{4,5}$ = 2.75 Hz (1:4) ratio), 1 H, H_5), 5.14–5.3 (m, J_{gem} = 15 Hz, 2 H, OCH_2), 5.02–5.1 (m, 1 H, H_4), 2.3 and 1.78 (2 s (1:4 ratio), 3 H, OCH_3); high-resolution mass spectrum, exact mass calcd for $C_{21}H_{20}N_2O_4$ 364.1429, found 364.1430.

7-Acetyl-3,8-diphenyl-4a,7,8,8a-tetrahydropyrido[4,3-*e*]-1,4,2-dioxazine (4c). A solution of **2c** (0.0334 g, 1 mmol) in 5 mL of dry dimethyl sulfoxide was heated at 55–60 °C with stirring for 48 h. The solution was cooled to 25 °C and water (10 mL) was added. Extraction with ether (5 × 20 mL), drying (Na_2SO_4), and removal of the solvent in vacuo afforded **4c** (0.32 g, 95.8%): mp 176–177 °C (EtOH); IR (KBr) 1677 ($NCOCH_3$), 1647 (C=N), 1614 (C=C) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.75 and 7.3–7.6 (dd and m, 10 H, 2 Ph), 7.24 (br d, $J_{5,6}$ = 8.5 Hz, $J_{4a,6}$ = 1 Hz, $J_{6,8}$ < 1 Hz, 1 H, H_6), 5.82 and 5.7 (d and br s, $J_{8,8a}$ = 3.25 Hz, 1 H, H_8), 5.13 and 4.95 (br d and d, $J_{5,6}$ = 8.5 Hz of d, $J_{4a,5}$ = 3.25 Hz of d, $J_{8a,8}$ = 3.25 Hz of d, $J_{5,8a}$ = 2.0 Hz, 1 H, H_8), 2.32, 2.02 (2 s, 3 H, $COCH_3$). Anal. Calcd for $C_{20}H_{18}N_2O_3$: C, 71.85; H, 5.38; N, 8.38. Found: C, 71.77; H, 5.59; N, 8.18.

7-Acetyl-8-*n*-butyl-4a,7,8,8a-tetrahydropyrido[4,3-*e*]-1,4,2-dioxazine (4a). Compound **2a** upon standing at 25 °C for 15 days rearranged completely to **4a**: viscous oil; IR (neat) 1678 (CO), 1642 (C=N), 1612 (C=C) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.70 and 7.42–7.56 (dd and m, 5 H, Ph), 7.15 and 6.98 (2 br d, $J_{5,6}$ = 8.5 Hz, $J_{4a,6}$ = 1.5 Hz, $J_{6,8}$ = 1 Hz, 1 H, H_6), 5.32–5.38 (m, $J_{4a,5}$ = 2.2 Hz, $J_{4a,8a}$ = 2.2 Hz, 1 H, H_{4a}), 5.04 and 4.92 (d, $J_{5,6}$ = 8.5 Hz of d, $J_{5,4a}$ = 2.2 Hz of d, $J_{5,8a}$ = 2.2 Hz, 1 H, H_5), 4.70 and 4.34 (d, $J_{8,8a}$ = 3.0 Hz of t, J_{8,CH_2} = 7.58 Hz, 1 H, H_8), 4.18–4.28 (m, $J_{8a,8}$ = 3.0 Hz, $J_{8a,4a}$ = 2.2 Hz, $J_{8a,5}$ = 2.2 Hz, 1 H, H_{8a}), 2.16 (s, 3 H, $COCH_3$), 1.20–1.60 (m, 6 H, $(CH_2)_3CH_3$), 0.86 (t, 3 H, $(CH_2)_3CH_3$); high-resolution mass spectrum, exact mass calcd for $C_{18}H_{22}N_2O_3$ 314.1630, found 314.1626.

7-(Methoxycarbonyl)-3-phenyl-4a,7,8,8a-tetrahydropyrido[4,3-*e*]-1,4,2-dioxazine (4b). Compound **2b** upon standing at 25 °C for 15 days rearranged completely to **4b**: mp 128–130 °C; IR (KBr) 1715, 1705 (CO), 1652 (C=N), 1614 (C=C) cm^{-1}; ^1H NMR (Me_2SO-d_6, +70 °C) δ 7.74–7.80 and 7.44–7.56 (2 m, 5 H, Ph), 6.96 (br d, $J_{5,6}$ = 8.5 Hz, 1 H, H_6), 5.24–5.29 (m, $J_{4a,5}$ = 2.0 Hz, $J_{4a,6}$ = 2 Hz, $J_{4a,8a}$ = 3.0 Hz, 1 H, H_{4a}), 5.02 (br d, $J_{5,6}$ = 8.5 Hz, 1 H, H_5), 4.34–4.40 (m, $J_{8a,8_{eq}}$ = 5 Hz, $J_{8a,8_{ax}}$ = 2.5 Hz, $J_{8a,4a}$ = 3.0 Hz, 1 H, H_{8a}), 4.0 (d, $J_{8\,gem}$ = 14.5 Hz of d, $J_{8_{eq},8a}$ = 5 Hz, 1 H, $H_{8_{eq}}$), 3.77 (s, 3 H, $COOCH_3$), 3.72 (br d, $J_{8\,gem}$ = 14.5 Hz of d, $J_{8_{ax},8a}$ =2.5 Hz, 1 H, $H_{8_{ax}}$). Anal. Calcd for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.10; N, 10.21. Found: C, 60.98; H, 5.01; N, 10.0.

8-*n*-Butyl-5,7-bis(methoxycarbonyl)-4a,7,8,8a-tetrahydropyrido[4,3-*e*]-1,4,2-dioxazine (4d). Compound **2d** upon standing at 25 °C for 15 days rearranged completely to **4d**: mp 92–93 °C; IR (KBr) 1737, 1712 (CO_2CH_3, NCO_2CH_3), 1635 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.12 (br s, $J_{6,8}$ < 1 Hz, 1 H, H_6), 7.87 and 7.38–7.52 (dd and m, 5 H, Ph), 5.40 (d, $J_{4a,8a}$ = 4 Hz of d, $J_{4a,6}$ = 1 Hz, 1 H, H_{4a}), 4.60 (br d, $J_{8,8a}$ = 3.5 Hz of t, J_{8,CH_2} = 7.0 Hz, 1 H, H_8), 4.26 and 4.24 (2 d, $J_{4a,8a}$ = 4 Hz of d, $J_{8,8a}$ = 3.5 Hz, 1 H, H_{8a}), 3.90 and 3.81 (2 s, 3 H each, CO_2CH_3, NCO_2CH_3), 1.32–1.76 (m, 6 H, $(CH_2)_3CH_3$), 0.93 (t, 3 H, $(CH_2)_2CH_3$); high-resolution mass spectrum, exact mass calcd for $C_{20}H_{24}N_2O_6$ 388.1634, found 388.1635.

3-[(Benzyloxy)carbonyl]-5-(methoxycarbonyl)-2,3,5-oxadiazabicyclo[2.2.2]oct-7-ene (7b), 6-Hydroxy-1-(methoxycarbonyl)-3(*R*(*S*))-[*N*-hydroxy-*N*-((benzyloxy)carbonyl)-amino]-1,2,3,6-tetrahydropyridine (11), and 6-Hydroxy-1-(methoxycarbonyl)-3(*R*(*S*))-[*N*-hydroxy-*N*-((benzyloxy)-carbonyl)amino]-1,2,3,6-tetrahydropyridine (12). The reaction of **1b** with benzyl nitrosoformate was carried out as outlined in the general procedure. The reaction mixture, containing **7b** and **8b**, was separated by using a silica gel column. The early ether eluant fractions afforded pure **7b** (500 mg). Continued elution gave a mixture of **7b**, **11**, and **12** (750 mg) in which **7b** was the major component. Further elution with ethyl acetate gave a mixture of **11** and **12** (0.66 g), which was separated by preparative silica gel TLC using plates 0.75 mm in thickness with ethyl acetate as development solvent. Extraction of the fractions having R_f 0.35 gave **11** (171 mg) and R_f 0.3 gave **12** (88 mg).

The product **11** was obtained in 13.6% yield as a foam: IR (KBr) 3250–3480 (NOH, OH), 1704, 1684 ($NCOOCH_2$, $NCOOCH_3$) cm^{-1}; ^1H NMR (Me_2SO-d_6, +70 °C) δ 9.30 (s, 1 H, NOH, exchanges with deuterium oxide), 7.30–7.46 (m, 5 H, Ph), 5.82 (br s, 2 H, H_4, H_5), 5.89 (d, $J_{6,OH}$ = 5.5 Hz, 1 H, OH, exchanges with deuterium oxide), 5.57 (br d, $J_{6,OH}$ = 5.5 Hz, $J_{6,3} \approx$ 1 Hz, 1 H, H_6), 5.12–5.22 (m, 2 H, CH_2Ph), 4.54 (d, $J_{3,2_{ax}}$ = 11.5 Hz of d, $J_{3,2_{eq}}$ = 5.5 Hz, 1 H, H_3), 3.90 (d, $J_{2\,gem}$ = 11.5 Hz of d, $J_{2_{eq},3}$ = 5.5 Hz, 1 H, $H_{2_{eq}}$), 3.67 (s, 3 H, CH_3), 3.26 (d, $J_{2\,gem}$ = 11.5 Hz of d, $J_{2_{ax},3}$ = 11.5 Hz, 1 H, $H_{2_{ax}}$); high-resolution mass spectrum, exact mass calcd for $C_{15}H_{16}N_2O_5$ (M^+ – 18) 304.1059, found 304.1050; CI mass spectrum, $(M + NH_4)^+$ 340.

The product **12** was obtained in 6.8% yield as a low-melting solid: IR (KBr) 3492–3250 (OH), 1695, 1660 ($NCOOCH_2$, $NCOOCH_3$) cm^{-1}; ^1H NMR (Me_2SO-d_6, +50 °C) δ 9.08 (s, 1 H, NOH, exchanges with D_2O), 7.32–7.48 (m, 5 H, Ph), 6.06 (d, $J_{4,5}$ = 10.1 Hz of d, $J_{5,6}$ = 4.95 Hz, 1 H, H_5), 5.78–5.88 (m, $J_{6,OH}$ = 4.95 Hz, $J_{4,3}$ = 4.95 Hz, $J_{4,5}$ = 10.1 Hz, 2 H, C_6-OH, exchanges with deuterium oxide, 1 H, H_4), 5.60 (d, $J_{6,OH}$ = 4.95 Hz of d, $J_{6,5}$ = 4.95 Hz, becomes a d, $J_{6,5}$ = 4.95 Hz, after deuterium oxide exchange, 1 H, H_6), 5.16 (s, 2 H, CH_2Ph), 4.40 (br d, $J_{4,3}$ = 4.95 Hz of d, $J_{3,2_{ax}}$ = 4.95 Hz of d, $J_{3,5}$ = 1 Hz, 1 H, H_3), 4.10 (d, $J_{2\,gem}$ = 14.3 Hz, $J_{2_{eq},4}$ = <1 Hz, 1 H, $H_{2_{eq}}$), 3.60 (s, 3 H, CH_3), 3.36 (d, $J_{2\,gem}$ = 14.3 Hz of d, $J_{2_{ax},3}$ = 4.95 Hz, 1 H, $H_{2_{ax}}$); high-resolution mass spectrum, exact mass calcd for $C_{15}H_{16}N_2O_5$ (M^+ – 18) 304.1059, found 304.1056; CI mass spectrum, $(M + NH_4)^+$ 340.

1-Acetyl-2(*R*(*S*))-*n*-butyl-6-methoxy-3(*R*(*S*))-[*N*-hydroxy-*N*-((benzyloxy)carbonyl)amino]-1,2,3,6-tetrahydropyridine (10). A solution of **9** (0.362 g, 1 mmol) in dry methanol (10 mL) was heated at reflux for 2 h. The solvent was removed in vacuo, and the residue was triturated first with hexane and then with ether. The product **10** was removed by filtration as a white solid, (0.35 g, 93%): mp 123–124 °C; IR (KBr) 3261 (OH), 1723 ($NCOOCH_2$), 1691, 1675 ($NCOCH_3$), 1627 (C=C) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 9.26 and 9.10 (2 s, (6.5:3.5 ratio), 1 H, NOH, exchanges with D_2O), 7.34–7.50 (m, 5 H, Ph), 6.26 and 6.13 (2 d, $J_{5,4}$ = 9.5 Hz of d, $J_{5,6}$ = 3.6 Hz of d, $J_{5,3}$ = 1.5 Hz (3.5:6.5 ratio), 1 H, H_5), 5.88 and 5.74 (2 d (3.5:6.5 ratio), $J_{4,5}$ = 9.5 Hz of d, $J_{4,3}$ = 5.4 Hz of d, $J_{4,2}$ = 1.1 Hz of d, $J_{4,6}$ = 1.2 Hz, 1 H, H_4), 5.87 and 5.20 (2 d (6.5:3.5 ratio), $J_{6,5}$ = 3.6 Hz of d, $J_{6,4}$ = 1.2 Hz of d, $J_{6,3}$ < 1 Hz, 1 H, H_6), 5.10–5.26 (m, 2 H, CH_2Ph), 4.70, 3.91, and 3.88 (t and dd, J_{2,CH_2} = 7.6 Hz, $J_{2,4}$ = 1.1 Hz, 1 H, H_2), 4.42 and 4.38 (2 br d, $J_{3,4}$ = 5.4 Hz, 1 H, H_3), 3.34 and 3.32 (2 s, 3 H, OCH_3), 2.10 and 2.0 (2 s, 3 H, $COCH_3$), 1.12–1.72 (m, 6 H, $(CH_2)_3CH_3$), 0.64–0.88 (m, 3 H, $(CH_2)_3CH_3$). Anal. Calcd for $C_{20}H_{28}N_2O_5$: C, 63.82; H, 7.44; N, 7.44. Found: C, 63.56; H, 7.62; N, 7.31.

Acknowledgment. We are grateful to the Medical Research Council of Canada (Grant MT-4888) for financial support of this work and to the Alberta Heritage Foun-

dation for Medical Research for a Fellowship awarded to one of us (S.K.D.). The grant from the Alberta Hertiage Foundation to purchase the Bruker AM-300 spectrometer is also gratefully acknowledged.

Registry No. **1a**, 61340-79-2; **1b**, 33707-36-7; **1c**, 35022-78-7; **1d**, 52358-23-3; **2a**, 96212-65-6; **2b**, 96212-66-7; **2c**, 96212-67-8; **2d**, 96212-68-9; **3**, 96212-69-0; **4a**, 96212-70-3; **4b**, 95610-88-1; **4c**, 96212-71-4; **4d**, 96227-28-0; **5a**, 96212-72-5; **5b**, 96212-73-6; **5c**, 96212-74-7; **6**, 96212-75-8; **7a**, 96212-76-9; **7b**, 96212-77-0; **7c**, 96212-78-1; **8a**, 96212-79-2; **8b**, 96212-80-5; **8c**, 96227-29-1; **9**, 96212-81-6; **10**, 96212-82-7; **11**, 96212-83-8; PhCONHOH, 495-18-1; PhOCONHOH, 38064-07-2; *N*-[(benzyloxy)carbonyl]hydroxylamine, 3426-71-9.

Chelate and Macrocycle Effects in the 2,2′-Bipyridine *N*,*N*′-Dioxide Complexation of Alkyltin Trichlorides

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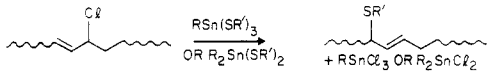
Received December 11, 1984

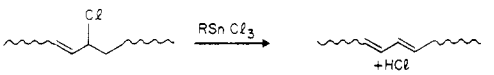
The synthesis of macrocyclic ligands **3**, **4**, and **7** for alkyltin trichloride ($RSnCl_3$) encapsulation is described. Key reactions were the condensation of *p*-$MeOCH_2C_6H_4MgBr$ with 6,6′-dibromo-2,2′-bipyridine, ring closures in dimethylformamide containing Cs_2CO_3, and oxidation of a bipyridyl precursor (**1**) to its *N*,*N*′-dioxide with buffered aqueous H_2O_2 in AcOH. The preparation of 4,4′-di-*tert*-butyl-2,2′-bipyridine 1,1′-dioxide (**8**) is also reported. The affinity of **8** for $MeSnCl_3$ was greater than that of 4-*tert*-butylpyridine 1-oxide, while the affinity of **7** was less than that of **5**. However, **7** was a better inhibitor of the $BuSnCl_3$-catalyzed degradation of *trans*-4-chloro-5-decene than **5**. The ability of the ligands to bind $RSnCl_3$ is evaluated in light of earlier work on organotin chloride–Lewis base interactions, and the relevance of the experiments to the design of additives for alkyltin trithiolate stabilizers for poly(vinyl chloride) is considered.

Monoalkyltin(IV) thiolates ($RSn(SR')_3$) are effective short-term color stabilizers[1] for poly(vinyl chloride) (PVC). This may be attributed to their ability to convert allylic and tertiary chloride moieties at defect sites on the polymer into much more stable alkyl sulfide groups, thereby preventing dehydrochlorination reactions that lead to the unwanted formation of colored polyene chains. Unfortunately, the byproducts of the stabilization process include Lewis acidic monoorganotin trichlorides ($RSnCl_3$), which catalyze[2] the very dehydrochlorinations that are supposed to be prevented by the stabilizers. Because of this serious disadvantage, $RSn(SR')_3$ stabilizers are of limited utility[2] in commercial PVC.

Model reactions for both the stabilization[3] and dehydrochlorination[4] processes have recently been described,



STABILIZATION REACTION



DEHYDROCHLORINATION REACTION

and the mechanisms seem to involve coordination of the chloride leaving group to the tin atom. It was demonstrated[4] that weak Lewis bases, which form complexes with $RSnCl_3$, retard the $RSnCl_3$-promoted elimination of HCl from an allylic chloride in nonpolar media, with a direct correlation between the effectiveness of the base as an inhibitor of dehydrochlorination and the affinity of the base for the tin atom in solution. In addition, the model stabilization reaction was found to occur even in the presence of the Lewis bases. Therefore, it was proposed that a PVC stabilizer formulation containing $RSn(SR')_3$ and a Lewis base might forestall the degradation of PVC over a longer time than would the thiolate alone.

Among the Lewis bases considered, pyridine *N*-oxide was the superior inhibitor of allylic chloride degradation and also the strongest complexing agent for $RSnCl_3$. It was therefore of interest to investigate the $RSnCl_3$-complexing behavior of pyridine *N*-oxide groups when incorporated into chelating and macrocyclic ligands. If chelating ligands were to exhibit stronger $RSnCl_3$ affinities than monodentate ligands, the former would be expected to act as improved dehydrochlorination inhibitors based on previous studies.[4] Macrocyclic ligands might further deactivate $RSnCl_3$ by sterically blocking access of the labile substrate to the catalytically important orbitals on the tin atom.

In this paper, we report full experimental details of the synthesis of novel chelating and macrocyclic ligands for $RSnCl_3$. The ability of the ligands to bind $RSnCl_3$ is evaluated in light of earlier work on organotin chloride–Lewis base interactions, and the action of a macrocyclic bipyridine *N*,*N*′-dioxide as an inhibitor of $RSnCl_3$-catalyzed allylic chloride degradation is briefly considered. Some of the synthetic methodology has been reported in a preliminary communication.[5]

Results

The synthesis of the bipyridine cycles is outlined in Schemes I and II. The Grignard reagent[6] from 1-bromo-4-(methoxymethyl)benzene was coupled to 6,6′-dibromo-2,2′-bipyridine[7] with $(PPh_3)_2NiCl_2$ to obtain di-

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