Unsaturated Heterocyclic Systems. LIII. Thermochemical Reactions of 1H-Azepine Derivatives. II. Aromatization and Sigmatropic Migrations Involving Nitrogen[1]

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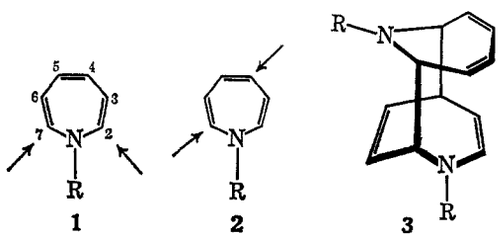
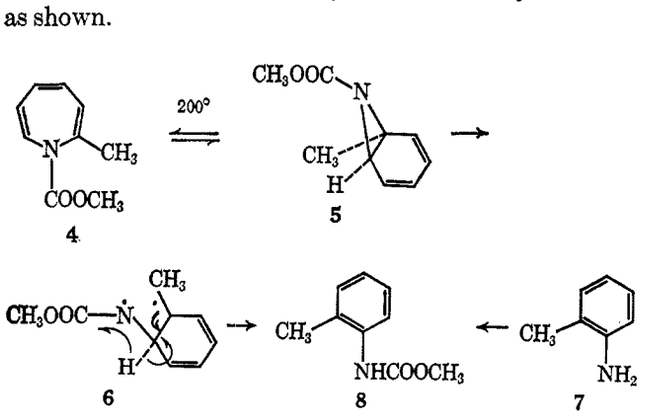
In contrast to N-carbalkoxy-1H-azepines and their 3- and 4-methyl derivatives which undergo ready dimerization at elevated temperatures, 2-methyl-N-carbomethoxyazepine and a number of disubstituted and annelated congeners are seen to aromatize or rearrange when heated. This behavior is not shared by 2,7-dimethyl-N-carbomethoxyazepine, which is stable at 250°, but decomposes above that temperature; no characterizable products are produced. A mechanistic interpretation of these results derived in part on product analysis and founded to some degree of thermodynamic considerations is advanced. Acid-catalyzed rearrangements of these same azepines are also discussed, since the bond reorganizations noted in this aspect of the work provide parallel mechanistic insight into the structural requirements for the changes which occur.

At temperatures approaching 130°, 1H-azepine derivatives lacking ring substituents and the 3- or 4-methyl derivatives undergo rapid kinetically controlled dimerization by way of a mechanism that involves (6 + 4)π *exo* cycloaddition to give the dimer **3**.[3] No aromatization was detected under the conditions used. We were then led to examine the behavior of azepines with substituents at the positions directly involved in the dimerization (*cf.* **1** and **2**). In this paper we report the sharply contrasting behavior of variously substituted derivatives.



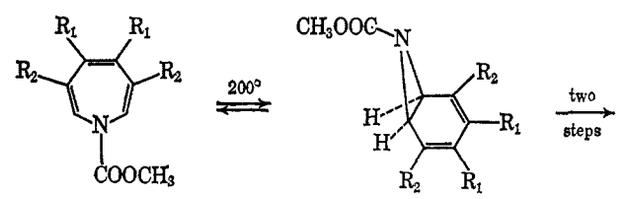
1 **2** **3**

Thermal Rearrangement of Monocyclic 1H-Azepines. —Heating of 2-methyl-N-carbomethoxyazepine (**4**) at 130° for periods of time ranging up to 2 hr led to no reaction, but at 200° **4** was converted in 64% yield to the aromatic urethan **8**, which was synthesized as shown.



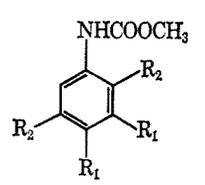
4 **5** **6** **8** **7**

Similarly, the 4,5-dimethyl congener (**9**) was transformed in this temperature range to **11** (68% yield), and the 3,6-dimethyl derivative **12** led to **14**. There was no evidence of dimerization on any of these reactions.



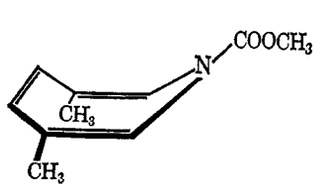
9, $R_1 = CH_3$; $R_2 = H$
12, $R_1 = H$; $R_2 = CH_3$

10, $R_1 = CH_3$; $R_2 = H$
13, $R_1 = H$; $R_2 = CH_3$



11, $R_1 = CH_3$; $R_2 = H$
14, $R_1 = H$; $R_2 = CH_3$

These observations suggest that the dimerization of 1H-azepines is subject to pronounced steric rate retardation. Because the presence of methyl groups at the "strategic" 2, 4, and 7 positions of the ring substantially retards the rate of the (6 + 4)π cycloaddition process, aromatization becomes the kinetically favored reaction pathway. In the case of **12**, methyl groups at positions 3 and 6 also inhibit dimerization. Dreiding models of **12** provide further support for the steric argument, because the location of the methyl substituents in this azepine blocks facile approach to the bottom side of its boat conformation (see **15**).



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The major structural changes involved in passing from **4**, **9**, and **12** to the corresponding aromatic isomers can best be rationalized in terms of azanorcaradiene valence tautomers as **5**, **10**, and **13**. Homolytic rupture

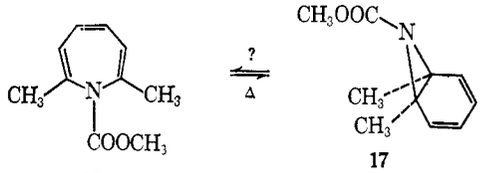
(1) For previous paper, see L. A. Paquette, D. E. Kuhla, J. H. Barrett, and R. J. Haluska, *J. Org. Chem.*, 2866 (1969).

(2) National Institutes of Health Predoctoral Fellow, 1965–1968.

(3) L. A. Paquette, J. H. Barrett, and D. E. Kuhla, *J. Amer. Chem. Soc.*, **91**, 3616 (1969).

of the more highly substituted C–N bond[4] with synchronous hydrogen atom transfer leads to benzenoid stabilization. Since signals due to azanorcaradiene tautomers are not seen in the nmr spectra of these azepines,[1] the concentration of such reactive intermediates is not large. It is striking that thermally induced suprafacial sigmatropic shifts of order [1,5][5] of the type observed in tropilidene skeletal rearrangements[6] are not operative in these heterocyclic examples under the conditions examined.

The 2,7-dimethyl derivative **16** was remarkably stable and withstood prolonged heating (24 hr) at 200° without noticeable dire effects. No spectral changes (nmr) were noted on heating a solution of **16** in Cl_2=

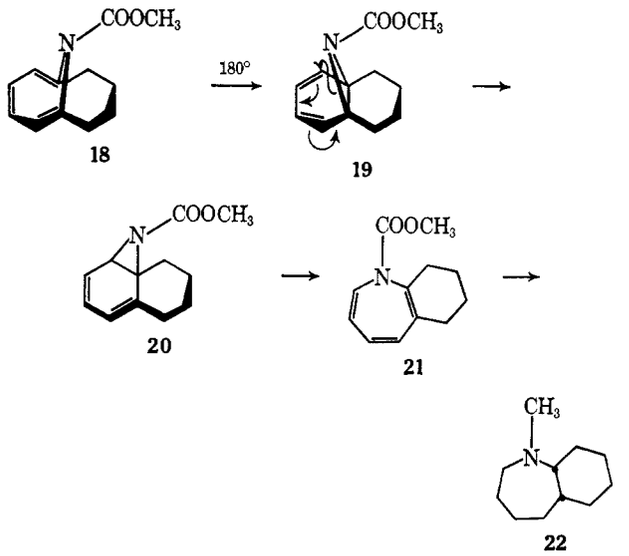


16 **17**

CCl_2 under nitrogen at 250° for 30 min; at 300° the sample darkened gradually and the various nmr signals were seen to fade. No characterizable product could be isolated.

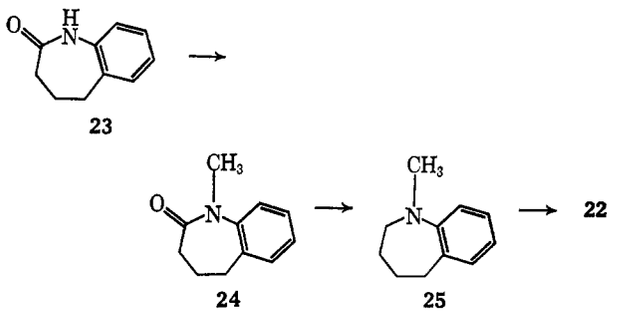
Thermal Rearrangement of Annelated Azepines.— We next investigated the thermochemical behavior of the related annelated substances **18** and **26**. As reported earlier,[1] the structures of **18** and **26** differ significantly; whereas the former is simply a bridged 2,7-disubstituted 1H-azepine, steric factors produced by the trimethylene bracket force **26** to exist in the aziridine form. Models indicate that valence tautomeric ring opening of the central bond in **26** is severely inhibited, and any rearrangements in **26** would likely occur from the tricyclic structure.

Pyrolysis of a neat sample of **18** in a sealed tube proceeded at a convenient rate at 180°. The process of the rearrangement was initially followed by thermolysis of small samples and gas chromatographic analysis at various intervals. After an optimal time of 30 min, molecular distillation of the crude mixture afforded a new azepine (**21**) in 87% yield. The structure of **21** was elucidated by spectra and partial degradation. The uv spectrum of **21** in ethanol displays the typical two bands characteristic[1] of several substituted N-carbalkoxyazepines at 213.5 (ϵ 19,500), and 289.5 mμ (ϵ 1500). The nmr spectrum of **21** in carbon tetrachloride solution shows four vinyl protons in the δ 5.39–6.11 region, a sharp three-proton methoxyl singlet at 3.58, and a broad eight-proton multiplet at 1.14–2.92, in excellent agreement with this azepine formulation. Structure **21** was further confirmed by catalytic hydrogenation and lithium aluminum hydride reduction to *cis*-2-azabicyclo-



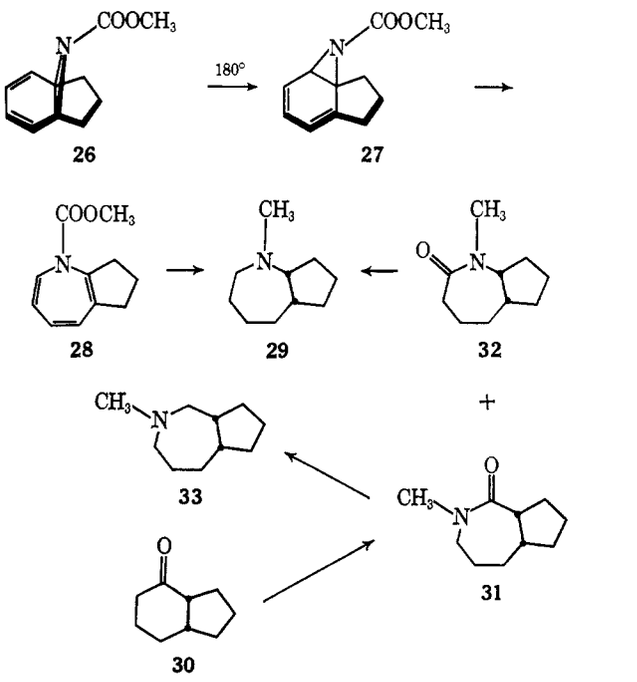
18 **19** **20** **21** **22**

[5.4.0]undecane (**22**). An authentic sample of **22** was synthesized in three well-precedented steps from homodihydrocarbostyril (**23**).



23 **24** **25** **22**

The thermal behavior of **26** was completely analogous to that of **18**. When heated at 180° for 30 min, **26** was transformed in 93% yield into 2,3-trimethylene-N-carbomethoxyazepine (**28**), the identity of which was similarly established by spectroscopic and chemical means. In this instance, the rate of the rearrangement could be measured by nmr techniques. The following



26 **27** **28** **29** **32** **33** **31** **30**

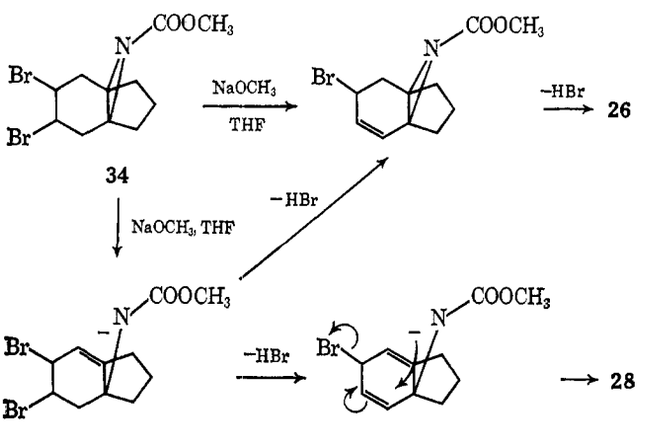
(4) A radical mechanism for these thermal reactions has not been established experimentally. However, the intervention of radicals seems most plausible in view of the elevated temperatures required for aromatization and the general acceptance of diradicals in somewhat related thermal bond reorganizations [J. A. Berson, *Accounts Chem. Res.*, **1**, 152 (1968); M. R. Wilcott, III, and C. J. Boriack, *J. Amer. Chem. Soc.*, **90**, 3287 (1968)]. For these reasons, radical intermediates are utilized herein, although it should be understood that the dipolar alternative to this mechanism has not been ruled out (however, see below).

(5) R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, **87**, 2511 (1965).

(6) (a) J. A. Berson and M. R. Wilcott, III, *ibid.*, **88**, 2494 (1966); (b) J. A. Berson, P. W. Grubb, R. A. Clark, D. R. Hartter, and M. R. Wilcott, III, *ibid.*, **89**, 4076 (1967).

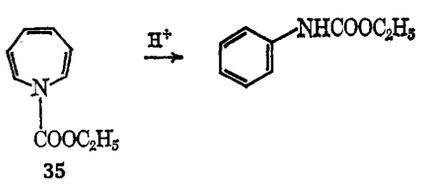
first-order rate constants and thermodynamic parameters were determined: $k_{158°} = 1.32 \times 10^{-4}$ sec^{-1}; $k_{168°} = 4.31 \times 10^{-4}$ sec^{-1}; $\Delta H^{\ddagger} = 4.38$ kcal/mol; $\Delta S^{\ddagger} = 24.6$ eu.[7] The simplest representation of the conversion of **26** to **28** requires the intervention of azanorcaradiene tautomer **27**. In principle, two mechanisms for the initial isomerization of **26** to **27** could be operative: (a) concerted suprafacial sigmatropic rearrangement of order [1,5] without intermediates, or (b) intramolecular 1,5 shift of nitrogen *via* diradical intermediates. The first process is permitted, but not required, by orbital symmetry considerations.[5,8] The large positive entropy of activation suggests a two-step mechanism for the rearrangement of **26** to **27**. That is to say, whereas a concerted mechanism would be expected to have a negative entropy, a transition state leading to a diradical should have more degrees of freedom than the ground state, resulting in a positive $\Delta S^{\ddagger}$. This conclusion is, of course, based on the reasonable assumption that **26** → **27** is rate determining.

Before discussing the acid-catalyzed rearrangements of 1H-azepines, the anomalous behavior[1] of dibromide **34** on dehydrobromination should be mentioned. Thus, it was shown that treatment of **34** with powdered sodium methoxide in anhydrous tetrahydrofuran gave rise not only to **26**, but also to substantial quantities of **28**.[1] Since **26** proved to be totally stable to the alkaline reaction conditions base-catalyzed rearrangement of **26** to **28** cannot be implicated. Rather, **28** must arise directly from dibromide **34**. Two plausible mechanisms are advanced below. Apparently the carba-



mate function can compete successfully with a bromine substituent as the preferred leaving group, perhaps for reasons of internal strain; recyclization to a new, less strained aziridine with ejection of bromide ion ultimately affords **28**.

Acid-Promoted Rearrangements.—Hafner has noted that reaction of N-carbethoxyazepine (**35**) with dilute



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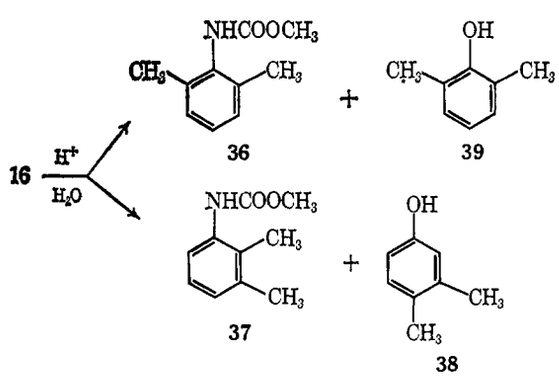
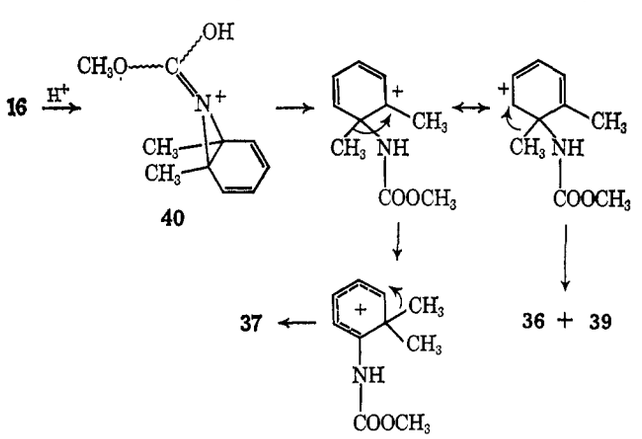
acids leads rapidly to N-phenylcarbamate.[9] More recently, Marsh and Simmons reported that acid hydrolysis of the mixture of isomeric fluoro-N-cyanoazepines obtained from fluorobenzene and cyanogen azide gave *o*- and *p*-fluorophenylureas in a 1:1 ratio containing less than 0.5% *meta* isomer.[10] Because of the relationship to the thermally induced bond reorganizations just discussed, we undertook an investigation of this cationic rearrangement with selected 1H-azepines. Most significantly, the temperatures of the two reactions differed widely.

Initially, attention was directed to the differing behavior of 3,6-dimethyl- (**12**) and 2,7-dimethyl-N-carbomethoxyazepines (**16**) toward acid. After exposure of a dilute dioxane solution of **12** to 10% sulfuric acid at room temperature for 2 hr, an 82% yield of **14** was obtained. Similar treatment of **16** for 4 hr led only to a high-yield recovery of unreacted starting material. However, when the same mixture was heated at reflux for 1 hr, **16** was completely transformed into a viscous brown oil. The major identifiable component (16%) of this oil was shown to be 2,6-dimethyl-N-carbomethoxyaniline (**36**). A second carbamate which was isolated in 1% yield was identified as the 2,3-dimethylaniline derivative **37**. In addition, two phenols were produced in equally low yield. These were defined as 3.4-dimethylphenol (**38**, 6%) and 2,6-dimethylphenol (**39**, 1%). The remainder of the crude product was polymeric in nature.



A mechanistic rationalization of the formation of **36**–**39** involves the assumption that **16** is first converted to **40**, which leads to **36**, **37**, and **39** through a series of carbonium ion rearrangements. On the other hand, the



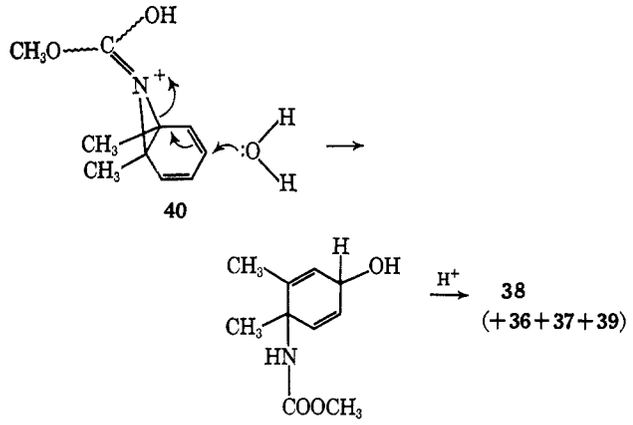
(7) Similar studies with **18** were complicated because of interference of crucial nmr absorptions by peaks due to minor by-products arising from aromatization of **21**.

(8) The observed rearrangement finds analogy in the thermal rearrangement of certain tropilidenes [ref 6 and E. Ciganek, *J. Amer. Chem. Soc.*, **89**, 1458 (1967)] and 1,6-methano[10]annulene [footnote 2, V. Rautenstrauch, H. J. Scholl, and E. Vogel, *Angew. Chem. Intern. Ed. Engl.*, **7**, 288 (1968)].

(9) K. Hafner, *Angew. Chem.*, **75**, 1041 (1963); *Angew. Chem. Intern. Ed. Engl.*, **3**, 165 (1964).

(10) F. D. Marsh and H. E. Simmons, *J. Amer. Chem. Soc.*, **87**, 3529 (1965).

formation of 3,4-dimethylphenol (**38**) appears to be the result of a direct attack of water on **40**. In mechanistic

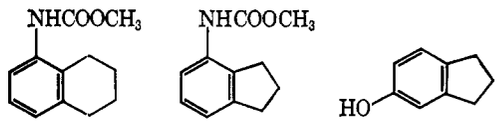


40

38 (+36+37+39)

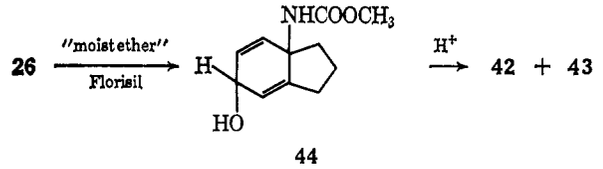
detail, the acid-catalyzed rearrangement of **16** parallels closely the behavior of 2,7-dimethyloxepin under similar conditions.[11]

At room temperature in the presence of small quantities of dilute sulfuric acid, azepines **18** and **21** undergo almost quantitative conversion to **41**. 2,3-Trimethylene-N-carbomethoxyazepine (**28**) behaved analogously to give **42** in 86% yield. Under the same conditions, the more highly strained tricyclic isomer **26** was likewise converted to **42**, but in low yield (7%). The major product of the rearrangement was 5-indanol (**43**, 42%). Presumably, therefore, attack by water on the protonated intermediate is kinetically favored over 1,5-sigmatropic shift of nitrogen, a property that allows for the formation of major amounts of **43**. Since an analogous phenol was not detected in the rearrangement of **18**, it would seem that the less strained nature of protonated **18** is more conducive to the migration of nitrogen.



41 **42** **43**

Strong support for the proposed mechanistic schemes was derived from chromatography of **26** on Florisil and elution with "moist ether," a process which afforded 1-(N-carbomethoxy)amino-4-hydroxybicyclo[4.3.0]nona-2,5-diene (**44**) in 82% yield. Evidence for this



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structure was derived from elemental analysis and the various spectra of the substance (see Experimental Section). Acid-catalyzed rearrangement of **44** gave rise only to **42** (8%) and **43** (56%), the ratio approximating that seen in the direct aromatization of **26**. Significantly, 1,2 migration of the carbamate group during the dienol–benzene rearrangement of **44** attests to the high probability that the quantity of **42** produced from acid treatment of **26** does not arise uniquely, if at all, from a 1,5-sigmatropic nitrogen shift.

Lastly, azepine **18** was seen to be inert to the above chromatographic conditions.

(11) E. Vogel and H. Günther, *Angew. Chem. Intern. Ed. Engl.*, **6**, 385 (1967).

Experimental Section[12]

Pyrolysis of 2-Methyl-N-carbomethoxyazepine (4).—A 1.10-g (6.65-mmol) sample of **4**[4] was heated in a sealed tube at 200° for 10 min. The dark product was chromatographed on Florisil (50 g). Elution with hexane–ether (19:1) yielded 685 mg (62.4%) of **8** as a fluffy white solid, mp 60.0–60.5° (from hexane–ether); ir $\nu_{max}^{CCl_4}$ 3345 (NH) and 1740 cm^{-1} (C=O). No other product was obtained on continued elution of the column with solvents of increasing polarity.

Anal. Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.32; H, 6.51; N, 8.61.

2-Methyl-N-carbomethoxyaniline (8).—*o*-Toluidine (10.7 g, 0.10 mol) and methyl chloroformate (4.72 g, 0.05 mol) in 100 ml of tetrahydrofuran were stirred at room temperature for 30 min. The precipitated hydrochloride salt was removed by filtration and the filtrate was concentrated *in vacuo* to give 8.25 g (100%) of **8**, mp 60–60.5° (from ether–hexane); nmr $\delta_{TMS}^{CCl_4}$ *ca.* 7.6 (m, 1 H, H-6), *ca.* 6.95 (m, 3 H, H-3,-4,-5), 6.4 (br, 1 H, NH), 3.17 (s, 3 H, $-OCH_3$), and 2.14 (s, 3 H, $-CH_3$).

Pyrolysis of 4,5-Dimethyl-N-carbomethoxyazepine (9).—A 200-mg (1.1 mmol) sample of **9** was heated in a sealed tube at 200° for 10 min. Chromatography of the dark product on Florisil (elution with hexane) gave 136 mg (68%) of **11**, mp 59–60° (from ether–hexane); ir $\nu_{max}^{CCl_4}$ 3448 (NH) and 1755 cm^{-1} (C=O). No other product was obtained on continued elution of the column.

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.12; H, 7.40; N, 7.67.

3,4-Dimethyl-N-carbomethoxyaniline (11).—Reaction of 12.1 g (0.10 mol) of 3,4-dimethylaniline with 4.72 g (0.05 mol) of methyl chloroformate in the predescribed manner afforded 8.95 g (100%) of **11**, mp 59–60°; nmr $\delta_{TMS}^{CDCl_3}$ 7.05 (m, 4 H, aromatic protons and NH), 3.69 (s, 3 H, $-OCH_3$), and 2.15 (s, 6 H, $-CH_3$).

Pyrolysis of 3,6-Dimethyl-N-carbomethoxyazepine (12).—A 600-mg (3.34 mmol) sample of **12**[1] was heated in a sealed tube at 200° for 10 min. The dark product was chromatographed on Florisil (50 g). Elution with hexane–ether (19:1) yielded 281 mg (46.8%) of **14** as a fluffy white solid, mp 86.5–87.0°; ir $\nu_{max}^{CCl_4}$ 3400 (NH) and 1740 cm^{-1} (C=O). No other product was obtained on continued elution of the column.

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.86; H, 7.31; N, 7.95.

2,5-Dimethyl-N-carbomethoxyaniline (14).—Reaction of 12.1 g (0.10 mol) of 2,5-dimethylaniline with 4.72 g (0.05 mol) of methyl chloroformate in the above manner gave 8.95 g (100%) of **14**, mp 86.5–87.0° (from ether–hexane); nmr $\delta_{TMS}^{CDCl_3}$ 7.46 (m, 1 H, H-6), 6.90 (m, 2 H, H-3,-4), 6.50 (br, 1 H, NH), 3.61 (s, 3 H, $-OCH_3$), 2.16 and 2.03 (s, 3 H each, $-CH_3$).

Pyrolysis of 1-Carbomethoxy-11-azabicyclo[4.4.1]undec-1,3,5-triene (18).—A 286-mg (1.44 mmol) sample of **18**[1] sealed in a Pyrex test tube was placed in an oil bath preheated to 180° for 30 min. Molecular distillation of the dark product [bp 100–110° (0.05 mm)] gave 248 mg (87%) of **21** as a pale yellow viscous liquid, ir $\nu_{max}^{CCl_4}$ 1718 cm^{-1} (C=O); uv λ_{max}^{hexane} 213.5 (ε 19,500) and 299 mμ (ε 1340); λ_{max}^{EtOH} 212 (ε 19,440), and 289.5 mμ (ε 1500); nmr $\delta_{TMS}^{CCl_4}$ 5.39–6.11 (m, 4 H, vinyl protons), 3.58 (s, 3 H, $-OCH_3$), 1.14–2.92 (m, 8 H, $-CH_2-$).

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.83. Found: C, 70.44; H, 7.52; N, 6.80.

Conversion of 21 to 2-Methyl-*cis*-azabicyclo[5.4.0]undecane (22).—A solution of 200 mg (0.97 mmol) of **21** in 75 ml of tetrahydrofuran was hydrogenated over 5% rhodium on carbon at 60 psig for 36 hr. The catalyst was separated by filtration and the filtrate was added dropwise to a stirred slurry of 2.0 g of

(12) Melting points are corrected and boiling points are uncorrected. The microanalyses were performed by the Microanalytical Laboratory, Herlev, Denmark. Infrared spectra were determined with a Perkin-Elmer Model 237 spectrometer fitted with a sodium chloride prism. Ultraviolet spectra were recorded with a Cary Model 14 spectrometer. The nmr spectra were determined with Varian A-60 or A-60A spectrometers purchased with funds made available through the National Science Foundation.

lithium aluminum hydride in 50 ml of anhydrous tetrahydrofuran. The reaction mixture was refluxed for 18 hr and worked up in the customary alkaline manner.[1] There was obtained 146 mg (89.6%) of **22** as a light yellow oil. An analytically pure sample was prepared by preparative scale vpc (5 ft × 0.25 in. aluminum column packed with 10% SF-96 on 60–80 mesh Chromosorb G at 152°). The spectral data of this sample were identical to those of the authentic sample of **22**. The picrate was obtained as yellow crystals, mp 171–172° (from ethanol); a mixture melting point was undepressed.

Alternative Synthesis of 22. A. N-Methylhomodihydrocarbostyril (24).—To a solution of 10.0 g (0.062 mol) of homodihydrocarbostyril (**23**)[13] in 50 ml of dry dimethylformamide was added 2.5 g of 60% sodium hydride–mineral oil dispersion (0.062 mol) and the mixture was heated at 50° for 1 hr. The flask was then cooled in ice while 14.2 g (0.10 mol) of methyl iodide was added dropwise during 5 min. The ice bath was removed and the mixture was stirred at room temperature for 1 hr. Ether (150 ml) was added and the precipitated solid was separated by filtration. The filtrate was evaporated *in vacuo* and the residual brown oil was vacuum distilled to give 9.66 g (89.0%) of **24** as a colorless liquid, bp 97–100° (0.1 mm); ir $\nu_{max}^{CCl_4}$ 1665 cm^{-1} (C=O); nmr $\delta_{TMS}^{CCl_4}$ 6.99–7.26 (m, 4 H, aromatic protons), 3.25 (s, 3 H, NCH_3), 2.51–2.85 (br t, 2 H, benzylic protons), and 1.90–2.26 (m, 4 H, methylene protons).

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 8.00. Found: C, 75.82; H, 7.77; N, 8.02.

B. N-Methyl-2,3-benzohexamethylenimine (25).—A 7.90-g (0.045-mol) sample of **24** was reduced with 4.0 g of lithium aluminum hydride in 150 ml of tetrahydrofuran as previously described. There was isolated 6.92 g (94.5%) of **25** as a colorless liquid, bp 58–60° (0.1–0.2 mm). The derived picrate melted at 144–145.5°.

Anal. Calcd for $C_{17}H_{18}N_4O_7$: C, 52.31; H, 4.68; N, 14.35. Found: C, 52.29; H, 4.69; N, 14.35.

C. Hydrogenation of 25.—A solution of 1.0 g (6.2 mmol) of **25** in 50 ml of ethanol was hydrogenated over 5% rhodium on carbon at 60 psig for 72 hr. The catalyst was filtered, the filtrate was concentrated, and the residue was distilled to give 920 mg (88.9%) of **22** as a colorless liquid, bp 72–74° (2 mm). The picrate melted at 171–172°.

Anal. Calcd for $C_{17}H_{24}N_4O_7$: C, 51.51; H, 6.10; N, 14.14. Found: C, 51.36; H, 6.35; N, 13.98.

Pyrolysis of 10-Carbomethoxy-10-azatricyclo[4.3.1.0^{1,6}]deca-2,4-diene (26).—A 100-mg (0.52 mmol) sample of **26**[1] was heated in a sealed tube for 30 min at 180°. Sublimation of the crude product at 50° and 0.05 mm afforded 93 mg (93%) of **28** as a light yellow solid, mp 61–63° (from pentane); ir $\nu_{max}^{CCl_4}$ 1727 cm^{-1} (C=O); uv λ_{max}^{hexane} 217 (ε 20,725), 253 sh (ε 1165), and 324 mμ (ε 1060); λ_{max}^{EtOH} 216.5 (ε 18,950), 249 sh (ε 905), and 312 mμ (ε 1270); nmr $\delta_{TMS}^{CDCl_3}$ 5.37–6.18 (m, 4 H, vinyl protons), 3.75 (s, 3 H, $-CH_3$), and 1.70–2.85 (m, 6 H, methylene protons).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.17; H, 7.00; N, 7.10.

Conversion of 28 to 2-Methyl-*cis*-2-azabicyclo[5.3.0]decane (29).—A 152-mg (0.80 mmol) sample of **28** was hydrogenated and reduced with lithium aluminum hydride as described for **21**. The resulting pale yellow oil was subjected to vpc purification (same column, 126°); there was obtained 68 mg (55.6%) of **29** as a colorless liquid. The picrate of **29** was obtained as light yellow needles from ethanol, mp 192.5–194°.

Anal. Calcd for $C_{16}H_{22}N_4O_7$: C, 50.25; H, 5.80; N, 14.65. Found: C, 50.56; H, 6.03; N, 14.67.

Unequivocal Synthesis of 29. A. Schmidt Ring Expansion of *cis*-Bicyclo[4.3.0]nonan-2-one (30).—A stirred ice-cold solution of 5.53 g (0.04 mol) of *cis*-bicyclo[4.3.0]nonan-2-one (**30**)[14] in 25 ml of concentrated hydrochloric acid was treated with 4.04 g (0.062 mol) of powdered sodium azide in small portions. After stirring for 3 hr, the mixture was evaporated *in vacuo* and the residue was dissolved in 35 ml of water and basified with 30% sodium hydroxide solution. The organic product was extracted with chloroform, dried, and evaporated to give 6.0 g of yellow-white solid. This material was recrystallized with difficulty from acetone–hexane to give 4.71 g (77%) of a mixture of isomeric amides, mp 102–109°.

Methylation of 4.15 g (0.027 mol) of this mixture with sodium hydride and methyl iodide in dimethylformamide in the predescribed manner yielded 4.02 g (88.4%) of a colorless liquid, bp 78–82° (0.1–0.25 mm), composed of approximately equal amounts of **31** and **32**.

B. Hydride Reduction of 31 and 32.—A 3.0-g (0.018 mol) sample of the mixture of **31** and **32** was reduced with 1.5 g (0.039 mol) of lithium aluminum hydride in 150 ml of tetrahydrofuran to produce 2.48 g (89.8%) of amine mixture, bp 68–70° (2–4 mm). The two amines (**29** and **33**) were cleanly separated by preparative vpc [10 ft × 0.25 in. aluminum column packed with 20% Apiezon L/KOH (4:1) on 60–80 mesh Chromosorb W at 134°]. The most rapidly eluted amine (**29**) was identical in all respects with the saturated amine prepared from azepine **28**; the picrate melted at 192.5–194°; a mixture melting point was undepressed.

The second amine was assigned structure **33**. Its picrate was obtained as yellow crystals from ethanol, mp 166–168° dec.

Anal. Calcd for $C_{16}H_{22}N_4O_7$: C, 50.25; H, 5.80; N, 14.65. Found: C, 50.19; H, 5.85; N, 14.59.

Acid-Catalyzed Rearrangement of 3,6-Dimethyl-N-carbomethoxyazepine (12).—To a solution of 600 mg (3.34 mmol) of **12** in 90 ml of dioxane was added 10 ml of 10% sulfuric acid, and the mixture was stirred at room temperature for 2 hr. The major portion of the solvent was removed *in vacuo* and the residue was treated with 400 ml of water and 500 ml of ether. The aqueous phase was further extracted with two 150-ml portions of ether and the combined organic layers were dried, filtered, and evaporated. There was obtained 548 mg of an off-white solid. Recrystallization of this material from ether–hexane gave 496 mg (82.6%) of **14**, mp 86–87°, identical in all respects with the authentic sample.

Acid-Catalyzed Rearrangement of 2,7-Dimethyl-N-carbomethoxyazepine (16).—A solution of 2.0 g (11.2 mmol) of **16** in 90 ml of dioxane and 10 ml of 10% sulfuric acid was refluxed for 1 hr. After cooling, 300 ml of water was added and the aqueous mixture was extracted with four 200-ml portions of ether.[15] There was obtained a viscous brown oil which was chromatographed on neutral alumina (activity I). Elution with hexane–ether (7:3) separated two fractions, each of which was found (vpc analysis) to be composed of a major and a minor component. Preparative vpc separation (5 ft × 0.25 in. aluminum column packed with 10% Carbowax 20M on 60–80 mesh Chromosorb W at 136°) afforded 81 mg (6%) of 3,4-dimethylphenol (**38**), mp 66–68°, identical with an authentic sample. The minor product (15 mg, 1%) was shown to be 2,6-dimethylphenol (**39**). The yield of the phenol mixture prior to vpc separation was 121 mg (9%).

Preparative vpc separation of the second fraction (5 ft × 0.25 in. aluminum column packed with 10% SF-96 on 60–80 mesh Chromosorb G at 148°) yielded 320 mg (16%) of 2,6-dimethyl-N-carbomethoxyaniline (**36**), mp 103–105°, and 20 mg (1%) of 2,3-dimethyl-N-carbomethoxyaniline (**37**), mp 90–92°.

2,6-Dimethyl-N-carbomethoxyaniline (36).—An authentic sample of **36** was obtained in quantitative yield from 2,6-dimethylaniline (12.1 g, 0.10 mol) and methyl chloroformate (4.72 g, 0.05 mol) under the above conditions as a fluffy white solid, mp 103–105° (from ether–hexane); ir $\nu_{max}^{CCl_4}$ 3365 (NH) and 1742 cm^{-1} (C=O); nmr $\delta_{TMS}^{CDCl_3}$ 6.89 (s, 3 H, aromatic protons), 6.65 (br, 1 H, NH), 3.59 (s, 3 H, $-OCH_3$), and 2.12 (s, 6 H, $-CH_3$).

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.99; H, 7.36; N, 7.85.

2,3-Dimethyl-N-carbomethoxyaniline (37).—Reaction of 2,3-dimethylaniline with methyl chloroformate in the predescribed fashion afforded a quantitative yield of **37** as a fluffy white solid, mp 90.5–92° (from ether–hexane); ir $\nu_{max}^{CCl_4}$ 3355 (NH) and 1748 cm^{-1} (C=O); nmr $\delta_{TMS}^{CDCl_3}$ 6.52–7.19 (m, 3 H, aromatic protons), 6.26 (br, 1 H, NH), 3.57 (s, 3 H, $-OCH_3$), 2.13 and 1.98 (s, 3 H each, $-CH_3$).

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.01; H, 7.36; N, 7.72.

Acid-Catalyzed Rearrangement of 18.—A solution of 150 mg (0.73 mmol) of **18** in 50 ml of dioxane was treated with 10 ml of 10% sulfuric acid for 2 hr at room temperature according to the generalized procedure described above. Recrystallization of the

(13) L. H. Briggs and G. C. Death, *J. Chem. Soc.*, 456 (1937).

(14) W. Hückel and E. Goth, *Chem. Ber.*, **67**, 2104 (1934); see also E. W. Warnhoff, D. G. Martin, and W. S. Johnson, "Organic Syntheses," Coll. Vol. IV, John Wiley & Sons, Inc., New York, N. Y., 1963, p 164, note 1.

(15) The remaining acidic aqueous layer was basified with 30% sodium hydroxide solution and the extraction process was repeated. A few milligrams of a yellow oil was isolated; this substance was not examined further.

residual solid (146 mg) from ether–pentane gave 133 mg (88.5%) of **41** as a fluffy white solid, mp 58.5–60°.

Acid-Catalyzed Rearrangement of 21.—Treatment of 350 mg (1.7 mmol) of **21** as above gave 326 mg of crude product. Recrystallization of this solid from ether–pentane afforded 294 mg (84%) of **41**, mp 58.5–60°, identical in all respects with an authentic sample.

1-(N-Carbomethoxy)amino-5,6,7,8-tetrahydronaphthalene (14).—Reaction of 1-amino-5,6,7,8-tetrahydronaphthalene (Aldrich Chemical Co.) with methyl chloroformate in the predescribed fashion yielded pure **41** in 91.5% yield, mp 58.5–60°; ir $\nu_{max}^{CCl_4}$ 1742 cm^{-1} (C=O).

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.35; H, 7.49; N, 6.80.

Acid-Catalyzed Rearrangement of 28.—A solution of 396 mg (2.07 mmol) of **28** in 50 ml of dioxane was treated with 10 ml of 10% sulfuric acid for 2 hr at room temperature according to the generalized procedure described above. Recrystallization of the crude product from ether–pentane yielded 341 mg (86%) of **42**, mp 69–70.5°, identical in all respects with an authentic sample.

4-(N-Carbomethoxy)aminoindan (42). A. 4- and 5-Aminoindans.—Indane (100 g) was nitrated according to the procedure of Lindner and Bruhin[16] to give a mixture of 4- and 5-nitroindans in approximately 70% yield. Reduction of the mixture with ferrous chloride in aqueous ethanol[16] afforded the derived amines in 80% yield (ratio of isomers 2:3).

B. Carbomethoxylation of 4- and 5-Aminoindans. Reaction of 13.32 g (0.10 mol) of the aminoindan mixture prepared above with 4.73 g (0.05 mol) of methyl chloroformate according to the above procedure gave 9.21 g (96.3%) of a brownish oil. Preparative vpc separation of this two-component mixture (5 ft × 0.25 in. aluminum column packed with 10% SF-96 on 60–80 mesh Chromosorb G, 152°) yielded the two pure carbamates, mp 69–70.5° and mp 63–65°.

The more rapidly eluted component was identified as **42**, mp 69–70.5°; ir $\nu_{max}^{CCl_4}$ 1715 cm^{-1} (C=O), by difference (see below).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.06; H, 6.83; N, 7.31.

The less rapidly eluted component was identified as 5-(N-carbomethoxy)aminoindan, mp 63–65°, on the basis of independent synthesis from authentic 5-aminoindan (Aldrich Chemical Co.); ir $\nu_{max}^{CCl_4}$ 1745 cm^{-1} (C=O).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33. Found: C, 69.25; H, 6.79; N, 7.38.

Acid-Catalyzed Rearrangement of 26.—A solution of 100 mg (0.576 mmol) of **26** in 50 ml of dioxane was treated with 10 ml of 10% sulfuric acid for 2 hr at room temperature as above. Column chromatography of the residue (no **26** remaining on the basis of nmr spectrum) on Florisil afforded 32 mg (42%) of 5-hydroxyindan (**43**), mp 51–53°, identical with an authentic sample (K + K Laboratories), and 7 mg (7%) of **42**, mp 69–70.5°. Elution of the column was achieved with hexane–ether (9:1).

Rearrangement of 26 on Florisil.—A mixture of 250 mg (1.31 mmol) of **26**, 50 ml of ether, 5 ml of water and 1 g of Florisil was evaporated to dryness at room temperature on a rotary evaporator. The resulting powder was placed on top of a column of 50 g of Florisil. Elution with hexane–ether (99:1) yielded 22 mg of unrearranged **26**. Elution with hexane–ether (19:1) afforded 186 mg (81.5%) of **44** as white needles, mp 137–138° (from ether–hexane); ir $\nu_{max}^{CCl_4}$ 3448, 3310 (-OH and NH) and 1725 cm^{-1} (C=O); uv λ_{max}^{EtOH} only end absorption; mass spectrum *m/e* 209; nmr $\delta_{TMS}^{CDCl_3}$ 5.87–6.39 (m, 3 H, vinyl protons), 5.52 (br, 1 H, NH), 4.22–4.48 (br, 2 H, CHOH), 3.65 (s, 3 H, $-OCH_3$), 1.34–2.73 (m, 6 H, methylene protons). Addition of D_2O results in the disappearance of the 5.52 peak and gross simplification of the 4.22–4.48 absorption (intensity decreasing to 1 H).

Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.34; H, 7.27; N, 6.78.

Acid-Catalyzed Rearrangement of 44.—A solution of 150 mg (0.72 mmol) of **44** in 50 ml of dioxane was treated with 10 ml of 10% sulfuric acid at room temperature for 2 hr in the above fashion. The resulting viscous brown oil (94 mg) was chromatographed on Florisil. Elution with hexane–ether (9:1) afforded 54 mg (56%) of 5-hydroxyindan (**43**), mp 51–53°, and 11 mg (8%) of **42**, mp 68–70°.

Registry No.—**8,** 14983-92-7; **11,** 20642-87-9; **14,** 20642-88-0; **21,** 20642-89-1; **22,** 20642-49-3; **22** (picrate), 20642-68-6; **24,** 20678-82-4; **25,** 20642-90-4; **25** (picrate), 20642-91-5; **28,** 20642-92-6; **29** (picrate), 20642-50-6; **31,** 20642-51-7; **32,** 20642-52-8; **33** (picrate), 20642-53-9; **36,** 20642-93-7; **37,** 20642-94-8; **38,** 95-65-8; **41,** 20642-96-0; **42,** 20642-97-1; **44,** 20642-98-2; 5-(N-carbomethoxy)aminoindan, 20642-99-3.

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(16) J. Lindner and J. Bruhin, *Chem. Ber.*, **60**, 435 (1927).