of water before being dried over anhydrous magnesium sulfate. After filtration, the ether was removed under reduced pressure, leaving a residue that still retained traces of acetic acid. The residue (32.3 g.) was dissolved in a small volume of methanol (~50 ml.) and cooled in an Dry Ice–acetone bath. The resulting solid was quickly filtered and washed with cold methanol. After air drying, the solid (17.2 g., 40%) was found to melt at 38°. The infrared spectrum of the product was superimposable on the spectrum of 2-nitrocyclohexanone (I) obtained from the chromic acid oxidation of 2-nitrocyclohexanol (II).

The Reaction of Acetyl Nitrate with Cyclopentene.—The acetyl nitrate reagent was prepared in an identical manner with that used for the cyclohexene reaction. Cyclopentene (20.5 g., 0.3 mole) was added in one portion to the acetyl nitrate at −20°. The temperature of the reaction mixture rose to 4° while the Dry Ice–acetone bath was maintained at −60 to −70°. After allowing the reaction mixture to cool to −20°, it was immediately poured into 1.5 l. of cold water. The solution was allowed to stand for 2 hr. and was then diluted with 800 ml. of a saturated sodium chloride solution. The resulting solution was extracted with four 200-ml. portions of ether which were combined, washed with two 200-ml. portions of water, and dried over anhydrous sodium sulfate. The ether was removed under reduced pressure, giving 23.9 g. of residue. Distillation of the residue provided two fractions. The first fraction [4.1 g., 13%, b.p. 37–38° (0.08 mm.)] was identified as being a mixture of 3-nitrocyclopentene (XI) and 4-nitrocyclopentene (XII). The infrared spectrum of this fraction shows λ_{max}^{neat} 3.25, 3.44, 3.53, 6.18, 6.45, 7.27, 13.13, and 14.20 μ. Although there is some overlapping of peaks, the n.m.r. spectrum of the mixture shows the spectrum of both XI and XII. The proton on the nitro-bearing carbon of XII appears at 5.14 p.p.m., while the same proton for XI appears at 5.46 p.p.m. Both patterns are complex multiplets. The olefinic protons of XII appear as a virtual singlet (5.70 p.p.m.), while the olefinic protons of XI appear as a highly split AB multiplet at 6.10 p.p.m. The methylenes of XII occur as an unsymmetrical doublet at 2.97 p.p.m., while the methylenes of XI occur as a complex multiplet at 2.48 p.p.m. The second fraction [13.4 g., b.p. 88–90° (0.08 mm.)] was identified[5a] as a mixture of 2-nitrocyclopentyl acetate (IX) and 2-nitrocyclopentyl nitrate (X) by infrared analysis. The infrared spectrum of the mixture shows λ_{max}^{neat} 5.78, 6.13, 6.44, 7.26, 8.05, and 8.71 μ.

Reactions of 14-Hydroxy-14-azadispiro[5.1.5.2]pentadec-9-ene-7,15-dione and Related Compounds. I. The 3,11-Dimethyl Derivative[1a]

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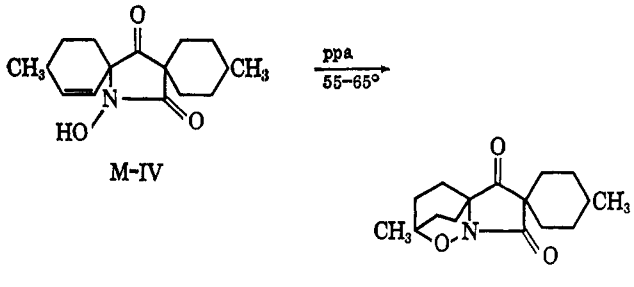
When 3,11-dimethyl-14-hydroxy-14-azadispiro[5.1.5.2]pentadec-9-ene-7,15-dione (M-IV) is heated with polyphosphoric acid at 65–70°, the 9,10 olefinic double bond migrates and the 14-hydroxyl group cyclizes with it to form M-VI, from which a variety of unusual compounds have been obtained. The oxime of M-IV undergoes a Beckmann rearrangement to form a predicted product (M-II) and a cyclized isomer, M-IIa.

The report of Conley and Nowak[2] of abnormal Schmidt reactions of spiro ketones in polyphosphoric acid led us to study the behavior of 3,11-dimethyl-14-hydroxy-14-azadispiro[5.1.5.2]pentadec-9-ene-7,15-dione (M-IV)[3] with sodium azide in this reagent. The product could be either a lactam identical with the Beckmann rearrangement product of M-I (an oxime of M-IV) or abnormal compounds analogous to those obtained by Conley and Nowak.

The product, M-VI, obtained from the attempted Schmidt reaction was not the expected lactam but had the formula, $C_{16}H_{23}NO_3$, as calculated from the elemental analyses and was isomeric with M-IV. Apparently, hydrazoic acid had not taken part in the reaction; so M-IV was heated alone with polyphosphoric acid to form M-VI in 67% yield.



M-IV

M-VI

The infrared spectrum of M-VI has a ketone carbonyl band at 1740 cm.$^{-1}$ and an amide carbonyl band at 1680 cm.$^{-1}$ (Table I) but no absorption for a hydroxyl group, an N–H, or an olefinic linkage. These data were substantiated by the formation of an oxime (M-XI) of M-VI which subsequently underwent a Beckmann rearrangement, a negative ferric chloride test, and the failure of M-VI to acylate.

The disappearance from the infrared spectrum of M-IV of the bands due to the lactam hydroxyl group and the olefinic linkage suggested that cyclization could have taken place between these two groups in a manner analogous to the formation of isoxazolines from α,β-unsaturated ketones in the presence of sulfuric acid.[4]

Cyclization of M-IV at the 11-carbon rather than at the 10-carbon was established by the n.m.r. spectrum of M-VI. The peaks appearing at 1.31 and 0.99 p.p.m. below tetramethylsilane are both assigned to the methyl groups on the basis of their location. The peak at 0.99 p.p.m. is in the typical area for a methyl group α to a saturated cyclic ring. The peak at 1.31 p.p.m. is in the location expected for a methyl group which is β to an oxygen atom, and the line sharpness indicates that there is no proton on the adjacent carbon atom. In addition to the peaks due to the methyl groups at the 3- and 11-positions, the spectrum shows peaks at 2.04 and 1.66 p.p.m. due to aliphatic methylene groups.

Hydrogenation of M-VI over Raney nickel at room temperature and 2 atm. reduced the ketone group to

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[1] (a) Abstract of a portion of the Ph.D. Dissertation of D. N. Heintz, University of Missouri, June 1965. Presented in part at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964. (b) Gregory Fellow, 1963–1964.

[2] R. T. Conley and R. E. Nowak, *J. Org. Chem.*, **26**, 692 (1961).

[3] Only the numbers I, IV, XV, and XIV correspond to compounds previously described. The prefix M signifies two methyl groups in the 3,11-positions of the azadispiro[5.1.5.2]pentadec-9-enes or -pentadecanes. The compounds having other ring systems also have two methyl groups.

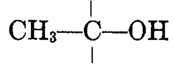
[4] K. von Auwers and H. Brink, *J. Prakt. Chem.*, [2] **133**, 154 (1932).

TABLE I

SIGNIFICANT INFRARED ABSORPTION (CM.$^{-1}$) OF PRINCIPAL COMPOUNDS

Compd.	C-OH	N-H	=N-OH	-N-OH	-C=N-	C=O	C=C
M-I			3270	3125	1725	1670	1646
M-II		3150		3280		1675	1640
		3030		2650			
M-IIa		3280				1670	
		3175					
		3050					
M-III		3270				1680	
		3160					
		3070					
		3030					
M-IIIa		3270				1680	
		3160					
		3070					
		3030					
M-IV				3100		1680	1645
				2660		1770	
M-IVi				3050		1675	1640
				2640		1770	
M-VI						1680	
						1750	
MVII	3500	3150				1680	
		3050				1750	
M-VIII	3220	3210				1670	
M-X	3300						
M-XI			3250		1700	1670	
M-XV		3160				1680	
		3050				1750	
M-XVa		3200				1690	
		3050				1680	
M-XVIi						1680	
						1760	
M-XIXa		3150				1675	
		2670				1775	
M-XIXb		3150				1680	
		2660				1760	
M-XXIII		3300				1660	

secondary alcohol to form M-XXIII, $C_{16}H_{25}NO_3$, but did not cleave the nitrogen–oxygen bond (see Chart I). The infrared spectrum of this compound had alcohol and carbonyl bands at 3300 and 1660 cm.$^{-1}$ but no N-H absorption. Additional evidence which showed that hydrogenolysis did not occur was the oxidation of M-XXIII with potassium dichromate in acetic acid to M-VI in 92% yield.

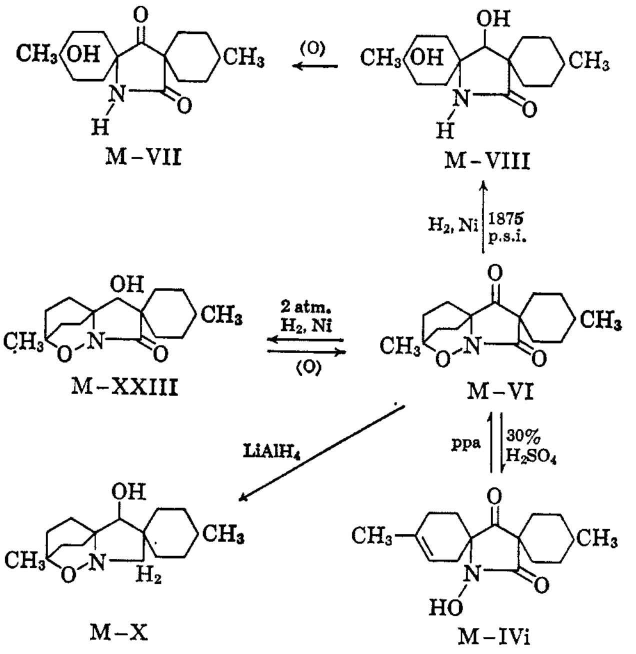
As would be expected, hydrogenation of M-VI at high pressure over Raney nickel caused reduction of the ketone group to secondary alcohol and hydrogenolysis of the nitrogen–oxygen bond[5] to  $CH_3—\overset{|}{\underset{|}{C}}—OH$ and >N-H to form M-VIII.

Oxidation of M-VIII with potassium dichromate in acetic acid gave M-VII. Since a hydroxyl group is still present in M-VII, the alcohol must be tertiary as it is in M-VIII and thus further substantiates the cyclization of M-IV at the 11-position.

Lithium aluminum hydride reduced the amide carbonyl group of M-VI to methylene and the ketone carbonyl group to secondary alcohol to form M-X.

When M-VI was refluxed with 30% sulfuric acid, a base-soluble compound, M-IVi, $C_{16}H_{33}NO_3$, isomeric with both M-VI and M-IV, was obtained. This solid gave a violet color with ferric chloride and formed N-methoxy and N-acetoxy derivatives.

CHART I



The infrared absorption spectrum of M-IVi[6] shows the presence of an N-hydroxylactam, ketone and amide carbonyl groups, and an olefinic double bond. This spectrum is very similar to that of M-IV. This similarity, their chemical properties, and the fact M-IVi readily cyclized to form M-VI when warmed with polyphosphoric acid suggested that M-IV and M-IVi were double-bond isomers. The n.m.r. spectra of the two compounds confirmed this view.

Comparison of the spectra in the vinyl proton region shows that in the spectrum of M-IV there are two vinyl protons, while the spectrum of M-IVi shows only one vinyl proton. The n.m.r. spectrum of M-IV contains two doublets (J = 10.2 c.p.s.), a simple one centered at 5.3 p.p.m. (C-9 olefinic proton, which has no adjacent aliphatic protons) and a more complex one centered at 6.1 p.p.m. (C-10 olefinic proton). With M-IV, in which the C-10 proton is coupled to the single C-11 proton, each member of the C-10 proton doublet is itself a finely split doublet (J = 3 c.p.s.). The n.m.r. spectrum of M-IVi shows only one vinyl proton as a broad peak centered at 5.3 p.p.m. This peak should appear as a triplet, but this was not observed at either 60 or 100 Mc.

Additional evidence for these compounds as double-bond isomers is in the region of absorption by the methyl groups. The secondary methyl group of the saturated ring in M-IVi gives the broad peak at 0.95 p.p.m. (doublet, 100 Mc.). This is to be compared with the same region of the spectrum of M-IV of known structure[7] which shows, in addition to the broad peak, a doublet centered at 1.1 p.p.m. (J = 7.2 c.p.s.) corresponding to the secondary methyl α to the double bond. In the spectrum of M-IVi, the resonance of this second methyl group has moved to about 8.3 p.p.m., which is expected for a typical olefinic methyl group.

Low-pressure hydrogenation of M-IVi over platinum catalyst gave a white solid, m.p. 163–193°, from which two products, $C_{16}H_{25}NO_3$, M-XIXa, m.p. 213–217°, and M-XIXb, m.p. 167–171°, were isolated by fractional crystallization from methanol. Both of them gave a violet color with ferric chloride and are

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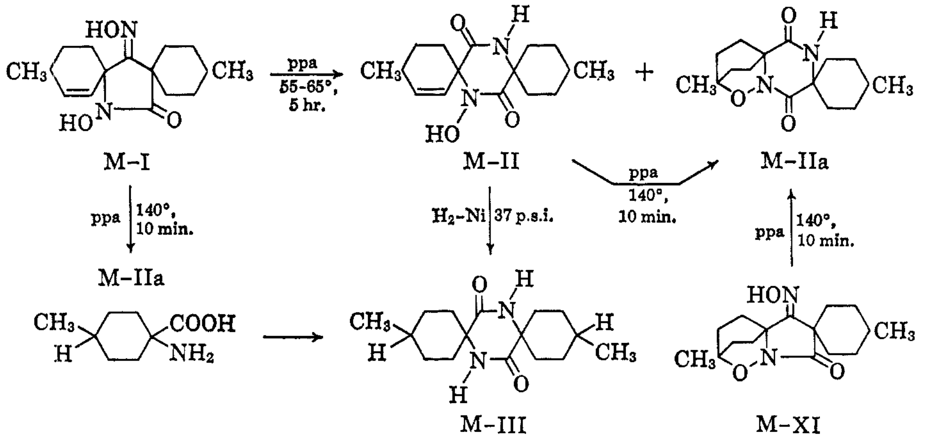
(5) (a) A. H. Lindemann and W. Pickert, *Ann.*, **456**, 275 (1927); (b) W. Stuhmer and W. Heinrich, *Ber.*, **84**, 224 (1951).

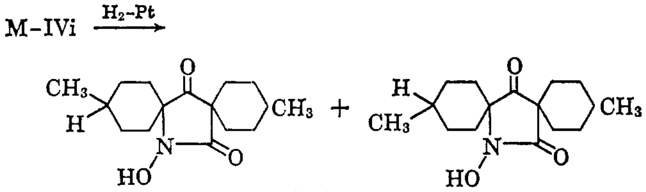
(6) Published in the NMR at Work Series, No. 87, Varian Associates Palo Alto, Calif., 1963.

(7) W. E. Noland and R. J. Sundberg, *J. Org. Chem.*, **28**, 647 (1963).

CHART II



believed to be mixtures of geometric isomers, owing to different configurations of the methyl groups in the 3- and 11-positions.



M-XIXa and b

The 4° melting point range suggests that M-XIXa may contain a small amount of the low-melting isomer, and M-XIXb may contain a small amount of the high-melting isomer. The infrared spectra of these products are identical in the 4000–1675-cm.$^{-1}$ region and differ only slightly in the fingerprint region. It was not possible to effect further separation by recrystallization or by chromatographic adsorption.

Low-pressure hydrogenation of M-XIXa over Raney nickel gave a solid, m.p. 233–240°. Fractional crystallization of this material from ethanol yielded two isomeric compounds, M-XV (5%) of established structure and M-XVa (85%), which gave no color with ferric chloride. Since the infrared spectra of these compounds are identical except for slight differences in the fingerprint region, they are also believed to be geometric isomers owing to the methyl groups.

Low-pressure hydrogenation of M-XIXb gave a solid, m.p. 256–261°, from which M-XV was obtained in 69% yield. It is likely that the configuration of the methyl groups in M-XVa are the same as their configuration in M-XIXa and that the configuration of the methyl groups in M-XV are the same as their configuration in M-XIXb.

Low-pressure hydrogenation of M-IVi over Raney nickel gave a product, m.p. 233–243°, from which only one compound, M-XVa, was isolated by fractional crystallization and by column chromatography.

Dehydration of M-VII with 30% sulfuric acid gave M-XVIi in 90% yield. Hydrogenation of this compound over Raney nickel at room temperature and atmospheric pressure gave a mixture from which M-XV (26%) and M-XVa (40%) were isolated by fractional crystallization from ethanol.

When M-I was warmed with polyphosphoric acid at 55–65° (Chart II), two isomeric compounds, 3,12-dimethyl-7-hydroxy-7,15-diazadispiro[5.2.5.2]hexadec-1-ene-8,16-dione (M-II) and 2′,4-dimethyl-3′,4′-dihydrospiro[cyclohexane-1,7′(8′H)-[2H-2,4a]ethanopyrazine[1,2-*b*][1,2]oxazine]-5′,8′(6′H)-dione (M-IIa), were obtained. Compound M-II, a normal Beckmann rearrangement product, is soluble in base, gives a violet color with ferric chloride, and has both N–OH and N–H absorption bands in the infrared spectrum.

Compound M-II is only slightly soluble in deuteriochloroform, but its n.m.r. spectrum shows the presence of two vinyl protons as multiplets centered at about 5.4 and 6.1 p.p.m., thus establishing the location of the double bond in the 1,2-position. It was not possible to determine accurately the coupling constants and the degree of splitting for these protons.

Compound M-IIa is insoluble in base, gives no color with ferric chloride, and shows no N–OH absorption in its infrared spectrum. The reaction of 2′,4-dimethyl-3′,4′-dihydrospiro[cyclohexane-1,6′(7′H)-[5H-2,4a]ethano(2H)pyrrolo[1,2-*b*][1,2]oxazine]-5′,7′-dione 7′-oxime (M-XI), the oxime of M-VI, yields only M-IIa when heated with polyphosphoric acid at 140°, thus establishing that the structure of the nitrogen-oxygen ring system is the same in M-IIa as it is in M-VI.

When M-I and M-II were heated with polyphosphoric acid at 140°, M-IIa was the only product isolated from each reaction. This suggests that M-II is an intermediate in the transformation of M-I to M-IIa.

Low-pressure hydrogenation of M-II over Raney nickel formed M-III, $C_{16}H_{26}N_2O_2$. The infrared spectrum of this compound shows strong absorption in both the amide carbonyl and the N–H regions, but no N–OH or olefinic absorption.

Thermal cyclization of 1-amino-*cis*-4-methylcyclohexanecarboxylic acid gave M-IIIa, $C_{16}H_{26}N_2O_2$. The infrared spectra of M-III and M-IIIa are identical from 4000 to 1500 cm.$^{-1}$, but differ slightly in the fingerprint region. Since these compounds are not soluble in the conventional solvents for spectral determinations, it was not possible to obtain n.m.r. spectra or infrared spectra in solution. Their solubilities in dimethylformamide and their melting point behaviors are somewhat different. Compound M-III is somewhat more soluble in dimethylformamide than is M-IIIa. Both M-III and M-IIIa began to decompose around 365° with extensive charring up to 400° but did not melt. When the sealed melting point tubes were inserted directly into a flame, M-III immediately liquified and sublimed, but M-IIIa sublimed without melting. These facts suggest that these two compounds are either dimorphic forms or perhaps geometric isomers.

Three products can be isolated from the Beckmann rearrangement product of 14-hydroxy-14-azadispiro-[5.1.5.2]pentadec-9-ene-7,15-dione 7-oxime (C-I). Two of these are cyclized products and one has a diketopiperazine structure. These and other reactions of the C series of compounds will be described in a subsequent paper.

Experimental Section[8]

3,11-Dimethyl-14-hydroxy-14-azadispiro[5.1.5.2]pentadec-9-ene-7,15-dione 7-oxime (M-I) was prepared as previously described,[9] using piperazine as the catalyst. Better yields were obtained when the amount of benzene was reduced by 30%.

3,11-Dimethyl-14-hydroxy-14-azadispiro[5.1.5.2]pentadec-9-ene-7,15-dione (M-IV).—This compound was more conveniently prepared by the hydrolysis of M-I with hydrochloric acid in 1-butanol rather than with dilute aqueous sulfuric acid.[9] M-I (8 g.), 130 ml. of concentrated hydrochloric acid, and 120 ml. of 1-butanol were refluxed for 2 hr. The solvent was removed by distillation until crystals began to separate. Water (200 ml.) was added to the residue, and, after the mixture had cooled, the solid was collected on a filter and washed with water to yield 7.5 g. (99%) of M-IV, m.p. 156–157° after crystallization from aqueous ethanol, lit.[9] m.p. 160–162°.

Hydrogenations.—All of the catalytic hydrogenations were carried out in conventional equipment for either high- or low-pressure reactions. After the mixture was removed from the container, the catalyst was separated from the solvent, heated if necessary, by filtration and the filtrate was evaporated, leaving a residue which was purified by crystallization from a suitable solvent.

Hydrogenation of M-IV. A. Low Pressure.—A solution of 7.8 g. of M-IV in 155 ml. of ethanol was hydrogenated over 2.5 g. of Raney nickel at an initial pressure of 130 p.s.i. and a final temperature of 50°. After the contents of the liner had cooled, an additional 2000 ml. of hot ethanol was required to dissolve all of the M-XV in order to remove the catalyst. After the solution had cooled, the separated solid was collected and crystallized from ethanol to yield 4.1 g. (56%) of M-XV, m.p. 300–302°.

Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.85; H, 9.49; H, 5.54.

B. High Pressure.—A solution of 6.46 g. of M-IV in 150 ml. of ethanol was hydrogenated over 1.0 g. of Raney nickel at an initial pressure of 2975 p.s.i. and a final temperature of 180°. Crystallization of the product from methanol yielded 3.85 g. (60%) of M-XIV, m.p. 246–248°.

Anal. Calcd. for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.26; N, 5.28. Found: C, 72.17; H, 10.33; N, 5.54.

Reduction of M-XV with Lithium Aluminum Hydride.—In a 500-ml. flask fitted with a condenser, stirrer, and dropping funnel were placed 1.0 g. of lithium aluminum hydride and 50 ml. of dry ether. To this well-stirred mixture was added a suspension of 1.0 g. of M-XV in 250 ml. of dry ether. After the mixture had refluxed for 22 hr., the complex was decomposed with 30% potassium hydroxide solution, and the aluminate was collected on a filter. The filtrate was evaporated until crystals began to separate. The yield of M-V was 0.7 g. (74%), m.p. 193–194° after crystallization from methanol.

Anal. Calcd. for $C_{16}H_{29}NO$: C, 76.44; H, 11.63; N, 5.57. Found: C, 76.24; H, 11.93; N, 5.28.

2′,4-Dimethyl-3′,4′-dihydrospiro[cyclohexane-1,6′(7′H)-[5H-2,4a]ethano(2H)pyrrolo[1,2-*b*][1,2-oxazine]-5′,7′-dione (M-VI).—M-IV (20 g.) was heated with 400 g. of polyphosphoric acid at 65–70° for 15 hr. and then allowed to stand overnight at room temperature. With stirring, cold water was added to the mixture until the polyphosphoric acid had dissolved. The cold solution was extracted with benzene and the benzene extracts were washed, dried, and evaporated nearly to dryness. Petroleum ether (b.p. 30–60°) was added to the warm residue until crystals began to separate. After the solution had cooled, the solid was collected on a filter, extracted with 10% sodium hydroxide to remove unreacted M-IV, and then washed with water to yield 13.5 g. (67.5%) of M-VI, m.p. 176–177° after recrystallization from benzene–petroleum ether (b.p. 60–70°).

Anal. Calcd. for $C_{16}H_{23}NO_3$: C, 69.28; H, 8.36; N, 5.05. Found: C, 69.40; H, 8.30; N, 5.06.

Hydrogenation of M-VI over Raney Nickel. A. Low Pressure.—A solution of 2.7 g. of M-VI in 100 ml. of absolute ethanol was hydrogenated over 0.5 g. of Raney nickel at room temperature and 2 atm. Crystallization of the product from ethanol yielded 2.07 g. (77%) of M-XXIII, m.p. 233–235°.

Anal. Calcd. for $C_{16}H_{25}NO_3$: C, 68.78; H, 9.02; N, 5.01. Found: C, 68.59; H, 8.71; N, 4.96.

B. High Pressure.—A solution of 2.8 g. of M-VI in 100 ml. of abolute ethanol was hydrogenated over 0.5 g. of Raney nickel at an initial pressure of 1875 p.s.i. at room temperature and a final temperature of 180°. The crude product was washed with hot benzene to remove unreacted starting material and then crystallized from methanol to yield 2.58 g. (92%) of M-VIII, m.p. 238–240°.

Anal. Calcd. for $C_{16}H_{27}NO_3$: C, 68.29; H, 9.67; N, 4.98. Found: C, 67.98; H, 9.57; N, 4.88.

Oxidation of M-XXIII.—To a solution of 1.0 g. of M-XXIII in 20 ml. of acetic acid was added dropwise and with stirring 560 mg. of potassium dichromate in 0.3 ml. of sulfuric acid in 4.6 ml. of water.[10] The mixture was stirred overnight at room temperature, diluted with water, and extracted with ether. The ether extracts were combined and washed with aqueous sodium bicarbonate, dried, and evaporated to dryness. Crystallization of the residue from benzene–petroleum ether (b.p. 60–70°) yielded 0.92 g. (92%) of M-VI, m.p. and m.m.p. (with authentic M-VI, m.p. 172–174°) 172–174°. The infrared spectra of this solid and of M-VI were identical.

Oxidation of M-VIII.—A solution of 1.0 g. of M-VIII in 20 ml. of acetic acid was oxidized with 1.2 g. of potassium dichromate and 0.6 ml. of sulfuric acid in 9.2 ml. of water as described above. The mixture was extracted with chloroform, the chloroform layer was washed with 10% sodium hydroxide and with water, dried, and evaporated to dryness to yield 0.89 g. (89.0%) of M-VII, m.p. 231.5–233° after crystallization from benzene.

Anal. Calcd. for $C_{16}H_{25}NO_3$: C, 68.78; H, 9.02; N, 5.01. Found: C, 68.81; H, 9.11; N, 5.04.

Reduction of M-VI with Lithium Aluminum Hydride.—In a 500-ml. three-neck flask fitted with a stirrer and a dropping funnel were placed 1.5 g. of lithium aluminum hydride and 50 ml. of dry ether. To this stirred mixture was added a suspension of 1.0 g. of M-VI in 150 ml. of dry ether. The mixture was refluxed for 21 hr., and the excess lithium aluminum hydride was decomposed with 50% potassium hydroxide solution. The aluminate was collected on a filter and the filtrate was evaporated to dryness. Recrystallization of the residue from methanol yielded 0.55 g. (55%) of M-X, m.p. 216–218°.

Anal. Calcd. for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.26; N, 5.28. Found: C, 73.16; H, 10.29; N, 5.01.

Oxime of M-VI.—The procedure was essentially that of Noland and Sundberg.[7] From 1 g. of M-VI, the yield of oxime M-XI was 1.5 g. (93%), m.p. 270–271° after crystallization from benzene.

Anal. Calcd. for $C_{16}H_{24}N_2O_3$: C, 65.72; H, 8.27; N, 9.58. Found: C, 65.72; H, 8.35; N, 9.83.

3,11-Dimethyl-14-hydroxy-14-azadispiro[5.1.5.2]pentadec-10-ene-7,15-dione (M-IVi).—Compound M-VI (2.5 g.), 75 ml. of concentrated sulfuric acid, and 175 ml. of water were refluxed 4 hr. After the solution had cooled, the separated solid was collected on a filter, washed with water, and crystallized from methanol to give 2.35 g. (94%) of M-IVi, m.p. 231–233°, as shiny pink needles.

Anal. Calcd. for $C_{16}H_{23}NO_3$: C, 69.28; H, 8.36; N, 5.05. Found: C, 68.99; H, 8.13; N, 5.27.

Derivatives of M-IVi.—The 14-methoxy derivative melted at 98–99°.

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(8) All melting points were determined in an open capillary tube in a copper block and are corrected. The microanalyses were performed at the Weiler-Strauss Laboratories, Oxford, England. The infrared spectra were determined in Nujol mulls with a Perkin-Elmer Infracord 237B. The n.m.r. spectra were determined and interpreted by the staff of Varian Associates.

(9) D. V. Nightingale, S. Miki, D. N. Heintz, and D. A. Reich, *J. Org. Chem.*, **28**, 642 (1963).

(10) H. O. House and R. W. Magin, *ibid.*, **28**, 647 (1923).

Anal. Calcd. for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.66. Found: C, 70.43; H, 8.60; N, 4.66.

The 14-acetoxy derivative melted at 68–69°.

Anal. Calcd. for $C_{18}H_{25}NO_4$; C, 67.69; H, 7.89; N, 4.39. Found: C, 67.53; H, 7.72; H, 4.34.

Cyclization of M-IVi.—Compound M-IVi (1.3 g.) was heated with 20 g. of polyphosphoric acid at 65–70° for 17 hr. The product, 1.2 g. (91%) of M-VI, was isolated as described above and melted at 172–173° after crystallization from petroleum ether (b.p. 60–70°). The infrared spectrum of this compound was identical with that of M-VI prepared directly from M-IV.

Hydrogenation of M-IVi. A. Over Platinum.—A solution of 3.6 g. of M-IVi in 200 ml. of glacial acetic acid was hydrogenated at room temperature and 18 p.s.i. over 400 mg. of catalyst. After 6.5 hr. of shaking, the catalyst was removed by filtration, and water was added to the filtrate until no more solid had separated. This product, m.p. 163–193°, gave a violet color with ferric chloride. Fractional crystallization from methanol yielded 0.8 g. (22%) of M-XIXa, m.p. 213–217°.

Anal. Calcd. for $C_{16}H_{25}NO_3$: C, 68.78; H, 9.02; N, 5.01. Found: C, 68.91; H, 9.07; N, 5.23.

Concentration of the filtrate finally yielded 1.7 g. (47%) of M-XIXb, m.p. 167–171° after recrystallization from methanol.

Anal. Calcd. for $C_{16}H_{25}NO_3$: C, 68.78; H, 9.02; N, 5.01. Found: C, 68.50; H, 8.97; N, 4.80.

B. Over Raney Nickel.—A solution of 3.3 g. of M-IVi in 220 ml. of absolute ethanol was hydrogenated over 0.75 g. of Raney nickel at an initial pressure of 20 p.s.i. at room temperature. The catalyst was removed by filtration of the hot solution, and the filtrate was evaporated to dryness under reduced pressure, leaving 2.9 g. of residue, m.p. 233–243°.

One gram of this solid was dissolved in 1:1 cyclohexane–benzene and chromatographed on alumina (30 cm. × 25 mm.). Benzene–cyclohexane solutions ranging from 0 to 66% benzene eluted no solid. Pure benzene (1200 ml.) eluted 0.06 g. of white solid, m.p. 268–276°. Benzene–chloroform (3:1) eluted 0.6 g. of solid, m.p. 233–245°, perhaps a xmiture of M-XV and M-XVa. Additional 3:1 benzene–chloroform (800 ml.) eluted another solid, m.p. 245–257°, which, when crystallized from ethanol, yielded 0.25 g. (23%) of M-XVa, m.p. 246–248°, as white needles.

Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 73.12; H, 9.55; N, 5.39.

Hydrogenation of M-XIXa.—A solution of 0.4 g. of XIXa in 75 ml. of ethanol was hydrogenated over 0.1 g. of Raney nickel at an initial pressure of 20 p.s.i. After 19 hr. of shaking, the catalyst was separated and the solvent was evaporated to yield 0.35 g. of residue, m.p. 233–240°, which gave a negative test with ferric chloride.

Fractional crystallization from ethanol yielded 0.02 g. (5%) of M-XV, m.p. 297–299°, identified by its infrared spectrum and a mixture melting point with authentic M-XV from the hydrogenation of M-IV.

Concentration of the filtrate yielded 0.32 g. of M-XVa, m.p. 244–246°, as white needles, after crystallization from ethanol.

Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 73.12; H, 9.55; N, 5.39.

Hydrogenation of M-XIXb.—A solution of 0.93 g. of M-XIXb in 110 ml. of ethanol was hydrogenated over 0.5 g. of Raney nickel at an initial pressure of 20 p.s.i. Fractional crystallization of the crude product from ethanol yielded 0.63 g. (69%) of M-XV, m.p. and m.m.p. (with authentic M-XV, m.p. 300–302°) 300–302°. The infrared spectra of the two compounds were identical.

Beckmann Rearrangement of M-I. A. At 55–65°.—Compound M-I (30 g.) was stirred with 600 g. of polyphosphoric acid at 55–65° for 5 hr. The yellow mixture was cooled to room temperature and stirred with cold water until the polyphosphoric acid had dissolved. The solution was extracted with chloroform and the chloroform layer was in turn extracted with 300 ml. of 10% sodium hydroxides solution and finally with water. The water washings and the basic solution were combined, acidified with hydrochloric acid, and extracted with chloroform. This latter chloroform extract was washed, dried, and evaporated to dryness to yield 8.4 g. (28%) of M-II as light yellow plates, m.p. 263–265° after crystallization from ethanol. This compound gave a violet color with ferric chloride.

Anal. Calcd. for $C_{16}H_{24}N_2O_3$: C, 65.72; H, 8.27; N, 9.58. Found: C, 65.73; H, 8.48; N, 9.49.

The first chloroform extract was washed and evaporated to dryness under reduced pressure. The reddish residue was dissolved in warm ether, the ether solution was concentrated, and the separated solid was collected on a filter. Crystallization of this material from chloroform–petroleum ether (b.p. 60–70°) gave 1.5 g. of M-IIa as light yellow needes, m.p. 255–258°. A mixture melting point of this compound and M-IIa (m.p. 259–261°) from a Beckmann rearrangement of M-XI was 258–260°. The infrared spectra of the two samples were identical.

B. At 140°.—After 2 g. of M-I was stirred and heated with 115 g. of polyphosphoric acid at 140° for 10 min.,[7] the brown mixture was cooled, diluted, and extracted with chloroform as described above. The reddish brown, semisolid oil obtained by evaporation of the solvent was dissolved in 2:1 chloroform–benzene and chromatographed on alumina. The same solvent pair (1300 ml.), but in a 1:2 ratio, eluted 2.1 g. of solid, which, when crystallized from benzene–petroleum ether (b.p. 60–70°), gave 1.79 g. (89%) of M-IIa, m.p. 260–262°. The infrared spectrum of this sample was identical with that of M-IIa from M-XI.

Conversion of M-II to M-IIa.—Compound M-II (5.0 g.) was heated with polyphosphoric acid at 140° for 10 min. The M-IIa was isolated from the reaction mixture and purified as described above. The yield of M-IIa was 1.25 g. (25%) of white needles, m.p. 258–260°, identical with M-IIa from M-XI.

Beckmann Rearrangement of M-XI.—Compound M-XI (1 g.) was stirred with 30 g. of polyphosphoric acid at 140° for 10 min. The product, M-IIa, was isolated as described above. The yield of M-IIa was 0.25 g. (25%) as white needles, m.p. 259–261° after crystallization from chloroform–petroleum ether (b.p. 60–70°).

Anal. Calcd. for $C_{16}H_{25}N_2O_3$: C, 65.72; H, 8.27; N, 9.58. Found: C, 65.84; H, 8.25; N, 9.72.

Only intractable, dark, oily residues were obtained by concentration of the solvent filtrates from all of the reactions with polyphosphoric acid.

Hydrogenation of M-II.—A solution of 0.4 g. of M-II in 100 ml. of absolute ethanol was hydrogenated over 0.4 g. of Raney nickel at 37.5 p.s.i. for 42 hr. Dimethylformamide was added to the mixture and the catalyst was removed by filtration of the boiling solvent mixture. The solid which separated from the cooled solution yielded 0.35 g. (88%) of M-III which, after crystallization from dimethylformamide, decomposed with extensive charring at 365–400°.

Anal. Calcd. for $C_{16}H_{26}N_2O$: C, 69.03; H, 9.41; N, 10.06. Found: C, 68.98; H, 9.41; N, 10.06.

Preparation of M-IIIa.—The procedure is essentially that of McElvain and Pryde[11] for the cyclization of 2-methyl-2-aminopropanoic acid. 1-Amino-*cis*-4-methylcyclohexane-1-carboxylic acid[12] (6.3 g.) and 50 ml. of β,β'-dihydroxyethyl ether were refluxed for 4 hr. in a 200-ml. round-bottom flask having a 4-in. neck. The brown solution was cooled and the solid which separated slowly was collected on a filter and washed first with 50 ml. of ethanol and then with 100 ml. of water. Crystallization of this product from dimethylformamide yielded 0.28 g. of (5%) of M-IIIa as a white granular solid which decomposed with extensive charring at 360–400°. The infrared spectra of M-III and M-IIIa were identical in the 4000–1500-cm.$^{-1}$ region.

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