Optimum Conditions for Benzophenone Formation.—In a series of three experiments the effect on the oxidation of diphenylmethane of varying the amount of manganese dioxide was studied under conditions otherwise identical with the standard conditions given below. As the amount of the dioxide was increased from 2.5 to 5.0 to 10.0 g. the yield of benzophenone increased from 40 to 68 to 74%.

When the temperature was decreased from the standard 125° to 100°, using 10 g. of manganese dioxide the yield of benzophenone was 38%. In this experiment the mixture was stirred magnetically throughout the heating period.

A decrease in time of heating from the standard 6 hr. to 3 hr., using 10.0 g. of manganese dioxide at 125°, decreased the yield of benzophenone from 74% to 38%.

When the reaction mixture was stirred magnetically throughout the heating period, under conditions otherwise standard, the yield of benzophenone was essentially unchanged.

Diaryl Ketone Experiments of Table I.—The standard procedure used for these experiments was as follows. One gram of diarylmethane and 10.0 g. of manganese dioxide were thoroughly mixed and placed in a 125-ml. erlenmeyer flask, the stopper of which was fitted with a Bunsen valve. Solid diarylmethanes were well ground before mixing. The reaction mixtures were heated at 125 ± 3.0° for 6 hr. in a magnetically stirred oil bath large enough to accommodate three flasks.

At the end of the heating period the flask contents were extracted with 250 ml. of chloroform for 12 hr. in a Soxhlet apparatus. After volatilization of the chloroform under reduced pressure the products, unless otherwise noted, were recrystallized from suitable solvents until their melting points agreed satisfactorily with the literature values.

The usual recrystallization techniques did not give a pure product from di-α-naphthylmethane. In an attempt to prepare the oxime a solution of the crude product in pyridine and absolute alcohol was heated under reflux 2 hr. with 1.0 g. of hydroxylamine hydrochloride. Recrystallization of the residue obtained upon removal of the solvents gave a 29% yield of di-α-naphthyl ketone instead of the expected oxime.

Supplementary Experiments.—The oxidation of tetraphenylethane was attempted under the standard conditions for diaryl ketones given above except that magnetic stirring was employed throughout the heating period. No ketone could be isolated but starting material was recovered in 61% yield. When the oxidation of 9,9'-bifluorenylidene was attempted in the same way only starting material (74%) was recovered.

The oxidations of benzhydrol, triphenylmethane and 9-chlorofluorene were carried out under the standard conditions for diaryl ketones.

Although p,p'-dibiphenylylmethane melts about 35° above the standard reaction temperature for diaryl ketones, magnetic stirring did not raise the rather low yield of ketone obtained from this compound.

Attempted oxidation of fluorene under the standard conditions for diaryl ketones gave no pure product. A 76% yield of fluorenone was obtained, however, at a temperature of 100° with magnetic stirring.[23]

No identifiable products were obtained when the oxidation of deoxybenzoin, xanthene, diphenylacetonitrile and 9-methylanthracene was attempted under the standard conditions for diaryl ketones.

The dehydration of manganese dioxide, referred to in the Discussion, was accomplished by heating a magnetically stirred suspension of 0.3 mole of manganese dioxide in 250 ml. of toluene under reflux (112°) in an apparatus equipped with a water trap. Water evolution ceased after 6.5 hr. at which time 2.82 ml. had collected. The oxide was filtered off and stored overnight in a desiccator under reduced pressure. When 10.0 g. of this dehydrated manganese dioxide was used in an attempted oxidation of diphenylmethane according to the standard procedure for the diaryl ketone experiments of Table I the yield of benzophenone was only 2%.

(23) This experiment was carried out by Dr. John F. Van de Castle.

Reactions of Nitroparaffins with Alicyclic Ketones. IV[1]

DOROTHY V. NIGHTINGALE, SHOZO MIKI, DANIEL N. HEINTZ, AND D. A. REICH

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Oximes of azadispiro keto cyclic hydroxamic acids have been obtained from the reaction of nitromethane and alicyclic ketones of five to eight carbons in the ring and from some 4-alkylcyclohexanones in the presence of pyrrolidine, piperidine, hexamethyleneimine, piperazine, 2-methylpiperazine, and morpholine as catalysts. With one exception, piperazine was the most satisfactory catalyst for the formation of these unusual compounds.

A previous publication[2] from this laboratory reported the preparation of a series of compounds from the solid product (C-I) from the reaction of nitromethane and cyclohexanone in the presence of piperidine. At that time, the structure of C-I was not known.

The structure of C-I has recently been determined by Noland and Sundberg[3] as 14-hydroxy-14-azadispiro[5.1.5.2]pentadec-9-ene-7,15-dione 7-oxime. The properties and reactions of the various compounds I agree well with those of an oxime of a keto cyclic hydroxamic acid. The structures of all of the compounds obtained in this laboratory from C-I and its analogs can be written with this atomic skeleton.

The numbers P-I, H-I, and O-I are assigned to the analogous solids obtained from the reaction of nitromethane with cyclopentanone, cycloheptanone, and cyclo-octanone respectively. These compounds and C-I all represent new ring systems.[4] Most of the Roman numbers designating the compounds in Chart I are those used in our preceding publication.[2]

The present study has been largely concerned with the effect of the amount and type of amine catalyst on the formation of the compounds I and with the effect of the size of the ring and the alkyl group of the 4-alkylcyclohexanones on the yields and properties of these compounds. These data are summarized in Table I.

Piperazine was in general the most satisfactory catalyst for the formation of the compounds I other

(1) Abstracted from the Masters thesis of S. Miki, 1961, the Ph.D. thesis of D. A. Reich, 1956, and the Ph.D. thesis to be submitted by D. N. Heintz.

(2) D. V. Nightingale, D. A. Reich, and F. B. Erickson, *J. Org. Chem.*, **23**, 236 (1958).

(5) W. E. Noland and R. J. Sundberg, *Tetrahedron Letters*, 295 (1962). These authors have recently reported in a personal communication that the double bond is in the 9 position.

(4) P-I: 12-Hydroxy-12-azadispiro[4.1.4.2]tridec-8-ene-6,13-dione 6-oxime. H-I: 16-Hydroxy-16-azadispiro[6.1.6.2]heptadec-10-ene-8,17-dione 8-oxime. O-I: 18-Hydroxy-18-azadispiro[7.1.7.2]nonadec-11-ene-9,19-dione 9-oxime.
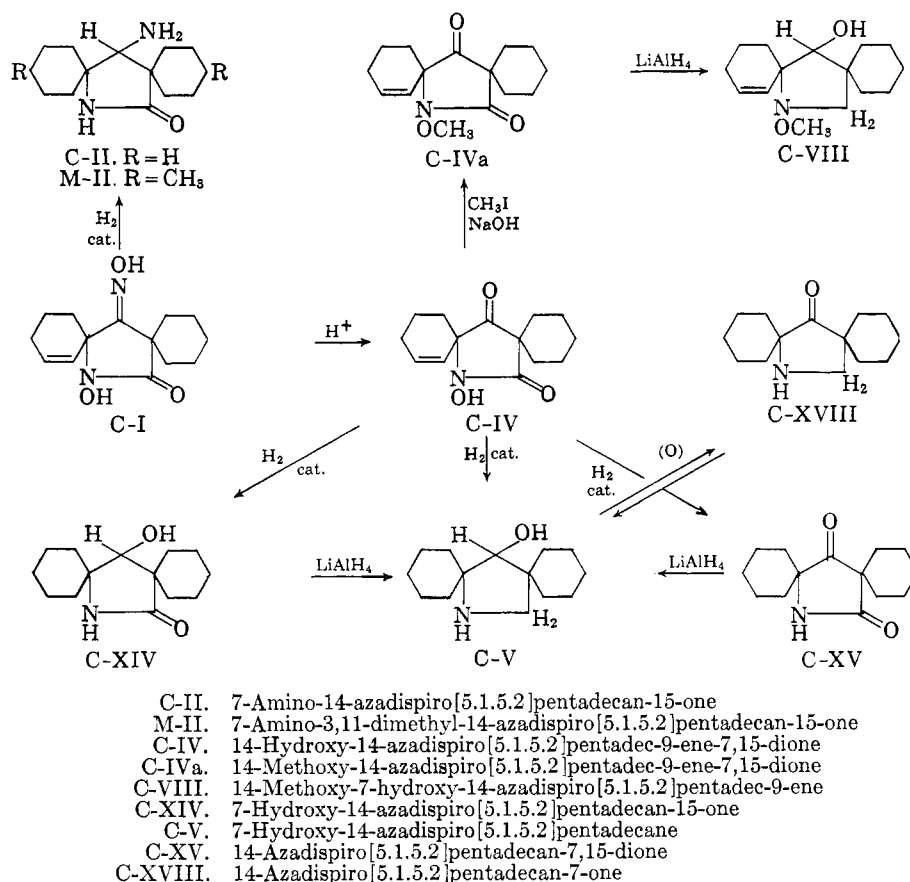
C-II. R = H
M-II. R = CH₃   C-IVa   C-VIII   C-I   C-IV   C-XVIII   C-XIV   C-V   C-XV

C-II.   7-Amino-14-azadispiro[5.1.5.2]pentadecan-15-one
M-II.   7-Amino-3,11-dimethyl-14-azadispiro[5.1.5.2]pentadecan-15-one
C-IV.   14-Hydroxy-14-azadispiro[5.1.5.2]pentadec-9-ene-7,15-dione
C-IVa.   14-Methoxy-14-azadispiro[5.1.5.2]pentadec-9-ene-7,15-dione
C-VIII.   14-Methoxy-7-hydroxy-14-azadispiro[5.1.5.2]pentadec-9-ene
C-XIV.   7-Hydroxy-14-azadispiro[5.1.5.2]pentadecan-15-one
C-V.   7-Hydroxy-14-azadispiro[5.1.5.2]pentadecane
C-XV.   14-Azadispiro[5.1.5.2]pentadecan-7,15-dione
C-XVIII. 14-Azadispiro[5.1.5.2]pentadecan-7-one

Chart I

Table I

Maximum Yields of Compounds I with Various Catalysts

I	Ketone moles	CH₃NO₂, moles	Catalyst	Moles	C₆H₆, ml.	Hr.	Yield, %	Ratio of ketone to catalyst
C-I	0.93	1.02	piperidine	0.13	115	100	23.7	7:1
C-I	1.86	2.04	piperazine	1.86	290	30	67.0	1:1
C-I	0.55	0.6	morpholine	0.5	100	64	22.3	1:1
C-I	0.55	0.6	pyrrolidine	0.13	82	75	23.0	4:1
C-I	0.9	1.02	hexamethyleneimine	0.13	115	53	24.5	7:1
M-I	0.55	0.63	piperidine	0.13	82	75	15.3	4:1
M-I	0.21	0.22	piperazine	0.10	50	64	40.5	2:1
M-I	0.54	0.63	pyrrolidine	0.13	82	75	15.2	4:1
M-I	0.55	0.63	hexamethyleneimine	0.13	82	75	25.0	4:1
i-Pr-I	0.20	0.21	piperazine	0.20	130	71	40.0	1:1
t-B-I	0.11	0.12	piperidine	0.17	63	63	16.3	7:1
t-B-I	0.24	0.28	piperazine	0.12	80	63	33.7	2:1
s-B-I	0.16	0.17	piperazine	0.08	100	118	23.0	2:1
Ch-I	0.20	0.21	piperazine	0.10	100	87	20.3	2:1
P-I	0.87	1.02	piperidine	0.06	115	57	24.3	4:1
H-I	0.21	0.23	piperazine	0.1	50	80	51.5	2:1
H-I	0.10	0.11	piperidine	0.1	50	72	48.0	1:1
H-I	0.10	0.11	morpholine	0.1	50	72	16.0	1:1
H-I	0.21	0.23	hexamethyleneimine	0.1	50	72	40.0	2:1
O-I	0.24	0.26	piperazine	0.12	57	·48	0.9	2:1

than P-I, as shown in Tables I and II. Yields of the 3,11-dialkyl analogs of C-I were lower and rather more variable than yields of C-I from the same amounts of reactants. The initial products from the piperazine catalyzed reactions of 4-methylcyclohexanone and of cycloheptanone proved to be the piperazine salts of M-I and H-I. Crude C-I apparently was a mixture of C-I and its salt, but crude t-B-I and i-Pr-I

contained very little salt. Much lower yields of C-I and M-I were obtained when 2-methylpiperazine was the catalyst.

The effect of the amount of piperazine on the rate of formation of C-I is striking. With 2:1 and 1:1 ratios of ketone to catalyst, crystals began to separate rapidly from the refluxing benzene solution after an hour and a half and fifteen minutes, respectively.

TABLE II

THE EFFECT OF THE AMOUNT OF CATALYST

I	Ketone	Catalyst	Ratio of ketone to catalyst	Yield, %
C-I	cyclohexanone	piperidine	14:1	14.0
C-I	cyclohexanone	piperidine	7:1	23.7
C-I	cyclohexanone	piperidine	1:1	15.4
C-I	cyclohexanone	piperazine	4:1	27.0
C-I	cyclohexanone	piperazine	2:1	47.2
C-I	cyclohexanone	piperazine	1:1	67.0
C-I	cyclohexanone	2-methyl-piperazine	2:1	27.0
i-Pr-I	4-isopropylcyclohexanone	piperazine	2:1	25.1
i-Pr-I	4-isopropylcyclohexanone	piperazine	1:1	40.0
H-I	cycloheptanone	piperidine	2:1	46.0
H-I	cycloheptanone	piperidine	1:1	48.0
H-I	cycloheptanone	piperazine	2:1	44.3
H-I	cycloheptanone	piperazine	1:1	28.0

C-I. R = H
M-I. R = CH₃
i-Pr-I. R = i-C₃H₇
t-B-I. R = t-C₄H₉
s-B-I. R = s-C₄H₉
Ch-I. R = C₆H₁₁

Piperidine in a 7:1 ratio of cyclohexanone to amine gave the best yield (23%) of C-I with this catalyst. Crystals began to separate after seven to eight hours of refluxing. Similar results were obtained from 4-methylcyclohexanone. Yields of C-I and M-I from pyrrolidine-catalyzed reactions were comparable with those from piperidine.

The morpholine-catalyzed reaction of cyclohexanone with nitromethane was interesting in that no solid separated from the reaction mixture, even at ice bath temperatures. The C-I separated only after the mixture was acidified with hydrochloric acid.[5] This may be due to the formation of a soluble salt of morpholine and C-I.

Similarly, no H-I separated from the reactions of nitromethane and cycloheptanone catalyzed by piperidine,[6] hexamethyleneimine, and morpholine until the mixture was acidified. Reich[2] apparently failed to obtain H-I from his piperidine catalyzed reaction because it remained in solution. All of the compounds I are very soluble in the secondary amines.

H-I is very soluble in ether, in marked contrast to the slight solubility of the other compounds I in this solvent. It is possible that H-I might not have the same structure as the other analogs of C-I, even though it forms a diacetate, yields H-IV on hydrolysis, gives the same violet color with ferric chloride solution and has the same significant bands in the infrared spectrum.

Yields of P-I from cyclopentanone were much more variable than yields of the other compounds I. This is well illustrated by the fact that from two reactions in which the same amounts of reactants were taken from the same bottles and refluxed for the same amount of time, yields were 24% and 12%.

The reaction of cyclooctanone with nitromethane will be studied further in an effort to improve the yield
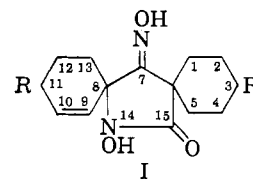
of O-I. The low yield reported is due in part to mechanical losses.

t-B-I and i-Pr-I were not appreciably hydrolyzed after boiling for days with 1:4 sulfuric acid, in which they were nearly insoluble.

Eckstein and co-workers[7] have obtained mainly 1-nitromethylcyclohexene and some C-I from the reaction of 1-piperidinocyclohexene with nitromethane in refluxing dioxane solution. They suggest that 1-nitromethylcyclohexene is formed from the reaction of the enamine with nitromethane. These results suggested to us that the formation of an enamine could be the first step in the formation of C-I and its analogs.

The reactions of 1-hexamethyleneiminocyclohexene, 1,4-bis(1-cyclohexenyl)piperazine, and 1,4-bis(1-cyclohexenyl-4-methyl)-piperazine with nitromethane to form C-I and M-I, respectively, in yields of 43%, 22%, and 20% agree with this supposition. The reaction of 1,4-bis(1-cyclohexenyl)piperazine in benzene solution with 1-nitromethylcyclohexene and with 1-nitromethyl-1-cyclohexanol formed C-I in yields of less than 1%.

When triethylamine and N-benzyltrimethylammonium hydroxide were used as catalysts, no compounds I were formed and no water collected in the trap. Tetramethylammonium hydroxide (10% aqueous solution) led to the formation of a black, amorphous solid.

The reaction of C-II and M-II with nitrous acid in dilute acetic acid yielded mixtures from which were obtained C-VII, $C_{14}H_{20}N_2O_2$, and M-VII, $C_{16}H_{24}N_2O_2$, respectively. These molecular formulas can be arrived at by assuming the replacement of —NH₂ by —OH, followed by loss of water and a nitrosation. Replacement of —NH₂ by —OH would form C-XIV and M-XIV, but these compounds cannot lose water without rearrangement of the ring system. Both compounds have bands in their infrared spectra in the —NH and —OH regions at $3.0/\mu$ and $3.2/\mu$, and at $5.9/\mu$. Hydrogenation of C-VII and M-VII and their hydrolysis with dilute sulfuric acid gave results of no immediate value. The structure of C-VII is currently under investigation by Noland and Chang.

The reactions of C-IVa, C-XV, and C-XIV with lithium aluminum hydride proceeded smoothly with reduction of the ketone carbonyl to —CHOH and the amide carbonyl to methylene. The oxidation of C-V formed the expected ketone C-XVIII. Currently in this laboratory we are studying other reactions of the ketones and alcohols shown on Chart I and their analogs which can be obtained from the various compounds I. The Schmidt reaction with C-IV and M-IV has not yielded normal products.

(5) A. Lambert and A. Lowe, J. Chem. Soc., 1517 (1947), isolated C-I in this manner from a diethylamine-catalyzed reaction.

(6) Z. Eckstein, A. Sacha, and T. Urbanski, Bull. acad. polon. sci., 5, 213 (1957); Chem. Abstr. 51, 1631 (1957), reported that the reaction of nitromethane with cycloheptanone in the presence of piperidine led to the formation of 1-nitromethylcycloheptene and a crystalline by-product for which they report no physical constants or analyses.

(7) Z. Eckstein, A. Sacha, and T. Urbanski, Bull. acad. polon. sci., 7, 295 (1959); Chem. Abstr., 54, 22637 (1960).

Table III

I	M.p.,[a] °C.	Infrared bands, μ (in Nujol mulls)				Formula	Calcd. C	H	N	Found C	H	N
C-I	273–274	3.1	3.2	5.8	6.1							
M-I	272–274[b,c]	3.1	3.2	5.9	6.05							
i-Pr-I	294–295	3.1	3.2	5.9	6.1	$C_{20}H_{32}N_2O_3$	68.92	9.26	8.04	69.17	9.48	7.99
t-B-I	320–321[d]	3.1	3.2	5.9	6.1	$C_{22}H_{36}N_2O_3$	70.17	9.64	7.44	70.08	9.29	7.23
s-B-I	285–286	3.1	3.2	5.9	6.1	$C_{22}H_{36}N_2O_3$	70.17	9.64	7.44	70.37	9.97	7.35
Ch-I	303–304	3.1	3.25	5.9	6.05	$C_{26}H_{40}N_2O_3$	72.86	9.41	6.54	73.09	9.36	6.56
H-I	250–251	2.9	3.2	5.9	6.1	$C_{16}H_{24}N_2O_3$	65.72	8.27	9.58	66.26	8.39	9.40
O-I	230–231	3.1	3.2	5.9	6.1	$C_{18}H_{28}N_2O_3$	67.47	8.81	8.74	67.41	8.52	8.78
P-I	246–247	3.2	3.3	5.9	6.1	$C_{12}H_{16}N_2O_3$	61.00	6.83	11.86	71.29	6.65	11.72

[a] These compounds all melt with decomposition and with some sublimation. [b] The 3,11-dialkyl analogs of C-I have two asymmetric carbons and two centers leading to geometric isomers, making eight possible racemates. No effort has been made to determine whether or not these products are single racemates. [c] This compound is from a reaction catalyzed with hexamethyleneimine. The previously reported melting point was 253–254° (dec.). [d] One sample of t-B-I melted at 284–285° (dec.). Found: C, 70.17; J, 9.86; N, 7.36.

Experimental[8]

A typical procedure is described for the use of the different catalysts in the reaction of nitromethane with cycloheptanone. Data for the formation of maximum yields of all of the compounds I with the various catalysts are listed in Table I. Physical constants, significant absorption bands, and analyses are listed in Table III. The compounds I were recrystallized from 95% ethanol, except t-B-I and Ch-I which were recrystallized from dimethylformamide.

Formation of H-I. (a) **With Piperidine as Catalyst.**—In a round-bottomed flask fitted with a Dean and Stark trap were placed 23 g. (0.21 mole) of cycloheptanone, 14.03 g. (0.23 mole) of nitromethane, 8.5 g. (0.10 mole) of piperidine, and 50 ml. of benzene, and the solution refluxed for 72 hr. No solid separated during the reaction, but after acidification of the reaction mixture with hydrochloric acid, crystals separated. They were collected on a filter, washed with hot water, and recrystallized from 95% ethanol to yield 14.2 g. (46%) of H-I, m.p. 247–249° (dec.).

(b) **With Hexamethyleneimine as Catalyst.**—The same amounts of reactants with 9.9 g. (0.10 mole) of hexamethyleneimine were refluxed for 72 hr. No solid separated during the reaction, but after acidification of the reaction mixture crystals separated. The crystals were washed with hot benzene and with hot water to yield 12 g. (40.0%) of H-I, m.p. 245–246° (dec.) after recrystallization from acetone.

(c) **With Piperazine as Catalyst.**—Cycloheptanone (33.6 g., 0.30 mole), 20.13 g. (0.33 mole) of nitromethane, 12.9 g. (0.15 mole) of piperazine, and 90 ml. of benzene were refluxed for 61 hr. The solid which separated was collected on a filter, washed first with ether and then with hot benzene, to yield 23 g. (44.3%) of the piperazine salt of H-I, m.p. 225–226° (dec.) after recrystallization from ethanol.

Anal. Calcd. for $C_{36}H_{54}N_2O_3$: C, 65.72; H, 8.27; N, 9.58. Found: C, 66.26; H, 8.38; N, 9.40.

When this salt was extracted with hot 1:1 hydrochloric acid for 40 min., it yielded H-I, m.p. 250–251° (dec.).

(d) **With Morpholine as Catalyst.**—Cycloheptanone (11.2 g., 0.10 mole), 6.71 g. (0.11 mole) of nitromethane, 10.3 g. (0.10 mole) of morpholine, and 50 ml. of benzene were refluxed for 72 hr. No crystals separated during the reaction, but after acidification of the reaction mixture and the addition of ether, crystals were obtained. The solid which separated was washed with hot water and hot benzene to yield 2.3 g. (16%) of H-I, m.p. 246–248° (dec.) after recrystallization from acetone.

When the reactions of the other alicyclic ketones with nitromethane were catalyzed with piperidine and with pyrrolidine, crystals began to separate slowly after several hours of refluxing. They were separated by filtration and washed thoroughly with ether prior to recrystallization. The only products identified in the filtrates from the solids were the 1-nitromethyl cyclic olefins.

The Piperazine Salt of M-I.—4-Methylcyclohexanone (61.6

g., 0.55 mole), 38.4 g. (0.63 mole) of nitromethane, 23.2 g. (0.27 mole) of piperazine, and 85 ml. of benzene were refluxed for 72 hr. The solid which separated was collected on a filter, washed with ether, and then with hot benzene to yield 33.1 g. (35.0%) of the piperazine salt of M-I, m.p. 270–271° (dec.) after recrystallization from ethanol.

Anal. Calcd. for $C_{36}H_{58}N_6O_6$: C, 65.45; H, 8.72; N, 12.53. Found: C, 64.19; H, 9.05; N, 12.89.

Derivatives.—The diacetate of M-I melted at 234–235°.

Anal. Calcd. for $C_{20}H_{28}N_2O_4$: C, 63.81: H, 7.50. Found: C, 63.65; H, 7.17.

The monobenzoate of M-I melted at 165–166°.

Anal. Calcd. for $C_{23}H_{28}N_2O_4$: C, 69.97; H, 7.12; N, 7.07. Found: 69.30: H, 7.31; N, 6.95.

The diacetate of t-B-I melted at 183–184°.

Anal. Calcd. for $C_{26}H_{40}N_2O_5$: C, 67.79; H, 8.75; N, 6.08. Found: 67.46; H, 8.70; N, 6.29.

The diacetate of H-I melted at 137–138°.

Anal. Calcd. for $C_{20}H_{28}N_2O_5$: C, 63.81; H, 7.50; N, 7.44. Found: C, 64.01; H, 7.49; N, 7.48.

The monobenzoate of P-I melted at 193–194°.

Anal. Calcd. for $C_{19}H_{20}N_2O_4$: C, 67.04; H, 5.92; N, 8.23. Found: C, 66.87; H, 5.63; N, 8.28.

Formation of C-I from 1,4-Bis(1-cyclohexenyl)piperazine.—The enamine (24 g., 0.1 mole), 13 ml. (0.24 mole) of nitromethane and 120 ml. of benzene were refluxed for 46 hr. Crystals separated after 8.5 hr. The solid was collected on a filter, washed with ether and dried. The yield of C-I was 5.84 g. (22.7%), m.p. 271–273° (dec.).

Formation of M-I from 1,4-Bis(1-cyclohexenyl-4-methyl)-piperazine.—The enamine (14 g., 0.05 mole), 65 ml. (0.12 mole) of nitromethane, and 60 ml. of benzene were refluxed for 46 hr. Crystals separated after 13 hr. and the yield of M-I was 3.08 g., (20.5%) m.p. 269–271° (dec.).

Formation of C-I from 1-Hexamethyleneiminocyclohexene.—The enamine (10.0 g., 0.05 mole), 28.0 g. (0.45 mole) of nitromethane and 110 ml. of benzene were refluxed 91 hr. No crystals separated and no water collected in the trap. When the reaction mixture was acidified with hydrochloric acid, a solid separated. It was collected on a filter, washed with hot water, and ether to yield C-I (3 g., 43%) m.p. 271–273° (dec.) after crystallization from ethanol.

Preparation of 1-Hexamethyleneiminocyclohexene.—The procedure is essentially that of Hunig, Benzig, and Lucke[9] for the preparation of 1-piperidinocyclohexene. In a flask fitted with a Dean and Stark trap were placed 52 ml. (0.5 mole) of cyclohexanone, 21.5 g. (0.25 mole) of hexamethyleneimine, 0.5 g. of p-toluenesulfonic acid, and 100 ml. of benzene. The mixture was refluxed until the water level became constant in the trap (10 hr.). After the solvent was removed from the reaction mixture by distillation, the residue was distilled at 15 mm., discarding the portion distilling below 139° (15 mm.). The yield of enamine was 59.9 g. (66%), b.p. 139–140° (15 mm.), $n^{29}D$ 1.5140.

Anal. Calcd. for $C_{12}H_{21}N$: C, 80.38; H, 11.75; N, 7.81. Found: C, 80.14; H, 11.75; N, 8.04.

Preparation of 1,4-Bis(1-cyclohexenyl)piperazine.—In a flask equipped with a Stark and Dean trap were placed 52 ml. (0.5 mole) of cyclohexanone, 21.5 g. (0.25 mole) of piperazine, a small amount of p-toluenesulfonic acid, and 100 ml. of benzene. The

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(8) The melting points were determined in an open capillary tube in a copper block and are uncorrected. For compounds I other than P-I, H-I, and O-I, the block was preheated to 250°, the tube inserted and heating continued at approximately 3° per minute. For the other compounds I, the block was preheated to 200°.

The elemental analyses were performed by the Weiler–Straus Laboratories, London, England.

The infrared absorption spectra were obtained with a Perkin–Elmer Infracord, Model 137, in Nujol mulls.

(9) S. Hunig, E. Benzig, and E. Lucke, Ber., 90, 2833 (1957).

mixture was gently refluxed for 5 hr. When the benzene was removed by distillation, 38.3 g. (62.5%) of a pale yellow solid was obtained. This crude product was extracted with ether, the ether insoluble piperazine was collected on a filter, and solvent was removed from the filtrate on a steam bath. The enamine so obtained melted at 112–113° after crystallization from cyclohexane.

Anal. Calcd. for $C_{16}H_{26}N_2$: C, 77.90; H, 10.64; N, 11.37. Found: C, 78.00; H, 10.51; N, 11.50.

Preparation of 1,4-Bis(1-cyclohexenyl-4-methyl)piperazine.— By the same procedure, 61.8 ml. (0.5 mole) of 4-methylcyclohexanone yielded 33.5 g. (49%) of crude enamine which melted at 118–119° after crystallization from cyclohexane.

Anal. Calcd. for $C_{18}H_3ON_2$: C, 78.77; H, 11.02; N, 10.21. Found: C, 78.72; H, 10.92; N, 10.51.

Hydrolysis of H-I.—H-I (5 g.) was refluxed with 400 ml. of 1:4 sulfuric acid for 56 hr. After the solution had cooled over night, the solid which separated was collected on a filter and washed with water. H-IV melted at 141–142° after crystallization from ethanol.

Anal. Calcd. for $C_{16}H_{23}NO_3$: C, 69.28; H, 8.36; N, 5.05. Found: C, 69.19; H, 8.46; N, 5.28.

The Hydrogenation of M-I.—M-I (35 g.) in 400 ml. of methanol was hydrogenated in conventional high pressure hydrogenation equipment over 6 g. of Raney nickel at an initial pressure of 1500 p.s.i. The yield of M-II was 26.1 g. (82.5%), m.p. 229–230° after crystallization from petroleum ether (b.p. 86–100°).

Anal. Calcd. for $C_{16}H_{28}N_2O$: C, 72.68; H, 10.67; N, 10.60. Found: C, 72.63; H, 10.35; N, 10.36.

The diacetate of M-II melted at 210–212° after crystallization from ethanol.

Anal. Calcd. for $C_{20}H_{32}N_2O_3$: C, 68.93; H, 9.26; N, 8.04. Found: C, 68.67; H, 9.30; H, 8.14.

The Hydrogenation of P-I.—P-I (19 g.) in 275 ml. of ethanol was hydrogenated over 6 g. of Raney nickel to form P-II (15.8 g., 95%), m.p. 165–166° after crystallization from petroleum ether (b.p. 86–100°).

Anal. Calcd. for $C_{12}H_{20}N_2O$: C, 69.19; H, 9.68; N, 13.45. Found. C, 69.47; H, 9.70; N, 13.11.

The diacetate of P-II melted at 183–184°.

Anal. Calcd. for $C_{16}H_{24}N_2O_3$: C, 65.72; H, 8.27; N, 9.58. Found: C, 66.03; H, 8.26; N, 9.41.

The Reaction of C-II with Nitrous Acid.—C-II (1 g.) was dissolved in 3 ml. of glacial acetic acid and 15 ml. of water in a three necked flask fitted with a stirrer and a dropping funnel. A saturated solution of 0.58 g. of sodium nitrite was added dropwise to the well stirred solution, which was then heated to 70–80° for 4 hr. The yellow solid (0.75 g.) m.p. 175–200° was collected on a filter and fractionally crystallized from ethanol to yield colorless C-VII, m.p. 257–259°.

Anal. Calcd. for $C_{14}H_{20}N_2O_2$. C, 67.71; H, 8.12; N, 11.28. Found: C, 67.45; H, 8.28; N, 11.48.

The Reaction of M-II with Nitrous Acid.—In a three-necked flask were placed 5.28 g. (0.02 mole) of M-II, 60. ml. of acetic acid, and 75 ml. of water. A saturated solution of 2.9 g. (0.04 mole) of sodium nitrite was added dropwise to the well stirred solution. After addition was complete, the mixture was heated

at 60–70° for 4 hr., cooled and filtered. The yellow solid (4.6 g.), m.p. 197–200°, was fractionally crystallized from methanol to give colorless M-VII, m.p. 263–264°.

Anal. Calcd. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.14. Found: C, 69.43; H, 8.69; N, 10.11.

Reduction of C-IVa with Lithium Aluminum Hydride.—C-IVa[2] (26.3 g., 0.1 mole) was dissolved in 500 ml. of dry ether and added dropwise to a well stirred suspension of lithium aluminum hydride (7.6 g., 0.2 mole) in 125 ml. of dry ether. After addition was complete, the mixture was refluxed for 3 hr., cooled, and the excess reducing agent decomposed with potassium hydroxide. The aluminate was collected on a filter and the filtrate evaporated. The acid soluble oil which remained was distilled to yield 17.8 g. of C-VIII, b.p. 143–145° (2 mm.)

Anal. Calcd. for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.03. Found: C, 71.62; H, 10.05.

The hydrochloride of C-VIII, melted at 193–195° (dec.).

Anal. Calcd. for $C_{15}H_{26}NO_2Cl$: C, 62.54; H, 9.18. Found: C, 62.10; H, 9.17.

Reduction of C-XV and C-XIV with Lithium Aluminum Hydride. —The reduction of each of these compounds[10] as described above, yielded C-V, m.p. and mixture m.p. with C-V, 161–163°.

The Oxidation of C-V. In a 100-ml. flask fitted with a drop funnel and a stirrer was placed 3 g. of C-V[2] dissolved in 30 ml. of water and 20 ml. of concd. sulfuric acid. A 10% solution of sodium dichromate was added dropwise until the solution was dark green and a solid had separated.

The mixture was poured onto ice and sodium hydroxide added until the solution was just basic. The mixture was extracted with ether and the ether extract washed and dried. After removal of the solvent, the white solid C-XVIII (2.5 g., 85%) was crystallized from ethanol and melted at 106–107°.

Anal. Calcd. for $C_{14}H_{23}NO$: C, 75.97; H, 10.47. Found: C, 75.54; H, 10.14.

Hydrogenation of C-XVIII over copper chromium oxide yielded C-V, m.p. and mixture m.p. with authentic C-V, 163–165°.

(10) The melting point of the analytical sample of C-XIV is 212–213° rather than 190–191° as previously reported.[2] The infrared spectra of this compound and of the C-XIV, m.p. 216–218° (sublimes) obtained similarly by Noland and Sundberg,[2] are identical.

The melting point of C-XV is 243–244° rather than 233–235°.