Ring Enlargements. XIII. Intramolecular Diazoalkane–Carbonyl Reactions

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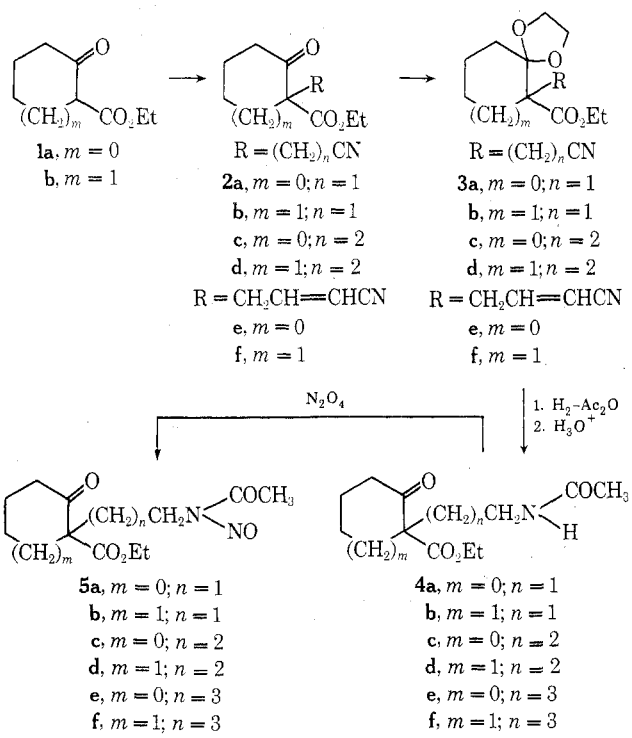
The scope of the intramolecular diazoalkane–carbonyl reaction, described in earlier papers in this series, has been extended by application to (a) 2-carbethoxycycloalkanones carrying acyclic side chains at the 2 position containing potential diazoalkyl moieties and (b) cycloalkanones carrying cyclic side chains at the 2 position containing potential diazoalkyl moieties. Of the several compounds studied, the three most synthetically useful ones are 2-carbethoxycyclopentanone carrying a three-carbon acyclic side chain (forming the bridged ring ketone **6** as the major product), 2-carbethoxycyclohexanone carrying a three-carbon acyclic side chain (forming the bridged ring ketone **9** as the major product), and cyclohexanone carrying an *N*-nitrosopyrrolidone-containing side chain (forming the bridged ring ketones **25** and **26** as the major products).

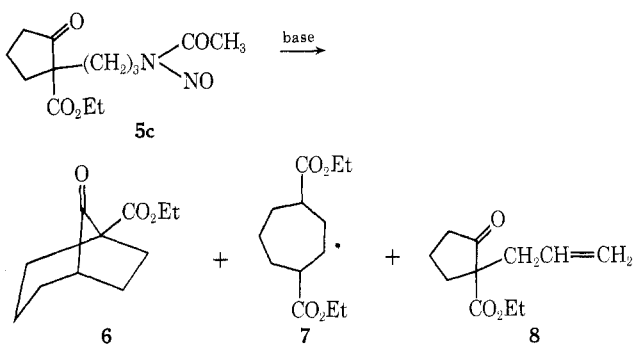
Earlier papers in this series have described diazoalkane–carbonyl reactions that are (a) intermolecular and involve cycloalkanones and *N*-nitrosolactams[1] and (b) intramolecular and involve cycloalkanones carrying potential diazoalkyl moieties.[2,3] The present paper is concerned with both of these aspects of the diazoalkane–carbonyl reaction, extending the scope of its application.

Reactions of 2-Carbethoxycycloalkanones Carrying Acyclic Side Chains at the C-2 Position Which Contain Potential Diazoalkyl Moieties (5). Following the general procedures that have been previously described,[2,3] 2-carbethoxycyclopentanone (**1a**) and 2-carbethoxycyclohexanone (**1b**) were converted to *N*-acetyl-(1′-carbethoxy-2′-ketocycloalkyl)alkylamines containing cyclopentanone and cyclohexanone rings carrying two-carbon, three-carbon, and four-carbon side chains (**4**), as illustrated in Scheme I. Nitrosation with dinitrogen tetroxide yields the corresponding *N*-nitroso compounds (**5**).

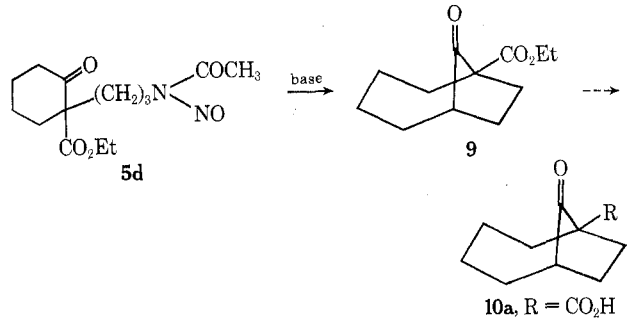
Scheme I
Preparation of *N*-Nitroso-*N*-acetyl-(1′-carbethoxy-2′-ketocycloalkyl)alkylamines (5)



Base-induced decomposition of the compounds carrying two-carbon side chains (**5a** and **5b**) results in the formation of complex mixtures which were not investigated further. Base-induced decompositions of the compounds carrying three-carbon side chains (**5c** and **5d**), on the other hand, proceed smoothly and yield more tractable reaction mixtures. Thus, potassium carbonate induced decomposition of **5c** at 25° gives a mixture containing 1-carbethoxybicyclo[3.2.1]octan-8-one (**6**) and 1,4-dicarbethoxycycloheptanone (**7**), the alcoholysis product from **6**. The structure of **6** is commensurate with a $C_{11}H_{16}O_3$ molecular formula, infrared stretching bands at 1760 and 1730 cm^{-1} for cyclopentanone and ester carbonyl functions, the observed nmr spectrum, and the failure to undergo oxidative cleavage with nitric acid.[4] The structure of **7** is commensurate with a $C_{13}H_{22}O_4$ molecular formula, a single stretching band at 1742 cm^{-1} for identical ester carbonyl functions, and the nmr spectrum showing a pair of identical OCH_2CH_3 functions. Under the more strenuous conditions of sodium ethoxide induced decomposition at 40–45°, **7** is the sole product, whereas under the milder conditions of potassium carbonate at −10° the bridged ring ketone **6** and the olefin **8** are formed in approximately equal amount.

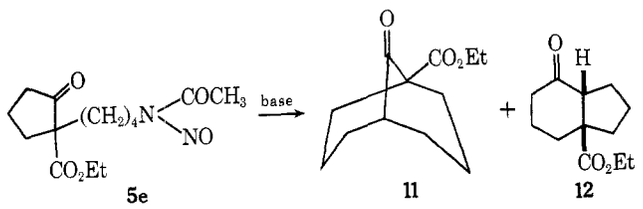


Compound **5d** reacts in the cleanest fashion of any of the compounds in this series and yields, under all of the conditions of base-induced decomposition that were employed, 1-carbethoxybicyclo[4.2.1]nonan-9-one (**9**) as the major product. The structure of **9** was established by hydrolyzing the compound to the corresponding acid **10a**, converting **10a** to the bromo compound **10b** *via* a Hunsdiecker reaction,[5] removing the bromine by reduction



with lithium in *tert*-butyl alcohol,[6] and oxidizing the hydroxyl group at C-9 back to a carbonyl function with 50% nitric acid to yield bicyclo[4.2.1]nonan-9-one identical with a sample prepared directly from *N*-nitroso-*N*-acetyl-3-(2′-ketocyclohexyl)propylamine.[2]

Base-induced decomposition of the compounds carrying four-carbon side chains (**5e** and **5f**) yields mixtures. In the case of **5e** the minor product (three parts) is the previously reported[7] 1-carbethoxybicyclo[3.3.1]nonan-9-one (**11**), and the major product (seven parts) is 1-carbethoxybicyclo[4.3.0]nonan-5-one (**12**), tentatively assigned the cis



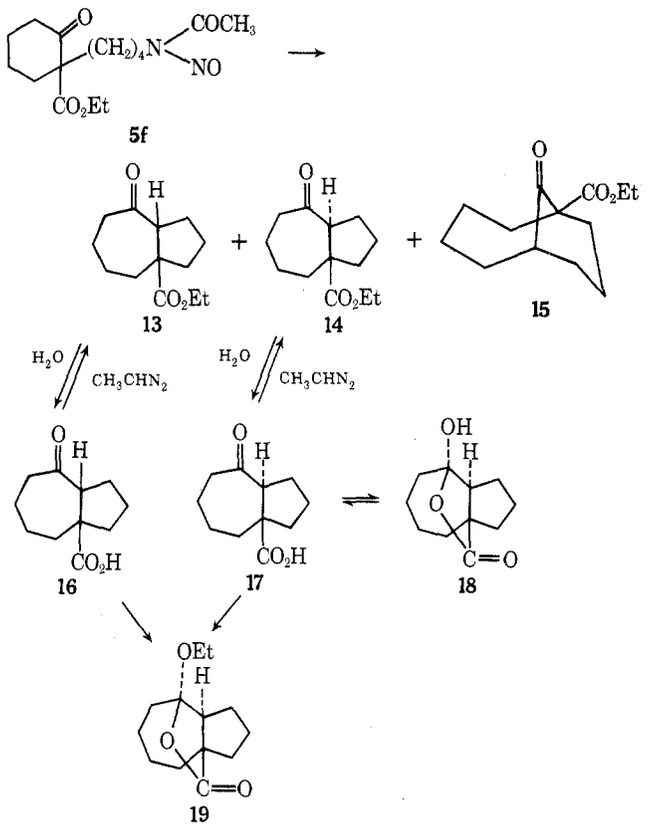
5e 11 12

configuration. The structure of **12** was inferred from its $C_{12}H_{18}O_3$ molecular formula, the presence of infrared stretching bands at 1735 and 1720 cm^{-1} for ester and cyclohexanone carbonyl functions, the one-hydrogen broad triplet in the nmr near δ 3.0 for a bridgehead hydrogen proximate to a keto group, and the susceptibility of the compound to oxidative cleavage by nitric acid[4] (in contrast to compound **11**, which is quite resistant to nitric acid oxidation). The stereochemistry of **12** was inferred from the effect of shift reagent on the nmr spectrum, described in more detail in the discussion of the products from **5e**.

There are two alternative pathways of decomposition to carbonyl products of the intermediate zwitterions produced in diazoalkane–carbonyl reactions. For the types of reactions dealt with in this paper, these pathways lead to bridged-ring and fused-ring ketones, and the factors governing these pathways have been previously discussed.[3] Accepting the premise that these two pathways are the most probable ones, the structure possibilities for the ring-expanded products in such instances are thereby clearly delimited. Thus, this premise complements the analytical and spectral data in establishing the structures of the compounds herein described.

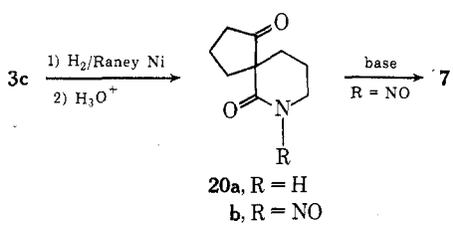
Employing the aforementioned premise, the products of base-induced decomposition of **5f** are thought to be nine parts of the fused ring compound *cis*-1-carbethoxybicyclo-[5.3.0]decan-6-one (**13**), one part of its corresponding trans isomer (**14**), and one part of the bridged ring ketone 1-carbethoxybicyclo[4.3.1]decan-1-one (**15**). The structure of **13** is based on its $C_{13}H_{20}O_3$ molecular formula, the presence of infrared stretching bands at 1725 and 1705 cm^{-1} for ester and cycloheptanone carbonyl functions, and the presence of a one-hydrogen triplet in the nmr at δ 3.83 for a bridgehead hydrogen proximate to the keto function; the characteristics of **14** are very similar to those of **13**. The structure of **15** is based on a direct comparison with an authentic sample prepared by a different route.

The stereochemistry of compounds **13** and **14** was inferred from the nmr shift data. The fused-ring compounds **12** and **13** obtained from **5e** and **5f**, respectively, both showed a downfield shift of 16 ± 1 ppm in the resonances arising from the bridgehead hydrogen adjacent to the keto group when the nmr spectrum was measured in the presence of 1.15 equiv of 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione [Eu(fod)$_3$]. The minor product (**14**) obtained from **5f**, on the other hand, showed a shift of only 13.5 ppm under the same conditions, suggesting a cis configuration for **12** and **13** and a trans configuration for **14**. Base-induced hydrolysis of the crude reaction mixture yielded a mixture of carboxylic acids from which the cis and trans isomers (**16** and **17**) corresponding to the fused ring keto esters **13** and **14** were obtained in pure form, the trans isomer existing primarily in the lactol form (**18**). Treatment of the acids with diazoethane afforded the original keto esters **13** and **14**; treatment of the acids with boron trifluoride and ethanol yielded a pseudo-ester **19** which is assumed to correspond to the trans isomer.



The products that are obtained in the 2-carbethoxycycloalkanone series just described parallel very closely those that are obtained in the cycloalkanone series lacking the carbethoxy group;[2,3] *viz.* the two-carbon side chain compounds yield side-chain decomposition products, the three-carbon side chain compounds yield bridged ring ketones, and the four-carbon side chain cyclopentanone compound yields a mixture of bridged-ring and fused-ring ketone (the four-carbon cyclohexanone compound was not included in the earlier study). Clearly, the carbethoxy group has little effect on the course of the reaction.

Reactions of Cycloalkanones Carrying Cyclic Side Chains Containing Potential Diazoalkyl Moieties. When the ketal **3c** is hydrogenated in a nonacetylating medium and the ketal group then removed by hydrolysis the lactam **20a** is produced. Nitrosation of **20a** to **20b** followed by base-induced decomposition of **20b** at 40–45° affords 1,4-dicarbethoxycycloheptane (**7**), in similarity with the decomposition of **5c**.

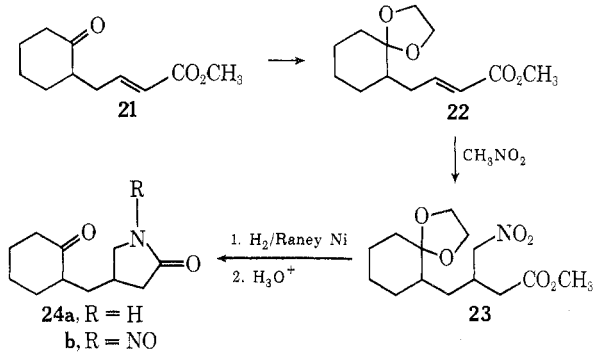


20a, R = H
b, R = NO

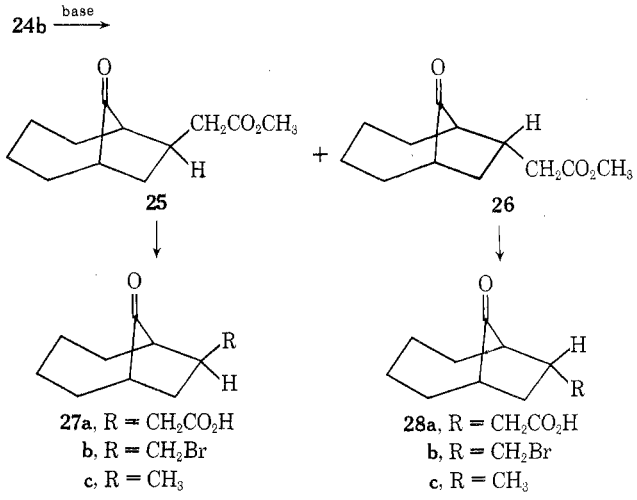
The intramolecular analog of the previously investigated *N*-nitrosolactam–cycloalkanone reaction[1] was

sought in the base-induced decomposition of compound **24,** prepared as outlined in Scheme II. Starting with the α,β-unsaturated ester **21,**[8] the keto group was protected *via* ketalization and a Michael addition of nitromethane was carried out to afford **23** in 57% overall yield from **21.** Reduction of the nitro group followed by lactam formation yielded 88% of **24a,** which was then nitrosated to **24b.**

Scheme II
Preparation of
***N*-Nitroso-4-(2′-ketocyclohexylmethyl)pyrrolidone-2 (24b)**



Base-induced decomposition of **24b** produces 82% of a mixture containing three parts of *exo*-7-carbomethoxymethylbicyclo[4.2.1]nonan-9-one (**25**) and two parts of *endo*-7-carbomethoxymethylbicyclo[4.2.1]nonan-9-one (**26**). The structures of the purified samples were established by the elemental analyses, the resistance to nitric acid oxidation,[4] the ir and nmr spectral characteristics, and conversion to the previously prepared[9] *exo*- and *endo*-7-methylbicyclo[4.2.1]nonan-9-ones (**27c** and **28c**). The stereochemistry of **27c** and **28c,** previously inferred from indirect evidence,[9] was put on firmer ground by observations of the downfield shift of certain nmr resonances of these compounds in the presence of $Eu(fod)_3$. Thus, the compound designated as the exo isomer shows a smaller downfield shift in the resonance of the hydrogen at the 7 position and a greater downfield shift in the resonance of the methyl group attached to the 7 position than the compound designated as the endo isomer (Figure 1). On the well-founded assumption that the lanthanide reagent associates with the ketone function[10] and that the magnitudes of the paramagnetic shifts that are induced by the lanthanide reagent are inversely related to the distance between the hydrogen atom and the lanthanide atom,[11] these observations are in accord with the stereochemical designations that have been given to **27c** and **28c** and, by chemical correlation, to **25** and **26.**



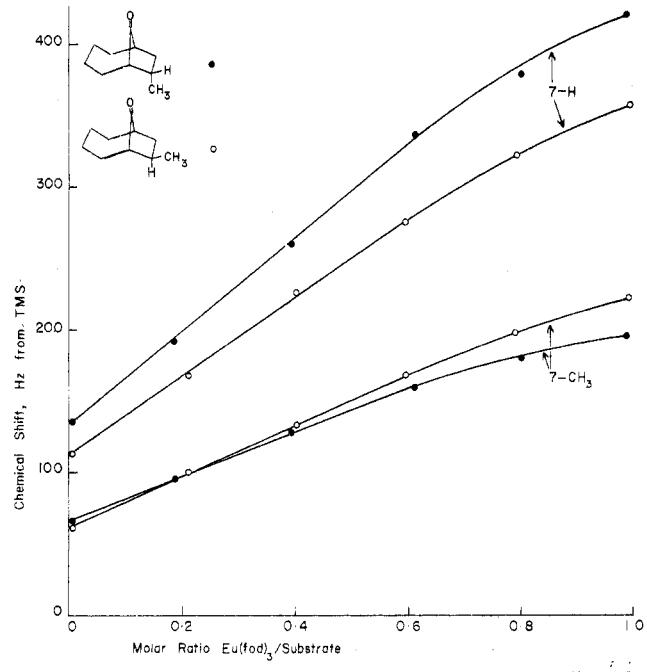


Figure 1. Nmr resonances of *endo*- and *exo*-7-methylbicyclo[4.2.1]nonan-9-one in the presence of tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium(III) [$Eu(fod)_3$].

The exo and endo stereochemistry of **25** and **26** is introduced primarily, if not exclusively, at the point in the synthesis sequence where diastereoisomers first appear, *i.e.,* in the conversion of **22** to **23.** This was demonstrated by preparing one of the diastereoisomers of **24a** in relatively pure form, subjecting it to base-induced decomposition, and obtaining a product which contained the exo and endo isomers in a ratio of 13:1.

Experimental Section[12]

Preparation and Decomposition of *N*-Nitroso-*N*-acetyl-2-(1′-carbethoxy-2′-ketocyclopentyl)ethylamine (5a). Alkylation of 2-carbethoxycyclopentanone with chloroacetonitrile and sodium in refluxing toluene yielded 78% of 2-cyanomethyl-2-carbethoxycyclopentanone (**2a**), obtained as a colorless liquid: bp 104–108° (0.08 mm); ir (liquid) 2272 (CN), 1755 (cyclopentanone C=O), 1738 cm^{-1} (ester C=O); nmr (CCl_4) δ 1.27 (t, 3, J = 7.0 Hz, OCH_2CH_3), 1.94–2.60 (m, 6, CH_2), 2.57 (d, 1, J = 16.4 Hz, CH_2CN), 2.90 (d, 1, J = 16.4 Hz, CH_2CN), 4.19 ppm (q, 2, J = 7.0 Hz, OCH_2CH_3).

Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17. Found: C, 61.32; H, 7.05; N, 6.95.

The 2,4-dinitrophenylhydrazone of **2a** was obtained after two recrystallizations from aqueous ethanol, as orange crystals, mp 95–96°.

Anal. Calcd for $C_{16}H_{17}N_5O_6$: C, 51.20; H, 4.57; N, 18.66. Found: C, 51.09; H, 4.59; N, 18.50.

The semicarbazone of **2a** was obtained, after two recrystallizations from aqueous ethanol, as fine, colorless needles, mp 150.5–151.5°.

Anal. Calcd for $C_{11}H_{16}N_4O_3$: C, 52.37; H, 6.39; N, 22,21. Found: C, 52.69; H, 6.55; N, 22.45.

The ethylene ketal **3a** was prepared as described below for **3c** and was obtained in 87% yield as a colorless oil: bp 120–125° (0.07 mm); ir (liquid) 2250 (CN), 1742 cm^{-1} (ester C=O); nmr (CCl_4) δ 1.30 (t, 3, J = 6.9 Hz, OCH_2CH_3), 1.54–1.95 (m, 6, CH_2), 2.41 (d, 1, J = 16.4 Hz, CH_2CN), 2.81 (d, 1, J = 16.4 Hz, CH_2CN), 3.80–3.94 (m, 4, OCH_2CH_2O), 4.16 ppm (q, 2, J = 6.9 Hz, OCH_2CH_3).

Anal. Calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; H, 5.85. Found: C, 60.40; H, 6.91; N, 6.07.

Reductive acetylation of a 24.6-g sample of **3a,** as described below for **3c,** yielded 21.6 g (90%) of ***N*-acetyl-2-(1′-carbethoxy-2′-ketocyclopentyl)ethylamine (4a)** as a pale yellow, very viscous liquid that could not be distilled without decomposition. Nitrosation yielded an orange oil, which was dissolved in 150 ml of

methylene chloride. Treatment of 50-ml portions of this solution with sodium methoxide in ethanol at 40–45°, with potassium carbonate in ethanol at 25–27°, or with potassium carbonate in ethanol at −10 to −5° yielded, in all instances, mixtures containing at least seven components; no attempt was made to characterize these materials.

Preparation and Decomposition of *N*-Nitroso-*N*-acetyl-2-(1′-carbethoxy-2′-ketocyclohexyl)ethylamine (5b). Alkylation of 2-carbethoxycyclohexanone with chloroacetonitrile and sodium in refluxing toluene yielded 53% of **2-cyanomethyl-2-carbethoxycyclohexanone (2b)** as a colorless liquid: bp 98–103° (0.08 mm); ir (liquid) 2275 (CN), 1742 (ester C=O), 1720 cm^{-1} (cyclohexanone C=O); nmr (CCl_4) δ 1.31 (t, 3, J = 7.0 Hz, OCH_2CH_3), 1.55–2.60 (m, 8, CH_2), 2.70 (s, 2, CH_2CN), 4.25 ppm (q, 2, J = 7.0 Hz, OCH_2CH_3).

Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.12; H, 7.14; N, 6.60.

The 2,4-dinitrophenylhydrazone of **2b** was obtained, after two recrystallizations from aqueous ethanol, as orange crystals, mp 124–125°.

Anal. Calcd for $C_{17}H_{19}N_5O_6$: C, 52.44; H, 4.92; N, 17.99. Found: C, 52.18; H, 4.97; N, 18.12.

The ethylene ketal **3b** was prepared by the procedure described below for **3c** and was obtained in 75% yield as a colorless liquid: bp 119–122° (0.05 mm); ir (liquid) 2275 (CN), 1725 cm^{-1} (ester C=O); nmr (CCl_4) δ 1.32 (t, 3, J = 7.1 Hz, OCH_2CH_3), 1.47–2.20 (m, 8, CH_2), 2.46 (d, 1, J = 16.1 Hz, CH_2CN), 2.91 (d, 1, J = 16.1 Hz, CH_2CN), 3.92 (s, 4, OCH_2CH_2O), 4.20 ppm (q, 2, J = 7.1 Hz, OCH_2CH_3).

Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.69; H, 7.56; N, 5.53. Found: C, 61.70; H, 7.91; N, 5.51.

Reductive acetylation of a 26.6-g sample of **3b**, as described below for **3c**, followed by selective hydrolysis yielded 23.0 g (90%) of ***N*-acetyl-2-(1′-carbethoxy-2′-ketocyclohexyl)ethylamine (4b)** as a pale yellow, viscous liquid that could not be distilled without decomposition. Nitrosation yielded an orange oil which was dissolved in 150 ml of methylene chloride. Treatment of 50-ml portions in the manner described above yielded mixtures containing six or more components; no attempt was made to characterize these materials.

Preparation and Decomposition of *N*-Nitroso-*N*-acetyl-3-(1′-carbethoxy-2′-ketocyclopentyl)propylamine (5c). A 64.4-g sample of 2-β-cyanoethyl-2-carbethoxycyclopentanone[13] was refluxed for 30 hr in a solution of benzene containing 20.5 g of ethylene glycol and 0.2 g of *p*-toluenesulfonic acid, the water formed during the reaction being withdrawn in a Dean–Stark trap. A 28-g sample of the crude ketal **3c**, obtained in 84% yield, bp 125–130° (0.07 mm), was reductively acetylated at 100° and 1.8 atm with 100 ml of acetic anhydride,[14] 5–8 g of Raney nickel W-2,[15] and 8 g of anhydrous sodium acetate contained in a thick-walled glass bottle. The cooled mixture was then treated with 100 ml of 4% sulfuric acid and 35 ml of acetic acid and allowed to stand at room temperature of 12 hr. Distillation of the crude product yielded 20.8 g (74%) of **4c** as a colorless, viscous liquid: bp 182–184° (0.08 mm); ir (liquid) 3355, 3125 (amide NH), 1742 (cyclopentanone C=O), 1718 (ester C=O), 1647 (NHCO), 1538 cm^{-1} (NHCO); nmr (CCl_4) δ 1.25 (t, 3, J = 7.0 Hz, OCH_2CH_3), 1.45–2.65 (m, 10, CH_2), 1.92 (s, 3, $NCOCH_3$), 2.92–3.24 (m, 2, NCH_2), 4.14 (q, 2, J = 7.0 Hz, OCH_2CH_3), 7.65 ppm (t, 1, NH). Treatment of a 20.8-g sample of **4c** with 26.3 g of anhydrous sodium acetate and 31 ml of a 5.2 M solution of dinitrogen tetroxide in methylene chloride yielded the *N*-nitrosoamide **5c** as an orange oil which was dissolved in 150 ml of methylene chloride. A 50-ml portion of this solution was treated at 40–45° with a solution of 1 g of sodium in 100 ml of anhydrous ethanol. The resulting product was distilled to yield 1.8 g of **4c** and 1.7 g of 1,4-dicarbethoxycycloheptane (**7**) as a colorless liquid: ir (liquid) 1742 cm^{-1} (ester C=O); nmr (CCl_4) δ 1.22 (t, 6, J = 7.2 Hz, OCH_2CH_3), 1.45–2.65 (m, 12, CH_2), 4.07 ppm (q, 4, J = 7.2 Hz, OCH_2CH_3).

Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.77; H, 9.08.

A second 50-ml portion of the solution of **5c** was treated at 25–27° with 1 g of potassium carbonate in 100 ml of absolute ethanol and yielded 1.7 g of **4c** and 1.7 g of **1-carbethoxybicyclo[3.2.1]octan-8-one (6)** as a colorless liquid: ir (liquid) 1760 (cyclopentanone C=O), 1730 cm^{-1} (ester C=O); nmr (CCl_4) δ 1.26 (t, 3, J = 7.1 Hz, OCH_2CH_3), 1.50–2.65 (m, 11, CH_2), 4.14 ppm (q, 2, J = 7.1 Hz, OCH_2CH_3).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.18; H, 8.20.

The 2,4-dinitrophenylhydrazone of **6** was obtained, after two recrystallizations from 95% ethanol, as long, yellow needles, mp 187–188°.

Anal. Calcd for $C_{17}H_{20}N_4O_6$: C, 54.25; H, 5.36; N, 14.89. Found: C, 53.92; H, 5.48; N, 15.02.

The semicarbazone of **6** was obtained, after two recrystallizations from 30% ethanol, as clusters of colorless needles, mp 179.8–180°.

Anal. Calcd for $C_{12}H_{19}N_3O_3$: C, 56.93; H, 7.50; N, 16.59. Found: C, 56.76; H, 7.43; N, 16.46.

Treatment of **6** with boiling nitric acid left it unchanged, in accordance with the bridged ring structure.[4]

A third 50-ml portion of the solution of **5c** was treated at −10 to −5° with 1 g of potassium carbonate in 100 ml of anhydrous ethanol and yielded 2.0 g of **4c** and 1.9 g of a colorless liquid, bp 110–124° (0.5 mm), which was shown by glc on column 3[12] to consist of 92% of equal quantities of **6** and 3-(1′-carbethoxy-2′-ketocyclopentyl)propene-1 (**8**), obtained as a colorless liquid: ir (liquid) 3120 (=CH), 1752 (cyclopentanone C=O), 1726 (ester C=O), and 1639 cm^{-1} (C=C); nmr (CCl_4) δ 1.26 (t, 3, J = 7.1 Hz, OCH_2CH_3), 1.55–2.83 (m, 8, CH_2), 4.14 (q, 2, J = 7.1 Hz, OCH_2CH_3), 4.83–6.08 ppm (m, 3, =CH).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.10; H, 8.40.

Preparation and Decomposition of *N*-Nitroso-*N*-acetyl-3-(1′-carbethoxy-2′-ketocyclohexyl)propylamine (5d). Following the procedure described above, a 100-g sample of 2-β-cyanoethyl-2-carbethoxycyclohexanone[16] was converted to the ketal **3d** in 86% yield, bp 134–138° (0.06 mm), and a 30.7-g sample of the ketal was reductively acetylated to yield 25 g (81%) of *N*-acetyl-3-(1′-carbethoxy-2′-ketocyclohexyl)propylamine (**4d**) as a colorless, viscous liquid: ir (liquid) 3355, 3145 (CONH), 1742 (shoulder, ester C=O), 1712 (cyclohexanone C=O), 1661 (CONH), 1542 cm^{-1} (CONH); nmr (CCl_4) δ 1.27 (t, 3, J = 7.0 Hz, OCH_2CH_3), 1.45–2.60 (m, 12, CH_2), 1.88 (s, 3, $COCH_3$), 2.90–3.27 (m, 2, NCH_2), 4.15 (q, 2, J = 7.0 Hz, OCH_2CH_3), 7.41 ppm (t, 1, NH).

Anal. Calcd for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.53; H, 8.38; N, 5.48.

A 34-g sample of **4d** was converted to the *N*-nitroso compound **5d** by treatment with 54 g of anhydrous sodium acetate and 25 ml of an 8.3 M solution of dinitrogen tetroxide in methylene chloride. The resulting orange solution was added to a solution of 1 g of sodium in 100 ml of anhydrous ethanol at 40–45° to yield, after distillation of the crude product, 18.3 g (69%) of a colorless oil which was shown by glc on column 3[12] to contain more than 97% of 1-carbethoxybicyclo[4.2.1]nonan-9-one (**9**): ir (liquid) 1751 (cyclopentanone C=O), 1728 cm^{-1} (ester C=O); nmr (CCl_4) δ 1.25 (t, 3, J = 7.1 Hz, OCH_2CH_3), 1.45–2.78 (m, 13, CH_2), 4.13 ppm (q, 2, J = 7.1 Hz, OCH_2CH_3).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.25; H, 8.78.

The 2,4-dinitrophenylhydrazone of **9** was obtained, after several recrystallizations from aqueous ethanol, as orange needles, mp 181.5–182.5°.

Anal. Calcd for $C_{18}H_{22}N_4O_6$: C, 55.38; H, 5.68; N, 14.35. Found: C, 55.03; H, 5.50; N, 14.54.

The semicarbazone of **9** was obtained, after three recrystallizations from 30% ethanol, as white, feathery crystals, mp 175–176°.

Anal. Calcd for $C_{13}H_{21}N_3O_3$: C, 58.41; H, 7.92; N, 15.72. Found: C, 58.33; H, 7.90; N, 15.75.

Decomposition of the nitroso compound at 25–27° with 1 g of potassium carbonate in 100 ml of absolute ethanol also yielded **9** as the major reaction product.

Conversion of 1-Carbethoxybicyclo[4.2.1]nonan-9-one (9) to Bicyclo[4.2.1]nonan-9-one (10c). A 10-g sample of **9** was treated with 60 ml of 5% sodium hydroxide, allowed to stand for 6 hr at room temperature, and worked up to yield 6.5 g of 1-carboxybicyclo[4.2.1]nonan-9-one (**10a**) as colorless, feathery crystals after recrystallization from ether: mp 107–108° (reported[17] mp 105.5°); ir (KBr) 3500–2600 (OH), 1748 (cyclopentanone C=O), 1708 cm^{-1} (carboxyl C=O); nmr ($CDCl_3$) δ 1.30–2.90 (m, 13, CH_2), 10.70 ppm (s, 1, CO_2H).

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.90; H, 7.76. Found: C, 65.77; H, 7.89.

A 4.4-g sample of **10a** was taken up in methanol and treated with an equivalent amount of potassium hydroxide and then with silver nitrate dissolved in aqueous methanol to yield the silver salt of **10a**. This was thoroughly dried, slurried with 100 ml of anhydrous carbon tetrachloride, and treated at room temperature with 5.7 g of bromine in 25 ml of anhydrous carbon tetrachloride

to yield, after work-up, 3.0 g (57%) of **1-bromobicyclo[4.2.1]nonan-9-one (10b)** as a slightly yellow liquid with a faint camphoraceous odor: bp 90–92° (0.1 mm); ir (liquid) 1755 cm^{-1} (cyclopentanone C=O). The 2,4-dinitrophenylhydrazone of **10b** was obtained, after one recrystallization from ethanol–ethyl acetate (1:1), as fine, orange crystals, mp 200–200.5°.

Anal. Calcd for $C_{15}H_{17}N_4O_4Br$: C, 45.35; H, 4.32; Br, 20.11. Found: C, 45.28; H, 4.32; Br, 20.07.

Following a published procedure[6] a 200-mg sample of **10b** was heated at 75–80° for 6 hr with 20 mg of lithium dissolved in 5 ml of anhydrous tetrahydrofuran and 0.3 ml of *tert*-butyl alcohol. The crude product, consisting of 90 mg of a colorless liquid, was separated by preparative glc on column 3[12] into two components. The more volatile, more abundant of these was bicyclo[4.2.1]nonan-9-one (**10c**), obtained as a colorless oil possessing a strong camphoraceous odor and which on standing slowly crystallized: mp 104–106° (lit.[18] mp 109–111°); glc retention time and ir spectrum identical with those of an authentic sample.[18]

Preparation and Decomposition of *N*-Nitroso-*N*-acetyl-4-(1′-carbethoxy-2′-ketocyclopentyl)butylamine (5e). Using a literature procedure as a model[19] a 78-g sample of 2-carbethoxycyclopentanone was converted to the sodium enolate and treated with 75 g of 4-bromobutenonitrile. The crude product was distilled through a 35-cm Vigreux column to yield 64 g (58%) of 4-(1-carbethoxy-2-ketocyclopentyl)butenonitrile (**2e**), obtained as a pale yellow liquid: bp 130–135° (0.15 mm); ir (liquid) 2240 (CN), 1753 (cyclopentanone C=O), 1728 (ester C=O), 1636 cm^{-1} (C=C); nmr (CCl_4) δ 1.26 (t, 3, J = 7.1 Hz, OCH_2CH_3), 1.70–2.96 (m, 8, CH_2), 4.15 (q, 2, J = 7.1 Hz, OCH_2CH_3), 5.43 (d, 1, J = 16.2 Hz, =CHCN), 6.51 and 6.67 ppm (doublet of triplets, 1, J = 7.1 and 16.2 Hz, =CH). The 2,4-dinitrophenylhydrazone of **2e** was obtained, after five recrystallizations from aqueous ethanol, as fine, yellow needles, mp 92–93°.

Anal. Calcd for $C_{18}H_{19}N_5O_6$: C, 53.86; H, 4.77; N, 17.45. Found: C, 53.60; H, 4.76; H, 17.11.

The semicarbazone of **2e** was obtained, after three recrystallizations from aqueous ethanol, as fine, colorless needles, mp 155.5–157.5°.

Anal. Calcd for $C_{13}H_{18}N_4O_3$: C, 56.10; H, 6.52; N, 20.13. Found: C, 55.99; H, 6.57; N, 19.92.

The ketal **3e**, obtained in 80% yield by the procedure described above, was reductively acetylated and selectively hydrolyzed to afford a 77% yield of *N*-acetyl-4-(1′-carbethoxy-2′-ketocyclopentyl)butylamine (**4e**) as a colorless, very viscous liquid: bp 185–187° (0.05 mm); ir (liquid) 3380, 3135 (CONH), 1750 (cyclopentanone C=O), 1722 (ester C=O), 1650 (CONH), 1540 cm^{-1} (CONH); nmr (CCl_4) δ 1.24 (t, 3, J = 7.2 Hz, OCH_2CH_3), 1.50–2.60 (m, 12, CH_2), 1.88 (s, 3, $COCH_3$), 2.92–3.24 (m, 2, NCH_2), 4.13 (q, 2, J = 7.2 Hz, OCH_2CH_3), 7.45 ppm (t, 1, NH).

Anal. Calcd for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.31; H, 8.37; N, 5.22.

A 24.3-g sample of **4e** was converted to the *N*-nitroso compound as described above and dissolved in 150 ml of methylene chloride. Treatment of a 50-ml portion with a solution of 1 g of sodium in 100 ml of absolute ethanol at 40–45° yielded 1.0 g of **4e** and 3.8 g of a colorless liquid, bp 94–102° (0.1 mm), containing two components in the ratio of 7:3 which were separated by glc on column 3.[12] The more volatile, more abundant component was destroyed by the action of hot 50% nitric acid,[4] in accord with the structure **1-carbethoxybicyclo[4.3.0]nonan-5-one (12)**: ir (liquid) 1735 (ester C=O), 1720 cm^{-1} (cyclohexanone C=O); nmr (CCl_4) δ 1.26 (t, 3, J = 7.2 Hz, OCH_2CH_3), 1.42–2.44 (m, 12, CH_2), 2.86–F.15 (t, 1, bridgehead H), 4.15 ppm (q, 2, J = 7.2 Hz, OCH_2CH_3).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.29; H, 8.55.

The less volatile, less abundant component was unchanged by the action of hot 50% nitric acid[4] in accord with the structure **1-carbethoxybicyclo[3.3.1]nonan-9-one (11)**: mp 37–39° (lit.[7] mp 26–32°, 38–39.5°, 43.5–45°); ir (liquid) 1735 (ester C=O), 1720 cm^{-1} (shoulder, cyclohexanone C=O); nmr (CCl_4) δ 1.26 (t, 3, J = 7.2 Hz, OCH_2CH_3), 1.44–2.80 (m, 13, CH_2), 4.15 (q, 2, J = 7.2 Hz, OCH_2CH_3).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.35; H, 8.81.

The 2,4-dinitrophenylhydrazone of **11** was obtained as orange crystals, mp 174–176° (lit.[7] mp 174–177°).

Hydrolysis of the crude reaction mixture yielded **1-carboxybicyclo[4.3.0]nonan-5-one** as a solid after crystallization from ether–hexane: mp 116–117°; ir (KBr) 3500–2600 (OH), 1730 (cyclohexanone C=O), and 1695 cm^{-1} (carboxyl C=O); nmr ($CDCl_3$) δ 1.54–2.54 (m, 12, CH_2), 2.92–3.25 (t, 1, bridgehead CH), and 10.35 ppm (CO_2H).

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.74; H, 7.75.

Treatment of the crude product with hot 50% nitric acid followed by base-induced hydrolysis yielded 1-carboxybicyclo[3.3.1]nonan-9-one, obtained after two recrystallizations from water as colorless prisms, mp 138–139° (lit.[7] mp 138.5–139.5°).

Decomposition of the nitroso compound **5e** with potassium carbonate in absolute ethanol at 25–27° and at −10 to −5° yielded results identical with those described above.

Preparation and Decomposition of *N*-Nitroso-*N*-acetyl-4-(1′-carbethoxy-2′-cyclohexyl)butylamine (5f). Following the procedure described above, a 25.5-g sample of 2-carbethoxycyclohexanone was alkylated with 23 g of 4-bromobutenonitrile to yield 67% of **4-(1-carbethoxy-2-ketocyclohexyl)butenonitrile (2f)** as a pale yellow liquid: bp 132–136° (0.12 mm); ir (liquid) 2240 (CN), 1740 (shoulder, ester C=O), 1720 (cyclohexanone C=O), 1634 cm^{-1} (C=C); nmr (CCl_4) δ 1.31 (t, 3, J = 7.1 Hz, OCH_2CH_3), 1.50–2.85 (m, 10, CH_2), 4.22 (q, 2, J = 7.1 Hz, OCH_2CH_3), 5.20–5.56 (m, 1, =CHCN), 6.29–6.93 ppm (m, 1, =CH).

Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.29; H, 7.36; N, 5.87.

The 2,4-dinitrophenylhydrazone of **2** was obtained, after five recrystallizations from ethyl acetate, as fine, yellow needles, mp 165–166°.

Anal. Calcd for $C_{19}H_{21}N_5O_6$: C, 54.94; H, 5.10; N, 16.86. Found: C, 54.95; H, 5.21; N, 16.90.

Following the procedure described above **2f** was converted to 79% yield to the ketal **3f**, obtained as a colorless oil: bp 136–140° (0.1 mm); ir (liquid) 2240 (CN), 1730 (ester C=O), 1632 cm^{-1} (C=C); nmr (CCl_4) δ 1.28 (t, 3, J = 7.1 Hz, OCH_2CH_3), 1.45–2.95 (m, 10, CH_2), 3.84–3.95 (m, 4, OCH_2CH_2O), 4.16 (q, 2, J = 7.1 Hz, OCH_2CH_3), 5.15–5.52 (m, 1, =CHCN), 6.32–6.78 ppm (m, 1, =CH).

Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.45; H, 7.73; N, 5.06.

Reductive acetylation of **3f** followed by selective hydrolysis as described above afforded *N*-acetyl-4-(1′-carbethoxy-2′-ketocyclohexyl)butylamine (**4f**) in 78% yield as a colorless, viscous liquid: bp 185–190° (0.07 mm); ir (liquid) 3390, 3165 (CONH), 1725 (shoulder, ester C=O), 1712 (cyclohexanone C=O), 1662 (CONH), 1550 cm^{-1} (CONH); nmr (CCl_4) δ 1.27 (t, 3, J = 7.0 Hz, OCH_2CH_3), 1.30–2.67 (m, 14, CH_2), 1.88 (s, 3, $COCH_3$), 2.93–3.36 (m, 2, CH_2N), 4.17 (q, 2, J = 7.0 Hz, OCH_2CH_3), 7.53 ppm (t, 1, NH).

Anal. Calcd for $C_{15}H_{25}NO_4$: C, 63.58; H, 8.89; N, 4.94. Found: C, 63.29; H, 8.89; N, 5.05.

A 17-g sample of **4f** was converted to the *N*-nitroso compound as described above and dissolved in 100 ml of methylene chloride. One-half of this solution (*i.e.*, 50 ml) was treated at 40–45° with a solution of 1 g of sodium in 100 ml of anhydrous ethanol to yield 4.8 g (70%) of a colorless liquid, bp 100–116° (0.2 mm). Analysis by glc on column 6[12] showed three major components, present in the ratio of 9:1:1. Preparative-scale glc on column 5[12] yielded a pure sample of the most abundant component, *cis*-**1-carbethoxybicyclo[5.3.0]decan-6-one (13)**, as a colorless liquid: ir (liquid) 1725 (ester C=O) and 1705 cm^{-1} (cycloheptanone C=O); nmr (CCl_4) δ 1.32 (t, 3, J = 7.2 Hz, OCH_2CH_3), 1.46–2.60 (m, 14, CH_2), 3.83 (t, 1, J = 7.3 Hz, bridgehead CH), and 4.22 ppm (q, 2, J = 7.2 Hz, OCH_2CH_3).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.89; H, 9.03.

The 2,4-dinitrophenylhydrazone of **13** was obtained, after four recrystallizations from 95% ethanol, as very fine, orange flakes, mp 132.5–133.5°.

Anal. Calcd for $C_{19}H_{24}N_4O_6$: C, 56.42; H, 5.99; N, 13.86. Found: C, 56.43; H, 5.93; N, 13.84

The two minor components (**14** and **15**) were obtained as a mixture by preparative glc on column 5.[12] A pure sample of *trans*-**1-carbethoxybicyclo[5.3.0]decan-6-one (14)**, however, was obtained by acid-catalyzed isomerization of **13** followed by separation from unchanged **13** by glc on column 5:[12] ir (liquid) 1725 (ester C=O) and 1700 cm^{-1} (cycloheptanone C=O); nmr (CCl_4) 1.25 (t, 3, J = 7.1 Hz, OCH_2CH_3), 1.40–2.80 (m, 15, CH_2), and 4.12 ppm (q, 2, J = 7.1 Hz, OCH_2CH_3).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.34; H, 8.91.

A pure sample of **1-carbethoxybicyclo[4.3.1]decan-10-one (15)** was obtained by treating 148 mg of a sample containing **14** and **15**

with 2 ml of 10% boron trifluoride in anhydrous ethanol at reflux temperature for 5 min (to convert **14** to **13**) followed by glc on column 5.[12] The product was a colorless liquid which possessed an ir spectrum identical with that of an authentic sample.[20]

The Pseudo Ethyl Ester of 1-Carboxybicyclo[5.3.0]decan-6-one (19) was obtained as a colorless liquid by heating a mixture of **16** and **17** with 10% boron trifluoride in anhydrous ethanol: ir (liquid) 1770 cm^{-1} (γ-lactone); nmr (CCl_4) δ 1.20 (t, 3, J = 7.2 Hz, OCH_2CH_3), 1.20–2.70 (m, 15, CH_2), and 3.73 ppm (q, 2, J = 7.2 Hz, OCH_2CH_3).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.72; H, 9.00.

trans-**1-Carboxybicyclo[5.3.0]decan-10-one (17)** was obtained by heating a 6.1-g sample of the crude product from **5f** for 4 hr on a steam bath with 60 ml of a 5% sodium hydroxide solution. The product consisted of 2.6 g of colorless crystals, mp 93–95°, which was shown by glc of the trimethylsilyl derivative on column 2 to contain the cis and trans isomers in approximately equal amount. Fractional crystallization of the product from hexane–ether yielded pure **17** as colorless crystals: mp 149.5–151°; ir (KBr) 3480 (OH) and 1735 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.40–2.43 (m, 14, CH_2), 2.67 (t, 1, J = 4.8 Hz, bridgehead CH), 5.85 ppm (s, 1, OH). The spectral data indicate that the compound exists primarily in the tricyclic lactol form **18**.

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.30; H, 8.10.

From the mother liquors from the crystallization of the trans compound, *cis*-**1-carboxybicyclo[5.3.0]decan-10-one (16)** was obtained as clusters of thick, white needles: mp 132.2–132.4°; ir (KBr) 3300–2500 (CO_2H), 1728 (cycloheptanone C=O), and 1690 cm^{-1} (carboxyl C=O); nmr ($CDCl_3$) δ 1.17–2.70 (m, 14, CH_2), 3.83 (t, 1, J = 7.5 Hz, bridgehead CH), and 9.84 ppm (s, 1, CO_2H).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.15; H, 8.12.

Treatment of **16** with ethereal diazoethane produced the ester **13**; treatment of **17** with ethereal diazoethane produced the ester **14**.

Preparation and Decomposition of *N*-Nitroso-2-azaspiro[5.4]decane-1,7-dione (20b). A 7.6-g sample of the ethylene ketal of 2-β-cyanoethyl-2-carbethoxycyclopentanone (**2c**), synthesized as described above, was mixed with 50 ml of absolute ethanol and 6–10 g of Raney nickel W-2 catalyst[15] and hydrogenated at 80–100° and 50–70 atm for 2 hr. The crude product was treated with 2 *N* hydrochloric acid, allowed to stand at room temperature for 2 hr, and worked up to give a 30% yield of **2-azaspiro[5.4]decane-1,7-dione (20a)** as white crystals after recrystallization from acetone: mp 166–167.5°; ir ($CHCl_3$) 3475 (NH), 1740 (cyclopentanone C=O), 1656 cm^{-1} (δ-lactam C=O); nmr (CCl_4) δ 1.50–2.80 (m, 10, CH_2), 3.10–3.50 (m, 2, NCH_2), 7.04 (s, 1, CONH).

Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.64; H, 7.78; N, 8.58.

A 0.9-g sample of **20a** was converted to the *N*-nitroso compound, dissolved in 75 ml of methylene chloride, and treated at 40–45° with a solution of 1 g of sodium in 100 ml of anhydrous ethanol. The crude product consisted of 0.6 g of a colorless oil which was shown by glc on column 3[12] to contain one major product identified as 1,4-dicarbethoxycycloheptane (**7**) (see above).

Preparation and Decomposition of *N*-Nitroso-4-(2′-ketocyclohexylmethyl)pyrrolidone-2 (24b). A mixture of 110 g (0.56 mol) of methyl γ-(2-ketocyclohexyl)crotonate (**21**),[8] 37 g (0.06 mol) of ethylene glycol, and 150 ml of benzene was refluxed in an apparatus fitted with a Dean–Stark trap. After 7 hr of refluxing, the theoretical amount of water had been collected, and the solution was worked up to yield, after distillation through a 35-cm Vigreux column, 120 g (89%) of the ethylene ketal **22**, obtained as a colorless liquid: bp 108–110° (0.2 mm); ir (liquid) 1730 (ester C=O), 1662 (C=C), 1157, 1136, 1123, 1089 cm^{-1} (dioxolane bands[21]).

Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.75; H, 8.51.

Patterning the procedure after a published method,[22] a 1-l. three-necked flask equipped with a magnetic stirrer, a reflux condenser, and an immersion thermometer was charged with 132 g (0.55 mol) of the ethylene ketal **22**, 134 g (2.2 mol) of nitromethane, 75 g of trimethylbenzylammonium hydroxide solution (40% in methanol), and 60 ml of 1-butanol. The mixture was stirred for 27 hr at 60–65° and then worked up to give, after distillation through a 20-cm Vigreux column, 82 g (57%) of the ethylene ketal of methyl γ-(2-ketocyclohexyl)-β-nitromethylbutyrate (**23**) as a yellow oil: bp 163–168°; ir (liquid) 1742 (ester C=O), 1550 cm^{-1} (NO_2). A 24-g sample of this material was dissolved in 100 ml of absolute ethanol, treated with 5–8 g of Raney nickel W-2 catalyst,[15] and hydrogenated at 80–100° for 2 hr at 50–70 atm pressure. The crude product was treated with 60 ml of 2 *N* hydrochloric acid, and the solution was allowed to stand at room temperature for 2 hr. Work-up gave 14 g (88%) of **4-(2′-ketocyclohexylmethyl)pyrrolidone-2 (24a)** as powdery, white solid, mp 100–105, which was recrystallized from benzene–petroleum ether (bp 65–80°) to yield colorless needles: mp 128–130°; ir (mull) 3270, 3175 (NH), 1705 (shoulder, cyclohexanone C=O), 1695 cmA^{1} (CONH).

Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78. Found: C, 67.66; H, 8.65.

A solution of 78 g (0.4 mol) of a crude sample of **24a** in 500 ml of methylene chloride was added over a period of 10 min to a stirred solution containing 0.65 mol of dinitrogen tetroxide and 180 g (2.2 mol) of anhydrous sodium acetate in 1 l. of methylene chloride cooled to −50°. The mixture was allowed to warm to room temperature, recooled to −5°, and filtered, and the filtrate was washed with ice-cold 10% aqueous sodium bicarbonate followed by ice-cold water, dried, and concentrated under vacuum to yield the *N*-nitroso compound **24b** as an orange-colored oil. A 1-l. three-necked flask equipped with a condenser and two addition funnels was charged with 200 ml of anhydrous methanol. The methanol was heated to reflux, and a solution of nitroso compound **24b** from 78 g (0.4 mol) of **24a** in 100 ml of methylene chloride was added, dropwise, over a period of 15 min. Simultaneously, a 25-ml portion of a 0.4 *M* solution of sodium methoxide in methanol was added from the other addition funnel. After the addition was complete, the mixture was refluxed for an additional 10 min, and it was then worked up to yield, after distillation through a 20-cm Vigreux column, 68 g (81%) of a pale yellow liquid, bp 60–78° (0.1 mm). Analysis by glc on column 1 or 4[12] indicated that 82% of the product comprised two materials, present in the ratio of 3:2, and treatment of the mixture with hot 50% nitric acid showed that neither was readily oxidized; the remaining 18%, on the other hand, was destroyed by this oxidation procedure.[4] Separation by preparative glc on column 4[12] yielded the more volatile and abundant component, *exo*-**7-carbomethoxymethylbicyclo[4.2.1]nonan-9-one (25)** as a colorless liquid: ir (liquid) 1742 cm^{-1} (ester and cyclopentanone C=O); nmr (CCl_4) δ 1.40–2.20 (m, 11, CH_2), 2.33 (d, 4, α protons), 3.63 ppm (s, 3, OCH_3).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.27; H, 8.53.

The 2,4-dinitrophenylhydrazone of **25** was obtained, after four recrystallizations from aqueous ethanol, as fine, orange needles, mp 151–151.5°.

Anal. Calcd for $C_{18}H_{22}N_4O_6$: C, 55.38; H, 5.68; N, 14.34. Found: C, 55.46; H, 5.62; N, 14.37.

The less volatile and less abundant component, *endo*-**7-carbomethoxymethylbicyclo[4.2.1]nonan-9-one (26)**, was also obtained as a colorless liquid: ir (liquid) 1742 cm^{-1} (ester and cyclopentanone C=O); nmr (CCl_4) δ 1.58 (m, 9, CH_2), 2.46 (m, 6, includes four α protons), 3.64 (s, 3, OCH_3).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.25; H, 8.73.

The 2,4-dinitrophenylhydrazone of **26** was obtained, after two recrystallizations from 95% ethanol, as yellow crystals, mp 147.5–148.5°.

Anal. Calcd for $C_{18}H_{22}N_4O_6$: C, 55.38; H, 5.68; N, 14.34. Found: C, 55.49; H, 5.47; N, 14.17.

The melting point of the mixture of the 2,4-dinitrophenylhydrazones from **25** and **26** was 128–130°.

When 4.5 g of a purified sample of **24a**, mp 128–130°, was converted to the *N*-nitroso compound and decomposed in the manner described above, 2.8 g (57%) of a colorless liquid was obtained, bp 60–80° (0.1 mm), which was shown by glc on column 4[12] to contain 76% of the exo isomer **25**, 6% of the endo isomer **26**, and 18% of a mixture of four unidentified compounds. Using the material in the mother liquor from the purification of **24a** as the starting material and carrying through the nitrosation and base-induced decomposition in the same fashion, a product containing 33% of the exo isomer **25**, 43% of the endo isomer **26**, and 24% of a mixture of unidentified compounds was obtained.

endo-**7-Carboxymethylbicyclo[4.2.1]nonan-9-one (28a)** was obtained by heating a 1.6-g sample of a mixture of the exo and endo esters **25** and **26** for 3.5 hr on a steam bath with 25 ml of 5% sodium hydroxide solution. Fractional crystallization of the crude product, mp 65–75°, from ether at *ca.* −70° yielded **28a** as clusters

of fine, white needles: mp 98–99°; ir (KBr) 3500–2600 (OH), 1735 (cyclopentanone C=O), and 1708 cm^{-1} (carboxyl C=O); nmr ($CDCl_3$) δ 1.60 (m, 9, CH_2), 2.58 (m, 6, includes four α protons), and 14.31 ppm (s, 1, CO_2H).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.37; H, 8.11.

From the mother liquors from the crystallization of the endo compound, ***exo*-7-carboxymethylbicyclo[4.2.1]nonan-9-one (27a)** was obtained, after two recrystallizations from hexane, as clusters of white feathers: mp 80.5–81.5°; ir (KBr) 3500–2600 (OH), 1742 (cyclopentanone C=O), and 1715 cm^{-1} (carboxyl C=O); nmr ($CDCl_3$) δ 1.20–2.35 (m, 13, CH_2), 2.46 (s, 2, CH_2CO_2), and 14.30 ppm (s, 1, CO_2H).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.12; H, 8.12.

Treatment of **27a** with ethereal diazomethane produced the methyl ester **25**; treatment of **28a** with ethereal diazomethane produced the methyl ester **26**.

Conversion of *exo*-7-Carboxymethylbicyclo[4.2.1]nonan-9-one (27a) to *exo*-7-Methylbicyclo[4.2.1]nonan-9-one (27c). A 0.14-g sample of **27a** was dissolved in 10 ml of methanol and treated with 1 equiv of methanolic potassium hydroxide followed by an equivalent amount of silver nitrate dissolved in aqueous methanol. The silver salt of **27a** was separated, thoroughly dried, and then slurried with 10 ml of anhydrous carbon tetrachloride. The slurry was treated with a solution of 0.17 g of bromine in 10 ml of carbon tetrachloride, and the mixture was heated on the steam bath for 45 min. Work-up of the reaction mixture yielded **27b** as a yellow liquid with a pungent odor; ir (liquid) 1742 cm^{-1} (cyclopentanone C=O). Following a literature procedure,[5] this material was heated at reflux for 30 min with 25 mg of lithium metal in 8 ml of *tert*-butyl alcohol to produce a mixture of alcohol and ketone corresponding to **27c**. Treatment of the mixture with 2 ml of 50% nitric acid for 30 min on the steam bath afforded 54 mg of a material which was purified by preparative scale glc on column 3,[12] yielding **27c** as a colorless liquid with a strong camphoraceous odor. The 2,4-dinitrophenylhydrazone of **27c** was obtained as orange needles, mp 144.5–145° (lit.[9] mp 142–143°).

Conversion of *endo*-7-Carboxymethylbicyclo[4.2.1]nonan-9-one (28a) to *endo*-7-Methylbicyclo[4.2.1]nonan-9-one (28c). Following the procedure described above, an 80-mg sample of **28a** was converted to 36 mg of **28c**, obtained as a colorless liquid with a strong camphoraceous odor. The 2,4-dinitrophenylhydrazone of **28c** was obtained as orange needles, mp 147–148° (lit.[9] mp 145–146°).

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Registry No. **1a**, 611-10-9; **1b**, 1655-07-8; **2a**, 42894-03-1; **2a** 2,4-dinitrophenylhydrazone, 42894-04-2; **2a** semicarbazone, 42894-05-3; **2b**, 42894-06-4; **2b** 2,4-dinitrophenylhydrazone, 42894-07-5; **2c**, 4668-82-0; **2d**, 42894-09-7; **2e**, 42894-10-0; **2e** 2,4-dinitrophenylhydrazone, 42894-11-1; **2e** semicarbazone, 42894-12-2; **2f**, 42894-13-3; **2f** 2,4-dinitrophenylhydrazone, 42894-14-4; **3a**, 42894-15-5; **3b**, 42894-16-6; **3c**, 42894-17-7; **3d**, 42894-18-8; **3f**, 42894-19-9; **4a**, 42894-20-2; **4b**, 42894-21-3; **4c**, 42894-22-4; **4d**, 42894-23-5; **4e**, 42894-24-6; **4f**, 42894-25-7; **5c**, 42894-26-8; **5d**, 42894-27-9; **5e**, 42894-28-0; **5f**, 42894-29-1; **6**, **42894-30-4**; **6** 2,4-dinitrophenylhydrazone, 42894-31-5; **6** semicarbazone, 42894-32-6; **7**, 42894-33-7; **8**, 41975-67-1; **9**, 30144-00-4; **9** 2,4-dinitrophenylhydrazone, 42894-36-0; **9** semicarbazone, 42894-37-1; **10a**, 42894-38-2; **10b**, 42894-39-3; **10b** 2,4-dinitrophenylhydrazone, 42894-40-6; **11**, 4696-09-7; **12**, 42894-42-8; **12** (free acid), 42894-43-9; **13**, 42894-44-0; **13** 2,4-dinitrophenylhydrazone, 42894-45-1; **14**, 42894-46-2; **16**, 42894-47-3; **17**, 42894-48-4; **19**, 42878-89-7; **20a**, 42878-90-0; **20b**, 42878-91-1; **21**, 1134-74-3; **22**, 42878-93-3; **23**, 42878-94-4; **24a**, 42878-95-5; **24b**, 42878-96-6; **25**, 42878-97-7; **25** 2,4-dinitrophenylhydrazone, 42878-98-8; **26**, 42878-99-9; **26** 2,4-dinitrophenylhydrazone, 42879-00-5; **27a**, 42879-01-6; **28a**, 42879-02-7; chloroacetonitrile, 107-14-2; 4-bromobutenonitrile, 42879-03-8.

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