Diels-Alder Cycloadditions of *N*-Substituted-1,2-Dihydropyridines with 1,2,4-Triazoline-3,5-diones and Maleimides

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The reaction of *N*-substituted-1,2-dihydropyridines **1** with 1,2,4-triazoline-3,5-diones **2** and maleimides **9** proceeds stereospecifically to afford *endo* cycloaddition products. *N*-Acetyl-1,2-dihydropyridines react with **2** to afford a stereo isomeric mixture of **3** and **4** whereas those possessing a *N*-ethoxycarbonyl, methoxycarbonyl, methanesulfonyl or benzenesulfonyl substituent yield **3** exclusively: similar results are also obtained in reactions employing maleimides. Stereochemistry was assigned on the basis of nmr data and use was made of the anisotropic effects of the 7,8 unsaturation on the R_1 and R_2 substituents.

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The ($\pi 2 + \pi 4$) cycloaddition of dienamines with alkenes (the Diels-Alder reaction) is an attractive method for the synthesis of pharmacologically interesting bicyclic compounds. Recent examples involve reaction of *N*-methyl-2-pyridone with maleic anhydride and *N*-phenylmaleimide (1). In an earlier study it was shown that reaction of *N*-lithio-1,2-dihydropyridines with acyl chlorides and esters afford *N*-substituted-1,2-dihydropyridines (2). We now describe the facile reaction of these dienamines with 1,2,4-triazoline-3,5-diones and maleimides (3).

The major drug classes used clinically as antiepileptic agents include the hydantoin, barbiturate, succinimide, oxazolidinedione and more recently the benzodiazepine ring structure. A common structural feature of these compounds is the -CONH- unit which may be the biologically active center or requirement for antiepileptic activity. It would be of interest, therefore, to develop new bicyclic ring structures possessing this pharmacophoric group (4).

Treatment of 4-phenyl-1,2,4-triazoline-3,5-dione **2a** with *N*-ethoxycarbonyl-2-phenyl-1,2-dihydropyridine **1a** at -65° results in a discharge of the red color and a quantitative yield of 5-*endo*-ethoxycarbonyl-6-*exo*-phenyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic acid *N*-phenylimide **3a**. On the basis of mechanistic considerations for ($\pi 2 + \pi 4$) cycloadditions, **2a** should add to the less hindered face of **1a** to form the *endo* adduct **3a** with the phenyl group on the side of the molecule away

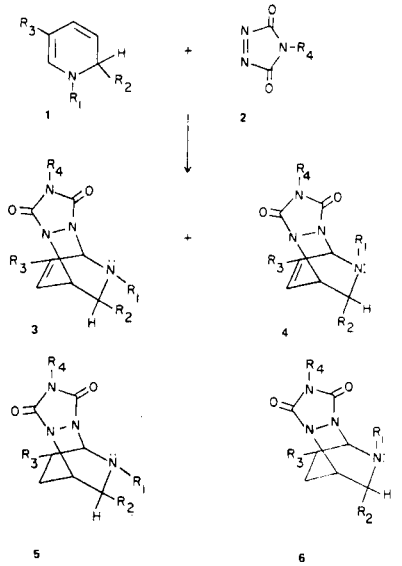


Table I

Reaction of *N*-Substituted-1,2-dihydropyridines with 1,2,4-Triazoline-3,5-diones

	1			2		Yield of Products (%)	
	R_1	R_2	R_3	R_4	Temp (°C)	3	4
(a)	CO_2Et	C_6H_5	H	C_6H_5	-65	100	
(b)	COMe	C_6H_5	H	C_6H_5	-65	68	32
	COMe	C_6H_5	H	C_6H_5	25	67	33
(c)	CO_2Me	H	H	C_6H_5	25	100	
(d)	SO_2Me	H	H	C_6H_5	25	100	
(e)	$SO_2C_6H_5$	H	H	C_6H_5	25	100	
(f)	COC_6H_5	C_6H_5	H	C_6H_5	25	100	
(g)	CO_2Me	n-C_4H_9	H	C_6H_5	25	100	
(h)	CO_2Me	n-C_4H_9	CO_2Me	C_6H_5	25	100	
(i)	$PO(OEt_2)$	n-C_4H_9	H	C_6H_5	25	97	
(j)	CONHEt	C_6H_5	H	C_6H_5	25	100	
(k)	CO_2Me	H	H	Et	-65	92	
(l)	SO_2Me	H	H	Et	25	89	
(m)	COMe	C_6H_5	H	Et	25	69	31
(n)	COMe	C_6H_5	H	H	0	43	26
(o)	CO_2Me	C_6H_5	H				

from the urazole moiety (5,6). Attack on the hindered face to give an *exo* adduct is less favourable due to the steric effect of the R_1 and R_2 substituents. The stereochemistry of substituents R_1 and R_2 in **3a** was assigned on the basis of nmr spectral evidence. It has been reported that reduction of the double bond in bicyclo[2.2.2]octane systems results in a shift of the signal for the *endo* 6-H to a lower magnetic field by 0.23 δ while that of the *exo* 6-H remains unchanged (7). Reduction of **3a** using 10% Palladium-charcoal and hydrogen gave rise to **5a**. Examination of the nmr data shown in Table II shows that the chemical shift of the 6-H is deshielded by 0.39 δ in the reduced compound which means it must be in the *endo* position. It therefore follows that the C-6 phenyl group must be in the *exo* configuration. By analogy the absorptions due to the methylene and methyl protons of the R_1 substituent are deshielded by 0.06 and 0.14 δ respectively which indicates that the R_1 substituent is also affected by the diamagnetic anisotropy of the double bond and that the structure assigned to **3a** must therefore be 5-*endo*-ethoxycarbonyl-6-*exo*-phenyl-2,3,5-triazabicyclo[2.2.2]-oct-7-ene-2,3-*endo*-dicarboxylic acid *N*-phenylimide rather than **4a**.

Reaction of *N*-acetyl-2-phenyl-1,2-dihydropyridine **1b** with **2b** at -65° gave rise to a mixture of **3b** (68%) and **4b** (32%) which could not be separated by fractional crystallization or thin layer chromatography. The nmr spectrum of the mixture exhibited two absorptions at 5.16 and 5.42 δ due to the H-6 proton: and at 1.79 and 2.34 δ for the acetyl methyl group which integrated for one and three protons respectively. The 7,8-double bond is expected to shield the *endo* H-6 and R_1 substituent of **3b** but to exhibit no effect on the *exo* H-6 and R_1 substituent of **4b**.

Table II

Relative Chemical Shifts of Unsaturated and Reduced Products

Compound	H_6	$-O-CH_2-$	$-CH_3$
3a	5.21	4.08	1.1
5a	5.60	4.14	1.24
3b	5.16		1.79
4b	5.42		2.34
5b and **6b**	5.4		2.36

Examination of the nmr data in Table II shows that after catalytic reduction, the *endo* H-6 of **3b** at 5.16 δ is deshielded by 0.24 δ and the methyl absorption at 1.79 δ is deshielded by 0.57 δ. The reaction product must therefore be composed of 5-*endo*-acetyl-6-*exo*-phenyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic acid *N*-phenylimide **3b** and 5-*exo*-acetyl-6-*endo*-phenyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic acid *N*-phenylimide **4b**.

The results shown in Table III indicate the product ratio **3**:**4** for the reaction of *N*-acetyl-1,2-dihydropyridines **1b**, **1m** and **1n** with **2b**, **2m** and **2n** is relatively constant and is independent of the reaction temperature as well as the R_4 substituent of **2**. The temperature study indicates that the *endo*-adduct which probably arises *via* a kinetic reaction does not undergo conversion to the thermodynamically more stable *exo* adduct. The fact that the yield of **3** always exceeds that of **4** when R_1 is acetyl suggests there is less steric hindrance to the approach of **2** when the R_2 substituent is *exo* and R_1 is *endo*. The reaction of **1** possessing ethoxycarbonyl, methoxycarbonyl, methanesulfonyl, diethylphosphate and ethyliminocarbonyl substituents at the R_1 position with **2** results in the exclusive

Table III

Isomeric Product Ratio's for Reaction of *N*-Acetyl-2-phenyl-1,2-dihydropyridine

Product Mixture	Reaction Temp °C	δ CH_3 3	δ CH_3 4	Ratio 3:4 (a)
3b and **4b**	-65	1.79	2.34	23:11
3b and **4b**	25	1.79	2.34	24:12
3b and **4b** (b)	-65	1.79	2.34	23:12
	0	1.79	2.34	21:11
	31	1.79	2.34	22:10
3m and **4m**	25	1.78	2.30	22:10
3n and **4n**	0	1.72	2.30	18:11

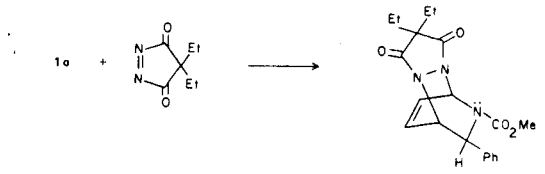
(a) Determined from the nmr integration curve. (b) Reaction was effected at -65° in an nmr tube and the spectrum was obtained at -65°, 0° and 31° respectively.

Table IV

Reaction of *N*-Substituted-1,2-dihydropyridines with Maleimides

	1 R_1	1 R_2	1 R_3	9 R_4	Catalyst	Yield of Products 10	Yield of Products 11
(b)	COMe	C_6H_5	H	C_6H_5	None	75	25
(b)	COMe	C_6H_5	H	C_6H_5	$AlCl_3$ (5 equiv)	34	15
(o)	CO_2Me	C_6H_5	H	Me	$AlCl_3$ (5 equiv)	56	
(p)	CO_2Me	C_6H_5	H	H	$AlCl_3$ (5 equiv)	52	

formation of **3**. Dreiding models indicate these R_1 substituents likely exert a steric effect which prevents the approach of the dienophile **2** when R_2 is in the *endo* and R_1 in the *exo* position. Treatment of 4,4-diethyl-1,2-pyrazoline-3,5-dione **7** with **1o** afforded **8** (100%). The reaction of other *N*-substituted-1,2-dihydropyridines **1** with **2** are shown in Table I.



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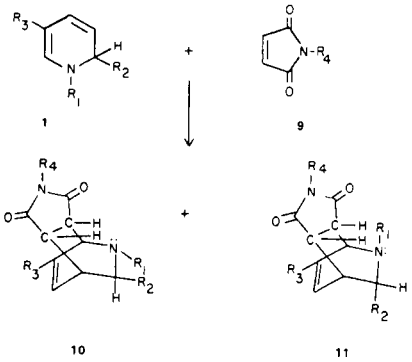
The reaction of *N*-substituted-1,2-dihydropyridines **1** with maleimides **9** was also investigated. For example, reaction of *N*-acetyl-2-phenyl-1,2-dihydropyridine **1b** with *N*-phenylmaleimide **9b** afforded a mixture of **10b** (75%) and **11b** (25%) which could not be separated by fractional crystallization or thin layer chromatography. It has been reported that the conformation of adducts similar to **10** and **11** can be determined by ^1H nmr from the magnitude of the coupling constants for the protons at the bridgehead positions (H-1, H-4) and the adjacent protons H-2



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and H-3 (8-10). The nmr spectrum of a mixture of **10** and **11** exhibited coupling constants $J_{1,2}$ = 3 Hz and $J_{3,4}$ = 4 Hz which is consistent with the *endo* conformation. The nmr spectrum of the mixture exhibited two absorptions at 4.80 (*endo*) and 5.09 (*exo*) δ for the H-6 proton and at 1.77 and 2.30 δ for the C-5 acetyl methyl groups of **10b** and **11b**. The 7,8 double bond is expected to shield the *endo* H-6 and R_1 substituent of **10b** but to exert no effect on the *exo* H-6 and R_1 substituent of **11b**. The aluminum chloride catalyzed reaction of **1b** with **9b** gave rise to **10b** (34%) and **11b** (15%). On the other hand, the reaction of **1o** and *N*-methylmaleimide **9o** proceeded to yield **10o** (56%) only if catalyzed. Optimum yields were obtained by employing five equivalents of aluminum chloride as

catalyst which was superior to boron trifluoride diethereate. Similarly, the reaction of **1p** with maleimide **9p** gave rise to **10p** (52%). The absence of **11o** and **11p** in the latter two reactions suggests there is steric hindrance to approach of the maleimide **9** by the *exo* R_1 methoxycarbonyl substituent when the 6-phenyl substituent is *endo*.

Pharmacological Test Results.

Ten selected compounds *viz:* **3a, 3c, 3d, 3g, 3h, 3k, 3l** and isomeric mixtures of **3b** and **4b, 3m** and **4m,** and **3n** and **4n** (Table 1) have been evaluated as antiepileptic agents for their ability to modify or prevent electrically (maximal electroshock) and chemically (metrazol) induced seizures. Although these compounds were non-toxic even at high doses ($TD_{50} > 1600$ mg/kg) they were ineffective. The ED_{50} for maximal electroshock and metrazol protection was greater than 1600 mg./kg. It was noted that **3g** offered a very light protection and that the **3m-4m** mixture potentiates the action of metrazol. Further studies are now in progress to prepare less rigid structures.

EXPERIMENTAL

Melting points were determined with a Büchi capillary apparatus and are uncorrected. Nmr spectra were determined for solutions of deuteriochloroform unless otherwise noted with TMS as internal standard with a Varian A-60, HA-100 or 220 spectrometer. Infrared spectra (in potassium bromide unless otherwise noted) were taken on a Unicam SP-1000 spectrometer. Mass spectra were measured with an AEI-MS-9 mass spectrometer.

5-*endo*-Ethoxycarbonyl-6-*exo*-phenyl-2,3,5-triazabicyclo[2.2.2]-oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3a**).

To a solution of 0.189 g. (1.08 mmoles) 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) in 10 ml. of dry dichloromethane was added dropwise a solution of 0.247 g. (1.08 mmoles) of *N*-ethoxycarbonyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at -65° with stirring under nitrogen. After warming to room temperature the solvent was removed *in vacuo* to give **3a** (100%), m.p. 150-154°; ir: 1790, 1718 cm^{-1} (C=O); nmr (13): δ 7.0-7.6 (m, 10, Ph), 6.74 (m, 2, C_4-H, C_8-H), 6.12 [d ($J_{7,8}$ = 9.5) of d ($J_{1,7}$ = 5), 1, C_7-H], 5.21 [d ($J_{1,6}$ = 2.5), 1, C_6-H], 5.11 [d ($J_{1,7}$ = 5) of d ($J_{1,6}$ = 2.5), 1, C_1-H], 4.08 (q, 2, OCH_2), 1.1 (t, 3, CH_3); Mass Calcd. for $C_{22}H_{20}N_4O_4$: 404.1478. Found: 404.1485.

5-Acetyl-6-phenyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3b** and **4b**).

To a solution of 0.100 g. (0.57 mmole) of PTAD in 10 ml. of dry dichloromethane was added dropwise a solution of 0.113 g. (0.57 mmole) of *N*-acetyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at -65° with stirring under nitrogen. Warming to room temperature and evaporation of solvent gave an off-white solid (**3b** and **4b**) in 100% yield (68% **3b**, 32% **4b**), m.p. 181-183°; ir: 1784, 1715(sh), 1709 cm^{-1} (C=O); nmr (13): δ 7.05-7.58 (m, 11, Ph, C_4-H), 6.82 [d ($J_{7,8}$ = 8) of d ($J_{4,8}$ = 5.5) of d ($J_{1,8}$ = 1.75), 1, C_8-H], 6.05-6.50 (m, 1, C_7-H), 5.16, 5.42 (m, 1, *endo*-C_6-H, *exo*-C_6-H), 5.08 (m, 1, C_1-H), 1.79, 2.34 (s, 3, *endo*-CH_3, *exo*-CH_3); Mass Calcd. for $C_{21}H_{18}N_4O_3$: 374.1379. Found: 374.1377.

5-*endo*-Methoxycarbonyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3c**).

To a solution of 1.5 g. (8.57 mmoles) of PTAD in 10 ml. of dry dichloromethane was added dropwise a solution of 1.19 g. (8.57 mmoles) of *N*-methoxycarbonyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen.

Stirring at room temperature for 4.5 hours and solvent evaporation gave an off-white solid (**3c**) in 100% yield, m.p. 152-156° dec.; ir: 1779, 1725, 1710(sh) cm^{-1} (C=O); nmr (13): δ 7.36 (m, 5, Ph), 6.36-6.76 (m, 3, C_4-H, C_7-H, C_8-H), 5.04 [d ($J_{1,7}$ = 5) of d ($J_{1,6}$ = 2.75), 1, C_1-H], 3.8 [d ($J_{6,6^1}$ gem = 11) of d ($J_{1,6}$ = 2.75), 1, C_6-H or $C_6{}^1$-H], 3.73 (s, 3, OCH_3), 3.17 [d ($J_{6,6^1}$ gem = 11) of d ($J_{1,6}$ = 2.75), 1, C_6-H or $C_6{}^1$-H]; Mass Calcd. for $C_{15}H_{14}N_4O_4$: 314.1015. Found: 314.1020.

5-*endo*-Methanesulfonyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3d**).

To a solution of 1.5 g. (8.57 mmoles) of PTAD in 40 ml. of dry dichloromethane was added dropwise a solution of 1.36 g. (8.57 mmoles) of *N*-methanesulfonyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen.

Stirring at room temperature for 0.5 hour and solvent evaporation gave an off-white solid (**3d**) in 100% yield, m.p. 170-175° (acetone washed); ir: 1794, 1725 cm^{-1} (C=O), 1155, 1340 cm^{-1} (SO_2); nmr (DMSO-d_6) (13): δ 7.45 (m, 5, Ph), 6.6-6.96 (m, 2, C_7-H, C_8-H), 6.06 [d ($J_{4,8}$ = 6) of d ($J_{4,7}$ = 1.5), 1, C_4-H], 5.2 (m, 1, C_1-H), 3.81 [d ($J_{6,6^1}$ gem = 10.5) of d ($J_{1,6}$ = 3), 1, C_6-H or $C_6{}^1$-H], 3.24 [d ($J_{6,6^1}$ gem = 10.5) of d ($J_{1,6}$ = 3), 1, C_6-H or $C_6{}^1$-H], 3.08 (s, 3, SO_2CH_3); Mass Calcd. for $C_{14}H_{14}N_4O_4S$: 334.0736. Found: 334.0752.

5-*endo*-Benzenesulfonyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3e**).

To a solution of 0.070 g. (0.4 mmole) of PTAD in 25 ml. of dry dichloromethane was added dropwise a solution of 0.088 g. (0.4 mmole) of *N*-benzenesulfonyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen. Solvent evaporation gave a pale yellow solid (**3e**) in 100% yield, m.p. 145°; ir: 1780, 1720 cm^{-1} (C=O); 1355, 1170 cm^{-1} (SO_2); nmr: δ 7.16-8.16 (m, 10, Ph), 6.14-6.76 (m, 3, C_4-H, C_7-H, C_8-H), 4.96 (m, 1, C_1-H), 3.61 [d ($J_{6,6^1}$ gem = 10.5) of d ($J_{1,6}$ = 2.5), 1, C_6-H or $C_6{}^1$-H], 3.16 [d ($J_{6,6^1}$ gem = 10.5) of d ($J_{1,6}$ = 1.8), 1, C_6-H or $C_6{}^1$-H]; Mass Calcd. for $C_{19}H_{16}N_4O_4S$: 396.0893. Found: 396.0870.

5-*endo*-Benzoyl-6-*exo*-phenyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3f**).

To a solution of 0.338 g. (1.93 mmoles) of PTAD in 40 ml. of dry dichloromethane was added dropwise a solution of 0.500 g. (1.93 mmoles) of *N*-benzoyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen. Stirring at room temperature for 0.5 hour, and solvent evaporation gave an off-white solid (**3f**) in 100% yield, m.p. 202-204° (from DMSO); ir: 1790, 1720, 1700(sh) cm^{-1} (C=O); nmr (DMSO-d_6): δ 7.33, 7.46, 7.59 (m, 15, Ph), δ 6.94-7.33 (m, 1, C_4-H), δ 6.27-6.63 (m, 2, C_7-H, C_8-H), δ 5.62 [d ($J_{1,6}$ = 2.5), 1, C_6-H], δ 5.35 (m, 1, C_1-H); Mass Calcd. for $C_{26}H_{20}N_4O_3$: 436.1535. Found: 436.1531.

5-*endo*-Methoxycarbonyl-6-*exo*-*n*-butyl-2,3,5-triazabicyclo[2.2.2]-oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3g**).

To a solution of 0.350 g. (2.00 mmoles) of PTAD in 10 ml. of

dry dichloromethane was added dropwise a solution of 0.390 g. (2.00 mmoles) of *N*-methoxycarbonyl-2-*n*-butyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen. Stirring at room temperature for 0.5 hour and solvent evaporation gave a light yellow semi-solid (**3g**) in 100% yield, m.p. 35-38°; ir (neat): 1782, 1726, 1712(sh) cm^{-1} (C=O); nmr: δ 7.23-7.52 (m, 6, Ph, C_4-H), 6.28-6.67 (m, 2, C_7-H, C_8-H), 5.06 (m, 1, C_1-H), 3.79-4.2 (m, 1, C_6-H), 3.79 (s, 3, OCH_3), 0.70-1.53 (m, 9, *n*-Bu); Mass Calcd. for $C_{19}H_{22}N_4O_4$: 370.1641. Found: 370.1654.

5-*endo*-8-Dimethoxycarbonyl-6-*exo*-*n*-butyl-2,3,5-triazabicyclo-[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3h**).

To a solution of 0.277 g. (1.58 mmoles) of PTAD in 20 ml. of dry dichloromethane was added dropwise a solution of 0.400 g. (1.58 mmoles) of 1,5-dimethoxycarbonyl-2-*n*-butyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen. Stirring at room temperature for 0.5 hour and solvent evaporation gave a light yellow semi-solid (**3h**) in 100% yield, m.p. 55-60°; ir: 1780, 1728, 1715(sh) cm^{-1} (C=O); nmr: δ 7.23-7.50 (m, 6, Ph, C_4-H), 6.95 (m, 1, C_7-H), 5.21 [d ($J_{1,7}$ = 5) of d ($J_{1,6}$ = 2.5), 1, C_1-H)], 3.84-4.25 (m, 1, C_6-H), 3.84 (s, 3, OCH_3), 3.81 (s, 3, OCH_3), 0.77-1.62 (m, 9, *n*-Bu); Mass Calcd. for $C_{21}H_{24}N_4O_6$: 428.1696. Found: 428.1680.

5-*endo*-Diethylphosphoryl-6-*exo*-*n*-butyl-2,3,5-triazabicyclo-[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3i**).

To a solution of 0.079 g. (0.45 mmole) of PTAD in 20 ml. of dry dichloromethane was added dropwise a solution of 0.123 g. (0.45 mmole) of *N*-diethylphosphoryl-2-*n*-butyl-1,2-dihydropyridine in 5 ml. of dry dichloromethane at 25° with stirring under nitrogen. Evaporation of solvent *in vacuo* gave a light yellow oil (**3i**) in 97% yield. ir: 1770, 1720 cm^{-1} (C=O), 1250 cm^{-1} (P=O); nmr (DMSO-d_6): 7.3-7.64 (m, 5, Ph), 6.87 (m, 1, C_4-H), 6.56 (m, 1, C_8-H), 5.76-6.00 (m, 2, C_7-H, C_1-H), 5.08 (m, 1, C_6-H), 4.02 [q ($J_{CH_2CH_3}$ = 7), 4, CH_2], 0.70-1.90 (m, 15, CH_3, C_4H_9); Mass Calcd. for $C_{21}H_{29}N_4O_5P$: 448.1877. Found: 448.1873.

5-*endo*-Ethyliminocarbonyl-6-*exo*-phenyl-2,3,5-triazabicyclo-[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**3j**).

To a solution of 0.140 g. (0.8 mmole) of PTAD in 20 ml. of dry dichloromethane was added dropwise a solution of 0.182 g. (0.8 mmole) of *N*-ethyliminocarbonyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen. Solvent evaporation gave a white solid (**3j**) in 100% yield, m.p. 130-132°; ir: 1778, 1720 cm^{-1} (C=O); nmr (DMSO-d_6) (13): δ 7.1-7.7 (m, 5, Ph), 6.76-7.02 (m, 2, C_4-H, C_8-H), 6.62 [t (J_{NH,CH_2} = 5), 1, NH, exchanges with deuterium oxide], 6.25 (m, 1, C_7-H), 5.65 (m, 1, C_6-H), 5.29 (m, 1, C_1-H), 3.05 (m, 2, CH_2), 0.98 [t (J_{CH_2,CH_3} = 7), 3, CH_3]; **3j** did not give m/e 403 (M^+).

Anal., Calcd. for $C_{22}H_{21}N_5O_3$: C, 65.50; H, 5.28; N, 17.36. Found: C, 65.70; H, 5.37; N, 17.47.

5-*endo*-Methoxycarbonyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Ethylimide (**3k**).

To a solution of 0.750 g. (5.91 mmoles) of 4-ethyl-1,2,4-triazoline-3,5-dione (ETAD) in 10 ml. of dry dichloromethane was added dropwise a solution of 0.821 g. (5.91 mmoles) of *N*-methoxycarbonyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at -65° with stirring under nitrogen. Warming to room temperature and evaporation of solvent gave a yellow semi-solid (**3k**) in 92% yield; ir: 1756, 1708 cm^{-1} (C=O); nmr: δ 5.75-6.3 (m, 2, C_8-H, C_7-H or C_4-H), 5.33-5.67 (m, 1, C_4-H or C_7-H), 4.19-4.56 (m, 1, C_1-H), 3.33-4.19 (m, 7, OCH_3, CH_2, C_6-H, $C_6{}^1$-H), 1.24 [t (J_{CH_2,CH_3} = 7), 3, CH_3]; Mass Calcd. for $C_{11}H_{14}N_4O_4$: 266.1015. Found: 266.1016.

5-*endo*-Methanesulfonyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Ethylimide (**3l**).

To a solution of 0.359 g. (2.80 mmoles) of ETAD in 10 ml. of dry dichloromethane was added dropwise a solution of 0.450 g. (2.80 mmoles) of *N*-methanesulfonyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen. Stirring at room temperature for 0.5 hour and solvent evaporation gave a yellow semi-solid (**3l**) in 89% yield; ir: 1768, 1702 cm^{-1} (C=O); nmr: δ 5.71-6.52 (m, 3, C_4-H, C_7-H, C_8-H), 5.25 (m, 1, C_1-H), 3.24-4.18 (m, 4, C_6-H, $C_6{}^1$-H, CH_2), 3.02 (s, 3, SO_2CH_3), 1.25 [t (J_{CH_2,CH_3} = 7), 3, CH_3]; Mass Calcd. for $C_{10}H_{14}N_4O_4S$: 286.0736. Found: 286.0740.

5-Acetyl-6-phenyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Ethylimide (**3m** and **4m**).

To a solution of 0.924 g. (7.28 mmoles) of ETAD in 10 ml. of dry dichloromethane was added dropwise a solution of 1.448 g. (7.28 mmoles) of *N*-acetyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at 25° with stirring under nitrogen. Stirring at room temperature for 0.5 hour and solvent evaporation gave a yellow solid (**3m** and **4m**) in 100% yield (69% **3m**, 31% **4m**), m.p. 70°; ir: 1782, 1720 cm^{-1} (C=O); nmr: δ 6.91-7.5 (m, 6, Ph, C_4-H), 6.68 (m, 1, C_8-H), 6.08 (m, 1, C_7-H), 4.82-5.39 (m, 1, C_1-H, *endo*-C_6-H, *exo*-C_6-H), 3.47 [q (J_{CH_2,CH_3} = 7), 2, CH_2], 1.78, 2.30 (s, *endo*-CH_3, *exo*-CH_3), 1.17 [t (J_{CH_2,CH_3} = 7), 3, CH_3]; Mass Calcd. for $C_{17}H_{18}N_4O_3$: 326.1379. Found: 326.1374.

5-Acetyl-6-phenyl-2,3,5-triazabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid Imide (**3n** and **4n**).

A solution of 0.153 g. (0.77 mmole) of *N*-acetyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane was added dropwise to a solution of 1,2,4-triazoline-3,5-dione in 100 ml. of dry dichloromethane at 0° with stirring under nitrogen until the red color was discharged. Stirring to room temperature and evaporation of solvent gave a light yellow solid (**3n** and **4n**) in 69% yield (43% **3n**, 26% **4n**), m.p. 217-219° (chloroform washed); ir: 1778, 1720 cm^{-1} (C=O); nmr (DMSO-d_6): δ 7.04-7.56 (m, 5, Ph), 6.63-7.00 (m, 2, C_4-H, C_8-H), 6.00-6.59 (m, 2, C_7-H, NH, exchanges with deuterium oxide), 5.42, 5.73 (m, 1, *endo*-C_6-H, *exo*-C_6-H), 5.16 (m, 1, C_1-H), 1.72, 2.30 (s, 3, *endo*-CH_3, *exo*-CH_3); Mass Calcd. for $C_{15}H_{14}N_4O_3$: 298.1066. Found: 298.1059.

4,4-Diethylpyrazoline-3,5-dione Adduct of *N*-Methoxycarbonyl-2-phenyl-1,2-dihydropyridine (**8**).

A solution of 0.412 g. (1.92 mmoles) of *N*-methoxycarbonyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane was added dropwise to a solution of 4,4-diethyl-1,2-pyrazoline-3,5-dione (11) in 100 ml. of dry dichloromethane at 0° with stirring under nitrogen until the blue color was discharged. Warming to room temperature and evaporation of solvent gave a yellow solid (**8**) in 100% yield (12): ir: 1745, 1712, 1700(sh) cm^{-1} (C=O); nmr: δ 7.05-7.47 (m, 6, Ph, C_4-H), 6.78 (m, 1, C_8-H), 6.12 (m, 1, C_7-H), 5.06-5.35 (m, 2, C_1-H, C_6-H), 3.61 (s, 3, OCH_3), 1.80 [q (J_{CH_2,CH_3} = 7), 2, CH_2CH_3], 1.75 [q (J_{CH_2,CH_3} = 7), 2, CH_2CH_3], 0.95 [t (J_{CH_2,CH_3} = 7), 3, CH_2CH_3], 0.79 [t J_{CH_2,CH_3} = 7), 3, CH_2CH_3]; Mass Calcd. for $C_{20}H_{23}N_3O_4$: 369.1683. Found: 369.1686.

5-Acetyl-6-phenyl-5-azabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Phenylimide (**10b** and **11b**).

To a solution of 1.190 g. (6.88 mmoles) of *N*-phenylmaleimide in 50 ml. of dry dichloromethane was added dropwise a solution of 1.369 g. (6.88 mmoles) of *N*-acetyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at reflux (40°) with stirring. Refluxing for 5 days and solvent evaporation gave an off-white solid (**10b** and **11b**) in 100% yield (75% **10b**, 25% **11b**), m.p. 269-271° (acetone washed); ir: 1775, 1710 cm^{-1} (C=O); nmr (220 MH_z)(13): δ 7.02-7.50 (m, 10, Ph), 6.61 [d ($J_{7,8}$ = 8) of d ($J_{4,8}$ = 6) of d ($J_{1,8}$ = 1.25), 1, C_8-H], 5.93-6.14 (m, 2, C_4-H, C_7-H), 4.80, 5.09 (m, 1, *endo*-C_6-H, *exo*-C_6-H), 3.64 (m, 1, C_1-H), 3.52 [d ($J_{2,3}$ = 8) of d ($J_{3,4}$ = 4), 1, C_3-H], 3.34 [d ($J_{2,3}$ = 8) of d ($J_{1,2}$ = 3), 1, C_2-H], 1.77, 2.30 (s, 3, *endo*-CH_3, *exo*-CH_3); Mass Calcd. for $C_{23}H_{20}N_2O_3$: 372.1474. Found: 372.1465.

5-*endo*-Methoxycarbonyl-6-*exo*-phenyl-5-azabicyclo[2.2.2]oct-7-ene-2,3-*endo*-dicarboxylic Acid *N*-Methylimide (**10o**).

To a solution of 0.207 g. (1.86 mmoles) of *N*-methylmaleimide and 1.240 g. (9.30 mmoles) of aluminum chloride in 50 ml. of dry dichloromethane was added dropwise a solution of 0.400 g. (1.86 mmoles) of *N*-methoxycarbonyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at reflux (40°) with stirring under argon. Refluxing for 1 hour, washing with water (100 ml.), 5% sodium bicarbonate (2 x 100 ml.), water (100 ml.), drying (sodium sulfate), and solvent evaporation *in vacuo* gave a low melting off-white solid which was chromatographed on a 2.5 x 35 cm silica column. Elution with 750 ml. of benzene-ether (1:2 v/v) gave **10o** in 56% yield; ir: 1772 (broad) cm^{-1} (C=O); nmr: δ 6.84-7.38 (m, 5, Ph), 6.37 (m, 1, C_8-H), 5.78 (m, 1, C_7-H), 5.32 (m, 1, C_4-H), 4.75 (m, 1, C_6-H), 3.10-3.80 (m, 6, C_1-H, C_2-H, C_3-H, OCH_3), 2.80s(s, 3, NCH_3); Mass Calcd. for $C_{18}H_{18}N_2O_4$: 326.1267. Found: 326.1251.

5-*endo*-Methoxycarbonyl-6-*exo*-phenyl-5-azabicyclo[2.2.2]oct-7-ene, 2,3-*endo*-dicarboxylic Acid Imide (**10p**).

To a solution of 0.198 g. (2.05 mmoles) of maleimide and 1.364 g. (10.2 mmoles) of aluminum chloride in 100 ml. of dry dichloromethane was added dropwise a solution of 0.440 g. (2.05 mmoles) of *N*-methoxycarbonyl-2-phenyl-1,2-dihydropyridine in 10 ml. of dry dichloromethane at reflux (40°) with stirring under argon. Refluxing for 1.5 hours, washing with water (100 ml.), 5% sodium bicarbonate (2 x 100 ml.), water (100 ml.), drying (sodium sulfate) and solvent evaporation *in vacuo* gave a yellow semi-solid which precipitated from benzene-cyclohexane-methanol (10:35:1) (10 ml.) giving **10p** in 52% yield: ir: 1765 (broad) cm^{-1} (C=O); nmr (220 MH_z) (13); δ 8.64 (s, 1, NH, exchanges with deuterium oxide), 7.00-7.48 (m, 5, Ph), 6.53 (m, 1, C_8-H), 5.95 (m, 1, C_7-H), 5.39 (m, 1, C_4-H), 4.75 (m, 1, C_6-H), 3.34-3.82 (m, 5, C_1-H, C_3-H, OCH_3), 3.25 (m, 1, C_2-H); Mass Calcd. for $C_{17}H_{16}N_2O_4$: 312.1110. Found: 312.1118.

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