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AZATRICYCLES FROM SUBSTITUTED PYRIDINES SYNTHESIS AND REARRANGEMENT OF N-ETHOXYCARBONYL-2-AZATRICYCLO[4 3 1 $0^{3,7}$]DEC-8-ENES

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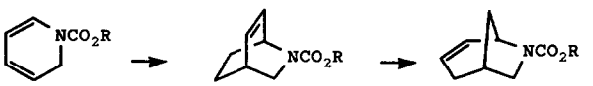
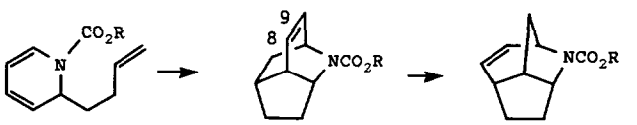
Abstract The scope and relative rates of intramolecular cycloaddition reactions of methyl-substituted 2-[3-butenyl]-1,2-dihydropyridines 4 have been studied Cycloadducts 5 can be rearranged to 14 upon reaction with bromine, except when olefinic methyl groups are present

Utilization of an N-acyl-1,2-dihydropyridine 1 as the diene component in a Diels-Alder reaction provides ready access to derivatives of the N-acyl bridged bicyclic amine 2 [1,2] Cycloadducts 2 have been converted to the rearranged N-acyl-7-azabicyclo[3 2 1]oct-2-ene skeleton 3 upon reaction with electrophilic bromine reagents [3]



1 2 3

The intramolecular version of the cycloaddition route to bridged nitrogen heterocycles is shown by the conversion of 2-(3-butenyl)-1,2-dihydropyridine 4 to the tricyclic structure 5 [4] The present study was initiated to determine how alkyl substituents at positions 3-6, 3′, 4′, and R of 1,2-dihydropyridines 4 affect the formation of cycloadducts 5

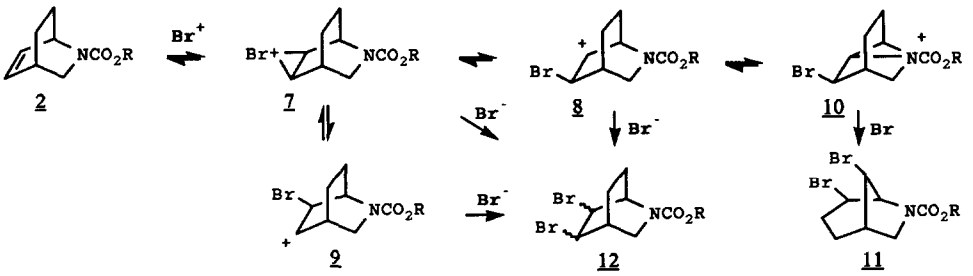


4 5 6

Further, it was of interest to see how olefinic substituents at positions 8 and 9 of tricycles 5 might influence the propensity for rearrangement during electrophilic bromination reactions As depicted in Scheme 1, addition of bromine to azabicycle 2 can give rearranged dibromide 11 or unrearranged dibromide 12 via potentially equilibrating bromonium ion 7, shown as its anti isomer, cations 8 and 9, or an aziridinium ion 10 Olefinic substituents

on 2 would be expected to influence the partitioning of the intermediates 7-10 and thus affect the ratio of products 11 and 12

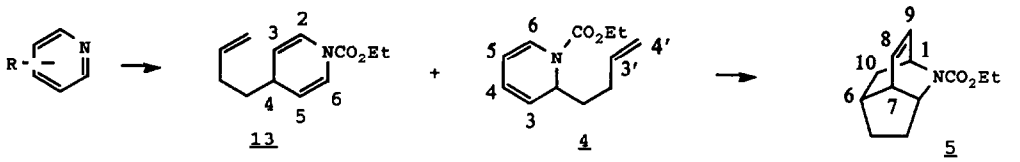
Scheme 1 Formation of rearranged and unrearranged dibromides 11 and 12 from 2 via bromonium ions 7, open cations 8 and 9, and aziridinium ion 10



RESULTS AND DISCUSSION

Synthesis N-ethoxycarbonyl-2-(3-butenyl)-1,2-dihydropyridines 4 were synthesized by addition of 3-butenyl magnesium bromide (or homologs with alkyl groups on the olefinic bond) to pyridine, or the appropriate substituted pyridine, at 0° in tetrahydrofuran, followed by reaction with ethyl or methyl chloroformate [4a 4c] Although the 1,2-dihydropyridines 4 were admixed occasionally with isomeric 1,4-dihydropyridines 13, the latter did not interfere with the subsequent cycloadditions The 1,2-dihydropyridines 4 were added to refluxing decalin to afford cycloadducts 5 At the conclusion of each reaction, the cycloadducts 5 were separated from 1,4-dihydropyridines 13 by chromatography over silica gel Appreciable loss of cycloadduct was observed during chromatography of cycloadducts 5 which had a 6-alkyl substituent [5] A single regioisomeric cycloadduct 5 was obtained from each 1,2-dihydropyridine 4 Structures 5 were assigned to cycloadducts by consideration of earlier studies[4a,4c] and by consideration of the structure of the rearrangement product 14a formed from cycloadduct 5a upon bromination/dehydrobromination (vide infra) If the regioisomeric cycloadduct 15a had been formed, dehydrobromination of a rearranged dibromide 16 to give 17 would not be possible because of bridgehead strain effects in 17

Kinetics The rates of disappearance of 4 and appearance of cycloadducts 5 shown in Table 1 were monitored by gas chromatography, the 1,4-dihydropyridines 13 remained unchanged At the times required to monitor the cycloadditions all reactions showed first order kinetics The derived rates k (hr^{-1}) and half-lives $t^{1/2}$ (hr) are for reactions followed through at least three half-lives Since in general these experiments were not performed using a device to rigorously control temperature, the boiling point of decalin fluctuated around 192° Thus, use of this data must be restricted to a comparison of those cycloadditions where clear rate differences were observed The kinetic data in Table 1 has been analyzed in the discussion to follow according to substitution patterns

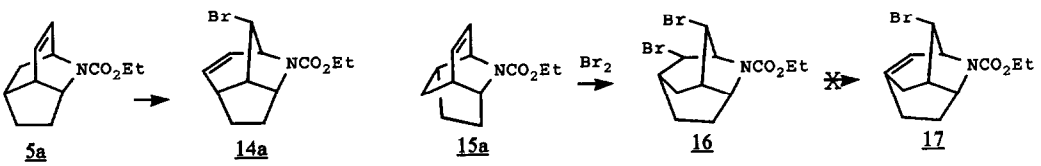


13 4 5

13a Parent
13b 3-Me
13c 4-Me
13e 2-Me
13f 2-Me,Et=Me
13g 3-Et
13i 2-Et
13p 2,5-di-Me
13q 3,4-di-Me
13r 2,4-di-Me
13s 3,5-di-Me
13u 2,3-di-Me
13v 3'-Me
13x 4'-*trans*-Et

4a Parent
4b 3-Me
4c 4-Me
4d 5-Me
4e 6-Me
4f 6-Me,Et=Me
4g 3-Et
4h 4-Et
4i 5-Et
4j 6-Et
4k 4-Pr
4l 4-*iso*-Pr
4m 4-*iso*-Pent
4n 4-*t*-Bu
4o 4-Ph
4p 3,6-di-Me
4q 3,4-di-Me
4r 4,6-di-Me
4s 3,5-di-Me
4t 4,5-di-Me
4u 5,6-di-Me
4v 3'-Me
4w 4'-*cis*-Et
4x 4'-*trans*-Et

5a Parent
5b 7-Me
5c 8-Me
5d 9-Me
5e 1-Me
5f 1-Me,Et=Me
5g 7-Et
5h 8-Et
5i 9-Et
5j 1-Et
5k 8-Pr
5l 8-*iso*-Pr
5m 8-*iso*-Pent
5n 8-*t*-Bu
5o 8-Ph
5p 1,7-di-Me
5q 7,8-di-Me
5r 1,8-di-Me
5s 7,9-di-Me
5t 8,9-di-Me
5u 1,9-di-Me
5v 6-Me
5w 10-*syn*-Et
5x 10-*anti*-Et

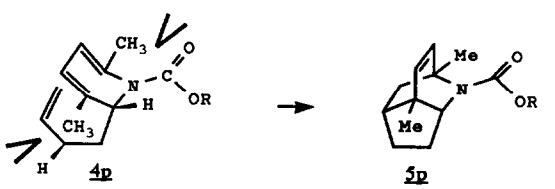


5a 14a 15a 16 17

Monoalkyl Substitution

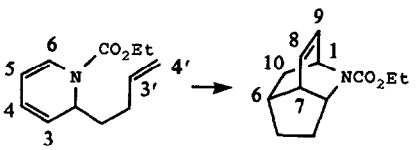
Relative cycloaddition rates for the monomethylated 1,2-dihydropyridines 4b-4e are 5-methyl > parent > 4-methyl > 3-methyl > 6-methyl It has been shown that the rate retarding effect of the 3-methyl and 6-methyl substituents are steric in origin by observing the two-fold and nearly four-fold decrease in cycloaddition rates of 3-ethyl- and 6-ethyl-1,2-dihydropyridines 4g and 4j relative to 3-methyl- and 6-methyl-1,2-dihydropyridines 4b and 4e [4c 4d] As depicted in Figure 1, molecular models of the dihydropyridine 4p with a pseudo-axial 3-butenyl side chain[6] indicate that during reaction to give cycloadduct 5p the 3-alkyl substituent interacts sterically with a methylene group of the side chain as it twists to orient over the diene This same twisting motion during cycloaddition moves the alkoxycarbonyl and the 6-methyl groups closer together, thus accounting for the rate retardation by a 6-methyl substituent Consistent with this picture of the reaction, replacement of the N-ethoxycarbonyl group of the 6-methyl derivative 4e by the smaller N-methoxycarbonyl of 4f results in a 30% rate increase

Figure 1



4p 5p

Table 1 Kinetic Data for Conversions of 4 to 5 in Decalin at 192°



	Reactant	Product	k (hr^{-1})	$t^{1/2}$(hr)
4a	Parent	5a Parent	1 33 ± 0 02	0 52 ± 0 01
		Monoalkyl Homologs		
4b	3-Me	5b 7-Me	0 50 ± 0 01	1 40 ± 0 02
4c	4-Me	5c 8-Me	0 95 ± 0 08	0 75 ± 0 08
4d	5-Me	5d 9-Me	1 75 ± 0 14	0 4 ± 0 05
4e	6-Me	5e 1-Me	0 20 ± 0 01	3 4 ± 0 2
4f	6-Me[a]	5f 1-Me	0 31 ± 0 01	2 24 ± 0 07
4g	3-Et	5g 7-Et	0 25 ± 0 01	2 8 ± 0 1
4h	4-Et	5h 8-Et	1 11 ± 0 05	0 62 ± 0 02
4i	5-Et	5i 9-Et	2 26 ± 0 08	0 31 ± 0 01
4j	6-Et	5j 1-Et	0 055 ± 0 002	12 6 ± 0 5
4k	4-Pr	5k 8-Pr	1 11 ± 0 05	0 62 ± 0 02
4l	4-*iso*-Pr	5l 8-*iso*-Pr	1 17 ± 0 08	0 59 ± 0 04
4m	4-iso-Pent	5m 8-iso-Pent	1 02 ± 0 06	0 68 ± 0 04
4n	4-t-Bu	5n 8-t-Bu	1 14 ± 0 06	0 61 ± 0 03
4o	4-Ph	5o 8-Ph	3 5 ± 0 4	0 20 ± 0 03
		Dialkyl homologs		
4p	3,6-di-Me	5p 1,7-di-Me	0 04 ± 0 01	16 5 ± 0 4
4q	3,4-di-Me	5q 7,8-di-Me	0 30 ± 0 03	2 3 ± 0 2
4r	4,6-di-Me	5r 1,8-di-Me	0 19 ± 0 01	3 6 ± 0 2
4s	3,5-di-Me	5s 7,9-di-Me	1 0 ± 0 3	0 68 ± 0 02
4t	4,5-di-Me	5t 8,9-di-Me	1 65 ± 0 17	0 42 ± 0 04
4u	5,6-di-Me	5u 1,9-di-Me	0 67 ± 0 06	1 0 ± 0 1
		Side-chain Homologs		
4v	3'Me	5v 6-Me	0 20 ± 0 01	3 4 ± 0 1
4w	4'-cis-Et	5w 10-syn-Et	0 10 ± 0 003	7 0 ± 0 2
4x	4'-trans-Et	5x 10-anti-Et	0 57 ± 0 02	1 22 ± 0 06

(a) Et = Me

The 4-methyl substituent in 1,2-dihydropyridine 4c results in a 60% reduction of rate relative to the parent 4a Larger substituents, even t-butyl at the 4-position as in 4n, result in smaller 20-30% rate reductions and present no synthetic difficulties The combination of FMO factors for a neutral electron demand Diels-Alder reaction[7a] and conformational effects, which might give rise to these small differences, has been discussed previously [4d] It has been suggested that although 4-alkyl substitution, which raises the energy of the diene HOMO and LUMO, results in an increase in stabilization by the normal HOMO diene/LUMO dienophile interaction, there is a counterbalancing decrease in stabilization of the inverse HOMO dienophile/LUMO diene interaction It can be noted that a 4-phenyl group of 4o, which raises the diene HOMO to a greater extent than does a 4-alkyl group, reacts 2 5 times faster than the parent 4a [8]

The 5-methyl- and 5-ethyl-1,2-dihydropyridines 4d and 4i react 20% and 40% faster than the parent 4a Although 5-alkyl substituents also raise the diene HOMO and LUMO energies, the increase in the normal stabilization due to a better HOMO diene/LUMO dienophile interaction is greater than the decrease in stabilization from a poorer inverse HOMO dienophile/LUMO diene interaction [4d,8]

Dialkyl Substitution.

Comparison of the kinetic data for the monomethyl and dimethyl 2-(3-butenyl)-1,2-dihydropyridines 2p-2u indicates that introduction of a second methyl group decreases the cycloaddition rate, unless a 5-methyl group is added As shown in Table 2, this is the same effect that was observed when the reactivities of monomethyl 1,2-dihydropyridines 4b-4e were compared to the parent 4a The greatest rate retardation was observed for the 3,6-dimethyl-1,2-dihydropyridine 4p The 30-fold rate retardation is likely steric in origin, since the buttressing of the two methyls with the carbamate and 3-butenyl side chain is increased in the cycloaddition transition state [8]

Alkyl Substitution on the dienophile

Modification of the 3-butenyl side chain by introduction of alkyl groups at its three olefinic positions did not affect the ability to prepare cycloadducts in yields comparable to reaction of the parent 4a The effect of substituent on reaction rate varied A 3'-methyl substituent in 4v resulted in over 6-fold rate retardation relative to the parent 4a, this was as severe an effect as that seen upon introduction of the 6-methyl group in 4e The 4'-cis-ethyl and 4'-trans-ethyl compounds 4w and 4x also reacted at 7% and 42% slower rates than the parent 2a The rate retardations relative to the parent 2a may be partly steric in origin, but they also are as expected according to FMO theory [7] Alkyl substitution on the dienophile should, by raising the energy of the LUMO, increase the FMO gap and thus slow the rate of a normal Diels-Alder reaction [8]

Table 2 Relative Cycloaddition Rates of N-ethoxycarbonyl-1,2-dihydropyridines 4 Following addition of a Methyl Group to a Base Structure at the Indicated Ring Position

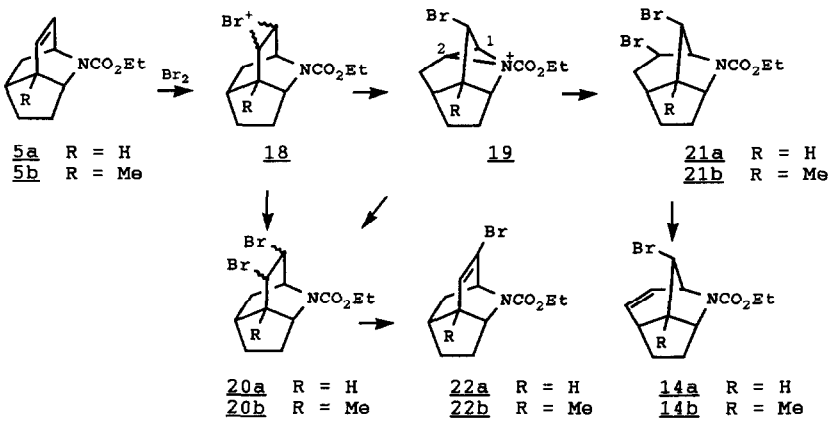
Base Structure		Relative rates/Site of Me Substitution
4a	Parent	5-Me > 4-Me > 3-Me > 6-Me
4b	3-Me	5-Me > 4-Me > -- > 6-Me
4c	4-Me	5-Me > -- 3-Me > 6-Me
4d	5-Me	-- 4-Me > 3-Me > 6-Me
4e	6-Me	5-Me > 4-Me > 3-Me > --

Bromination/Dehydrobromination of Cycloadducts 5

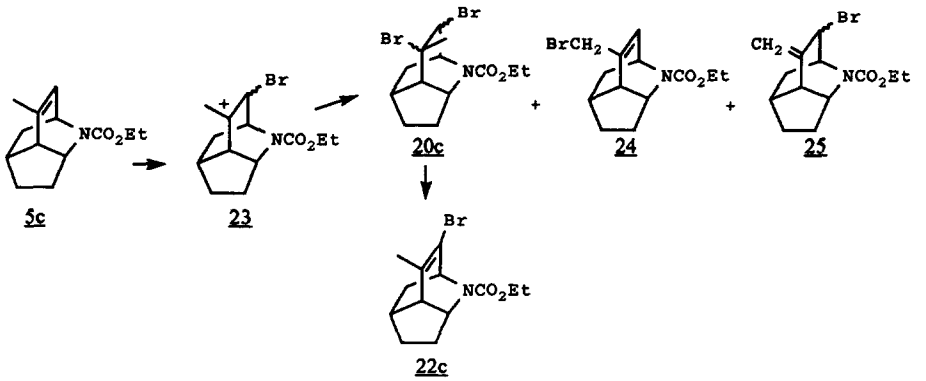
Participation of an N-alkoxycarbonyl substituent during addition of bromine to a nearby olefinic site can lead to rearranged structures [3a,3b] As earlier described in Scheme 1,

substituents on the double bond of a tricycle 5 might influence the equilibria between bromonium ions, open cations and aziridinium ion species and affect rearrangements In order to test this hypothesis, the cycloadducts 5a (parent), 5b (7-methyl), 5c (8-methyl), and 5s (7,9-dimethyl) were reacted with bromine in methylene chloride [3a]

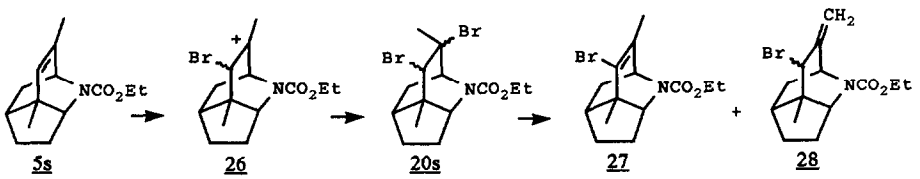
Bromination of azatricyclic compound 5a was carried out at -78° C in dichloromethane Formation of the anti-bromonium ion 18 by attack from the face opposite the bulky carbamate substituent could be followed by attack of bromide ion to give dibromide 20a In the alternative, nitrogen participation can result in rearrangement of the bromonium ion 18 to the aziridinium ion 19, which can be attacked by bromide ion position 1 and 2 to give a mixture of the dibromides 20a and 21a Dehydrobromination of the dibromides with diazabicyclo[5 4 0]undecene (DBU) in refluxing xylene gave in 76% isolated yield a 32 68 mixture of vinyl bromide 22a, which showed a single olefinic proton at δ6 34 (H-8), and rearranged azatricycle 14a, which showed two olefinic resonances at δ6 0 (H-2) and δ5 72 (H-3) Azatricycle 5b similarly afforded in 75% yield a 33 67 mixture of vinyl bromide 22b and rearranged azatricycle 14b The doublet (J = 5 Hz) at δ4 00 indicates that the H-9 proton of 14b is anti to the olefinic bond with an H-1/H-9 dihedral angle of about 40° rather than syn to the olefinic bond with an H-1/H-9 dihedral angle of nearly 90°



Bromination of azatricycle 5c, which is methyl substituted at the olefinic C-8 position, can afford a tertiary cation 23 This ion can compete favorably with either a bromonium ion or an aziridinium ion Loss of a proton from ion 23 and allylic isomerization afforded 30% of a 90 10 mixture of allylic bromides 24, which showed an ^{1}H NMR olefinic resonance at δ6 56, and 25, of undefined stereochemistry, whose exo-methylene resonance appeared at δ5 28 Attack of bromide ion on 23 led to 52% of a dibromide 20c, which upon treatment with DBU afforded 92% of vinyl bromide 22c identified by the absence of vinyl protons Notably, base removes the most acidic proton nearest to the electron-withdrawing carbamate substituent



The azatricycle 5s, which is methyl substituted at the olefinic position C-9, afforded 85% of a mixture of dibromides 20s The 9-methyl group stabilizes the tertiary cation 26 and eliminates nitrogen participation via the aziridinium ion pathway Dibromide 20s was dehydrobrominated with difficulty to give an inseparable 56 44 (NMR) mixture of vinyl bromide 27, which has no olefinic protons, and allylic bromide 28, of undefined stereochemistry, which has ^{1}H NMR resonances at δ5 45 (2H) for the exo-methylene protons



Conclusion

It has been shown that azatricycles 5 can be synthesized with alkyl substitution at C-1, and C-6 through C-10 using the intramolecular Diels-Alder cycloaddition of appropriate alkyl-substituted N-alkoxycarbonyl-2[3-butenyl]-1,2-dihydropyridines 4 The latter are derived from 3-butenyl Grignard reagents, alkyl chloroformates and alkyl pyridines If C-8 and C-9 of 5 are unsubstituted, interception of bromonium ions by neighboring group participation of the carbamate group leads to an aziridinium ion 19, which gives rise to a rearranged azatricycle 14 Alkyl substitution at C-8 or C-9 of 5 suppresses the onset of nitrogen migration to form rearranged structures and leads to formation of allylic bromides and unrearranged dibromides 20 Reaction of unrearranged dibromides 20 with DBU affords vinyl bromides 22 rather than allylic bromides

EXPERIMENTAL

Infrared spectra were recorded as neat oils on sodium chloride plates using a Perkin-Elmer 710B or 727B spectrometer Routine proton NMR spectra were obtained in $CDCl_3$ solutions

with tetramethylsilane as internal standard using a Perkin-Elmer R-32 90MHz spectrometer or 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 Carbon-13 spectra were recorded on a Varian XL-100 instrument operating at 25 2 MHz using a Nicolet NTCFT 1180 pulse system $CDCl_3$ was assigned as 76 910 ppm as the standard, chemical shifts were computer generated Exact mass measurements were taken on an RMH-2 Hitachi Perkin-Elmer mass spectrometer or a VG Micromass 7035 spectrometer at an ionization energy of 70 eV at the University of Pennsylvania Mass Spectrometry Center Ultraviolet spectra were recorded on an H P 8450 A Hewlett Packard UV/VIS spectrophotometer or a Perkin Elmer 330 spectrometer Gas chromatograms were recorded on a Varian Aerograph 702 with a 10% SE-30 column (1/4" x 3m) at flow rates of 60 mL/min and column temperature of 160°C Analyses were performed by Microtech Labs, Inc , Skokie, Il

Materials Tetrahydrofuran was freshly distilled from sodium, decalin was distilled over calcium hydride and stored over sodium spheres Flash column chromatography was performed using Baker Silica gel 250-400 mesh, and thin layer chromatography was performed using Analtech silica gel plates (GF) containing fluorescent indicator The substituted pyridines were purchased from Aldrich Chemical Co or Reilly Coal Tar Co , 1-bromo-3-methyl-3-butene, cis-1-bromo-3-hexene, and trans-1-bromo-3-hexene were prepared from commercially available alcohols according to the procedure of Maercker and Weber [9]

General procedure for synthesis of N-ethoxycarbonyl-2-(3-butenyl)-1,2-dihydropyridines 4 To a suspension of 0 58 g (24 mmoles) of magnesium turnings in dry tetrahydrofuran (25 mL) under nitrogen there was added dropwise 3 25g of 4-bromo-1-butene (24 mmoles) After formation of the Grignard reagent was completed (30 min), the solution was cooled to 0° and the appropriate pyridine derivative (20 mmoles) in dry tetrahydrofuran (5 mL) was added followed by dropwise addition of ethyl chloroformate (2 16 g, 20 mmoles) over 30 min in such a way that the reaction temperature remained below 0° The resulting solution was stirred for one hr, then warmed to room temperature The reaction mixture was poured into ice water (100 mL), which was extracted with ether (3 x 50 mL) The combined organic layers were washed successively with 2% hydrochloric acid, cold water (50 mL) and brine solution (10 mL), then dried over magnesium sulfate, filtered, and the solvent was removed in vacuo to yield a mixture containing the N-ethoxycarbonyl-2-(3-butenyl)-1,2-dihydropyridine 4 and an N-ethoxycarbonyl-4-(3-butenyl)-1,4-dihydropyridine 13 The crude dihydropyridines were purified by flash chromatography using 4 1 hexane/ether as eluent The ratio of 1,2- to 1,4-dihydropyridines could be determined by gas chromatography or NMR analysis of mixtures using H-6 of 4 and 13 and H-4 of 13

N-Ethoxycarbonyl-2-(3-butenyl)-1,2-dihydropyridine (4a) Pyridine (1 58g) yielded 3 6g (82%) of a product mixture containing 65% 4a (GC retention time 5 7 min), NMR δ6 9-6 55 (m H-6), 5 8- 5 55 (m, H-3/H-4/H-3'), 5 20-5 00 (m, H-5/H-4'), 5 20 (m, H-2), 4 20 (q, J = 7 Hz, OCH_2), 2 3-1 9 (m, H-2'), 1 9-1 45 (m, H-1'), 1 25 (t, J = 7 Hz, CH_3), IR 1705 cm^{-1}, UV, λ_{max} 298 (ϵ = 6100) Admixed was 35% of N-ethoxycarbonyl-4-(3-butenyl)-1,2-dihydropyridine (13a) (GC retention time 8 1 min), NMR δ6 90-6 65 (br, H-2/H-6), 4 9 (m, H-5/H-3), 2 96 (m, H-4), other shifts overlapped with those of 4a HRMS for 4a and 13a calcd for $C_{12}H_{17}NO_2$ m/z 207 1259, found m/z 207 1262

N-ethoxycarbonyl-2-(3-butenyl)-3-methyl-1,2-dihydropyridine (4b) and N-ethoxycarbonyl-2-(3-butenyl)-5-methyl-1,2-dihydropyridine (4d) From 3-picoline (1 86 g) there was obtained 3 2 g (73%) of a mixture containing 48% 4b (GC retention time 7 0 min), NMR δ6 8-6 46 (m, H-6), 6 16-5 56 (m, H-4, H-3'), 5 26 (m, H-5), 5 18-4 82 (m, H-4'), 4 73 (m, H-2), 4 22 (q, J = 7 Hz, OCH_2), 2 23-1 9 (m, H-2'), 1 80 (s, Me), 1 85-1 50 (m, H-1'), 1 27 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 295 (ϵ = 5500) Also present was 12% 4d (GC retention time 7 0 min), NMR δ6 8-6 46 (m, H-6), 6 16-5 26 (m, H-4/H-3'/H-3), 5 18-4 82 (m, H-4'), 4 73 (m, H-2), 4 22 (q, J = 7 Hz, OCH_2), 2 23-1 9 (m, H-2'), 1 65 (s, Me), 1 85-1 5 (m, H-1'), 1 27 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 300 (ϵ = 5300) The third component was N-ethoxycarbonyl-4-(3-butenyl)-3-methyl-1,2-dihydropyridine (13) (GC retention time 10 min), NMR δ6 8-6 46 (m, H-2/H-6), 2 92 (q, J = 6 Hz, H-4), other peaks the same as for 4b HRMS of 4b and 4d calcd for $C_{13}H_{19}NO_2$ m/z 221 1415, found m/z 221 1412

N-Ethoxycarbonyl-2-(3-butenyl)-4-methyl-1,2-dihydropyridine (4c) From 4-picoline (1 86 g)

there was obtained 3 9 g (73%) of a mixture containing 83% 4c, NMR δ6 9-6 6 (m, H-6), 6 0-5 35 (m, H-3'/H-4'/H-3/H-5), 4 82-5 20 (m, H-2), 4 22 (q, J = 7 Hz, OCH_2), 2 23-1 90 (m, H-2'), 1 8-1 5 (m, H-1'), 1 26 (t, J = 7 Hz, Me), IR, 1710 cm^{-1}, UV, λ_{max} 295 (ε = 5600) The 13% component was N-ethoxycarbonyl-4-(3-butenyl)-4-methyl-1,4-dihydropyridine (13c), NMR δ6 92-6 55 (m, H-2/H-6), 5 10 (m, H-3/H-5), other peaks the same as for 4c HRMS of 4c and 13c calcd for $C_{13}H_{19}NO_2$ m/z 221 1416, found m/z 221 1407

N-Ethoxycarbonyl-2-(3-butenyl)-6-methyl-1,2-dihydropyridine (4e) From 2-picoline (1 86 g) there was obtained 2 3 g (52%) of a mixture containing 43% 4e (GC retention time 6 min), NMR δ6 0-5 4 (m, H-4/H-5/H-3'/H-3), 5 1-4 7 (m, H-4'), 4 7 (m, H-2), 4 15 (q, J = 7 Hz, OCH_2), 2 2-1 5 (m, H-2'/H-1'), 2 13 (s, Me), 1 25 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 290 (ε = 4900) The 57% component was N-ethoxycarbonyl-4-(3-butenyl)-6-methyl-1,2-dihydropyridine (13e) (GC retention time 10 3 min), NMR δ6 90 (m, H-6), 5 0-4 8 (m, H-3/H-5), 2 85 (m, H-4), other peaks as for 4e HRMS of 4e and 13e calcd for $C_{13}H_{18}NO_2$ (P - 1) m/z 220 1337, found m/z 220 1328

N-Methoxycarbonyl-2-(3-butenyl)-6-methyl-1,2-dihydropyridine (4f) From 2-picoline (1 86 g) and methyl chloroformate (1 89 g, 20 mmol) there was obtained 2 3 g (56%) of a mixture containing 49% 4f, NMR δ6 0-5 3 (m, H-3/H-4/H-5/H-3'), 5 15-4 62 (m, H-2/ H-4'), 3 74 (s, OMe), 2 13 (s, Me), 2 1-1 1 (m, H-1'/H-2'), IR 1720 cm^{-1}, UV, λ_{max} 288 (ε = 3700) The 51% component was N-methoxycarbonyl-4-(3-butenyl)-2-methyl-1,2-dihydropyridine (13f), NMR δ6 82 (d, J = 9 Hz), 6 0-5 5 (m, H-5/H-3'), 5 2-4 68 (m, H-3/H-4'), 3 73 (s, OMe), 2 8 (m, H-4), 2 15 (s, Me), 2 0-1 18 (m, H-1'/H-2') HRMS of 4f and 13f calcd for $C_{12}H_{17}NO_2$ m/z 207 1259, found m/z 207 1243

N-Ethoxycarbonyl-2-(3-butenyl)-3-ethyl-1,2-dihydropyridine (4g) and N-Ethoxycarbonyl-2-(3-butenyl)-5-ethyl-1,2-dihydropyridine (4i) From 3-ethylpyridine (2 14 g) there was obtained 3 7 g (78%) of a mixture containing 4g, 4i, and N-ethoxycarbonyl-4-(3-butenyl)-3-methyl-1,4-dihydropyridine 13g in a 1 1 1 ratio as determined by NMR integration and TLC enrichment of the isomers (4 1 hexane/ether) Spectral data for 4g are NMR δ6 8-6 4 (m, H-6), 6 1-5 5 (m, H-4/H-3'), 5 50-4 8 (m, H-5/H-4'/H-2), 4 25 (q, J = 7 Hz, OCH_2), 2 3-1 8 (m, CH_2), 1 80-1 45 (m, H-1', H-2'), 1 32 (t, J = 7 Hz, Me), 1 09 (t, J = 7 Hz, Me), IR 1720 cm^{-1}, UV, λ_{max} 297 (ε = 4900) Spectral data for 4i are NMR δ6 8-6 4 (m, H-6), 6 1-5 5 (m, H-3/H-4/H-3'), 5 2-4 8 (m, H-4'), 4 8-4 6 (m, H-2), 4 25 (q, J = 7 Hz, OCH_2), other peaks as for 4g, IR 1720 cm^{-1}, UV, λ_{max} 300 (ε = 5600) Spectral data for 13g are NMR δ6 9-6 4 (m, H-6/H-2), 5 2-4 8 (m, H-5), 3 2-2 9 (m, H-4), other peaks as for 4g HRMS of an isomeric mixture calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1573

N-Ethoxycarbonyl-2-(3-butenyl)-4-ethyl-1,2-dihydropyridine (4h) From 4-ethylpyridine (2 07 g) there was obtained 3 2 g (68%) of 4h, R_f = 0 9 (4 1 hexane/ether), NMR δ7 0-6 5 (m, H-6), 6 1-5 5 (H-3/H-3'), 5 5-4 65 (m, H-5/H-4'), 4 6-4 09 (m, H-2 and q, J = 7 Hz, OCH_2), 2 8-0 9 (br, 12 H), IR 1720 cm^{-1}, UV, λ_{max} 292 (ε = 5400) HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1576 No N-ethoxycarbonyl-4-(3-butenyl)-4-ethyl-1,2-dihydropyridine 13h was detected

N-ethoxycarbonyl-2-(3-butenyl)-6-ethyl-1,2-dihydropyridine (4j) From 2-ethylpyridine (2 14 g) there was obtained 2 03 g (43%) of a mixture containing 4j and N-ethoxycarbonyl-4-(3-butenyl)-2-ethyl-1,2-dihydropyridine 13j in a 40 60 ratio by NMR analysis Spectral data for 4j are NMR δ6 1-5 4 (m, H-3'/H-3/H-4/H-5), 5 2-4 7 (m, H-2/H-4'), 4 22 (q, J = 7 Hz, OCH_2), 2 3-1 4 (m, 6H), 1 28 (t, J = 7 Hz, Me), 1 03 (t, J = 7 Hz, Me), IR 1720 cm^{-1}, UV, λ_{max} 287 (ε = 6000) Spectral data for 13j are NMR δ6 85 (d, J = 8 Hz, H-2), 6 05-5 60 (m, H-3'/H-3), 4 80-5 20 (m, H-4'/H-5), 4 20 (q, J = 7 Hz, OCH_2), 2 80 (qnt, J = 6 Hz, H-4), 2 6-1 55 (m, 6H), 1 30 (t, J = 7 Hz, Me), 1 11 (t, J = 8 Hz, Me), IR 1720 cm^{-1} HRMS of the isomeric mixture calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1566

N-Ethoxycarbonyl-2-(3-butenyl)-4-propyl-1,2-dihydropyridine (4k) From 4-propylpyridine (2 42 g) there was obtained 3 6 g (72%) of 4k, R_f = 0 71 (4 1 hexane/ether), NMR δ6 82-6 45 (m, H-6), 6 0-5 4 (m, H-3/H-3'), 5 4-4 4 (m, H-5/H-2/H-4'), 4 10 (q, J = 7 Hz, OCH_2), 2 4-1 1 (m, 8H), 1 2 (t, J = 7 Hz, Me), 0 8 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 296 (ε = 5300), HRMS calcd for $C_{15}H_{23}NO_2$ m/z 249 1729, found m/z 249 1735

N-Ethoxycarbonyl-2-(3-butenyl)-4-isopropyl-1,2-dihydropyridine (41). From 4-isopropylpyridine (2 42 g) there was obtained 4 23 g (85%) of 41, R_f = 0 53 (4 1 hexane/ether), NMR δ6 85-6 5 (m, H-6), 6 0-5 4 (m, H-3/H-3'), 5 4-4 5 (m, H-5/H-4'/H-2), 4 15 (q, J = 7 Hz, OCH_2), 2 5-1 4 (m, 5H), 1 22 (t, J = 7 Hz, Me), 0 95 (d, J = 6 Hz, 6H), IR 1710 cm^{-1}, UV, λ_{max} 289 (ε = 6000), HRMS calcd for $C_{15}H_{23}NO_2$ m/z = 249 1729, found 249 1749

N-Ethoxycarbonyl-2-(3-butenyl)-4-isopentyl-1,2-dihydropyridine (4m) From 4-isopentylpyridine (2 98 g) there was obtained 4 76 g (86%) of 4m, R_f = 0 8 (4 1 hexane/ether), NMR δ6 90-6 55 (m, H-6), 6 10-4 60 (m, H-3/H-3'/H-4'/H-5/H-2), 4 23 (q, J = 7 Hz, OCH_2), 2 3-1 2 (m, 9H), 1 31 (t, J = 7 Hz, Me), 0 80 (t, J = 6 Hz, 6 H), IR 1710 cm^{-1}, UV, λ_{max} 292 (ε = 5000), HRMS calcd for $C_{17}H_{27}NO_2$ m/z 277 2042, found m/z 277 2050

N-Ethoxycarbonyl-2-(3-butenyl)-4-t-butyl-1,2-dihydropyridine (4n) From 4-t-butylpyridine (2 7 g) there was obtained 4 2 g (80%) of 4n, R_f = 0 65 (4 1 hexane/ether), NMR δ6 7-6 4 (m, H-6), 5 9-4 4 (m, H-3/H-5/H-3'/H-4'/H-2), 4 02 (q, J = 7 Hz, OCH_2), 2 1-1 25 (m, 4 H), 1 06 (t, J = 7 Hz, Me), 0 85 (s, 9H), IR 1700 cm_{-1}, UV, λ_{max} 293 (ε = 5500), HRMS calcd for $C_{16}H_{25}NO_2$ m/z 263 1885, found m/z 263 1874

N-Ethoxycarbonyl-2-(3-butenyl)-4-phenyl-1,2-dihydropyridine (4o) From 4-phenylpyridine (3 10 g) there was obtained 3 2 g (57%) of 4o, R_f = 0 8 (4 1 hexane/ether), NMR δ7 5-7 2 (m, Ph), 6 9 (m, H-6), 6 05-5 5 (m, H-3/H-3'), 5 2-4 8 (m, H-4'/H-5/H-2), 4 25 (q, J = 8 Hz, OCH_2), 2 5-1 5 (m, 4H), 1 32 (t, J = 8 Hz, Me), IR 1700 cm^{-1}, UV, λ_{max} 308 (ε = 4000), HRMS calcd for $C_{18}H_{21}NO_2$ m/z 283 1572, found m/z 283 1568

N-Ethoxycarbonyl-2-(3-butenyl)-3,6-dimethyl-1,2-dihydropyridine (4p) From 2,5-lutidine (2 14 g) there was obtained 3 2 g (73%) of a mixture containing 47% of 4p (GC retention time 7 7 min) and 53% of N-ethoxycarbonyl-4-(3-butenyl)-2,5-dimethyl-1,4-dihydropyridine 13p (GC retention time 11 2 min) Spectral data for 4p are NMR δ6 12-5 51 (m, H-3'/H-4), 5 40-5 32 (m, H-5), 5 2-4 78 (m, H-4'), 4 60 (m, H-2), 4 20 (q, J = 7 Hz, OCH_2), 2 15 (s, Me), 2 2-2 0 (m, H-2'), 1 90 (s, Me), 1 8-1 6 (m, H-1'), 1 30 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 286 (ε = 5300) Spectral data for 13p are NMR δ6 75 (br, H-6), 4 81 (br, H-3), 2 86 (br, H-4), other peaks are as for 4p HRMS of the mixture calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1545

N-Ethoxycarbonyl-2-(3-butenyl)-3,4-dimethyl-1,2-dihydropyridine (4q) and N-ethoxycarbonyl-2-(3-butenyl)-4,5-dimethyl-1,2-dihydropyridine (4t) From 3,4-lutidine (2 17 g) there was obtained 3 4 g (77%) of a mixture containing 61% of 4q (GC retention time 9 0 min), 15% of 4t and 24% of N-ethoxycarbonyl-4-(3-butenyl)-3,4-dimethyl-1,4-dihydropyridine 13q (GC retention times 10 4 min at 165°) Spectral data for 4q are NMR δ6 7-6 4 (m, H-6), 6 56-5 00 (m, H-3'/H-4'/H-5/H-2), 4 18 (q, J = 7 Hz, OCH_2), 2 12-1 90 (m, H-2'), 1 70 (s, Me), 1 85-1 50 (m, H-1'), 1 27 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 289 (ε = 4600) Spectral data for 4t are NMR δ6 7-6 4 (m, H-6), 6 56-5 0 (m, H-3'/H-4'/H-3/H-2), 4 18 (q, J = 7 Hz, OCH_2), 2 12-1 9 (m, H-2'), 1 70 (s, 6H), 1 85-1 50 (m, H-1'), 1 27 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 299 (ε = 4300) Spectral data for 13q are NMR δ6 7-6 4 (H-6/H-2), 5 20 (m, H-5), others are the same as 4t HRMS of the mixture calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1572

N-Ethoxycarbonyl-2-(3-butenyl)-4,6-dimethyl-1,2-dihydropyridine (4r) From 2,4-lutidine (2 14 g) there was obtained 3 6 g (77%) of an 87 13 mixture of 4r and N-ethoxycarbonyl-4-(3-butenyl)-2,4-dimethyl-1,2-dihydropyridine (13r) (GC retention time 8 7 min for both) Spectral data for the mixture of isomers are NMR δ6 86 (d, J = 8 Hz, H-6 of 13r, 13% of an OCH_2 proton), 6 05-4 8 (H-3'/H-4'/H-3/H-5), 4 7 (m, H-2), 4 17 (q, J = 7 Hz, OCH_2), 2 12 (s, 6-Me), 2 2-1 4 (m, 4H), 1 69 (s, 4-Me), 1 27 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV (corrected) for 4r, λ_{max} 287 (ε = 5100), HRMS of the mixture of isomers calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1570

N-Ethoxycarbonyl-2-(3-butenyl)-3,5-dimethyl-1,2-dihydropyridine (4s) From 3,5-lutidine (2 14 g) there was obtained 3 60 g (82%) of a 45 55 mixture of 4s (GC retention time 12 0 min) and N-ethoxycarbonyl-4-(3-butenyl)-3,5-dimethyl-1,4-dihydropyridine (13s) (GC retention time 12 0 min) Spectral data for 4s are NMR δ6 80-6 54 (m, H-6), 6 0-4 5 (m, H-3'/H-4'/H-4/H-2), 4 21 (q, J = 7 Hz, OCH_2), 2 8-1 4 (m, 4 H), 1 66 (s, 6H), 1 27 (t, J = 7 Hz, Me),

IR 1710 cm^{-1}, UV, λ_{max} 297 (ϵ = 6700) Spectral data for 13s are NMR δ6 48-6 25 (m, H-6/H-2), 2 84 (m, H-4), others as for 4s HRMS of the isomeric mixture calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1547

N-Ethoxycarbonyl-2-(3-butenyl)-5,6-dimethyl-1,2-dihydropyridine (4u) From 2,3-lutidine (2 14 g) there was obtained 2 6 g (59%) of a 1 3 mixture of 4u (GC retention time 7 7 min) and N-ethoxycarbonyl-4-(3-butenyl)-2,3-dimethyl-1,4-dihydropyridine (13u) (GC retention time 9 8 min) Spectral data for the mixture of isomers is NMR δ6 80 (d, J = 8 Hz, H-6 of 13u, 75% of an OCH_2 proton), 6 02-4 79 (m, H-4/H4'/H-3'/H-5/H-3/H-2), 4 17 (q, J = 7 Hz, OCH_2), 2 65 (m, H-4 of 13u), 2 2-1 86 (m, H-2'), 2 03 (s, 3H), 1 8-1 4 (m, H-1'), 1 67 (s, 3H), 1 25 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV of 4u, λ_{max} 287 (ϵ = 5600), HRMS of the isomeric mixture calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1574

N-Ethoxycarbonyl-2-(3-methyl-3-butenyl)-1,2-dihydropyridine (4v) Pyridine (0 79 g, 0 01 moles) was reacted with the Grignard reagent prepared from 1-bromo-3-methyl-3-butene and then acylated with ethyl chloroformate according to the general procedure to afford 1 2 g (54 %) of a 1 1 mixture of 4v, TLC R_f 0 68, and N-ethoxycarbonyl-4-(3-methyl-3-butenyl)-1,2-dihydropyridine (13v), which was not characterized Spectral data for 4v are NMR δ6 72 (m, H-6), 5 9 (m, H-4), 5 6 (m, H-3), 5 25 (m, H-5), 4 82 (m, H-2), 4 72 (s, H-4'), 4 25 (q, J = 8 Hz, OCH_2), 2 05 (m, H-2'), 1 9-1 5 (m, H-1'), 1 74 (s, Me), 1 30 (t, J = 8 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 299 (ϵ = 4200), HRMS calcd for $C_{13}H_{19}NO_2$ m/z 221 1416, found m/z 221 1414

N-Ethoxycarbonyl-2-(cis-3-hexenyl)-1,2-dihydropyridine (4w) Pyridine (0 79 g, 0 01 moles) was reacted with the Grignard reagent prepared from cis-1-bromo-3-hexene and then acylated with ethyl chloroformate according to the general procedure to afford 1 2 g (51%) of a 6 4 mixture of 4w, TLC R_f 0 70, and N-ethoxycarbonyl-4-(cis-3-hexenyl)-1,4-dihydropyridine 13w Spectral data are, for the mixture, NMR δ7 0-6 6 (m, H-6), 6 1-4 65 (H-3/H-4/H-5/H-3'/H-4'/H-2), 4 24 (q, J = 7 Hz, OCH_2), 3 1-2 9 (m, H-4 of 13w), 2 5-1 8 (m, 6 H), 0 98 (t, J = 7 Hz, Me), IR 1710 cm^{-1}, UV, λ_{max} 298 (ϵ = 4800) HRMS of the isomers calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1570

N-Ethoxycarbonyl-2-(trans-3-hexenyl)-1,2-dihydropyridine (4x) Pyridine (0 79 g, 0 01 moles) was reacted with the Grignard reagent prepared from trans-1-bromo-3-hexene and then acylated with ethyl chloroformate according to the general procedure to afford 1 2 g (54%) of a 60 40 mixture of 4x, TLC R_f 0 72, and N-ethoxycarbonyl-4-(trans-3-hexenyl)-1,2-dihydropyridine (13x), mixture NMR δ7 0-6 6 (bm, H-6), 6 5-4 68 (H-3'/H-4'/H-3/H-4/H-5/H-2), 4 25 (q, J = 7 Hz, OCH_2), 3 1-2 8 (m, H-4 of 13x), 2 5-1 5 (m, 6 H), 1 3 (t, J = 7 Hz, Me), 0 98 (t, J = 7 Hz, Me), IR 1720 cm^{-1}, UV (4x), λ_{max} 298 (ϵ = 5400), HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found 235 1569

General Procedure for intramolecular cycloaddition of N-ethoxycarbonyl-2-(3-butenyl)-1,2-dihydropyridines 4 to N-ethoxycarbonyl-2-azatricyclo-[4.3 1 $0^{3,7}$]dec-8-enes 5 After the quantity of the N-alkoxycarbonyl-1,2-dihydropyridine 4 was calculated from the known ratio of 4 to the isomeric 13, about 300 mg of 4 was dissolved in decalin (30 mL, approximately 1 mL/10 mg) and the solution was refluxed under nitrogen until the half-life data in Table 2 indicated most of 4 to be reacted The cooled reaction mixture was then poured through a column of silica gel, which was eluted with hexane (100 mL) to remove decalin, then 4 1 hexane/ether to elute unreacted 13 and the cycloadduct 5 Proton NMR peaks for adducts 5 are generally broad multiplets because of overlap of carbamate conformers Ethyl carbamate shifts are in the ranges δ156 8-153 5 (C=O), δ60 8-59 0 (CH_2), δ15 0-13 8 (CH_3)

Kinetic procedure for following conversion of 4 to 5 The N-alkoxycarbonyl-1,2-dihydropyridine 4 was added using a syringe into a 100 mL 3-necked flask provided with a thermometer, condenser and septum and containing 1 mL refluxing decalin (192°)/10 mg of substrate under a nitrogen atmosphere Immediately after the addition of the sample, 0 3 mL of the refluxing solution, collected using a syringe, was added to a vial and cooled in an ice bath Following this 0 hour sample, aliquots were collected at appropriate 30 min or hourly time intervals depending upon the reaction rate The aliquots collected either were injected into a gas chromatograph or, in the case of conversion of 4o to 5o, into a Waters HPLC Model 440 using a C_{18} reverse phase column with 2% water in methanol as eluent The quantity of reactants remaining and products (P) formed was analyzed from the areas of

the appropriate peaks using an integrating recorder or by cutting and weighing xeroxed copies of the recorded peaks The cutting and weighing method and integration methods agreed within a range of ± 3-5% Rate determinations were generally performed in duplicate for reproducibility of the rate constants (k) and half-lives ($t^{1/2}$), which were determined from the equations $k = 1/t \times \ln [100/(100 - \% P)]$ and $t^{1/2} = 0.693/k$

N-Ethoxycarbonyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5a). After 20 hr 4a (0 91 g) provided 590 mg (65%) of 5a (GC retention time 8 9 min), IR 1675 cm^{-1}, ^1H NMR δ6 53 (dd, J = 8 Hz, 6 Hz, H-9), 6 23 (ddd, J = 8 Hz, 6 Hz, 1 Hz), 4 55 (br, H-1), 4 10 (q, J = 7 Hz, OCH_2), 3 60 (br, H-3), 2 56 (br, H-7), 2 40-1 40 (m, 7 H), 1 20 (t, J = 7 Hz, Me), ^{13}C NMR δ134 6 (d, C-9), 129 5 (d, C-8), 56 3 (d, C-3), 44 1 (d, C-1), 42 2 (d, C-7), 38 0 (t, C-10), 31 9 (d, C-6), 30 8 and 30 4 (t and t, C4/C-5) Anal Calcd for $C_{12}H_{17}NO_2$ C, 69 54, H, 8 27, N, 6 76 Found C, 69 33, H, 8 12, N, 6 75

N-Ethoxycarbonyl-7-methyl-2-azatricyclo[4 3.1 $0^{3,7}$]dec-8-ene (5b) and N-ethoxycarbonyl-9-methyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5d). After 18 hr a 4 1 mixture of 4b and 4d (1 38 g) afforded 980 mg (71%) of a 4 1 mixture of 5b and 5d, which was separated by elution through silica gel with 4 1 hexane/ether Spectral data for 5b are ^1H NMR δ6 50 (dd, J = 8 Hz, 6 Hz, H-9), 5 88 (dd, J = 8 Hz, 1 Hz, H-8), 4 60 (m, H-1), 4 10 (q, J = 7 Hz, OCH_2), 3 34 (m, H-3), 2 4-1 4 (m, 7H), 1 20 (t, J = 7 Hz, Me), 1 12 (s, Me), ^{13}C NMR δ135 1 (d, C-9 and C-8), 61 2 (d, C-3), 45 4 (s, C-7), 44 2 (d, C-1), 39 5 (t, C-10), 37 4 (d, C-6), 29 0 and 28 3 (t and t, C4/C-5), 20 4 (q, CH_3), IR 1680 cm^{-1}, spectral data for 5d are ^1H NMR δ5 80 (br, H-8), 4 50 (br, H-1), 4 10 (q, J = 7 Hz, OCH_2), 3 65 (br, H-3), 2 45 (br, H-7), 2 1-1 4 (m, 7 H), 1 80 (s, Me), 1 20 (t, J = 7 Hz, Me), ^{13}C NMR δ134 8 (d, C-9), 121 6 (d, C-8), 56 6 (d, C-3), 49 1 (d, C-1), 42 5 (d, C-7), 37 6 (t, C-10), 33 0 (d, C-6), 30 5 and 30 1 (t and t, C4/C-5), 18 4 (q, CH_3), IR 1680 cm^{-1} Anal Calcd for $C_{13}H_{19}NO_2$ C, 70 24, H, 8 72, N, 6 11 Found C, 70 56, H, 8 65, N, 6 33

N-Ethoxycarbonyl-8-methyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5c) After 5 hr 4c (2 79 g) afforded 1 7 g (60%) of 5c, ^1H NMR δ6 12 (br, H-9), 4 50 (br, H-1), 4 11 (q, J = 7 Hz, OCH_2), 3 65 (br, H-3), 2 36 (br, H-7), 2 35-1 40 (m, 7 H), 1 81 (s, Me), 1 21 (t, J = 7 Hz, Me), ^{13}C NMR δ138 0 (s, C-8) 126 8 (d, C-9), 55 6 (d, C-3), 44 4 (d, C-1), 47 4 (d, C-7), 38 4 (t, C-10), 31 5 (d, C-6), 30 1 and 29 8 (t and t, C4/C-5), 19 3 (q, CH_3), IR 1680 cm^{-1} Anal Calcd for $C_{13}H_{19}NO_2$ C, 70 56, H, 8 65, N, 6 33 Found C, 70 59, H, 8 52, N, 6 26

N-Ethoxycarbonyl-1-methyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5e) After 19 hr 4e (990 mg) afforded 266 mg (27 %) of 5e, ^1H NMR δ6 4-6 1 (br, H-8/H-9), 4 04 (q, J = 7 Hz, OCH_2), 3 71 (br, H-3), 2 50 (br, H-7), 2 15-1 42 (m, 7 H), 1 73 (s, Me), 1 21 (t, J = 7 Hz, Me), ^{13}C NMR δ139 2 (d, C-9), 129 1 (d, C-8), 58 2 (d, C-3), 52 6 (s, C-1), 42 0 (d, C-7), 37 4 (t, C-10), 35 0 (d, C-6), 31 2 and 30 5 (t and t, C4/C-5), 24 3 (q, CH_3), IR 1680 cm^{-1} Anal Calcd for $C_{13}H_{19}NO_2$ C, 70 56, H, 8 65, N, 6 33 Found C, 70 29, H, 8 56, N, 6 18

N-Methoxycarbonyl-1-methyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5f) After 12 hr 4f (800 mg) afforded 83 mg (10 4%) of 5f, TLC R_f 0 33, ^1H NMR δ6 27 (br, H-8/H-9), 3 72 (br, H-3), 3 63 (s, OMe), 2 5 (br, H-7), 2 5-1 2 (m, 7H), 1 88 (s, Me), ^{13}C NMR δ139 6 (d, C-9), 129 2 (d, C-8), 58 3 (d, C-3), 51 1 (s, C-1), 52 8 (d, C-7), 42 2 (d, C-6), 35 1 (t, C-10), 31 3 and 30 6 (t and t, C4/C-5), 24 3 (q, CH_3), IR 1720 cm^{-1} HRMS calcd for $C_{12}H_{17}NO_2$ m/z 207 1259, found m/z 207 1256

N-Ethoxycarbonyl-7-ethyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5g) After 12 hr 4g (230 mg) afforded 166 mg (72%) of 5g, TLC R_f 0 38, ^1H NMR δ6 48 (br, H-9), 6 02 (br, H-8), 4 56 (br, H-1), 4 12 (q, J = 7 Hz, OCH_2), 3 47 (br, H-3), 2 5 (br, H-7), 2 35-1 4 (m, 9 H), 1 25 (t, J = 7 Hz, Me), 0 95 (t, J = 7 Hz, Me), ^{13}C NMR δ134 9 and 132 8 (d and d, C-8/C-9), 59 3 (d, C-3), 44 1 (d, C-1), 49 9 (s, C-7), 39 5 (t, C-10), 34 8 (d, C-6), 29 2 and 28 7 (t and t, C4/C-5), 25 1 (t, CH_2), 8 6 (q, CH_3), IR 1720 cm^{-1} HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1568

N-Ethoxycarbonyl-8-ethyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5h) After 3 hr 4h (420 mg) afforded 316 mg (75 %) of 5h, TLC R_f 0 42, ^1H NMR δ6 48 (br, H-9), 4 53 (br, H-1), 4 11 (q, J = 7 Hz, OCH_2), 3 65 (br, H-3), 2 45 (br, H-7), 2 35-1 4 (m, 9 H), 1 25 (t, J = 7 Hz, Me), 1 05 (t, J = 7 Hz, Me), ^{13}C NMR δ144 6 (s, C-8), 125 3 (d, C-9), 56 4 (d, C-3), 46 6 (d, C-

1), 44 7 (d C-7), 38 9 (t, C-10), 32 3 (d, C-6), 30 6 and 29 9 (t and t, C4/C-5), 25 1 (t, CH_2), 11 5 (q, CH_3), IR 1720 cm^{-1} HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1576

N-Ethoxycarbonyl-9-ethyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-9-ene (5i) After 4 hr 4i (58 mg), admixed with 42 mg of 4g as an impurity, afforded 45 mg (79%) of 5i, TLC R_f 0 33, ^1H NMR δ5 78 (br, H-8), 4 44 (br, H-1), 4 14 (q, J = 7 Hz, OCH_2), 3 60 (br, H-3), 2 51 (br, H-7), 2 35-1 45 (m, 9 H), 1 24 (t, J = 7 Hz, Me), 1 05 (t, J = 7 Hz, Me), ^{13}C NMR δ119 6 (d, C-8), 118 0 (s, C-9), 56 8 (d, C-3), 47 8 (d, C-1), 42 4 (d, C-7), 38 1 (t, C-10), 33 0 (d, C-6), 30 8, 30 6 (t and t, C4/C-5), 25 9 (t, CH_2), 11 4 (q, CH_3), IR 1720 cm^{-1} HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1564

N-Ethoxycarbonyl-1-ethyl-2-azatricyclo[4 3 1.$0^{3,7}$]dec-9-ene (5j) After 14 hr 4j (300 mg) afforded 28 mg (9%) of 5j, TLC R_f 0 35, ^1H NMR δ6 25 (br, H-9/H-8), 4 05 (q, J = 7 Hz, OCH_2), 3 75 (br, H-3), 2 45 (br, H-7), 2 3-1 38 (m, 9 H), 1 23 (t, J = 7 Hz, Me), 0 96 (t, J = 7 Hz, Me), ^{13}C NMR δ139 1 (d, C-9), 129 3 (d, C-8), 58 5 (d, C-3), 51 0 (s, C-1), 42 4 (d, C-7), 35 0 (t, C-10), 32 6 (d, C-6), 30 8 and 28 9 (t and t, C4/C-5), 25 3 (t, CH_2), 8 3 (q, CH_3), IR 1720 cm^{-1} HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found 235 1570

N-Ethoxycarbonyl-8-propyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5k) After 4 5 hr 4k (118 mg) afforded 109 mg (92%) of 5k, TLC R_f 0 39, ^1H NMR δ6 15 (br, H-9), 4 55 (br, H-1), 4 08 (q, J = 7 Hz, OCH_2), 3 65 (br, H-3), 2 45 (br, H-7), 2 30-1 38 (m, 11 H), 1 38-1 10 (t, J = 7 Hz, Me), 0 88 (t, J = 7 Hz, Me), ^{13}C NMR δ143 0 (s, C-8), 127 0 (d, C-9), 56 7 (d, C-3), 46 9 (d, C-1), 45 1 (d, C-7), 39 2 (t, C-10), 32 6 (d, C-6), 30 9 and 30 7 (t and t, C4/C-5), 29 6 and 28 1 (t, CH_2), 13 6 (q, CH_3), IR 1700 cm^{-1} HRMS calcd for $C_{15}H_{23}NO_2$ m/z 249 1729, found m/z 249 1735

N-Ethoxycarbonyl-8-isopropyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5l) After 5 hr 4l (160 mg) afforded 144 mg (90 %) of 5l, TLC R_f 0 25, ^1H NMR δ6 15 (br, H-9), 4 6 (br, H-1), 4 12 (q, J = 7 Hz, OCH_2), 3 65 (br, H-3), 2 42 (br, H-7), 2 4-2 2 (m, H-11), 2 2-1 35 (m, 7 H), 1 15 (t, J = 7 Hz, Me), 1 03 (d, J = 7 Hz, 6 H), ^{13}C NMR δ148 9 (s, C-8), 124 2 (d, C-9), 57 0 (d, C-3), 45 4 (d, C-1), 45 3 (d, C-7), 39 2 (t, C-10), 32 9 (d, C-6), 30 9 and 30 6 (t and t, C4/C-5), 32 6 (d, CH), 20 7 (q, CH_3), IR 1710 cm^{-1} HRMS calcd for $C_{14}H_{23}NO_2$ m/z 249 1729, found mz/ 249 1730

N-Ethoxycarbonyl-8-isopentyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5m) After 5 hr 4m (115 mg) afforded 105 mg (92%) of 5m, TLC R_f 0 36, ^1H NMR δ6 17 (br, H-9), 4 52 (br, H-1), 4 1 (q, J = 7 Hz, OCH_2), 3 67 (br, H-3), 2 45 (br, H-7), 2 9-1 05 (m, 16 H including Me of the carbamate), 0 80 (t, J = 7 Hz, 6 H), ^{13}C NMR δ145 1 (s, C-8), 128 6 (d, C-9), 57 0 (d, C-3), 48 6 (d, C-1), 45 1 (d, C-7), 44 3 (d, CH), 39 2 (t, C-10), 32 9 (d, C-6), 30 9 and 30 6 (t and t, C4/C-5), 25 8 (t, CH_2), 11 9 (q, CH_3), IR 1700 cm^{-1} HRMS calcd for $C_{17}H_{27}NO_2$ m/z 277 2042, found m/z 277 2034

N-Ethoxycarbonyl-8-t-butyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5n) After 5 hr 4n (163 mg) afforded 135 mg (83 %) of 5n, TLC R_f 0 34, ^1H NMR δ6 12 (br, H-9), 4 54 (br, H-1), 4 12 (q, J = 7 Hz, OCH_2), 3 64 (br, H-3), 2 69 (br, H-7), 2 40-1 45 (m, 7 H), 1 2 (t, J = 7 Hz, Me), 1 0 (s, 9 H), ^{13}C NMR δ151 3 (s, C-8), 123 2 (d, C-9), 57 1 (d, C-3), 45 2 (d, C-1), 43 7 (d, C-7), 39 1 (t, C-10), 33 0 (d, C-6), 30 9 and 30 6 (t and t, C4/C-5), 34 3 (s, C), 28 0 (q, CH_3), IR 1700 cm^{-1} HRMS calcd for $C_{16}H_{25}NO_2$ m/z 263 1885, found m/z 263 1877

N-Ethoxycarbonyl-8-phenyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5o) After 3hr 4o (325 mg) afforded 240 mg (74 %) of 5o, TLC R_f 0 3, ^1H NMR δ7 5-7 2 (m, Ph), 6 75 (br, H-9), 4 75 (br, H-1), 4 13 (q, J = 7 Hz, OCH_2), 3 82 (br, H-3), 3 09 (br, H-7), 2 35-1 42 (m, 7 H), 1 25 (t, J = 7 Hz, Me), ^{13}C NMR δ141 8 (s, C-8), 139 3 (d, C-9), 129 7 (d), 128 9 (d), 127 7 (s), 125 4 (d), 57 2 (d, C-3), 46 0 (d, C-1), 45 6 (d, C-7), 39 0 (t, C-10), 33 1 (d, C-6), 31 6 and 31 3 (t and t, C4/C-5), IR 1720 cm^{-1} HRMS calcd for $C_{18}H_{21}NO_2$ m/z 283 1572, found m/z 283 1574

N-Ethoxycarbonyl-1,7-dimethyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5p) After 44 hr 4p (1 5 g) afforded 436 mg (29 %) of 5p (GC retention time 9 7 min), ^1H NMR δ6 30 (d, J = 8 Hz, H-9), 5 85 (d, J = 8 Hz, H-8), 4 04 (q, J = 7 Hz, OCH_2), 3 43 (br, H-3), 2 1-1 4 (m, 7 H), 1 62 (s, Me), 1 20 (t, J = 7 Hz, Me), 1 12 (s, Me), ^{13}C NMR δ138 2 and 128 6 (C-8/C-9), 63 6 (C-

3), 53 1 (C-1), 49 7 (C-7), 45 4 (C-10), 40 4 (C-6), 29 8 and 29 3 (C4/C-5), 24 5 and 20 7 (CH_3), IR 1700 cm^{-1} Anal Calcd for $C_{14}H_{21}NO_2$ C, 71 51, H, 9 00, N, 5 95 Found C, 71 44, H, 8 83, N, 5 71

N-Ethoxycarbonyl-7,8-dimethyl-2-azatricyclo[4.3.1 $0^{3,7}$]dec-8-ene (5q) and N-ethoxycarbonyl-8,9-dimethyl-2-azatricyclo[4 3.1.$0^{3,7}$]-dec-8-ene (5t) After 20 hr a 4 1 mixture of 4q and 4t (2 56 g) afforded 2 28 g (89 %) of a 4 1 mixture of 5q (GC retention time 13 7 min) and 5t (GC retention time 11 3 min) Spectral data for 5q are ^1H NMR δ6 24 (br, H-9), 4 40 (br, H-1), 4 10 (q, J = 7 Hz, OCH_2), 3 35 (br, H-3), 2 10-1 50 (m , 7 H), 1 77 (s, 8-Me), 1 20 (t, J = 7 Hz, Me), 1 09 (s, 7-Me), ^{13}C NMR δ139 6 (s, C-8), 129 1 (d, C-9), 60 6 (d, C-3), 44 1 (d, C-1), 47 9 (s, C-7), 39 5 (t, C-10), 37 3 (d, C-6), 29 1 and 28 3 (t and t, C4/C-5), 17 7 and 17 1 (q, CH_3), IR 1680 cm^{-1} Anal Calcd for $C_{14}H_{21}NO_2$ C, 71 51, H, 9 00, N, 5 95 Found C, 71 29, H, 8 85, N, 5 88 Spectral data for 5t are ^1H NMR δ4 35 (br, H-1), 4 09 (q, J = 7 Hz, OCH_2), 3 68 (br, H-3), 2 30 (br, H-7), 2 2-1 5 (m, 7 H), 1 75 (s, 6 H), 1 19 (t, J = 7 Hz, Me), ^{13}C NMR δ128 6 and 128 0 (s and s, C-8/C-9), 56 6 (d, C-3), 50 6 (d, C-1), 48 8 (d, C-7), 38 4 (t, C-10), 33 3 (d, C-6), 30 9 and 30 6 (t and t, C4/C-5), 16 1 and 15 3 (q, CH_3), IR 1680 cm^{-1}, HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1573, found m/z 235 1573

N-Ethoxycarbonyl-1,8-dimethyl-2-azatricyclo[4.3 1 $0^{3,7}$]dec-8-ene (5r) After 5 hr 4r (2 0 g) afforded 420 mg (21 %) of 5r (GC retention time 11 0 min), ^1H NMR δ5 94 (s, H-9), 4 03 (q, J = 7 Hz, OCH_2), 3 72 (br, H-3), 2 30 (br, H-7), 2 20-1 43 (m, 7 H), 1 82 (s, 8-Me), 1 68 (s, 1-Me), 1 20 (t, J = 7 Hz, Me), ^{13}C NMR δ137 9 (C-8), 128 5 (C-9), 57 6 (C-3), 55 6 (C-1), 47 7 and 45 8 (C-7/C-10), 36 9 (C-6), 31 9 and 31 0 (C4/C-5), 24 1 and 21 0 (CH_3), IR 1700 cm^{-1} Anal Calcd for $C_{14}H_{21}NO_2$ C, 71 51, H, 9 00, N, 5 95 Found C, 71 55, H, 9 10, N, 5 94

N-Ethoxycarbonyl-7,9-dimethyl-2-azatricyclo[4.3 1 $0^{3,7}$]dec-8-ene (5s). After 18 hr 4s (1 62 g) afforded 972 mg (60%) of 5s (GC retention time 11 3 min), ^1H NMR δ5 43 (br, H-8), 4 49 (br, H-1), 4 10 (q, J = 7 Hz, OCH_2), 3 40 (br, H-3), 2 13-1 50 (m, 7 H), 1 85 (s, 9-Me), 1 20 (t, J = 7 Hz, Me), 1 09 (s, 7-Me), ^{13}C NMR δ144 3 (s, C-9), 127 6 (d, C-8), 61 6 (d, C-3), 49 4 (d, C-1), 48 9 (s, C-7), 39 2 (t, C-10), 38 9 (d, C-6), 29 2 and 28 4 (t and t, C4/C-5), 20 6 and 18 3 (q, CH_3), IR 1680 cm^{-1} Anal Calcd for $C_{14}H_{21}NO_2$ C, 71 51, H, 9 00, H, 5 95 Found C, 71 42, H, 8 78, H, 5 92

N-Ethoxycarbonyl-1,9-dimethyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5u) After 20 hr 4u (195 mg) afforded 45 mg (23 %) of 5u (GC retention time 10 3 min), ^1H NMR δ5 81 (dd, J = 6 Hz, 2 Hz, H-8), 4 03 (q, J = 7 Hz, OCH_2), 3 66 (br, H-3), 2 38 (br, H-7), 2 20-1 50 (m, 7 H), 1 68 (s, 1-Me), 1 40 (s, 9-Me), 1 21 (t, J = 7 Hz, Me), ^{13}C NMR δ146 1 (s, C-9), 123 0 (d, C-8), 58 3 (d, C-3), 54 9 (s, C-1), 47 8 (d, C-7), 47 8 (t, C-10), 35 0 (d, C-6), 31 5 and 30 9 (t and t, C4/C-5), 22 2 and 17 3 (q, CH_3), IR 1700 cm^{-1} Anal Calcd for $C_{14}H_{21}NO_2$ C, 71 51, H, 9 00, N, 5 95 Found C, 71 55, H, 9 10, N, 5 94

N-Ethoxycarbonyl-6-methyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5v) After 12 hr 4v (150 mg) afforded 105 mg (70 %) of 5v, TLC R_f 0 35, ^1H NMR δ6 55 (m, H-9), 6 18 (m, H-8), 4 53 (br, H-1), 4 10 (q, J = 7 Hz, OCH_2), 3 67 (br, H-3), 2 40-1 4 (m, 7 H), 1 22 (t, J = 7 Hz, Me), 0 98 (s, 6-Me), ^{13}C NMR δ135 4 and 130 0 (d and d, C-8/C-9), 57 5 (d, C-3), 49 1 (d, C-1), 45 9 (s, C-6), 45 0 (d, C-7), 39 1 (t, C-10), 30 9 and 30 6 (t and t, C4/C-5), 27 6 (q, CH_3), IR 1710 cm^{-1}, HRMS calcd for $C_{13}H_{19}NO_2$ m/z 221 1416, found m/z 221 1419

N-Ethoxycarbonyl-10-syn-ethyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5w) After 24 hr 4w (120 mg) afforded 64 mg (53 %) of 5w, TLC R_f 0 34, ^1H NMR δ6 58 (m, H-9), 6 18 (m, (H-8), 4 45 (br, H-1), 4 15 (q, J = 7 Hz, OCH_2), 3 6 (br, H-3), 2 55 (br, H-7), 2 2-0 8 (br, 14 H), ^{13}C NMR δ130 2 and 127 6 (d and d, C-8/C-9), 57 3 (d, C-3), 47 9 (d, C-1), 45 4 (d, C-7), 43 5 (d, C-10), 34 6 (d, C-6), 30 7 and 30 3 (t and t, C4/C-5), 21 8 (t, CH_2), 11 1 (q, CH_3), IR 1720 cm^{-1}, HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1569

N-Ethoxycarbonyl-10-anti-ethyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (5x) After 8 hr 4x (72 mg) afforded 49 mg (68 %) of 5x, TLC R_f 0 38, ^1H NMR δ6 30 (br, H-9/H-8), 4 5 (br, H-1), 4 15 (q, J = 7 Hz, OCH_2), 3 6 (br, H-3), 2 55 (br, H-7), 2 4-0 8 (m, 14 H), ^{13}C NMR δ131 3 and 130 5 (d and d, C-8/C-9), 56 1 (d, C-3), 52 1 (d, C-1), 48 7 (d, C-7), 43 4 (d, C-10), 40 7 (d, C-6), 31 2 and 30 9 (t and t, C4/C-5), 27 4 (t, CH_2), 14 9 (q, CH_3), IR 1710 cm^{-1}, HRMS calcd for $C_{14}H_{21}NO_2$ m/z 235 1572, found m/z 235 1569

Bromination/Dehydrobromination of 5a General Procedure Formation of rearrangement product N-ethoxycarbonyl-9-endo-bromo-10-azatricyclo[5.2.1.$0^{4,8}$]-dec-2-ene (14a) and Unrearranged N-ethoxycarbonyl-9-bromo-2-azatricyclo[4.3.1.$0^{3,7}$]dec-2-ene (22a) To 5a (200 mg, 0 97 mmol) in methylene chloride (15 mL) at -78°, there was added dropwise bromine (155 mg, 0 97 mmol) in methylene chloride (5 mL) The reaction mixture was stirred for 1 5 hr as the temperature slowly rose to 25° The mixture was then poured into a saturated solution of sodium carbonate (20 mL), the organic layer was separated, dried over magnesium sulfate, filtered and solvent was removed in vacuo to give an oily mixture of dibromides 20a and 21a (300 mg, 85 % based upon dibromide formation) NMR showed no olefinic protons In a scaled-up reaction, the crude oil (1 25 g, 3 4 mmol) was stirred at 95° for 16 hr with diazabicycloundecane (3 4 mL) The reaction was allowed to cool, water was added (30 mL), and the mixture was extracted with ether (3 x 30 mL) The combined ether extracts were washed with water (50 mL), 2% hydrochloric acid (50 mL), and water (50 mL), dried over magnesium sulfate, filtered and solvent was removed in vacuo to give 821 mg of a mixture The mixture was separated by flash column chromatography (1 1 hexane/ether) to give 502 mg (52%) of 14a, TLC R_f = 0 35, NMR δ6 0 (m, H-2), 5 72 (dd, J = 10 Hz major, H-3), 4 5-3 95 (m, H-1/H-7/H-9), 4 1 (q, J = 7 Hz, OCH_2), 2 85 (m, H-4/H-8), 2 0-1 6 (m, 4 H), 1 25 (t, J = 7 Hz, CH_3), IR 1720 cm^{-1}, HRMS calcd for $C_{12}H_{16}NO_2Br$ m/z 285 0364, found 285 0360 Also isolated was 233 mg (24 %) of 22a, TLC R_f 0 41, NMR δ6 34 (dd, J = 9 Hz, 2 Hz, H-5), 4 67 (m, H-1), 4 12 (q, J = 7 Hz, OCH_2), 3 72 (m, H-3), 2 85 (m, H-4), 2 0 (m, H-8), 1 95-1 4 (m, 6 H), 1 25 (t, J = 7 Hz, Me), IR 1720 cm^{-1}, HRMS calcd for $C_{12}H_{16}NO_2Br$ m/z 285 0364, found m/z 285 0363

Bromination/Dehydrobromination of 5b. N-Ethoxycarbonyl-9-endo-bromo-7-methyl-10-azatricyclo[5 2 1.$0^{4,8}$]dec-2-ene (14b) and N-Ethoxycarbonyl-9-bromo-7-methyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-8-ene (15b). A solution of 160 mg (1 mmol) of bromine in methylene chloride (5 mL) was reacted with 224 mg (1 0 mmol) of 5b according to the general procedure to afford 366 mg (95%) of a dibromide mixture, which was refluxed with diazabicycloundecane (1 mL) in xylene for 4 d Workup and silica gel chromatography (5 1 1 hexane-ether-methylene chloride) afforded 154 mg (51%) of 14b, NMR δ5 95 (m, H-3), 5 80 (dd, J = 3 Hz, 9 Hz, H-2), 4 40 (m, H-1), 4 11 (q, J = 7 Hz, OCH_2), 4 00 (d, J = 5 Hz, H-9), 3 78 (m, H-7), 2 45 (m, H-4), 1 20 (s, CH_3), 1 50-2 00 (m, 4H), 1 22 (t, J = 7 Hz, CH_3), HRMS calcd for $C_{13}H_{19}NO_2Br$ m/z 301 0501, found m/z 301 0503 Also isolated was 72 mg (24%) of 22b, NMR δ6 03 (d, J = 3 Hz, H-8), 4 65 (m, H-1), 4 14 (q, J = 7 Hz, OCH_2), 3 48 (m, H-3), 2 1-1 45 (m, 7 H), 1 14 (s, CH_3), 1 24 (t, J = 7 Hz, CH_3), HRMS calcd for $C_{13}H_{19}NO_2Br$ m/z 301 0501, found m/z 301 0495

Bromination/Dehydrobromination of 5c N-Ethoxycarbonyl-9-bromo-8-methyl-2-azatricyclo-[4 3 1 $0^{3,7}$]dec-2-ene (22c), N-Ethoxycarbonyl-8-bromomethyl-2-azatricy- clo[4 3 1 $0^{3,7}$]dec-2-ene (24) and N-Ethoxycarbonyl-9-bromo-8-exo-methylene-2-azatricy- clo[4 3 1.$0^{3,7}$]decane (25) A solution of 320 mg (2 mmol) of bromine in methylene chloride 5 (mL) was reacted with 370 mg (1 7 mmol) of 5c according to the general procedure to afford 540 mg of a mixture, which was separated by preparative TLC (2 1 hexane-ether) to afford 160 mg (30%) of an oil shown by H^1 NMR (comparison of vinyl resonances) to be a 90 10 mixture of major allylic bromide 24, NMR δ6 56 (d, J = 6 Hz, H-9), 4 65 (m, H-1), 4 10 (q, J = 7 Hz, CH_2), 3 76 (m, H-3), 2 1-1 4 (m, 7 H), 1 20 (t, J = 7 Hz, CH_3), and minor allylic bromide 25, NMR δ5 28 (dd, J = 2 Hz, 8 Hz, vinyl CH_2), 4 76 (m, H-8), 4 5 (m, H-1), 4 15 (q, J = 7 Hz, CH_2), 3 73 (m, H-3), 2 67 (m, H-7), 2 1-1 4 (m, 7 H), 1 20 (t, J = 7 Hz, CH_3), high resolution mass spectrum calculated for $C_{13}H_{19}NO_2Br$ m/z 299 0521, found m/z 299 0520 Also obtained was 340 mg (52%) of dibromide 20c, which was treated with diazabicycloundecane (1 mL) according to the general procedure to afford after workup 249 mg (92%, 49% based on 5c) of vinyl bromide 22c, NMR δ4 64 (m, H-1), 4 08 (q, J = 7 Hz, CH_2), 3 72 (m, H-3), 2 54 (t, J = 4 Hz, H-7), 2 2-1 4 (m 7 H), 1 82 (s, CH_3), 1 20 (t, J = 7 Hz, CH_3), HRMS calcd for $C_{13}H_{19}NO_2Br$ m/z 299 0521, found m/z 299 0521

Bromination/Dehydrobromination of 5s N-Ethoxycarbonyl-8-bromo-7,9-dimethyl-2-azatricyclo[4 3 1 $0^{3,7}$]dec-2-ene (27) and N-Ethoxycarbonyl-8-bromo-7-methyl-9-exo-methylene-2-azatricyclo[4 3 1 $0^{3,7}$]decane (28) A solution of 180 mg (1 1 mmol) of bromine in methylene chloride (5 mL) was reacted with 235 mg (1 0 mmol) of 5s by the general procedure to afford 335 mg (85%) of a mixture, which was treated with diazabicycloundecane (2 mL) at 90° for 15 h Workup provided 134 mg of oil which upon chromatography (5 1 1 hexane-ether-methylene chloride) afforded 34 mg of unreacted dibromides (R_f = 0 50) and 66 mg (17% based on 5s) of

an inseparable mixture (R_f = 0 45) shown by H^1 NMR to contain 56% vinyl bromide 27, NMR δ4 24 (m, H-1), 4 2 (m, CH_2), 3 27 (m, H-3), 2 1-1 5 (m, 10 H), 1 24 (t, J = 7 Hz, CH_3), 1 10 (s, CH_3), and also 44% of allylic bromide 28, NMR δ5 45-5 46 (two s, vinyl H), 4 39 (m, H-1), 3 34 (m, H-3), 4 40-4 01 (m, CH_2/H-8), 2 1-1 5 (m, 7 H), 1 25 (t, J = 7 Hz, CH_3), 1 10 (s, CH_3), HRMS calcd for $C_{14}H_{21}NO_2Br$ m/z 315 0656, found m/z 315 0680

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References and Notes

1 For reviews see Stout, D M and Meyers, A I Chem. Rev , 1982, **82**, 223-243, Eisner, U and Kuthan, J Chem. Rev , 1972, **72**, 1-42

2 (a) Krow, G R , Carey, J T , Cannon, K C , Henz, K J Tetrahedron Lett , **1982**, 2527-2528 (b) Sundberg, R J and Bloom, J D J. Org. Chem , 1981, **46**, 4836-4842 (c) Sundberg, R J and Bloom, J D J. Org. Chem , 1980, **45**, 3382-3387 (d) Knaus, E E , Avasthi, K , Giam, C S Can. J. Chem , 1980, **58**, 2447-2451 (e) Wender, P A , Schaus, J M , Torney, D C Tetrahedron Lett , **1979**, 2485-2488 (f) Wender, P A , Schaus, J M , White, A W J. Am. Chem. Soc , 1979, **1980**, 6157-6159 (g) Krow, G R , Cannon, K C , Carey, J T , Lee, Y B , Szczepanski, S W , Ramjit, H G J. Heterocycl. Chem , 1985, **22**, 131-135 (h) Sundberg, R J , Hamilton, G , Trindlee, C J. Org. Chem , 1986, **51**, 3672-3679 (i) Augelmann, G , Streith, J , Fritz, H Helv. Chim. Acta, 1985, **68**, 95-103 (j) Pavlov, A V and Mochalin, V B Zh. Org. Khim 1983, **19**, 234-235, Chem. Abstr 1983, **98** 179340j

3 (a) Krow, G R , Shaw, D A , Jovais, C S , Ramjit, H G Synthetic Commun , **1983**, 575-579 (b) Krow, G R , Shaw, D A , Szczepanski, S , Ramjit, H G Synthetic Commun , **1984**, 429-433 (c) Krow, G R , Rodebaugh, R , Hyndman, C , Carmosin, R , DeVicaris, G Tetrahedron Lett , **1973**, 2175-2178

4 (a) Comins, D L , Abdullah, A H , Smith, R K Tetrahedron Lett , **1983**, 2711-2714 (b) Greuter, H and Schmid, H Helv. Chim. Acta, 1974, **57**, 1204-1217 (c) Krow, G R , Lee, Y B , Szczepanski, S W , Raghavachari, R , Baker, A D Tetrahedron Lett , **1985**, 2617-2618 (d) Krow, G R , Lee, Y B , Raghavachari, R , Alston, P V , Baker, A D Tetrahedron Lett , **1988**, 3187-3190

5 Carbon-nitrogen bond cleavage can be initiated by acid to generate an allylic cation [3c] The 6-alkyl group in cycloadducts 5 can facilitate this process

6 Krow, G R , Raghavachari, R , Siatkowski, R , Chodash, D F J. Org. Chem , 1986, **51**, 1916-1918

7 (a) Sauer, J , Sustmann, R Angew. Chem. Int. Ed. Engl., 1980, **19**, 779-807 (b) Fleming, I "Frontier Orbitals and Organic Chemical Reactions," J Wiley and Sons, London, 1976, 110

8 An alternative to the pericyclic model for analysis of cycloaddition rates of 4 is a stepwise diradical or related diradicaloid mechanism, consideration of radical stabilities does not appear adequate to account for the observed rate data See, (a) Dewar, M J S , Olivella, S , Stewart, J J P J. Am. Chem. Soc , 1986, **108**, 5771-5779 (b) Dewar, M J S and Pierini, A B , J. Am. Chem. Soc , 1984, **106**, 203-208 (c) Dewar, M J S J. Am. Chem Soc , 1984, **106**, 209-219 (d) Firestone, R A. Tetrahedron, 1977, 33, 3009-3039

9 Maercker, von A and Weber, K Liebigs Ann. Chem , 1972, **756**, 43-78