scribed above for VIIb gave 13 g. of an oil which was shown to contain, in addition to IXa and Xa (R = C_2H_5), 5–10% of 2-allylcyclopentanone (XIa). An authentic sample of XIa was prepared for comparison by the procedure of Staudinger and Ruzicka[20] and obtained as an oil with b.p. 72–74° (12 mm.) [reported b.p. 86° (12 mm.)[20]]. In view of the discrepancy between the boiling points a p-nitrophenylhydrazone was prepared, m.p. 138–139.5° (reported m.p. 139°[20]).

α-7-3 Series[15] [Synthesis of 10-Ketobicyclo[5.2.1]decane (IXc)]

N-Acetyl-3-(2′-ketocycloheptyl)propylamine (VIc).—Cyanoethylation of cycloheptanone enamine (IIIc) from 112 g. (1 mole) of cycloheptanone yielded 84 g. (60% based on 15 g. of recovered cycloheptanone) of 2-cyanoethylcycloheptanone (IVc) as a colorless oil, b.p. 152–154° (9 mm.). The corresponding ketal Vc was prepared as described above, and the crude product was reduced with hydrogen and Raney nickel in a solution containing acetic anhydride and sodium acetate.[7] Selective hydrolysis by the procedure described above gave 82 g. (76% from IVc) of N-acetyl-3-(2′-ketocycloheptyl)propylamine (VIc) as a colorless oil, b.p. 146–148° (0.02 mm.).

Anal. Calcd. for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02. Found: C, 67.78; H, 9.97.

The 2,4-dinitrophenylhydrazone of VIc was obtained after recrystallization from dimethoxyethane-water as fine orange needles, m.p. 108–108.5°.

Anal. Calcd. for $C_{18}H_{25}N_5O_5$: C, 55.23; H, 6.44. Found: C, 55.09; H, 6.08.

N-Nitroso-N-acetyl-3-(2′-ketocycloheptyl)propylamine (VIIc) was prepared as described above for VIIb and was obtained in 96% yield as a red-orange oil which, on the basis of subsequent nitrogen evolution on decomposition, was indicated to be *ca.* 99% pure.

Ring Enlargement of N-Nitroso-N-acetyl-3-(2′-ketocycloheptyl)propylamine: (A) Reflux Method.—When N-nitroso-N-acetyl-3-(2′-ketocycloheptyl)propylamine (VIIc) was decomposed in a solution of ethanol containing sodium ethoxide heated to reflux under the conditions described above for VIIb only a small amount of bicyclic ketone (IXc) was formed, and the v.p.c. analysis indicated at least eight products to be present.

(B) Ice Bath Method.—To a stirred and cooled (below 10°) mixture of 250 ml. of absolute methanol and 0.4 g. of finely powdered potassium carbonate a solution of 0.25 mole of VIIc in 200 ml. of dichloromethane was added over a period of 2 hr. The mixture was stirred an additional hour and worked up as described above to give 33 g. of a mobile, yellow oil which was shown by v.p.c. analysis to contain *ca.* 60% of 10-ketobicyclo-[5.2.1]decane (IXc). Purification of a 1-g. sample of this material by passage through a preparative v.p.c. column yielded a solid, m.p. 112–115°, which showed no depression in m.p. when admixed with a sample of IXc as obtained *via* the bis-diazoalkane method.[5]

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[20] H. Staudinger and L. Ruzicka, *Helv. Chim. Acta.*, **7**, 442 (1942).

Ring Enlargements. X. The Reactions of Cycloalkanones Carrying Two-carbon and Four-carbon Side Chains Containing Potential Diazoalkyl Moieties[1]

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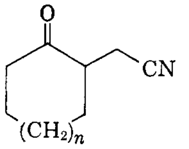
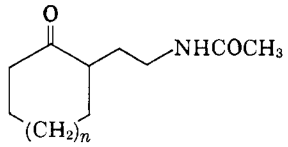
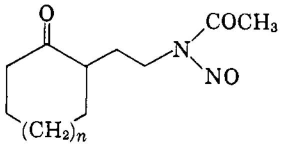
The syntheses of cyclopentanone, cyclohexanone, and cycloheptanone carrying a $—CH_2CH_2N(NO)COCH_3$ moiety in the 2-position, of cyclohexanone carrying a $—CH_2CH_2N(NO)CO_2C_2H_5$ moiety in the 4-position, and of cyclopentanone carrying a $—(CH_2)_4N(NO)COCH_3$ moiety in the 2-position are described. Base-catalyzed decomposition of these compounds results in the formation of solvolysis and elimination products in the case of the cycloalkanones with two-carbon side chains in the 2-position, in the formation of 2-ketobicyclo[3.2 1]octane in the case of cyclohexanone carrying a two-carbon side chain in the 4-position and in the formation of a mixture of 2-ketobicyclo[4.3.0]nonane and 9-ketobicyclo[3.3.1]nonane in the case of cyclopentanone carrying a four-carbon side chain in the 2-position.

The previous paper of this series[4] described the base-catalyzed decomposition of cycloalkanones carrying in the α-position a three-carbon side chain terminating in a potential diazoalkane moiety. The present paper extends the scope of the investigation to include examples of compounds carrying two- and four-carbon side chains in the α-position and a compound carrying a two-carbon side chain in the γ-position.







Ia (n = 0)	IIa (n = 0)	IIIa (n = 0)
b (n = 1)	b (n = 1)	b (n = 1)
c (n = 2)	c (n = 2)	c (n = 2)

Ketonitriles of structure I were prepared by treatment of the enamine of cyclopentanone (n = 0) and cyclohexanone (n = 1) with chloroacetonitrile and by ring enlargement (*in situ* method[5]) of cyclohexanone with β-(N-acetyl-N-nitrosoamino)propionitrile for n = 2. Protection of the carbonyl function by formation of the ethylene ketal followed by reductive acetylation[6] and selective hydrolysis yielded the 2-(β-acetylaminoethyl)cycloalkanone (II) from which the corresponding N-nitroso compound III was obtained by nitrosation with dinitrogen tetroxide.[7] Decomposition of the nitrosoamides III resulted in the evolution of 65–85% of the theoretical amount of nitrogen, but the volatile products were obtained in low yield and contained little or none of the fused ring or bridged ring ketones. The only identified products were methoxyethylcyclopentanone (IVa) and vinylcyclopentanone

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[1] This work was supported, in part, by grants-in-aid from the National Science Foundation (G-6282 and G-21323).

[2] Universal Match Company Fellow, 1959–1961.

[3] Universal Match Company Fellow, 1961–1962; National Science Foundation Summer Research Fellow, 1962.

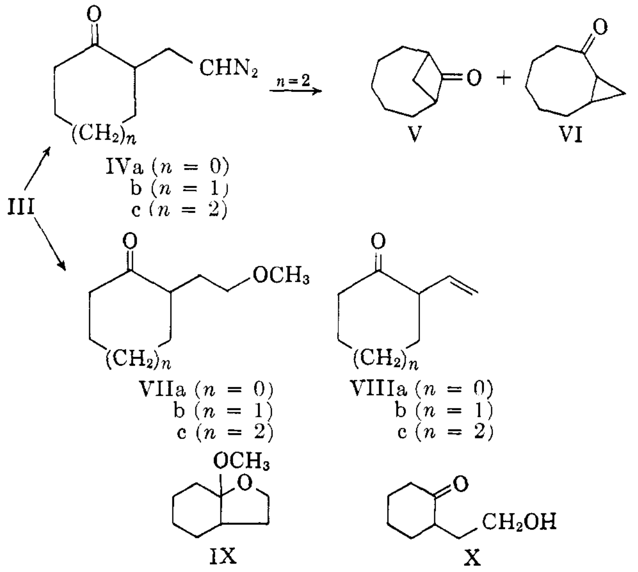
[4] C. D. Gutsche and D. M. Bailey, *J. Org. Chem.*, **28**, 607 (1963).

[5] See C. D. Gutsche, *Org. Reactions*, **VIII**, 364 (1954).

[6] F. E. Gould, G. S. Johnson, and A. F. Ferris, *J. Org. Chem.*, **25**, 1658 (1960).

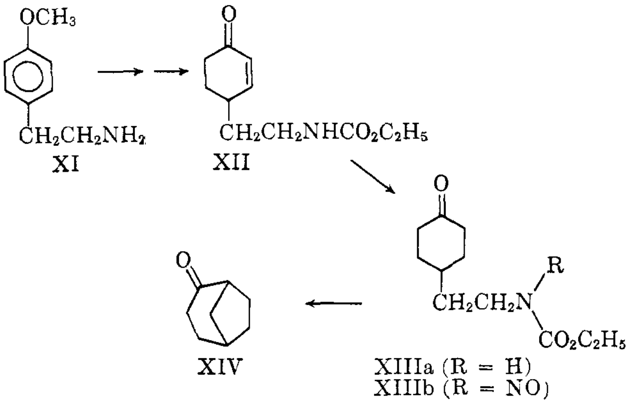
[7] E. J. White, *J. Am. Chem. Soc.*, **77**, 6008 (1955).

(VIIIa) from the decomposition of IIIa, methoxyethylcycloheptanone (IVc) and vinylcycloheptanone (VIIIc) from the decomposition of IIIc, and a material identified as IX from the decomposition of IIIb. The characterization of IX is based on a carbon and hydrogen analysis compatible with the formula $C_{10}H_{18}O_2$, a methoxyl value roughly in accord with one OMe,[8] an infrared spectrum which lacks a carbonyl band but shows strong absorption for C—O stretching bands at 1100 cm.$^{-1}$, and on acid-catalyzed conversion to 2-(β-hydroxyethyl)cyclohexanone (X) which was also prepared by an alternate route. Attempts to convert X back to IX, however, were unsuccessful, this being in accord with the very marked hydrolytic instability of IX.[8]



It is apparent that in the case of compounds carrying a two-carbon side chain in the α-position, solvolysis and elimination reactions (probably through a common intermediate) take precedence over diazoalkane formation. That this might be the result of intramolecular assistance of some sort is suggested by the fact that the reaction of cyclohexanone with the bisnitrosourethane from propane-1,3-diamine did yield, although in relatively small amount, a mixture of the bridged ring ketone V and the fused ring ketone VI (along with larger amounts of keto ether VIIc). This may be the result of the formation of 1,4-bisdiazobutane, *per se*, followed by its interaction with cyclohexanone to form IVc [rather than IIIc which would be formed from cyclohexanone and $N_2CH(CH_2)_3N(NO)COR$]. If so, it demonstrates that the diazoalkane, once formed, *can* engage in intramolecular reaction with a carbonyl removed from it by only two carbons, and it indicates that the failure to achieve such reactions from compounds of type III may be ascribed to the failure of the diazoalkane IV ever to form, other processes intervening.[9]

Moving the two-carbon side chain from the α- to the γ-position changes the course of the reaction back to the path of ring enlargement as demonstrated by the base-catalyzed decomposition of XIV. This material was obtained from *p*-methoxyphenylethylamine (XI) by a Birch reduction[10] to the dihydro compound, conversion to the corresponding carbamate with ethyl chloroformate, hydrolysis to the unsaturated ketone XII, catalytic reduction to the corresponding saturated ketone XIIIa and nitrosation to XIIIb. When XIIIb was decomposed in alcoholic base, nitrogen was evolved in quantitative amount, and 2-ketobicyclo-[3.2.1]octane (XXIV) was formed in *ca.* 50% yield. The structure of the bridged ring ketone was established by comparison with material obtained by a different method.[11] Although the preparation of XIV from XIII does not represent the synthesis of a new ring system, it does provide a new route to this compound and illustrates another aspect of the diazoalkane side chain method of ring enlargement.



The diazoalkane side chain method has been investigated in one case with a four-carbon side chain attached at the α-position of the cycloalkanone. γ-(2-Keto-1-cyclopentane)butyric acid (XV) was converted to the amide XVI, the carbonyl group was protected *via* ketal formation, and the amide group was converted to an amino group by reduction with lithium aluminum hydride. Acetylation followed by hydrolysis of the ketal yielded XVII which was converted to XVIII by nitrosation. Decomposition of XVIII in alcoholic base gave an almost quantitative yield of a mixture containing two materials in a ratio of *ca.* 2 to 1. Treatment of the mixture with ethyl formate converted the component present in larger amount to a hydroxymethylene derivative and allowed its separation from the other component.[12]

The structure of this fraction was established as 2-ketobicyclo[4.3.0]nonane (XIX) by its analysis (compatible with a $C_9H_{14}O$ formula), by a carbonyl absorption at 1710 cm.$^{-1}$ characteristic of a cyclohexanone, by its failure to react with neutral potassium permanganate (no olefinic bonds) or hydriodic acid (no methoxyl groups), by its facile bromination (enolizable α-protons), and by its conversion to the keto-amide XVI (*via* pertrifluoroacetic acid oxidation of XIX to the lactone, opening of the lactone to ethyl γ-(2-hydroxy-

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[8] Methoxyl values were very capricious and always low due, presumably, to the ease with which IX undergoes hydrolysis.

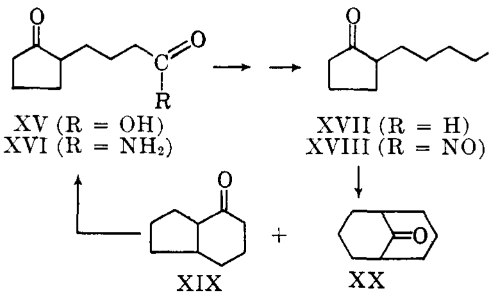
[9] The decomposition of N-nitrosobenzylurethanes in the presence of cyclohexanone and alcoholic base has been shown to lead to mixtures containing an increasingly large ratio of ring enlarged product to solvolysis product as the ability of the system to stabilize a benzyl carbonium ion increases [C. D. Gutsche and H. E. Johnson, *J. Am. Chem. Soc.*, **77**, 109 (1955)]. It has also been shown that phenyldiazomethane, *per se*, is unreactive toward methanol (to form methyl benzyl ether) but very reactive toward cyclohexanone (to form phenylcycloheptanone) [C. D. Gutsche and E. F. Jason, *ibid.*, **78**, 1184 (1956)].

[10] A. J. Birch and H. Smith, *Quart. Rev.*, **12**, 17 (1958).

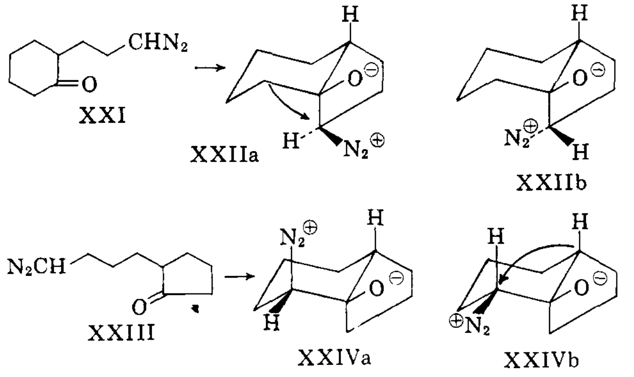
[11] We are indebted to Professor H. M. Walborsky for a generous sample of XXIV which had been prepared by the method of K. Alder [for ref., see A. A. Youseff, M. E. Baum, and H. M. Walborsky, *J. Am. Chem. Soc.*, **81**, 4709 (1955)].

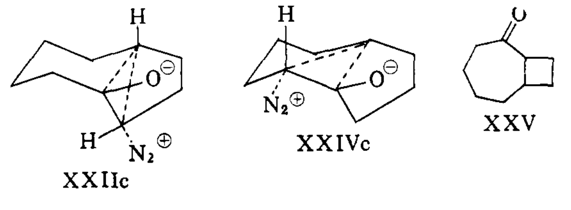
[12] W. S. Johnson and H. Posvic, *ibid.*, **69**, 1361 (1947).

cyclopentyl)butyrate, oxidation to ethyl γ-(2-ketocyclopentyl)butyrate, and conversion to the amide XVI). Although both isomers of XIX have been reported,[13] the structure proof of our material by the chemical sequence just outlined was deemed necessary, for its derivative agreed in melting point, even after extensive recrystallizations, with neither of those reported. Possibly the product of ring enlargement is a eutectic mixture of the *cis* and *trans* forms of XIX. The constituent which failed to form a hydroxymethylene derivative was identified as 9-ketobicyclo[3.3.1]nonane (XX) by its analysis (compatible with a $C_9H_{14}O$ formula), by a carbonyl absorption at 1715 cm.$^{-1}$ characteristic of a cyclohexanone, by its failure to react with neutral potassium permanganate or hydriodic acid or bromine, and by its conversion to the known bicyclo[3.3.1]nonane.[14] Comparison of both the hydrocarbon and the ketone with samples prepared by alternate methods[15,16] provided additional support for structure XX.



An α-substituted cyclopentanone was chosen for the four-carbon side chain example because of the interesting relationship between XXI and XXIII. The intermediates involved in the intramolecular diazoalkyl-carbonyl reaction of these two compounds are similar with respect to the ring system (*e.g.*, a fused 6-5 system) and differ only with respect to the position of the nitrogen substituent. Since XXI leads only to bridged ring ketone, while XXIII gives a mixture of bridged ring and fused ring ketone with the latter predominating, it is clear that the nature of the bicyclic ring system in the intermediate is less important in controlling the outcome of the reaction than is the size of the ring carrying the oxygen and nitrogen functions. An explanation for the data obtained in the bisdiazoalkane-cycloalkanone series has been advanced[17] which is based on three postulates, *viz.* (a) that the formation of product from the intermediate charge-separated structure is the result of backside displacement of nitrogen by the migrating carbon atom, (b) that the most stable conformation for the bicyclic, charge-separated intermediate will contain the highest population of molecules, and (c) that the configuration between the negatively charged oxygen and the positively-charged nitrogen in the charge-separated intermediate will be *cis* due to the electrostatic attraction between these two groups. To explain the present results, these postulates appear to be adequate if one makes the assumption that conformational preferences may outweigh electrostatic interactions. Thus, of the two configurations, XXIIa and XXIIb, the former might be the more stable because the differences in conformational interactions are negligible and the electrostatic attraction between the positive and negative groups will be the determining factor. In the two configurations, XXIVa and XXIVb, however, the latter might be the more favorable because of the tendency of the bulky group (nitrogen) to prefer an equatorial situation even at the expense of a somewhat diminished electrostatic attraction. Species XXIIa is well constituted to form bridged ring ketone by backside displacement of the nitrogen, while species XXIVb is well constituted to form fused ring ketone by a similar mechanism. The explanation for the difference in product ratio from XXI and XXIII may also be stated in terms of preferential formation of the fused ring system, partial bond intermediate XXIIc being less stable than partial bond intermediate XXIVc. In essence, this latter is simply a statement of the fact that the fused ring ketone XIX represents a less strained structure than the fused ring ketone XXV.





Experimental[18]

α-5-2 **Series.**[19]—2-Cyanomethylcyclopentanone (Ia) was prepared from 84 g. (1 mole) of cyclopentanone enamine and 75.5 g. (1 mole) of chloroacetonitrile and was obtained as 41 g. (33%) of a clear, very pale yellow oil, b.p. 122–124° (9 mm.).

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(13) W. Huckel and L. Schnitzpahn, *Ann.*, **505**, 274 (1933).

(14) A. C. Cope and M. E. Synerholm, *J. Am. Chem. Soc.*, **72**, 5228 (1950).

(15) We are indebted to Professor A. C. Cope for the melting point and infrared comparisons of the hydrocarbons and the ketones.

(16) A preparation of 9-ketobicyclo[3.3.1]nonane (XX) is described in the Ph.D. thesis of C. Foote, Harvard University, 1961, and m.p. 155.0–158.5° is reported. This synthesis has been repeated in modified form by A. C. Cope and co-workers (private communication), and a material with m.p. 152–153° was obtained. It is with the latter product that our compound (m.p. 151–152°) has been compared.[15] We are grateful to Professor Cope for calling our attention to the Harvard thesis.

(17) C. D. Gutsche and T. D. Smith, *J. Am. Chem. Soc.*, **82**, 4067 (1960).

(18) Melting points are corrected; boiling points are uncorrected. The infrared spectra were recorded on a Perkin-Elmer Model 21 spectrophotometer; the ultraviolet spectra were recorded on a Cary spectrophotometer. Analytical vapor phase chromatographic determinations were carried out with columns $^1/_4$ in. in diam. packed with firebrick (6-ft. column) or with glass beads (16-ft. column) with silicone oil (Dow-Corning 710) as the adsorbed phase. Preparative vapor phase chromatographic separations were carried out on a column $^1/_2$ in. × 10 ft. packed with silicone oil on firebrick. Nuclear magnetic resonance spectra were measured with a Varian high resolution spectrometer equipped with a Varian model V4311 fixed frequency rf unit operating at 56.4 Mc. The "side band" technique employing an audio oscillator equipped with a frequency counter was used to determine the positions of the resonance lines relative to the reference compound, tetramethylsilane. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill., and by Mikroanalytisches Laboratorium, Vienna, Austria.

Anal. Calcd. for C_7H_9NO: C, 68.27; H, 7.37. Found: C, 68.75; H, 7.50.

Conversion of 41 g. of Ia to the ethylene ketal, reductive acetylation, and selective hydrolysis to the keto-amide IIa were carried out by the procedures described in the previous paper[4] for the α-6-3 series and yielded 48 g. (85%) of IIa as a viscous oil. Attempts to distill this material resulted in decomposition, and it was therefore used directly in the subsequent step without purification. Nitrosation of a 42 g. sample of IIa was carried out as previously described,[4,7] and the resulting nitroso compound IIIa was dissolved in 50 ml. of dichloromethane and added, over a period of 45 min., to a stirred and cooled (below 10°) mixture of 100 ml. of absolute methanol and 0.4 g. of finely powdered potassium carbonate. The mixture was stirred an additional hour (total nitrogen evolution 66%). The solvent was then evaporated, the residue (40 g.) was chromatographed on an alumina column, and the fraction that was eluted with petroleum ether (16 g.) was fractionally distilled to give 1.6 g. with b.p. 60–72° (20 mm.), 9.7 g. with b.p. 98–100° (20 mm.), and a high-boiling residue weighing 4.7 g. The lower-boiling fraction contained three components, one of which was identified as 2-vinylcyclopentanone (VIIIa) by hydrogenation to 2-ethylcyclopentanone, an authentic sample of which was prepared for comparison. The higher-boiling fraction contained several components in minor amounts but consisted essentially of one material, **2-(β-methoxyethyl)cyclopentanone (VIIa)**. Purification by passage through a preparative v.p.c. column yielded a colorless oil; $\bar{\nu}^{\text{lip}}_{\text{cm}^{-1}}$ 1745 (cyclopentanone carbonyl), 1118 (ROR).

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.93. Found: C, 67.48; H, 9.95.

The 2,4-dinitrophenylhydrazone of 2-(β-methoxyethyl)cyclopentanone was obtained after recrystallization from absolute ethanol as orange needles, m.p. 125.5–126.5°.

Anal. Calcd. for $C_{14}H_{18}N_4O_5$: C, 52.17; H, 5.63. Found: C, 52.65; H, 5.81.

α-6-2 Series.[19]—Treatment of cyclohexanone enamine with chloroacetonitrile gave 2-cyanomethylcyclohexanone (Ib) in 44.5% yield. Conversion of 61 g. of Ib to the ethylene ketal, reductive acetylation, and selective hydrolysis yielded 71.5 g. (89%) of the ketoamide IIb as a viscous oil. Although distillation of this material resulted in conversion to a different material (probably N-acetyl-2,3,4,5,6,7-hexahydroindole), a semicarbazone of N-acetyl-2-(2′-ketocyclohexyl)ethylamine could be prepared from the crude material and was obtained as colorless small rhombs after recrystallization from water, m.p. 183.5–184.5° dec.

Anal. Calcd. for $C_{11}H_{20}N_4O_2$: C, 54.98; H, 8.39. Found: C, 55.13; H, 8.32.

Nitrosation of a 46-g. sample of IIb was carried out as previously described, and the resulting nitroso compound (IIIb) was decomposed in methanol at 10° as described above for IIIa (total nitrogen evolution 84%) and worked up in the same fashion to give 11.8 g. of a volatile fraction, b.p. 80–82° (20 mm.). Vapor phase chromatographic analysis of this material indicated it to be homogeneous, it gave a strong qualitative test for methoxy,[20] it rapidly absorbed bromine in carbon tetrachloride at 0° (with liberation of hydrogen bromide gas), and it slowly discolored a solution of potassium permanganate in acetone; $\bar{\nu}^{\text{liq.}}_{\text{cm}^{-1}}$ 1100, 1135, 1160 (ROR), n.m.r. 6.04 τ (multiplet, 2 protons), 6.92 τ (singlet, 3 protons), 7.82 and 8.62 τ (multiplet, 11 protons).

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32; OCH_3, 19.9. Found: C, 69.07; H, 10.54; OCH_3, 17.7.[8]

This material is thought to be 7a-methoxy 2,3,3a,4,5,6,7,7a-octahydrobenzofuran (IX) on the basis of these data and on the basis of its conversion, under acid-catalyzed conditions, to the 2,4-dinitrophenylhydrazone of 2-(β-hydroxyethyl)cyclopentanone (X) m.p. 150–151°, identical with an authentic sample prepared as described under "miscellaneous experiments."

α-7-2 Series[19]: N-acetyl-N-nitroso-β-aminopropionitrile, required for the ring enlargement of cyclohexanone, was prepared as follows. Employing the procedure of White,[7] an ice-cold solution of 84.5 g. (0.76 mole) of N-acetyl-β-aminopropionitrile,[21] m.p. 62–63°, in 300 ml. of dichloromethane was added to a mixture of 108 g. (1.17 moles) of dinitrogen tetroxide and 200 g. (2.44 moles) of anhydrous sodium acetate in 1.2 l. of dichloromethane cooled to −30°. The mixture was allowed to warm to 0°, maintained at that temperature with occasional stirring for 30 min., re-cooled to −30°, and poured into 1.5 l. of ice-cold 10% potassium carbonate solution. The organic layer was thoroughly extracted with cold 10% potassium carbonate solution, dried over anhydrous potassium carbonate, and concentrated in vacuum to a total volume of *ca.* 250 ml. with the temperature maintained below 35° during the concentration.

2-Cyanomethylcycloheptanone (Ic) was prepared by addition, over a period of 2 hr., of the solution of the nitroso compound described above to a cooled (5–10°) and stirred mixture of 98 g. (1.0 mole) of cyclohexanone, 450 ml. of anhydrous methanol, and 5 ml. of 1 *N* sodium methoxide solution. The reaction mixture was stirred an additional 2 hr. (total nitrogen evolution 100%) and then worked up by solvent evaporation and fractional distillation of the residue to give 86 g. (75.5%) of Ic as a clear, colorless oil, b.p. 130–135° (5 mm.).

Anal. Calcd. for $C_9H_{13}NO$: C, 71.49; H, 8.67. Found: C, 71.75; H, 8.77.

The 2,4-dinitrophenylhydrazone of 2-cyanomethylcycloheptanone was obtained as amber needles after recrystallization from absolute ethanol, m.p. 137–137.5°.

Anal. Calcd. for $C_{15}H_{17}N_5O_4$: C, 54.37; H, 5.17. Found: C, 54.17; H, 5.28.

Conversion of 86 g. of Ic to the ethylene ketal, reductive acetylation, and selective hydrolysis yielded 95 g. (85% of the ketoamide (IIc) as a viscous oil [$\bar{\nu}^{\text{liq}}_{\text{max}}$ cm.$^{-1}$ 3400 and 3200 (N–H), 1710 (cycloheptanone carbonyl), 1670 (amide)] which decomposed on distillation at reduced pressure and which, therefore, was used in the subsequent step without purification. Nitrosation of 49 g. of IIc was carried out as previously described, and the resulting nitroso compound IIIc was decomposed in methanol at 10° as described above for IIIa (total nitrogen evolution 76%) and worked up by steam distillation to give only 7 g. of a pale yellow oil which consisted mainly of one component. Purification by passage through a preparative v.p.c. column gave a colorless oil which showed a negative test for methoxyl groups[20] and which rapidly decolorized a solution of potassium permanganate in acetone. The material was transparent in the region 200–250 mμ of the ultraviolet (no α,β-unsaturated carbonyl) and had an infrared band at 1700 cm.$^{-1}$ for cycloheptanone carbonyl and bands at 1800 (weak), 1400 (medium), 1290 (medium), 1000 (strong), and 945 (strong) cm.$^{-1}$ for $CH{=}CH_2$. On the basis of these data the structure of 2-vinylcycloheptanone is suggested for this material.

δ-6-2 Series[19] [Synthesis of 2-Ketobicyclo[3.2.1]octane (XIV)]

N-Carbethoxy-2-(4′-ketocyclohexyl)ethylamine (XIIIa).—2-(*p*-Methoxyphenyl)ethylamine (XI) was prepared in 83% yield from *p*-methoxyphenylacetonitrile by reduction with lithium aluminum hydride and aluminum chloride in ether solution[22] and was obtained as a pale yellow oil, b.p. 138–140° (20 mm.) [reported b.p. 138–142° (20 mm.)[23]]. To a stirred mixture of 166.5 g. (1.1 moles) of XI, 350 ml. of dry ether, and 3 l. of anhydrous liquid ammonia contained in a 5-l. three-necked flask, 50.5 g. (7.25 g.-atoms) of lithium was added in small pieces over a period of 30 min. The mixture was stirred an additional 30 min., and 438 ml. (7.5 moles) of absolute ethanol was then added dropwise. Evaporation of the solvents and a small amount of unchanged starting amine (6.1 g.) left 163 g. (99% based on recovered XI) of crude product. This was suspended in a solution of 89.7 g. (1.6 moles) of potassium hydroxide in 1.5 l. of water, stirred and cooled to 0–5°, and treated with 163 g. (1.5 moles) of ethyl chloroformate, added dropwise. Work up in the usual way gave 219 g. (88%) of a clear yellow oil which was added to a mixture of 1 l. of ether and 1 l. of 5% aqueous sulfuric acid and stirred at 0–5° for *ca.* 4 hrs. From this mixture the ketourethan XII was obtained in 89% yield. An 80-g. sample of XII was dissolved in 500 ml. of ethanol, 5 g. of 10% palladium-on-charcoal catalyst was added, and the mixture was

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[19] In this and subsequent designations in the experimental section the Greek letter refers to the point of attachment of the side chain to the cycloalkanone, the first number refers to the ring size of the cycloalkanone, and the second number refers to the number of carbon atoms in the side chain.

[20] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., John Wiley and Sons, Inc., New York, N. Y., 1959, p. 116.

[21] S. R. Buc, J. H. Ford, and E. C. Wise, *J. Am. Chem. Soc.*, **67**, 92 (1954).

[22] R. F. Nystrom, *ibid.*, **77**, 2544 (1955).

[23] G. S. Walpole, *J. Chem. Soc.*, **97**, 942 (1909).

subjected to hydrogenation for 36 hr. at 28 p.s.i. The product was isolated in the usual manner and consisted of 80 g. (100%) of a waxy solid. Recrystallization from isopropyl ether gave 69 g. (85%) of XIIIa as colorless, waxy crystals, m.p. 49–50° (prev. sof.).

Anal. Calcd. for $C_{11}H_{19}NO_3$: C, 61.94; H, 8.98. Found: C, 61.85; H, 8.99.

The 2,4-dinitrophenylhydrazone of N-carbethoxy-2-(4′-ketocyclohexyl)ethylamine was obtained as orange needles after recrystallization from absolute ethanol, m.p. 162.5–163°.

Anal. Calcd. for $C_{17}H_{23}N_5O_6$: C, 51.90; H, 5.89. Found: C, 52.14; H, 5.58.

N-Nitroso-N-carbethoxy-2-(4′-ketocyclohexyl)ethylamine (XIIIb) was prepared as described previously[4,7] and was obtained in 99% yield as a red oil which, on the basis of subsequent nitrogen evolution on decomposition, was indicated to be *ca.* 92.5% pure.

Ring Enlargement of N-Nitroso-2-(4′-ketocyclohexyl)ethylamine.—To a stirred mixture of 200 ml. of absolute methanol and 0.4 g. of finely powdered potassium carbonate a solution containing 60 g. (0.25 mole) of XIIIb in 150 ml. of dichloromethane was added over a period of 1.5 hr. The mixture was stirred an additional 30 min. and then steam distilled and worked up in the usual fashion. The crude product consisted of 22 g. (72%) of a mushy solid which was shown to consist mainly of one component by v.p.c. analysis. Recrystallization from petroleum ether (b.p. 63–69°) gave 15 g. (48.5%) of 2-ketobicyclo[3.2.1]octane (XIV) with m.p. 115–122°, and repeated recrystallization raised this m.p. to 127–129° (reported m.p. 127–129°[11]). The semicarbazone of XIV was obtained as colorless, thin blades, m.p. 173–173.5° (reported m.p. 171–172°[11]). Mixed melting points of the ketone and its semicarbazone with ketone and semicarbazone obtained by another route[11] showed no depression in melting point.

α-5-4 Series.[16]—4-(2′-Ketocyclopentyl)butyric acid (XV) was prepared from 2-carbethoxycyclopentanone and ethyl γ-bromobutyrate followed by hydrolysis and decarboxylation of the resulting product. A 49-g. sample (0.29 mole) of XV was converted to the dry sodium salt and treated with oxalyl chloride[24] to yield the acid chloride which was then dissolved in chloroform and ammonolyzed with anhydrous ammonia. The resulting product was crystallized from benzene to give 26 g. (53%) of 4-(2′-ketocyclopentyl)butyramide (XVI) as a white solid. Several additional recrystallizations provided colorless needles with m.p. 85.5–86°.

Anal. Calcd. for $C_9H_{15}NO_2$: C, 63.88; H, 8.94. Found: C, 63.33; H, 8.86.

A 25-g. sample of XVI was converted to the ethylene ketal, and the amide group was reduced to the amino group with lithium aluminum hydride in dioxane. Acetylation of the amino function with acetic anhydride followed by selective hydrolysis of the ketal function (50 ml. of 1:25 sulfuric acid for 8 hr. at room temperature) provided 11 g. (32%) of N-acetyl-4-(2′-ketocyclopentyl)butylamine (XVII) as a colorless oil, b.p. 160–162° (0.05 mm.). A 2,4-dinitrophenylhydrazone of XVII was obtained as yellow needles after recrystallization from aqueous ethanol, m.p. 138.5–139.5°.

Anal. Calcd. for $C_{17}H_{23}N_5O_5$: C, 54.10; H, 6.14. Found: C, 53.85; H, 6.29.

Ring Enlargement of N-Nitroso-N-acetyl-4-(2′-ketocyclopentyl)butylamine (XVIII).—To 25 ml. of dichloromethane heated at reflux on a steam bath were simultaneously added a solution of XVIII, obtained from 10.0 g. (0.057 mole) of XVII by nitrosation in the usual way,[4,7] in 25 ml. of dichloromethane and 10 ml. of a 0.1 *N* solution of sodium methoxide in absolute methanol. After the addition was complete (*ca.* 10 min.) the reaction mixture was stirred an additional 15 min. and then subjected to steam distillation followed by the usual isolation procedure. The crude product, consisting of 6.6 g. of a yellow oil, was dissolved in 70 ml. of benzene, cooled to 0°, and treated with 5.5 g. of sodium methoxide and 17.4 g. of ethyl formate following the directions of Johnson and Posvic.[12] Extraction of reaction mixture with 20% sodium hydroxide solution brought the hydroxymethylene derivative of XIX into the aqueous phase and left XX in the benzene phase.

2-Ketobicyclo[4.3.0]nonane (XIX).—The aqueous phase of the reaction mixture described above was treated according to the general procedure,[12] and the parent ketone was isolated as a colorless liquid, $\bar{\nu}^{\text{liq}}_{\text{cm}^{-1}}$ 1710.

Anal. Calcd. for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.22; H, 10.26.

The semicarbazone of 2-ketobicyclo[4.3.0]nonane was obtained as colorless needles and even after numerous recrystallizations from aqueous ethanol the m.p. remained constant at 176–177° (reported for *cis* isomer 193°[13]; for the *trans* isomer 183°[13]).

Anal. Calcd. for $C_{10}H_{17}N_3O$: C, 61.51; H, 8.78. Found: C, 61.70; H, 8.77.

A sample of XIX was oxidized with trifluoroperacetic acid,[25] the crude lactone was hydrolyzed in 1.2 *N* alcoholic sodium hydroxide solution to the hydroxy acid, and the acid was oxidized by the procedure of Brown and Garg[26] to the keto acid XV. Conversion to the amide gave a material with m.p. 85–86° which, on the basis of mixed m.p. and infrared comparison, proved to be identical with 4-(2′-ketocyclopentyl)butyramide (XVI) described above.

9-Ketobicyclo[3.3.1]nonane (XX).—The benzene phase of the reaction mixture obtained from the ring enlargement product (described above) was concentrated *in vacuo*, and the residue was vacuum sublimed and twice recrystallized from petroleum ether (b.p. 63–69°), cooled to −70° (operation performed in a dry box) to give colorless needles; m.p. 151–152°; n.m.r. 7.69 τ (2 protons), 7.95 τ and 8.29 τ (11.75 protons combined). A mixed m.p. with a sample prepared by an alternate method[16] showed no depression.

Anal. Calcd. for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.89; H, 10.27.

The 2,4-dinitrophenylhydrazone of XX was obtained as yellow needles after recrystallization from aqueous ethanol, m.p. 191–192°.

Anal. Calcd. for $C_{15}H_{18}N_4O_4$: C, 56.59; H, 5.70. Found: C, 56.49; H, 5.69.

Following the procedure of Cope[14] for the reduction of 1-bromo-9-ketobicyclo[3.3.1]nonane, the ketone XX was converted to bicyclo[3.3.1]nonane, m.p. 145–146° (reported[14] 145–146°). A mixed m.p. and infrared comparison of this product with authentic material[15] showed the two substances to be identical.

Miscellaneous Experiments: Synthesis of 2-(β-Hydroxyethyl)-cyclohexanone (X).—β-(2-Ketocyclohexane)acetic acid, prepared by the method of Charlesworth, *et al.*,[27] was converted with diazomethane to the methyl ester, the 2,4-dinitrophenylhydrazone of which had m.p. 138–139° (reported[28] 138–139°). The keto ester was converted to the ethylene-ketal, reduced with with lithium aluminum hydride, and hydrolyzed with 1:25 aqueous sulfuric acid to yield X as a colorless liquid which formed a 2,4-dinitrophenylhydrazone, m.p. 150–151°, identical by mixed m.p. comparison with the material obtained from the α-6-2-series described above.

Anal. Calcd. for $C_{14}H_{18}N_4O_5$: C, 52.17; H, 5.63. Found: C, 52.25; H, 5.72.

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