and Bell, chromatographic quality) used as a solvent for the decompositions was dried by storage over activated molecular sieves and deoxygenated by bubbling purified nitrogen for 12 hr.

Samples (50–100 mg) of freshly recrystallized I or VI were weighed into a 5-ml glass ampoule kept under nitrogen and 2 ml of *p*-xylene was added. The system was then degassed by the freeze–vacuum–thaw method (3 times). The ampoule was sealed while the contents were frozen and still under high vacuum and then heated by the refluxing vapors of either xylene or toluene depending on the decomposition temperature desired. When decomposition was complete, the tube was allowed to cool and the solvent removed by freeze drying. In all cases, quantitative yields of bicyclopropyls (IX) were obtained. The ratios of products were determined by gas chromatography and results are summarized in Table II.

**Quantitative Determination of the Products from the Photolytic Decomposition of I and VI in Solution.**—The photolytic decompositions were carried out on approximately 50–100 mg of the freshly recrystallized I isomer mixture or pure isomer Ia,b dissolved in 30–40 ml of spectroquality dioxane. These solutions were irradiated in a Pyrex apparatus[22] (care was taken to exclude oxygen) with a Rayonet ultraviolet reactor (lamps with maximum emission at 350 nm were used). Nitrogen evolution was measured in a thermostated gas buret. Cessation of nitrogen evolution was taken as the end of the decomposition. In all cases, 95–100% of the theoretical nitrogen was evolved. After removal of the dioxane by freeze drying, the products were analyzed as before. Bicyclopropyls VIII were isolated in quantitative yields. The results are summarized in Table II.

**Registry No.**—*cis,trans*-I, 27694-29-7; IV, 27825-09-8; VIII, 27755-39-1.

**Acknowledgment.**—The authors gratefully acknowledge financial support of the National Science Foundation, Grant No. GP-7600.

(22) C. D. DeBoer, N. J. Turro, and G. S. Hammond, *Org. Syn.*, **47**, 65 (1967).

# Ring Expansion of a 1,2-Dihydropyridine to an Azepine

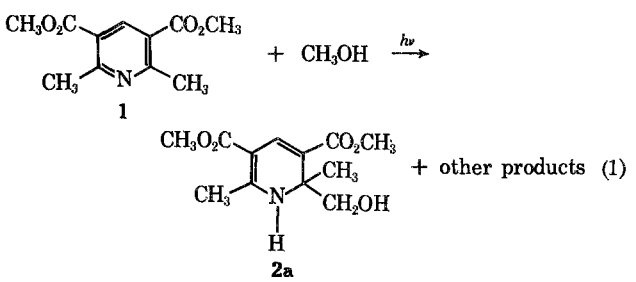
T. J. VAN BERGEN AND RICHARD M. KELLOGG*

*Department of Organic Chemistry, The University Zernikelaan, Groningen, The Netherlands*

*Received September 11, 1970*

Ring expansion of the tosylate of 3,5-dicarbomethoxy-2,6-dimethyl-2-hydroxymethyl-1,2-dihydropyridine (**2b**) is described. The product is 4,6-dicarbomethoxy-2,7-dimethyl-3*H*-azepine (**3**) which, in polar solvents, is in equilibrium with its dimer **5** formed by addition of the 2-methyl group of **3** to the $N_1$–$C_2$ double bond of another molecule of **3**. The structure of **3** is established from the nmr spectrum of its hydrogenation product. Ring expansion proceeds with the exclusive migration of a vinylic group ($C_2$–$C_3$ bond) of **2b** with no concomitant migration of the nitrogen atom. In the presence of diethylamine, **3** condenses with benzaldehyde to give 4,6-dicarbomethoxy-7-methyl-2-(*trans*-styryl)-3*H*-azepine (**8**). The nmr spectra for the methylene groups of both **3** and **8** are temperature dependent indicating ring-inversion barriers of $\Delta G^{\ddagger} = 13.7$ kcal/mol and $\Delta G^{\ddagger} = 14.2$ kcal/mol, respectively; no evidence of valence tautomerism was found. Limitations of this ring-expansion procedure are discussed.

Methanol adds to the pyridine derivative **1** upon irradiation yielding 1,2-dihydropyridine **2a** (eq 1).[1] The

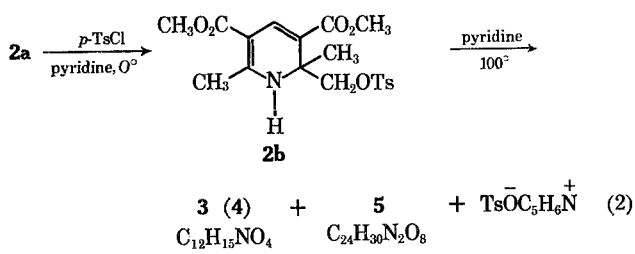


(1)

hydroxy methyl group of **2a** provides an obvious point at which to trigger ring expansion with either a vinylic group ($C_2$–$C_3$ bond) or the nitrogen atom ($N_1$–$C_2$ bond) being properly situated for a 1,2 shift.[2] We report here the successful ring expansion of the tosylate **2b** and subsequent transformations of the rearrangement product.

## Results

Dihydropyridine **2a**, which is stable at room temperature,[3] is obtained readily from other photochemical reaction products (eq 1) by thick layer chromatography (tlc). Tosylation of **2a** in pyridine in the cold gives the tosylate **2b** (eq 2); no substitution is observed at nitrogen consistent with the normal selectivity of tosyl chloride.[4] On heating at 100° in pyridine, **2b** reacts rapidly to produce *p*-toluenesulfonic acid (isolated in 85% yield as the pyridinium salt) and two neutral compounds one of which, isolated by tlc in 40–50% yield, was a rather unstable oil tentatively considered to be either 3*H*-azepine **3** or 2*H*-azepine **4**.[5] The neutral compound **5**, obtained in 18% yield, was a solid, mp 138–140°. The



(2)

(1) R. M. Kellogg, T. J. van Bergen, and H. Wynberg, *Tetrahedron Lett.*, 5211 (1969). The plethora of products which may be obtained from the photochemical reactions of pyridines are described in this article. Full details will be published in due course.

(2) For a review of ring-expansion reactions, see C. D. Gutsche and D. Redmore, "Carbocyclic Ring Expansion Reactions," Academic Press, New York, N. Y., 1968.

(3) (a) Most 1,2-dihydropyridines are notorious for their instability. See, for example, W. Traber and P. Karrer, *Helv. Chim. Acta*, **41**, 2066 (1958). (b) See, for a review on dihydropyridines, R. A. Barnes, "Pyridine and Derivatives," part I, E. Klingsberg, Ed., Interscience, New York, N. Y., 1960.

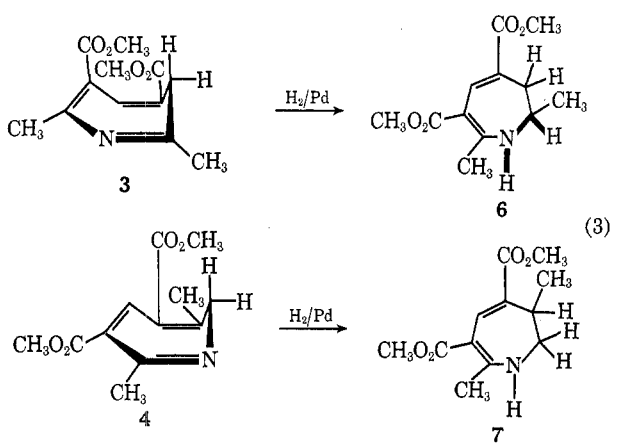
(4) L. F. Fieser and M. Fieser, "Reagents For Organic Synthesis," Wiley, New York, N. Y., 1968, p 1180.

(5) We felt it inadvisable to distil this compound in order to obtain an analytical sample; identification is based on spectral properties and chemical transformations (*vide infra*). Satisfactory elemental analyses were obtained for all of its precursors and derivatives.

molecular weight of the oil (mass spectral) accorded with the formula $C_{12}H_{15}NO_4$ consistent with the loss of the elements of *p*-toluenesulfonic acid from **2b**. Mass spectra and osmometry indicated **5** to have a dimeric composition, $C_{24}H_{30}N_2O_8$.

The ultraviolet spectrum of the oil showed major peaks at 305 mμ (log ε 3.82), 267 (3.83), and 215 (4.24) indicative of an azepine ring structure.[6] The nmr spectrum at room temperature showed nonequivalent allylic methyl groups, two nonequivalent methoxy groups, and a single vinylic proton. At temperatures below 0° a set of doublets, $J$ = 11.0 Hz, centered at δ 0.97 and 4.15, appeared. Above 100°, these doublets were replaced by a singlet at δ 2.61. The nmr spectrum is shown in Figure 1. Measurements at various temperatures established the coalescence temperature[7] to be 25 ± 5° with $\Delta G^{\pm}$ = 13.7 ± 0.2 kcal/mol in either chlorobenzene or carbon tetrachloride. These data are clearly consistent with an azepine capable of ring inversion but allow no distinction between the two possible structures **3** and **4** (vinyl and nitrogen migration, respectively). An unequivocal assignment is not possible on the basis of spectral observations: simple 2*H*-azepines are unknown[8] and no 3*H*-azepine with a substitution pattern analogous to **3** has been reported. A tentative indication for structure **3** is found in the observation of homoallylic[9] coupling ($J$ = 0.6 Hz) between the vinylic proton and the methyl group located at δ 2.56. In **4** the 2- and 7-methyl groups are equidistant from the vinylic proton, leading to the expectation that *both* methyl groups should show homoallylic coupling, whereas in **3** presumably only the 7-methyl group should be coupled.

Unambiguous evidence for the correctness of structure **3** was finally obtained by selectively reducing the imino portion of the azepine. Ample precedent exists for this type of conversion with other azepines.[6b] Low pressure hydrogenation in methylcyclohexane gave a single crystalline dihydro compound, mp 98–99°. Strong uv absorptions at 223 mμ (log ε 3.89), 280 (3.90), and 357 (3.86) point to a 1,2-dihydropyridine-like structure[10] requiring either 1,2 addition (1,2 bond) to **3** to give **6** or 1,6 addition (positions 1,3) to yield **7** (eq 3). The 100-Mc nmr spectrum of




3 6

(3)




4 7

(6) (a) L. A. Paquette, D. E. Kuhla, J. H. Barrett, and R. J. Haluska, *J. Org. Chem.*, **34**, 2866 (1969); (b) M. Anderson and A. W. Johnson, *J. Chem. Soc.*, 2411 (1965); (c) R. F. Childs and A. W. Johnson, *ibid.*, *C*, 1950 (1966).

(7) R. J. Kurland, M. B. Rubin, and W. B. Wise, *J. Chem. Phys.*, **40**, 2426 (1964); M. Oki, H. Iwamura, and N. Hayakana, *Bull. Chem. Soc. Jap.*, **37**, 1865 (1964).

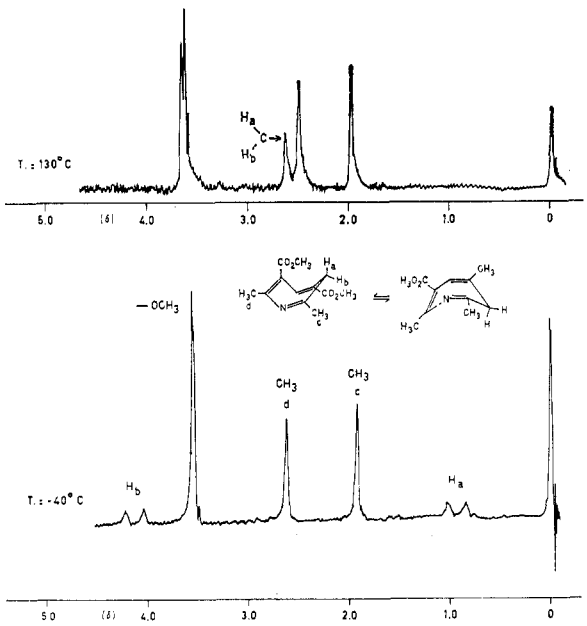



Figure 1.—Nmr spectrum of **3** at 60 Mc in $C_6H_5Cl$ solvent. The geminal coupling constant is $J$ = 11.0 Hz; homoallylic coupling between H-5 and the 7-methyl group ($H_d$) is $J$ = 0.6 Hz.

the hydrogenation product in carbon tetrachloride is shown in Figure 2; $J$ values were determined from decoupling experiments.[11] In DMSO vicinal coupling (inset, Figure 2) of the nitrogen-bound hydrogen was observed,[12] and decoupling experiments established the presence of the structural unit **HNC(CH$_3$)H** (heavy lines in **6**). These observations are consistent only with structure **6** and simultaneously *establish the ring-expansion product to be 3H-azepine* (**3**).

The structure of dimer **5** was unraveled by consideration of the following observations: (a) only three of the expected four methyl resonances could be located in the nmr spectrum (Figure 3) [of these, one is shifted to higher field (δ 0.94) suggesting it to be attached to a sp$^3$ rather than sp$^2$ hybridized carbon atom]; (b) the ultraviolet spectrum of **5** could be duplicated closely by *adding* the spectra of **3** and **6** (a 3*H*-azepine and a dihydroazepine); (c) **3** yields **5** only slowly in nonhydroxylic solvents (benzene) and more rapidly in hydroxylic solvents (methanol); (d) above 85° **5** is visibly in equilibrium with **3** and in refluxing chlorobenzene (135°) reversion to **3** is quantitative; (e) **5** contains *one* NH proton (ir 3360 cm$^{-1}$) as deduced from integration of the nmr resonances; (f) one methylene resonance in the nmr spectrum (Figure 3) is not seen suggesting an azepine ring. These data, coupled with the observation of two protons of the missing methyl group as an AB system ($J$ = 15.0 Hz, geminal coupling) at δ 2.28 and 2.48 and the third proton likely accounted for as NH suggest that

(8) See, for a review on azepines, L. A. Paquette in "Nonbenzenoid Aromatics," Vol. I, J. P. Synder, Ed., Academic Press, New York, N. Y., 1969.

(9) S. Sternhell, *Quart. Rev.*, **23**, 236 (1969).

(10) Compare, for example, compounds **2a,b** and ref 1. The blue shift of the long wavelength band is due to the greater ring size.

(11) We are indebted to Dr. K. Spaargaren and Mr. C. Kruk of the University of Amsterdam for measuring the 100-Mc spectra, carrying out decoupling experiments, and providing aid in interpretations.

(12) This trick has been successfully exploited with alcohols: O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, **86**, 1256 (1964).

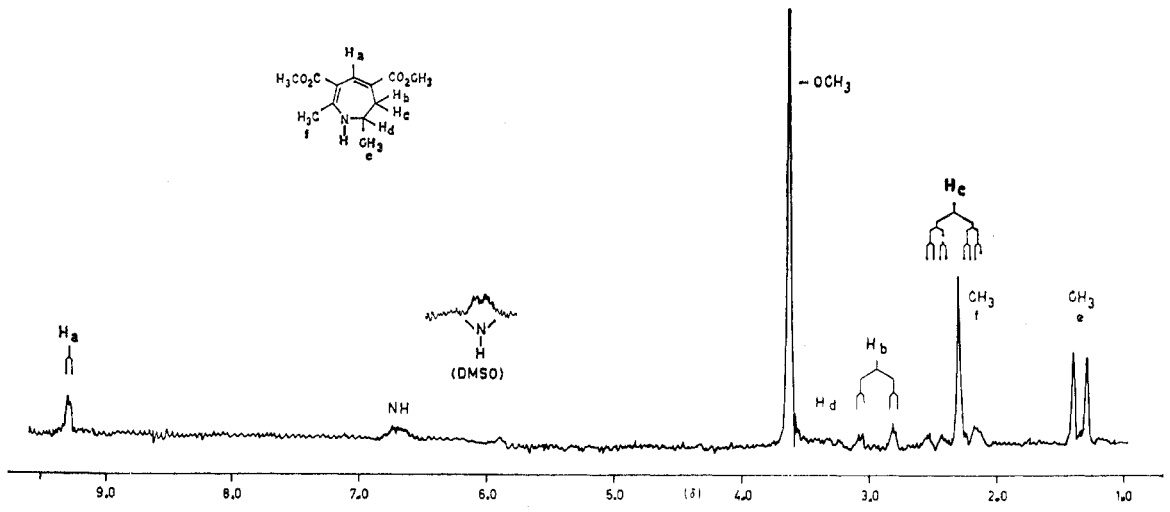



Figure 2.—Nmr spectrum of **6** at 100 Mc in $CCl_4$ (except for inset) taken at normal probe temperature (*ca.* 35°). Coupling constants are $J_{bc}$ = 16.0 Hz, $J_{cd}$ = 6.0 Hz, $J_{bd}$ = 2.0 Hz, $J_{ac}$ = 1.2 Hz, $J_{ab}$ = 0 Hz, and $J_{NH}$ = 5.0 Hz.

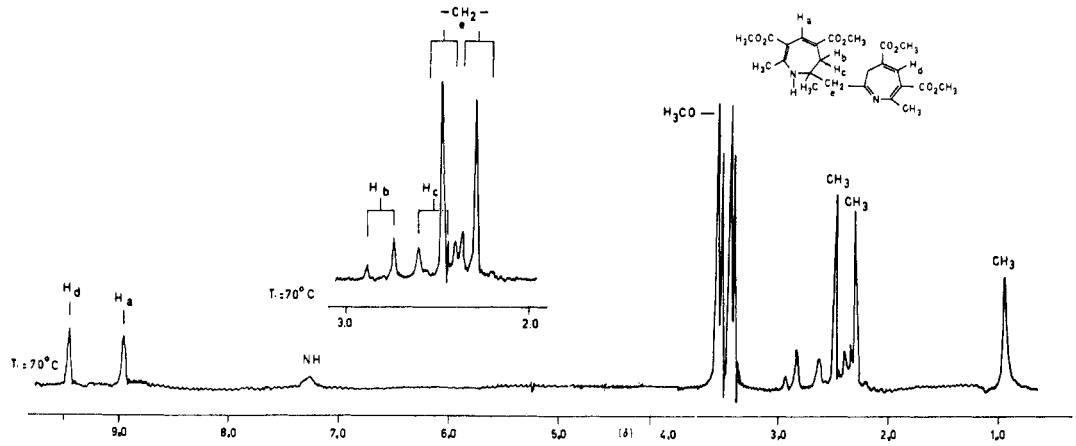
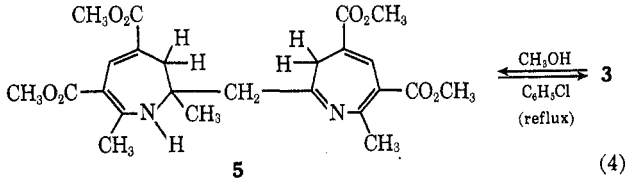


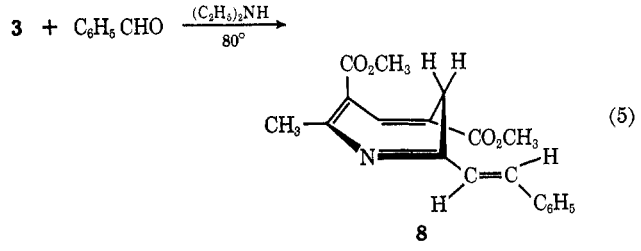

Figure 3.—Nmr spectrum of **5** at 100 Mc in $C_6D_6$: $J_{ab}$ = 0 Hz, $J_{ac}$ = *ca.* 1 Hz, $J_{bc}$ = 15.0 Hz, and $J_{ec(gem)}$ = 15.0 Hz. The 3*H*-methylene group of the azepine ring cannot be seen. Upon raising the temperature reversion to **3** occurred. Below 30° the spectrum becomes too diffuse to analyze.

the 2-methyl group of **3** has added across the $N_1{=}C_2$ bond of another molecule leading to **5** (eq 4).[13]




**5** (4)

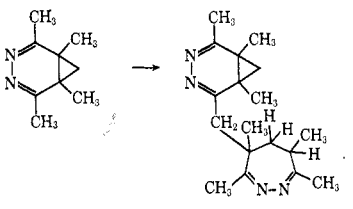
The acidic character of the 2-methyl group of **3** is not too surprising. In addition to the known base-catalyzed exchange at the 7-methyl group of 1,3-dihydro-1,3,5,7-tetramethyl-2*H*-azepin-2-one,[14] base-catalyzed condensations at the 2-methyl group of pyridines,[15] various methylated heterocycles,[16a] dihydro-1,3-oxazines,[16b] as well as benzodiazepines,[17] provide excellent precedent. We find that **3** readily undergoes deuterium exchange at the 2-methyl group and, in the presence of base, condenses with benzaldehyde to give in 32% yield (eq 5) the 2-styryl derivative **8**




**8** (5)

(trans geometry based on vinyl coupling, $J$ = 16.0 Hz). That condensation has occurred at the 2 position

(13) Most azepine dimerizations involve Diels–Alder-like cycloadditions. (a) L. A. Paquette and J. H. Barrett, *J. Amer. Chem. Soc.*, **88**, 2590 (1969). (b) A. L. Johnson and H. E. Simmons, *ibid.*, **89**, 3191 (1967). (c) K. Hafner and J. Mondt, *Angew. Chem.*, **78**, 822 (1966). (d) A most curious dimerization resembling that observed by us is shown in eq i: G. Maier, *ibid.*, **79**, 456 (1967).




(i)

(14) L. A. Paquette, *J. Org. Chem.*, **28**, 3590 (1963).

(15) For example, V. Boekelheide, H. Fritz, J. M. Ross, and H. X. Kaempfen, *Tetrahedron*, **20**, 33 (1964); S. M. McElvain and H. G. Johnson, *J. Amer. Chem. Soc.*, **63**, 2213 (1941).

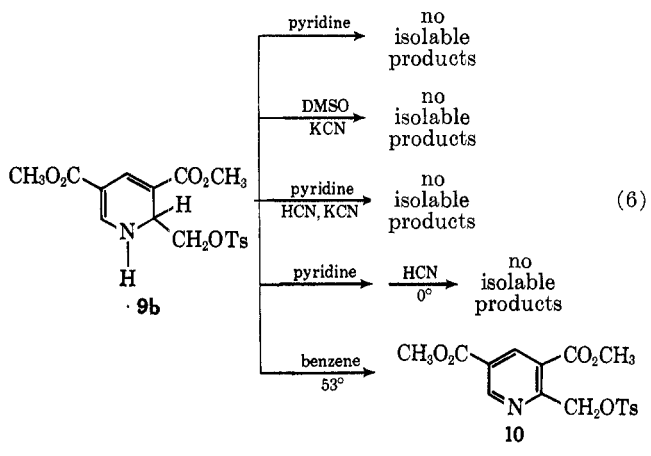
(16) (a) A. E. Siegrist and H. R. Meyer, *Helv. Chim. Acta*, **52**, 1282 (1969); (b) A. I. Meyers, A. Nabeya, H. W. Adickes, and I. R. Politzer, *J. Amer. Chem. Soc.*, **91**, 763 (1969).

(17) S. Motoki, C. Urakawa, A. Kano, Y. Fushimi, T. Hirano, and K. Murata, *Bull. Chem. Soc. Jap.*, **43**, 809 (1970); J. A. Baltrop, C. G. Richard, D. M. Russell, and G. Ryback, *J. Chem. Soc.*, 1132 (1959).

is indicated by the retention of homoallylic coupling between H-5 and the 7-methyl group. Ring inversion occurs in **8** with a coalescence temperature of 35 ± 5° ($\Delta G^{\pm}$ = 14.2 ± 0.2 kcal/mol) in either carbon tetrachloride or chlorobenzene.

The less than quantitative conversion of **2b** to **3** could be attributed either to work-up problems (tlc) or to formation of a second isomer, **4**, which decomposes under the reaction conditions. The ring expansion was investigated spectroscopically to resolve this question. When followed by uv the conversion of **2b** to **3** was calculated to proceed in 108% yield. No extraneous absorptions were seen and a clean isosbestic point was observed at 328 mμ. In a nmr tube the signals from **2b** were replaced exclusively by the signals from **3** (85% yield calculated using the tolylmethyl group as internal standard). The disappearance of **2b** in pyridine was cleanly first order at 53° with $k$ = $1.8 \times 10^{-4}$ l. mol$^{-1}$ sec$^{-1}$.

A number of attempts were made to effect ring expansion of **9b** (eq 6) obtained by tosylation of the



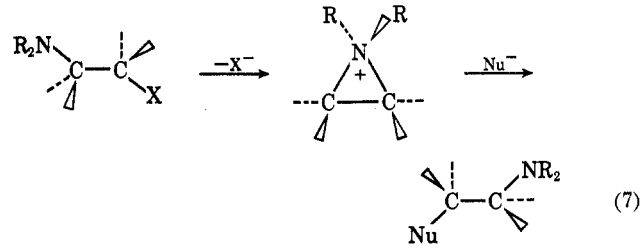
(6)

photochemically induced addition product of methanol to 3,5-dicarbomethoxypyridine **9a**. Conventional reaction in pyridine led to no isolable products. Reaction in DMSO/KCN[18] also failed. In benzene (nonsolvolytic) an 18% yield of the oxidation product 3,5-dicarbomethoxy-2-tosyloxymethylpyridine (**10**) was isolated. After a number of fruitless attempts to modify conditions or to trap an intermediate (HCN addition), we concluded that intrinsic difficulties in the system circumvent ring expansion of an azepine. Some of these problems are dealt with in the Discussion.

Descriptions of attempted Diels–Alder reactions and of photochemical experiments with **3** are given in the Experimental Section.

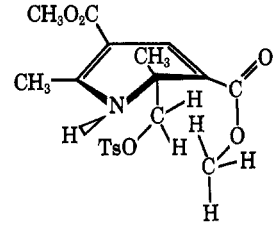
## Discussion

Many of the synthetic approaches to seven-membered rings hinge on the judicious exploitation of readily available six-membered precursors suitably constituted for ring expansion. In particular, solvolyses of cyclohexadienyl tosylates provide a workable route to cycloheptatrienes.[19] Replacement of carbon by a heteroatom is also feasible as attested, for example, by the successful conversion of 4-chloromethyl-1,4-dihydropyridines to 4*H*-azepines.[6b,20] In dihydropyridine **2b** either the vinylic group ($C_2$–$C_3$ bond) or the nitrogen ($N_1$–$C_2$ bond) are properly disposed for a 1,2 shift. Migration of the latter leading to 2*H*-azepine **4** is certainly not intrinsically prohibited. Various β-amino-substituted ethyl chlorides capable of forming aziridine intermediates undergo nitrogen shifts by the route depicted in eq 7,[21,22] and, moreover, even in a



(7)

case where the nitrogen lone pair is prevented sterically from forming an aziridine, rearrangement still occurs apparently by participation of only the nitrogen–carbon σ bond.[23] In **2b** the exclusive shift of the vinylic group is likely caused by dual interplay of steric and electronic factors. As depicted in eq 8 the antiperiplanar[24] conformation for a vinylic group shift involves less steric hindrance than for a nitrogen shift where tosylate–carbomethoxy interactions may develop. Second, the carbomethoxy groups of **2b** lower the nitrogen nucleophilicity by conjugative and inductive action; these combined effects apparently overweigh the deactivating tendency of the carbomethoxy group on the migrating vinylic group.[25]




(18) This technique has been exploited by Johnson and coworkers, ref 5b.

(19) N. A. Nelson, J. H. Fassnacht, and J. U. Piper, *J. Amer. Chem. Soc.*, **81**, 5009, (1959); O. L. Chapman and P. Fitton, *ibid.*, **85**, 41 (1963).

(20) M. Anderson and A. W. Johnson, *Proc. Chem. Soc.*, 263 (1964).

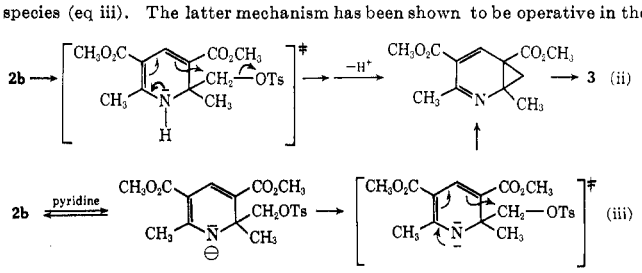
(21) See, for example, A. Streitweiser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N. Y., 1962, pp 105–108.

(22) R. C. Fuson and C. L. Zirkle, *J. Amer. Chem. Soc.*, **70**, 2760 (1948).

(23) R. B. Turner and R. B. Woodward, "The Alkaloids," Vol. III, R. H. F. Manske and H. L. Holmes, Ed., Academic Press, New York, N. Y., 1953, p 18.

(24) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley-Interscience, New York, N. Y., 1965, p 300.

(25) Two kinetically different processes may be imagined for the ring expansion: (a) a unimolecular process as crudely depicted in eq ii, or (b) prior ionization at *nitrogen* with the resultant anion being the rearranging species (eq iii). The latter mechanism has been shown to be operative in the




ring expansion of 2,6-dimethyl-4-chloromethyl-3,5-dicarbomethoxy-1,4-dihydropyridine in ethanol containing cyanide ion,[26] while the former mechanism must obtain in the ring expansion of the N-methylated derivative of the same compound where prior ionization is impossible.[6c] Ring expansion of **2b** does not lend itself to study since the reaction proceeds well only in pyridine and fails in other solvents such as acetonitrile, dioxane, and benzene (nonsolvolytic). No serious attempt to distinguish conclusively between these two mechanisms has been made.

(26) P. J. Brignell, U. Eisner, and H. Williams, *J. Chem. Soc.*, 4226 (1965).

No evidence for valence tautomerism in either **3** or **8** was obtained. The geminal coupling of the methylene hydrogens remained invariant at $J$ = 11.0 Hz and $J$ = 12.0 Hz, respectively, as the temperature was varied. This speaks strongly against the presence of measurable quantities of azanorcaradienes at readily reachable temperatures.[27-31] Azanorcaradienes are indicated as intermediates during ring expansion in eq ii and iii (ref 25) but a simple 1,2 shift proceeding directly to the azepine is indistinguishable. Particularly interesting are the ring-inversion barriers for **3** and **8** which are higher than ever reported for azepines not attached to condensed rings.[33] A general trend of increasing $\Delta G^{\ddagger}$ for ring inversion with increasing substitution can be discerned from the limited number of examples, but it is undoubtedly unwarranted to consider this the only causative factor.

All known 3*H*-azepines bear substituents in the 2 position.[8] Attempts to prepare an unsubstituted derivative by the solvolysis of **9b** met with failure although uv spectra (Experimental Section) suggested that an azepine may well have been formed. Most likely a 2 substituent fulfills the double role of protecting the $N_1$–$C_2$ bond from addition or dimerization reactions and, in the case of alkyl substituents, provides ylidic structures (note the acidity of the 2-methyl group of **3**) which lend further stability to the azepine. That the $N_1$–$C_2$ bond is quite sensitive to addition is shown by the replacement of a 2-ethoxy substituent in a 3*H*-azepine by a secondary amine, apparently by means of addition–elimination.[34,35]

## Experimental Section

Melting points were determined with a Reichert melting point microscope and are uncorrected. Ultraviolet spectra were recorded on a Zeiss PMQ II spectrophotometer. Nmr spectra were taken on a Varian A-60 spectrometer (except where otherwise reported) with tetramethylsilane as an internal standard. An AEI MS-902 mass spectrometer equipped with an all-glass heated inlet system at 150° was used. The ionization potential and current were 70 eV and 100 μA, respectively. Microanalysis were performed by the analytical department of this laboratory under the supervision of Mr. W. M. Hazenberg.

**3,5-Dicarbomethoxy-2,6-dimethylpyridine** (1) was obtained by a Hantzsch pyridine synthesis as described for the corresponding diethyl ester[36] and was isolated in 30% overall yield: bp 131° (1.3 mm) and mp 100–102° (recrystallized from petroleum ether, by 40–60°); uv max ($C_2H_5OH$) 235 mμ (log ε 4.07), 273 (3.63), and 282 (sh, 3.54).

*Anal.* Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.26, 59.37; H, 5.93, 5.91; N, 6.37, 6.23.

**3,5-Dicarbomethoxypyridine** was prepared by adding dropwise an excess of an ethereal solution of diazomethane to a stirred and ice-cooled suspension of 17 g of pyridine-3,5-dicarboxylic acid in 100 ml of diethyl ether. Stirring was continued overnight. The unreacted acid was recovered by filtration (5.5 g) and the filtrate was evaporated. Distillation of the residue yielded 9 g (67%) of 3,5-dicarbomethoxypyridine: bp 127–132° (1.4 mm); mp 82.5–84°, recrystallized from a petroleum ether (bp 40–60°)–ethanol solvent mixture (lit.[37] mp 84–85°); uv max ($CH_3OH$) 220 mμ (log ε 4.02), 262 (sh, 3.18), 267 (3.21), and 276 (sh, 3.07).

**3,5-Dicarbomethoxy-2,6-dimethyl-2-hydroxymethyl-1,2-dihydroxypyridine** (**2a**) was obtained by irradiating a solution of 1.5 g of 3,5-dicarbomethoxy-2,6-dimethylpyridine in 650 ml of methanol for 23 hr with a Rayonet photochemical reactor equipped with 2537-Å lamps. Evaporation of the solvent and separation of the residue by preparative tlc on silica gel $PF_{254}$ with diethyl ether as eluent afforded 1.050 g (60%) of crude **2a**. Recrystallization from ethanol gave an analytically pure sample: mp 186–188°; ir (KBr) 3520 (OH) and 3395 $cm^{-1}$ (NH); uv max ($C_2H_5OH$) 216 mμ (log ε 4.10), 283 (4.34), and 385 (3.84); pmr ($CD_3OD$) δ 1.40 and 2.32 (s, 3, $CH_3$), 3.36 and 4.00 (d, 1, $J$ = 11.5 Hz, $CH_2OH$), 3.67 (s, 6, ester $CH_3$), and 7.80 (s, 1, vinylic H).

*Anal.* Calcd for $C_{12}H_{17}NO_6$: C, 56.48; H, 6.70; N, 5.49. Found: C, 56.61, 56.24; H, 6.82, 6.78; N, 5.41, 5.45.

**3,5-Dicarbomethoxy-2-hydroxymethyl-1,2-dihydropyridine** (**9a**) was obtained from irradiation of 1.5 g of 3,5-dicarbomethoxypyridine as reported above for **2a** [1.361 g (79%) of the product **9a** was collected]: mp 139–142° (recrystallized from $C_2H_5OH$); ir (KBr) 3230 (NH) and 3350 $cm^{-1}$ (OH, associated); uv max ($C_2H_5OH$) 218 mμ (log ε 4.11), 282 (4.26), and 383 (3.76); pmr ($C_5D_5N$) δ 3.56 and 3.60 (s, 3, ester $CH_3$), 3.50–4.20 (m, 2, $CH_2OH$), 5.05 (q, 1, $CHCH_2OH$), 6.00 (2, OH and NH), 7.96 (d, 1, vinylic HCNH), 8.03 (s, 1, vinylic H).

*Anal.* Calcd for $C_{10}H_{13}NO_5$: C, 52.86; H, 5.77; N, 6.17. Found: C, 52.76, 52.60; H, 5.97, 5.92; N, 6.10, 6.20.

**3,5-Dicarbomethoxy-2,6-dimethyl-2-tosyloxymethyl-1,2-dihydropyridine** (**2b**) was obtained by adding 1.55 g of pure *p*-toluenesulfonyl chloride[38] to an ice-cooled solution of 0.960 g of **2a** dissolved in 10 ml of dry pyridine, and the reaction mixture was stored overnight in a refrigerator. The solution was poured out into 60 g of ice–water and crystallization of the tosylate was induced by cooling for several hours. Filtration and subsequent drying afforded 1.40 g (87%) of **2b**. An analytically pure sample was obtained by recrystallization at low temperature from methanol: mp 131–133°; ir (KBr) 3320 $cm^{-1}$ (NH); uv max ($C_2H_5OH$) 220 mμ (log ε 4.30), 278 (4.27), and 385 (3.79); pmr ($CD_3OD$) δ 1.48, 2.25, and 2.48 (s, 3, $CH_3$), 3.54 and 3.67 (s, 3, $OCH_3$), 3.54 and 3.67 (d, 1, $J$ = 10.0 Hz, $CH_2O$), 7.72 (s, 1, vinylic H), 7.40 and 7.80 (d, 2, $J$ = 7.0 Hz, aromatic hydrogens).

*Anal.* Calcd for $C_{19}H_{23}NO_7S$: C, 55.73; H, 5.66; N, 3.42; S, 7.83. Found: C, 55.37, 55.65; H, 5.64, 5.67; N, 3.29, 3.29; S, 8,00, 7.99.

**3,5-Dicarbomethoxy-2-tosyloxymethyl-1,2-dihydropyridine** (**9b**) could be obtained from **9a** in 66% yield by the same procedure as described above: mp 105–108° (recrystallized from a diethyl ether–methylene chloride solvent mixture); ir (KBr) 3290 $cm^{-1}$ (NH); uv max ($C_2H_5OH$) 222 mμ (log ε 4.33), 275 (4.20), and 380 (3.16); pmr ($CD_3OD$) δ 2.48 (s, 3, tolyl $CH_3$), 3.67 and 3.69 (s, 3, $OCH_3$), 3.60–4.20 (m, 2, $CH_2O$), 4.85 (q, 1, $CHCH_2O$), 7.20–7.90 (5, aromatic and vinylic hydrogens). Owing to difficulties in crystallization an analytical sample of **9b** could not be obtained.

**Solvolysis of 2b** was carried out by heating a solution of 1.120 g of **2b** in 10 ml of dry pyridine for 10 min at 100°. After this time the uv-absorption band of **2b** at 385 mμ had disappeared and a new band was present at 305 mμ. The pyridine was removed by evaporation and the residue dissolved in methylene chloride. This solution was extracted three times with water, dried ($Na_2SO_4$), and evaporated. The aqueous layer gave upon evaporation and drying the pyridinium tosylate salt (85%), characterized by its pmr spectrum. The residue from the organic layer afforded upon separation by preparative tlc (silica gel $PF_{254}$ and diethyl ether) 0.263 g (41%) of pure 4,6-dicarbomethoxy-2,7-dimethyl-3*H*-azepine (**3**) as an oil and 0.119 g

(27) For the oxygen case, existence of a benzene oxide form has been demonstrated unequivocally: E. Vogel, W. A. Böll, and H. Günther, *Tetrahedron Lett.*, 609 (1965); also ref 8.

(28) Geminal coupling in cyclopropanes and related systems is usually much smaller,[29] and in norcaradienes a value of $J$ = 4–5 Hz is found.[30] 3,4-Diazanorcaradienes are known, however.[31] Comments on the stabilization of norcaradienes have been made.[32]

(29) E. Ciganek, *J. Amer. Chem. Soc.*, **87**, 1149 (1965); **89**, 1454 (1967). F. Kaplan, C. O. Schultz, D. Weisleder, and C. Klopfenstein, *J. Org. Chem.*, **33**, 1728 (1968).

(30) E. Vogel, *Pure Appl. Chem.*, **20**, 237 (1969).

(31) G. Maier, *Angew. Chem.*, **79**, 827 (1967). The energy barrier for the conversion of 2,5-dicarbomethoxy-3,4-diazanorcaradiene to its diazepine analog has recently been determined accurately: D. A. Kleiner, G. Binsch, A. Steigel, and J. Sauer, *J. Amer. Chem. Soc.*, **92**, 3787 (1970).

(32) R. Hoffmann, *Tetrahedron Lett.*, 2907 (1970).

(33) A. Mannschreck, G. Rissmann, F. Vögtle, and D. Wild, *Ber.*, **100**, 335 (1967).

(34) (a) L. A. Paquette, *J. Amer. Chem. Soc.*, **85**, 4053 (1963); (b) *ibid.*, **86**, 4096 (1964); (c) W. von E. Doering and R. A. Odum, *Tetrahedron*, **22**, 81 (1966).

(35) E. Vogel, R. Erb, G. Lenz, and A. A. Bothner-By, *Justus Liebigs Ann. Chem.*, **682**, 10 (1965).

(36) A Singer and S. M. McElvain, *Org. Syn.*, **14**, 30 (1934).

(37) A. L. Searles and R. M. Warren, *J. Org. Chem.*, **18**, 1325 (1953).

(38) S. W. Pelletier, *Chem. Ind. (London)*, 1034 (1953).

(18%) of the dimer **5**. The oily product **3** showed ir (neat) 1727 and 1712 $cm^{-1}$ (C=O); uv max ($C_6H_{12}$) 215 mμ (log ε 4.24), 267 (3.83), and 305 (3.82). The dimer **5** had mp 138–140° (recrystallized from a cyclohexane–diethyl ether solvent mixture); ir (KBr) 3360 (NH), 1710 and 1680 $cm^{-1}$ (C=O); uv max ($C_2H_5OH$) 219 mμ (log ε 4.49), 274 (4.35), 314 (sh, 4.06), and 354 (4.12).

*Anal.* Calcd for $C_{24}H_{30}N_2O_8$: C, 60.75; H, 6.38; N, 5.90. Found: C, 60.71, 60.70; H, 6.37, 6.50; N, 6.10, 6.04.

**Dimerization of 3** was observed when a solution of 0.129 g in chloroform was refluxed for several hours. (Dimerization was also observed in methanol at room temperature and qualitatively proceeded more rapidly in this solvent.) A spot with the same $R_f$ value as the above-obtained dimer appeared on the tlc plate. Separation with preparative tlc (silica gel $PF_{254}$ and diethyl ether) yielded 0.024 g (19%) of **3** and 0.054 g (42%) of a solid, mp 130–134° (recrystallized from cyclohexane) with the same spectral properties as the earlier isolated dimer of the 3*H*-azepine **3**.

**Thermal reversion of the dimer 5 to 3** was observed when 0.200 g of **5** was refluxed for 15 min in chlorobenzene. On tlc **3** appeared as the main product, while the dimer **5** was present only in a trace amount. After removal of the solvent by evaporation and column chromatography of the residue over silica gel and diethyl ether as eluent, we collected 0.120 g (60%) of an oil with the same spectral properties as **3**.

**Dimerization of 3 in $CH_3OD$** was observed when a solution of 80 mg of **3** in 5 ml of $CH_3OD$ was refluxed for 16 hr. The solution contained at this stage almost only **5** as confirmed by tlc analysis. The methanol was removed by evaporation and the residue refluxed for 1 hr in chlorobenzene to convert the dimer **5** to monomer **3**. Evaporation of the solvent followed by column chromatography of the residue (silica gel with diethyl ether) yielded 52 mg (65%) of **3** with 53% deuterium incorporation in the 2-substituted methyl group as confirmed by pmr and mass spectral analysis.

**4,6-Dicarbomethoxy-2,7-dimethyl-1,2-dihydro-3*H*-azepine** (**6**) was obtained by shaking 200 mg of **3** dissolved in 50 ml of methylcyclohexane for 5 hr with 300 mg of Pt catalyst in a Parr apparatus under a hydrogen pressure of 2.5 atm. The catalyst was removed by filtration and washed carefully with methanol because of the insolubility of the reduction product in methylcyclohexane. The concentrated filtrate afforded upon preparative tlc (silica gel $PF_{254}$ and diethyl ether) 144 mg (72%) of **6**. An analytical sample was obtained by dissolving the compound in diethyl ether and slowly evaporating the solvent until crystallization started: mp 98–99°; ir (KBr) 3360 (NH), 1660 and 1650 $cm^{-1}$ (C=O); uv max ($C_2H_5OH$) 223 mμ (log ε 3.89), 280 (3.90), and 357 (3.86).

*Anal.* Calcd for $C_{12}H_{17}NO_4$: C, 60.23; H, 7.16; N, 5.86. Found: C, 59.86, 59.95; H, 7.34, 7.23; N, 5.92, 5.82.

**4,6-Dicarbomethoxy-7-methyl-2-(*trans*-styryl)-3*H*-azepine** (**8**) was formed when 260 mg of **3** was refluxed overnight with 120 mg of benzaldehyde and several drops of diethylamine in benzene. Evaporation of the solvent gave an oil that slowly solidified. Recrystallization from methanol afforded 118 mg (32%) of **8**. A second recrystallization gave an analytical sample: mp 122–123.5°; ir (KBr) 1690 and 1720 $cm^{-1}$ (C=O); uv max ($C_2H_5OH$) 224 mμ (log ε 4.28), 276 (4.43), and 346 (4.25); pmr ($CCl_4$) δ 2.52 (s, 3, $CH_3$), 3.75 and 3.80 (s, 3, $OCH_3$), 6.67 and 7.67 (d, 1, $J$ = 16.0 Hz, HC=CH trans), 7.20–7.60 (m, 5, aromatic hydrogens), and 7.75 (s, 1, vinylic H); pmr ($C_6H_5Cl$) at 10° δ 1.20 and 4.78 (d, 1, $J$ = 12.0 Hz, $CH_2$), at 125° δ 2.92 (s, 2, $CH_2$).

*Anal.* Calcd for $C_{19}H_{19}NO_4$: C, 70.08; H, 5.88; N, 4.31. Found: C, 69.84, 69.76; H, 5.83, 5.89; N, 4.31, 4.39.

**Hydrogen cyanide addition to 3**[6c] was tested by leading HCN gas through an ethereal solution of the azepine. The dimer **5** was observed as the only reaction product as confirmed by ir spectroscopy and tlc analysis.

**Diels–Alder reaction of 3** with dicarbomethoxyacetylene did not take place when equimolar quantities of both reagents were refluxed in benzene.

**Photolysis of 3**[6a] in diethyl ether for 24 hr with a mercury high-pressure lamp with a Vycor jacket did not yield any isolable product. The course of reaction was followed by uv spectroscopy: only slow decrease in the absorption of **3** was observed and no new peaks appeared.

**Solvolysis of 9b** was carried out (a) at 85° in pyridine, (b) at 85° in pyridine and subsequent addition of HCN at 0° to the reaction mixture, (c) by slowly warming up a solution of **9b** in pyridine saturated with HCN and KCN to 80°, (d) in dimethyl sulfoxide solution saturated with KCN at 40°.[6b] In all cases a sharp new uv absorption was observed at 345 mμ after solvolysis but no products could be isolated despite repeated attempts.

**3,5-Dicarbomethoxy-2-tosyloxymethylpyridine** (**10**) was obtained when 1.1 g of **9b** were refluxed for several hours in 50 ml of benzene. **10** (177 mg, 17%) was collected after evaporation of the solvent and preparative tlc (silica gel and a diethyl ether–benzene 1:1 solvent mixture) of the residue. Recrystallization from diethyl ether afforded an analytical sample: mp 89.5–90°: uv max ($C_2H_5OH$) 227 mμ (log ε 4.36) and 265 (3.52); pmr ($CCl_4$) δ 2.40 (s, 3, $CH_3$), 3.95 (s, 6, $OCH_3$), 5.48 (s, 2, $CH_2$), 7.25 and 7.72 (d, 2, $J$ = 8.0 Hz, phenyl hydrogens), 8.61 and 9.08 (d, 1, $J$ = 2.0 Hz, pyridyl hydrogens).

*Anal.* Calcd for $C_{17}H_{17}NO_7S$: C, 53.83; H, 4.52; N, 3.70; S, 8.46. Found: C, 53.98, 53,80; H, 4.74, 4.57; N, 3.56, 3.48; S, 8.47, 8.40.

**Determination of the yield of 3 by uv measurements** was carried out by heating a solution of 1.04 g of **2b** in 10 ml of dry pyridine as described above. The solution (0.1 ml) was diluted $10^4$ times and the absorptions were measured.

| mμ | Before reaction, $E$ | After reaction, $E$ | | Yield, % |
|---|---|---|---|---|
| 385 | 0.154 | 0.006 | 0.015 | |
| 305 | 0.041 | 0.174 | 0.185 | 105, 112 |

**Kinetic data** were obtained from $10^{-2}$ $M$ solutions of **2b**; 1-ml samples were diluted 50 times and the absorptions measured by uv.

**Registry No.**—**1**, 27525-74-2; **2a**, 27525-75-3; **2b**, 27525-76-4; **3**, 27525-77-5; **5**, 27525-78-6; **6**, 27525-79-7; **8**, 27525-80-0; **9a**, 26165-23-1; **9b**, 27525-82-2; **10**, 27525-83-3.