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Bicyclo[3.3.1]nonanes as Synthetic Intermediates. I. Improved Synthetic Methods for Bicyclo[3.3.1]nonan-3-one

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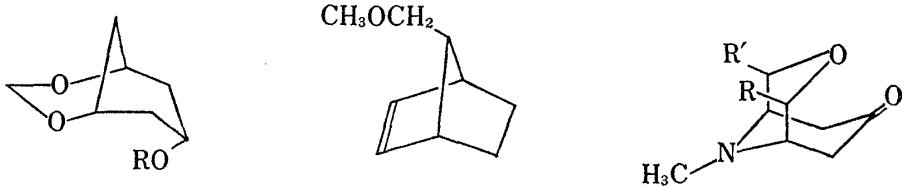
The syntheses of the title bicyclic ketone (IV) are described. The Michael-aldol condensation of ethyl acetoacetate (VI) with 2-cyclohexen-1-one (V) afforded a bicyclic β-keto ester, the ketonic cleavage of which gave 1-hydroxybicyclo[3.3.1]nonan-3-one (IX). Removal of the bridgehead hydroxyl in IX *via* the bromide (X) gave the desired ketone (IV). Another route to IV starting with bromination of adamantane followed by alkaline cleavage was established. Ozonolysis and subsequent ketalization converted 7-methylenebicyclo[3.3.1]nonan-3-one (XVII) into 7-ethylenedioxybicyclo[3.3.1]nonan-3-one (XIX), which was reduced to the desired ketone (IV) by means of the Huang-Minlon reduction. In addition, ozonolysis of 3-methylenebicyclo[3.3.1]nonane (XXII) gained by the Huang-Minlon reduction of XVII as a minor product was also found to give IV in good yield.

Keywords——bicyclo[3.3.1]nonane systems; cleavage of adamantane; Michael-aldol condensation; 'purple benzene' oxidation; Huang-Minlon reduction; 3-methyltricyclo-[3.3.1.$0^{3,7}$]nonane; transannular reaction; reductive dehalogenation; ^{13}C–NMR; ^{1}H–NMR

Bridged bicyclic compounds undergo a variety of bridge-fission reactions which provide novel approaches to medium and large ring compounds. Since most bicyclic compounds are constructed from simple, readily available intermediates, this process provides a useful route to specifically substituted rings: for example, the Beckmann[2] or Baeyer-Villiger[3] reaction converts a bridge ketone into a cyclic amino or hydroxy acid. Meanwhile, a recent report[4] of the synthesis of prostaglandin $F_{2\alpha}$ using a heterobicyclo[3.3.1]nonane system (I) as a stereoselective synthetic intermediate by Woodward, *et al.* has demonstrated an interesting synthetic utility of the bicyclic systems. The stereocontrolled synthesis of prostaglandins starting from a bicyclo[2.2.1]heptene derivative (II) by Corey, *et al.*[5] or the synthetic



I II III

Chart 1

1) Location: *133-1, Yamada-kami, Suita, Osaka 565, Japan.*
2) A.C. Cope and E.C. Hermann, *J. Am. Chem. Soc.*, **72**, 3405 (1950); A.C. Cope, F.S. Fawcett, and G. Munn, *ibid.*, **72**, 3399 (1950).
3) C.D. Gutsche, T.D. Smith, M.F. Sloan, J.J.Q. van Ufford, and D.E. Jordan, *J. Am. Chem. Soc.*, **80**, 4117 (1958).
4) R.B. Woodward, J. Gosteli, I. Ernest, R.J. Friary, G. Nestler, H. Raman, R. Sitrin, Ch. Suter, and J.K. Whitesell, *J. Am. Chem. Soc.*, **95**, 6853 (1973).
5) E.J. Corey, N.M. Weinshenker, T.K. Schaaf, and W. Huber, *J. Am. Chem. Soc.*, **91**, 5675 (1969); E.J. Corey, U. Koelliker, and J. Neuffer, *ibid.*, **93**, 1489 (1971); E.J. Corey, H. Shirahama, H. Yamamoto, S. Terashima, A. Venkateswarlu, and T.K. Schaaf, *ibid.*, **93**, 1490 (1971); E.J. Corey, S.M. Albonico, U. Koelliker, T.K. Schaaf, and R.K. Varma, *ibid.*, **93**, 1491 (1971); E.J. Corey and G. Moinet, *ibid.*, **95**, 6831 (1973) and refs. cited therein.

studies of laurencin and related compounds *via* a functionalized 9-aza-3-oxabicyclo[3.3.1]-nonan-3-one (III) by Masamune, *et al.*[6] also exemplify the synthetic utility of bicyclo[2.2.1]-heptane or bicyclo[3.3.1]nonane systems as important synthons for the stereoselective syntheses of various organic molecules.

Although there has been much continued interest in the structure-reactivity relationships[7] of the bicyclo[3.3.1]nonane system, synthetic routes to bicyclo[3.3.1]nonan-3-one (IV) are relatively few in number. Most of them[8] involve low-yield reactions and/or multi-step sequences which are synthetically unattractive. So, we have been particularly interested in developing an efficient route to IV, an important intermediate in some of our work, and have devised two practical methods, one *via* annelation of cyclohexenone and the other *via* cleavage of adamantane.

Annelation of Cyclohexenone

Our first attempt is summarized in Chart 2. Condensation of 2-cyclohexen-1-one (V) with ethyl acetoacetate (VI) in ethanol containing sodium ethoxide afforded a bicyclic keto ester (VII) in 74% yield. The structure of VII was evidenced by its infrared (IR) spectrum

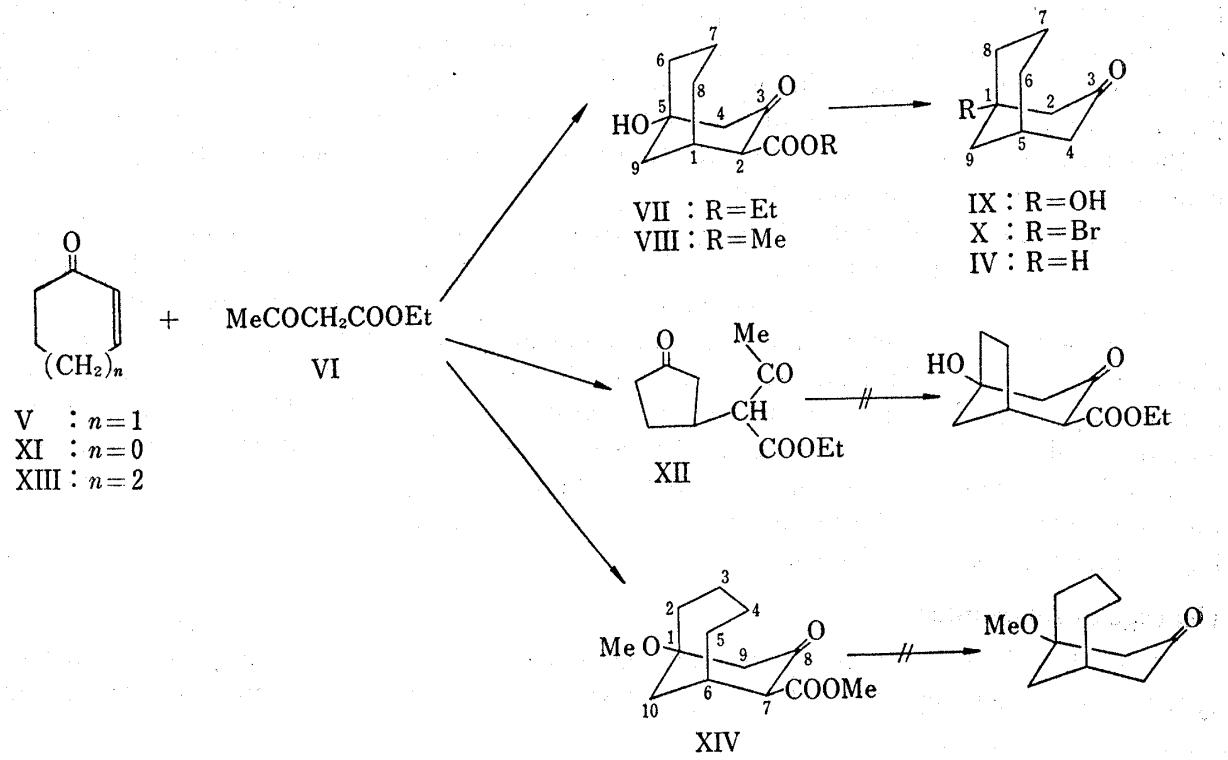


Chart 2

6) T. Masamune, S. Numata, H. Matsue, and A. Matsuyuki, *Bull. Chem. Soc. Jpn.*, **48**, 2294 (1975); T. Masamune and H. Matsue, *Chem. Lett.*, **1975**, 895; A. Murai, H. Murase, H. Matsue, and T. Masamune, *Tetrahedron Lett.*, **1977**, 2507.

7) See, for example, B.L. Buchanan, "Topics in Carbocyclic Chemistry," Vol. I, ed. by D. Lloyd, Logos Press Ltd., London, 1969, pp. 199—247; "Structure and Reactivity in Bicyclo[3.3.1]nonanes," by H. Kato, [*Yuki Gosei Kagaku Kyokai Shi*, **28**, 682 (1970)]; "Methods for the Preparation of Bridgehead Olefins," by R. Keese, [*Angew. Chem. Int. Ed. Engl.*, **14**, 528 (1975)]; "Polar Effects in Organic Reactions," by C.A. Grob, [*ibid.*, **15**, 569 (1976)].

8) *a*) Schaefer, *et al.* reported a method *via* the hydroboration of a highly sublimable olefin, bicyclo[3.3.1]-non-2-ene, which gave a poorly separable mixture of two regio-isomers of *exo*-alcohol, bicyclo[3.3.1]-nonan-2-ol and -3-ol [J.P. Schaefer, J.C. Lark, C.A. Flegal, and L.M. Honig, *J. Org. Chem.*, **32**, 1372 (1967)]; *b*) The method developed by Hall involves the cyclization of cyclohexane-1,3-diacetic acid to IV by means of either barium oxide or acetic anhydride, but is poor in yield [H.K. Hall, Jr., *ibid.*, **28**, 3213 (1963)].

displaying the bands characteristic of the enolized β-keto ester group in the range from 1580 to 1690 cm^{-1} and by the proton magnetic resonance (^1H-NMR) spectrum which displayed a one proton signal, at 3.02 ppm, due to the bridgehead proton and the one, at 12.10 ppm, due to the enol. A better yield (82%) was obtained when the condensation was carried out in methanol in the presence of sodium methoxide to give the corresponding methyl ester (VIII).

Decarboxylation of VIII in ethanol with 5% potassium hydroxide gave a hydroxy ketone (IX)[9] in 79% yield. Treatment of IX with phosphorous tribromide in benzene gave 1-bromobicyclo[3.3.1]nonan-3-one (X), in 91% yield, which was relatively unstable at room temperature. Conversion of IX into the corresponding halide by use of thionyl chloride was unsuccessful.[10] Reductive dehalogenation of X over Raney nickel catalyst was accomplished most selectively and effectively with diisopropylamine as solvent, and gave IV in 92% yield. Structural confirmation for IV was realized through its synthesis *via* an alternative route.[8a]

Attempts to extend this procedure to the general synthesis of the bicyclo[3.n.1]alkan-3-one system were unsuccessful. Reaction of VI with 2-cyclopenten-1-one (XI)[11] under a variety of conditions produced a complex mixture. The Michael adduct (XII) from the condensation of VI with XI was isolable in reasonable yield only from the run carried out in the presence of a catalytic amount of piperidine. The aldol cyclization of XII under various conditions was attempted in vain. According to the rules for ring closure by Baldwin,[12] this aldol cyclization should be favored as six-membered ring formation *via* the "*exo*-trigonal" path. So, either stereochemical inaccessibility of the acetyl group toward the cationic center in the transition state of the aldol cyclization or the preferred retrogression is suggested as a cause of the failure of this cyclization.

Condensation of VI with 2-cyclohepten-1-one (XIII)[13] gave an unexpected bicyclic adduct, methyl 1-methoxy-8-oxobicyclo[4.3.1]decan-7-carboxylate (XIV), instead of methyl 1-hydroxy-8-oxobicyclo[4.3.1]decan-7-carboxylate. The bridgehead methoxyl was evident from a three proton singlet at 3.16 ppm additional to the one, at 3.75 ppm, due to the carbomethoxy group in its ^1H-NMR spectrum and also from the two methoxyl signals at 50.76 and 48.13 ppm in the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum. Such a methoxyl substitution at the bridgehead was not observed to any extent in the reaction of V with VI. Transformation of XIV to the target ketone, bicyclo[4.3.1]decan-8-one, was unsuccessful because of the failure in its ketonic cleavage to remove the ester group under both acidic and basic conditions.

Cleavage of Adamantane

Recently, investigations concerning the correlation[14] between tricyclic and bicyclic systems have been reported with the progress of the adamantane chemistry. The second

9) A one pot synthesis of IX from V and VI has been described: see W.D.K. Macrosson, J. Martin, W. Parker, and A.B. Penrose, *J. Chem. Soc.*, (*C*), **1968**, 2323; P. Rabe, *Ber.*, **37**, 1671 (1904); P. Rabe and K. Appuhn, *Ber.*, **76**, 979 (1943). We could obtain the same product (IX) in better yield *via* isolation of the thermally labile intermediate (VII or VIII), and had some interesting information on the ketonic cleavage of these esters, which was mentioned briefly in a preliminary communication; T. Momose, S. Atarashi, and O. Muraoka, *Tetrahedron Lett.*, **1974**, 3697.

10) Successful conversion of 1-hydroxybicyclo[3.3.1]nonane into the corresponding bridgehead chloride on treatment with thionyl chloride has been reported: see W.G. Dauben and C.D. Poulter, *J. Org. Chem.*, **33**, 1237 (1968).

11) L.N. Owen and P.N. Smith, *J. Chem. Soc.*, **1952**, 4035; C.H. DePuy and K.L. Eilers, "Organic Syntheses," Coll. Vol. V, ed. by H.E. Baumgarten, John Wiley and Sons, Inc., New York, 1973, p. 326.

12) J.E. Baldwin, *J.C.S. Chem. Commun.*, **1976**, 734. J.E. Baldwin and L.I. Kruse, *ibid.*, **1977**, 233.

13) E.W. Garbisch, Jr., *J. Org. Chem.*, **30**, 2109 (1965).

14) See, for example, R.C. Fort, Jr. and P.V.R. Schleyer, *Chem. Rev.*, **64**, 277 (1964); R.C. Bingham and P.V.R. Schleyer, "Topics in Current Chemistry," Vol. 18, Springer Verlag, Berlin, 1971, pp. 32—40; E. Osawa, P.V.R. Schleyer, R.C. Bingham, and E.M. Engler, *Kagaku No Ryoiki*, **27**, 365 (1973); M. Nakazaki and K. Naemura., *Yuki Gosei Kagaku Kyokai Shi*, **32**, 905 (1974).

approach attempted was concerned with the conversion of adamantane to bicyclononanes. A straightforward route from adamantane to IV is summarized in Chart 3.

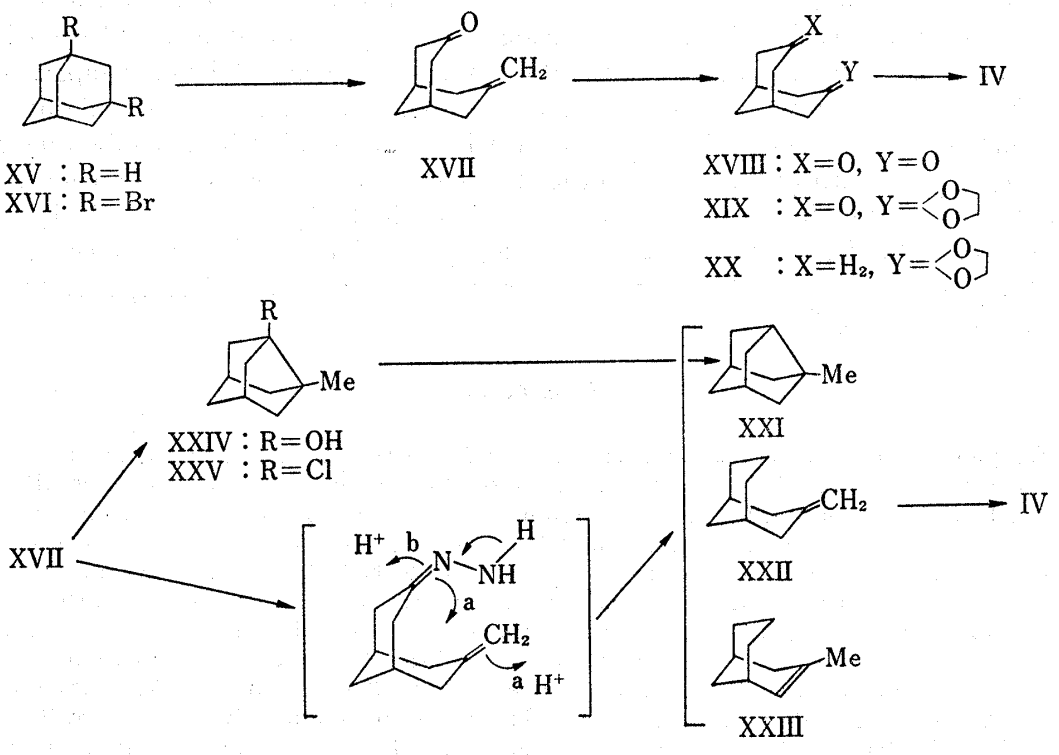


Chart 3

7-Methylenebicyclo[3.3.1]nonan-3-one (XVII) was obtained by the direct bromination[15] of adamantane (XV) with bromine and subsequent alkaline cleavage[16] of the resulting 1,3-dibromoadamantane (XVI). Conversion of XVII into a diketone (XVIII) was effected by ozonolysis[17] or oxidation with "purple benzene". Ketalization of XVIII with an excess of ethylene glycol gave a monoketal (XIX) as the sole product. The Huang-Minlon reduction of XIX gave a ketal (XX) in good yield, which was easily deketalized during work-up or storage in the presence of moisture to the desired ketone (IV). Its IR and ^{1}H–NMR spectra were completely in accord with those of an authentic sample.

Finally, we attempted the Huang-Minlon reduction of XVII expecting the *exo*-methylene compound (XXII) as a product. The Wolff-Kishner reduction of XVII was described by Eakin, *et al.*,[18] where adamantane was reported to be the only isolated product. Gas–liquid partition chromatography (GLC) analysis of the crude products showed three peaks

15) *a*) G.L. Baughman, *J. Org. Chem.*, **29**, 238 (1964); *b*) E.R. Talaty, A.E. Cancienne, Jr., and A.E. Dupuy, Jr., *J. Chem. Soc.*, (*C*), **1968**, 1902.

16) The fragmentation of the dibromide (XVI) yielding XVII has been described: see A.R. Gagneux and R. Meier, *Tetrahedron Lett.*, **1969**, 1365. However, Hamill, *et al.* [H. Hamill, A. Karim, and M.A. McKervey, *Tetrahedron*, **27**, 4317 (1971)] have recommended 1,3-dichloroadamantane as a starting material for XVII on the basis of criticism upon these procedures.[15] Following the refined method by Talaty, *et al.*,[15b] we prepared the dibromide most effectively, and the yield in the fragmentation of the dibromide to XVII (89%) was much better than that from the dichloride (55%). In addition, the diminished reaction period (18 hr), which was found enough for this cleavage, is another advantage as compared to that for the dichloride (70 hr). Use of a higher concentration of alkali in the present work was found to force the cleavage to completion in much shorter reaction period (12 hr, see Experimental).

17) H. Stetter and P. Tacke, *Chem. Ber.*, **96**, 694 (1963).

18) M. Eakin, J. Martin, and W. Parker, *Chem. Commun.*, **1965**, 206.

with the ratio of *ca.* 30: 10: 1, and no detectable amount of adamantane was obtained in spite of the repeated experiments. The mixture was chromatographed on silica gel impregnated with silver nitrate using pentane as eluent. The main component was identified as 3-methyltricyclo[3.3.1.$0^{3,7}$]nonane (XXI)[19] by its spectral data. Bridgehead methyl group was evident from its ^{1}H-NMR signal appearing at 1.15 ppm as a singlet and from the ^{13}C-NMR signal at 25.58 ppm. Final confirmation was performed by direct comparison of its IR and ^{13}C-NMR spectra with those of an authentic sample prepared from 7-methyltricyclo-[3.3.1.$0^{3,7}$]nonan-3-ol (XXIV)[18] by chlorination with thionyl chloride and subsequent reductive dehalogenation with lithium. The other two components were isomeric olefins, 3-methylenebicyclo[3.3.1]nonane (XXII)[20] and 3-methylbicyclo[3.3.1]non-2-ene (XXIII).[20,21] The structures were established by comparison of the physical data with those published. Ozonolysis or "purple benzene" oxidation of the exo-methylene compound (XXII) gave the desired ketone (IV) in good yield.

Experimental

Melting points and boiling points are uncorrected. IR spectra were taken on a Hitachi EPI-G3 grating spectrophotometer. ^{1}H-NMR spectra were measured for the 10% solution in CCl_4 or $CDCl_3$ with a Hitachi R-20A (60 MHz) or R-22 (90 MHz) spectrometer with tetramethylsilane as an internal standard. Coupling constants (J) are given in Hz, and the following abbreviations are used; s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, bs=broad singlet. The 22.63 MHz ^{13}C-NMR spectra were measured for the solution in CCl_4 or $CDCl_3$ with a Hitachi R-22CFT spectrometer, in conjunction with a HITAC 10-II computer, with tetramethylsilane as an internal standard. Mass spectra (MS) were taken on a Hitachi RMU-6E mass spectrometer. Gas-liquid partition chromatography (GLC) was carried out on a Perkin-Elmer 800 gas chromatograph equipped with a stainless column (2 mm×1.8 m) packed with 1.5% SE-52 on chromosorb W (60—80 mesh) with N_2 carrier gas: flow rate of 30 ml/min. GC-Mass spectra[22] were taken on a JEOL JMS-D100/JGC-20K system, in conjunction with a JEC-6 spectrum computer, equipped with a glass column (3 mm×1 m) packed with 5% OV-17 on chromosorb W (80—100 mesh) with CH_4 carrier gas: flow rate of 40 ml/min. Column chromatography was performed on Mallinckrodt silicic acid. All the organic extracts were dried over anhydrous magnesium sulfate prior to evaporation.

Ethyl 5-Hydroxy-3-oxobicyclo[3.3.1]nonane-2-carboxylate (VII)——Ethyl acetoacetate (VI, 8.1 g) and 2-cyclohexen-1-one (V, 5.0 g) were added to a solution of NaOEt prepared by dissolution of Na (1.4 g) in dry EtOH (75 ml), and the mixture was heated under reflux for 36 hr, poured into ice water, acidified with conc. HCl and extracted with benzene (3×50 ml). The extract was washed with water and evaporated. Crystallization of the residue from petroleum ether gave 8.7 g (74%) of VII as colorless crystals, mp 73—74°. IR ν_{max}^{KBr} cm^{-1}: 3280 (OH), 1650 and 1610 (enolized CO). ^{1}H-NMR (60 MHz, CCl_4) δ: 1.31 (3H, t, $-COOCH_2\underline{CH_3}$), 2.39 (2H, s, C_4–H), 2.60 (1H, s, bridgehead OH), 3.02 (1H, bs, C_1–H), 4.02 (2H, q, $-COO\underline{CH_2}CH_3$), 12.10 (1H, s, enol). ^{13}C-NMR (CCl_4) δ: 172.08 and 170.77 (C_3 and ester $\underline{C}O$), 99.26 (C_2), 68.35 (C_5), 59.57 ($-COO\underline{C}H_2CH_3$), 30.51 (C_1), 43.77, 41.15, 40.76, 28.74, 19.26 (ring methylene), 14.18 ($-COOCH_2\underline{C}H_3$). *Anal.* Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.66; H, 8.04.

Methyl 5-Hydroxy-3-oxobicyclo[3.3.1]nonane-2-carboxylate (VIII)——A mixture of VI (8.1 g), V (5.0 g), and NaOMe (from 1.4 g of Na) in dry MeOH (75 ml) was heated under reflux for 36 hr, and worked up in a manner similar to that for VII to give a brown oil, which on vacuum distillation gave 9.0 g (82%) of VIII as a colorless oil, bp 120° (0.05 mmHg). Distillation at the temperature above 150° was found to result in facile and complete polymerization. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3280 (OH), 1700 (CO), 1580—1670 (enolized CO). ^{1}H-NMR (90 MHz, CCl_4) δ: 2.38 (2H, s, C_4–H), 2.99 (1H, bs, C_1–H), 3.40 (1H, s, bridgehead OH), 3.71 (3H, s, $-COOC\underline{H_3}$), 12.15 (1H, s, enol). *Anal.* Calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.20; H, 7.64.

Reaction of Ethyl Acetoacetate with 2-Cyclopenten-1-one (XI)——a) A mixture of VI (1.9 g), XI (1.0 g), and NaOEt (from 330 mg of Na) in 30 ml of dry EtOH (or an equimolar amount of piperidine in dry EtOH,

19) Preferred transannular *exo*-protonation (a) over direct *exo*-protonation (b) in the first step of this reaction might be responsible for the predominant formation of XXI as depicted in Chart 3. Further discussion of this and related transannular reaction will be described in another paper.

20) Independent routes to XXII starting from endo-7-aminomethylbicyclo[3.3.1]nonan-3-one have been described: see Jih-Hua Liu, G.A. Gauger, and P. Kovacic, *J. Org. Chem.*, **38**, 543 (1973); Jih-Hua Liu and P. Kovacic, *ibid.*, **38**, 3462 (1973).

21) R.A. Appleton and S.H. Graham, *Chem. Commun.*, **1965**, 297.

22) We are grateful to Dr. H.K. Sasaki for his help in the GC-Mass measurement.

or an equimolar amount of NaOMe in dry MeOH) was heated under reflux for 24 hr, and worked up in a manner similar to that for VII to give a complex mixture as a brown oil, attempted fractionation of which was unsuccessful.

b) A mixture of VI (1.9 g), XI (1.0 g), a small amount of piperidine, and dry EtOH (30 ml) was heated under reflux for 6 hr, and worked up in a manner similar to that for VII to give a brown oil, which on vacuum distillation gave 1.95 g (76%) of XII as a mixture of the two diastereoisomers, bp 140° (1 mmHg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750, 1725 (CO). ^{1}H-NMR (90 MHz, CCl_4) δ: 1.26 and 1.28 (3H, t in pairs, $-COOCH_2\underline{C}H_3$), 2.16 and 2.18 (3H, s in pairs, $-COC\underline{H}_3$), 4.15 and 4.17 (2H, q in pairs, $-COOC\underline{H}_2CH_3$). ^{13}C-NMR (CCl_4) δ: 213.55 (ring CO), 199.29 ($-\underline{C}OCH_3$), 167.62 ($-\underline{C}OOC_2H_5$), 64.43 and 64.20 in pairs ($-CO\underline{C}HCOOC_2H_5$), 60.81 ($-COO\underline{C}H_2CH_3$), 28.59 and 28.44 in pairs ($-CO\underline{C}H_3$), 35.53 (ring tertiary carbon), 42.23 and 42.00 in pairs, 37.38, 27.28 and 27.13 in pairs (ring methylene), 13.95 ($-COOCH_2\underline{C}H_3$). GLC: retn. time, 8.0 min (temperature: column, 125°; injector, 160°; detector, 160°).

Attempted Aldol Cyclization of XII——A mixture of XII (212 mg) and NaOEt (from 30 mg of Na) in dry EtOH (5 ml) (or NaOMe in dry MeOH, or pyridine in dry EtOH) was heated under reflux for 8 hr and worked up in a manner similar to that for VII to give a complex mixture as a brown oil, attempted fractionation of which was unsuccessful.

Condensation of Ethyl Acetoacetate with 2-Cyclohepten-1-one (XIII)——A mixture of VI (2.8 g), XIII (2.0 g), and NaOMe (from 500 mg of Na) in dry MeOH (50 ml) was heated under reflux for 12 hr, and worked up in a manner similar to that for VII to give a brown oil, which on vacuum distillation gave 3.4 g (78%) of XIV as a colorless oil, bp 140° (0.02 mmHg), homogeneous on GLC (retn. time: 15.0 min. at the column temperature of 130°). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (CO, weak), 1650, 1610 (enolized CO). MS *m/e*: 240 (M^+, 14%). ^{1}H-NMR (90 MHz, CCl_4) δ: 2.90 (1H, bs, C_6–H), 3.16 (3H, s, $-OCH_3$), 3.75 (3H, s, $-COOCH_3$), 12.27 (1H, s, enol). ^{13}C-NMR (CCl_4) δ: 172.03 and 171.77 (C_8 and $-\underline{C}OOCH_3$), 50.76, 48.13 ($-COO\underline{C}H_3$, $-OCH_3$), 99.43 (C_7), 74.98 (C_1), 30.57 (C_6), 42.95, 38.96, 36.38, 33.38, 26.79, 23.19 (ring methylene).

1-Hydroxybicyclo[3.3.1]nonan-3-one (IX)——A solution of VIII (3.6 g) and potassium hydroxide (2.5 g) in 50% aq. EtOH (50 ml) was heated under reflux for 8 hr, and evaporated to remove ethanol under reduced pressure. The aqueous residue was thoroughly extracted with CH_2Cl_2 (5×5 ml), and the extract was washed with brine, and evaporated to afford a solid, which on sublimation gave IX (2.06 g, 79%) as colorless crystals, mp 189—191° (lit.,[9] mp 192—193°).

7-Methylenebicyclo[3.3.1]nonan-3-one (XVII)——The method described by Gagneux, *et al.*[16] was partially modified. A solution of 1,3-dibromoadamantane (XVI, 29.4 g) and 1.5 N NaOH (300 ml) in dioxane (300 ml) was heated in a stainless steel autoclave at 180° for 12 hr. The cooled solution was diluted with water (300 ml), and the mixture was extracted with ether (5×100 ml). The extract was washed with brine, and evaporated to give a colorless solid, which on recrystallization from EtOH gave XVII (13.4 g, 89.3%) as colorless crystals, mp 161—163° (lit., 160—163°,[16] 162—163°[17]). GLC: retn. time, 4.4 min (temperature: column, 110°; injector, 160°; detector, 160°).

Bicyclo[3.3.1]nonan-3,7-dione (XVIII)——To a mixture of potassium permanganate (0.47 g), dicyclohexyl-18-crown-6[23] (1.1 g), and benzene (30 ml) was added 0.15 g of methyleneketone (XVII), and the solution was stirred for 2 hr. The precipitate was filtered off, and the solution was concentrated. The residue was sublimed to give XVIII (85 mg, 56.2%) as colorless crystals, mp 252—254° (lit., 254—256°,[16] 254—255.5°[17]). Bissemicarbazone (from EtOH); mp 276° (dec.). *Anal.* Calcd. for $C_{11}H_{18}N_6O_2$: C, 49.61; H, 6.81; N, 31.56. Found: C, 49.43; H, 6.91; N, 30.90.

7-Ethylenedioxybicyclo[3.3.1]nonan-3-one (XIX)——A mixture of XVIII (1.5 g), ethylene glycol (2 ml), *p*-toluenesulfonic acid (80 mg), and benzene (60 ml) was heated under reflux for 3 hr, cooled, washed with satd. $NaHCO_3$, and then with water. Removal of the benzene gave a colorless solid, which on recrystallization from *n*-hexane gave XIX (1.67 g, 85.2%) as colorless crystals, mp 78—79°. IR ν_{max}^{KCl} cm^{-1}: 2945, 2880, 1697, 1228, 1145, 1090, 1071, 1028, 989, 948, 859. ^{1}H-NMR (90 MHz, CCl_4) δ: 1.15—1.90 (6H, m, C_6,C_8, C_9–H), 2.10—2.60 (6H, m, C_1,C_2,C_4,C_5–H), 3.65—4.03 (4H, m, $-OCH_2-$). *Anal.* Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.15; H, 8.20.

7-Methyltricyclo[3.3.1.0^{3,7}]nonan-3-ol (XXIV)[24]——To a solution of XVII (900 mg) in wet ether (80 ml) was added Na (1.0 g), and the suspension was stirred vigorously for 7 hr. The organic layer was decanted, and the excess Na was washed thoroughly with ether. The combined ether solution was neutralized with dil. HCl, washed with brine, and evaporated to give a colorless solid, which on recrystallization from *n*-hexane gave XXIV (800 mg, 87.7%) as colorless crystals, mp 168—168.5° (lit., 169—169.5°,[18] 165—166°,[25a] 169—170°[25b]). IR ν_{max}^{Nujol} cm^{-1}: 3300, 2918, 2850, 1453, 1309, 1140, 1028. ^{1}H-NMR (90 MHz, CCl_4) δ: 0.97 (3H, s, $-CH_3$), 1.36—1.68 (6H, m, C_6,C_8,C_9–H), 1.65 (1H, s, OH), 1.79 (4H, bs, C_2,C_4–H), 2.15

23) D.J. Sam and H.E. Simmons, *J. Am. Chem. Soc.*, **94**, 4024 (1972).

24) The procedure is essentially based on the method of Eakin, *et al.*,[18] who have, however, described no detail of the experimental procedure.

25) *a*) K. Kimoto and M. Kawanisi, *Chem. and Ind.*, **1971**, 1174; *b*) T. Mori, K.H. Yang, K. Kimoto, and H. Nozaki, *Tetrahedron Lett.*, **1970**, 2419.

(2H, bs, C_1,C_5–H). ^{13}C-NMR ($CDCl_3$) δ: 83.08 (C_3), 51.03 (C_2,C_4), 50.80 (C_6,C_8), 43.65 (C_7), 34.98 (C_1,C_5), 33.36 (C_9), 21.40 (–$\underline{C}H_3$). *Anal.* Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.56; H, 10.66. GLC: retn. time, 2.0 min (temperature: column, 110°; injector, 160°; detector, 160°).

3-Chloro-7-methyltricyclo[3.3.1.0^{3,7}]nonane (XXV)——A solution of XXIV (600 mg) in thionyl chloride (30 ml) was heated under reflux for 20 hr. The excess thionyl chloride was removed under reduced pressure, and to the resulting residue satd. $NaHCO_3$ was added. The organic material was taken in ether, and the extract was washed and evaporated to give a yellow solid, which on sublimation gave XXV (530 mg, 77.7%) as colorless crystals, mp 139—139.5°. IR ν_{max}^{Nujol} cm^{-1}: 2900, 1450, 1320, 1301, 1262, 1080, 990, 934, 895, 817, 628. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 1.14 (3H, s, –CH_3), 1.45—1.80 (6H, m, C_6C_8,C_9–H), 2.15 (6H, bs, C_1,C_2,C_4,C_5–H). ^{13}C-NMR (CCl_4) δ: 75.48 (C_3), 54.24 (C_2,C_4), 50.47 (C_6,C_8), 46.49 (C_7), 35.61 (C_1,C_5), 32.66 (C_9), 23.69 (–CH_3). *Anal.* Calcd. for $C_{10}H_{15}Cl$: C, 70.37; H, 8.86. Found: C, 69.88; H, 8.51. GLC: retn. time, 2.2 min (temperature: column, 110°; injector, 160°; detector, 160°).

3-Methyltricyclo[3.3.1.0^{3,7}]nonane (XXI) (Reductive Dehalogenation of XXV)[26]——The chloride (XXV, 550 mg) and absolute *tert*-BuOH (1.5 ml) were dissolved in dry THF (15 ml). Lithium (90 mg) was added to the solution, and the mixture was stirred at room temperature for 5 hr. Additional *tert*-BuOH (2 ml) was added to dissolve some remaining lithium, and the mixture was heated under reflux for 6 hr. Methanol was added, and the yellow reaction mixture was poured into 100 ml of ice water and extracted with pentane (3×25 ml). Evaporation of the extract gave XXI (260 mg, 59.1%) as highly sublimable crystals, mp 109—110°, which were homogeneous on GLC analysis. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2945, 2865, 1456, 1332, 1131, 1098, 1079, 669. ^{1}H-NMR (90 MHz, CCl_4) δ: 1.15 (3H, s, –CH_3), 1.35—2.00 (11H, m, C_3–H and ring methylene), 2.17 (2H, bs, C_1,C_5–H). ^{13}C-NMR (CCl_4) δ: 51.05 (C_2,C_4), 44.41 (C_3 or C_7), 44.14 (C_6,C_8), 37.88 (C_1,C_5), 36.89 (C_9), 25.58 (–CH_3). MS *m/e*: 136 (40%). *Anal.* Calcd. for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.30; H, 11.69.

The Huang-Minlon Reduction of XVII——A solution of XVII (3.0 g), 90% hydrazine hydrate (4.0 ml), and potassium hydroxide (4.0 g) in 40 ml of diethylene glycol was heated at 110° for 2 hr, and then at 190°. The sublimate trapped in the condenser was collected and taken up in ether (30 ml). The ethereal solution was washed with brine (3×5 ml), and careful removal of the ether from the solution gave a soft solid (1.96 g, 72%), which was stored at 0°. GLC analysis of the solid showed three peaks, in the ratio of *ca.* 30: 10: 1, corresponding to XXI, XXII, and XXIII, respectively. Chromatography of the solid (1.5 g) on silica gel (40 g) impregnated with silver nitrate (7.5 g)[27] with pentane as eluent gave XXI (900 mg) as extremely sublimable crystals, mp 109—111°. Its IR and ^{13}C-NMR spectra were identical with those of an authentic sample gained by the method mentioned above. Further elution with pentane–ether (5: 1) gave the *endo*-olefin (XXIII, 25 mg)[20,21] as an oil of 98% purity, followed by the *exo*-olefin (XXII, 320 mg)[20] as an oil.

Bicyclo[3.3.1]nonan-3-one (IV)——a) From IX *via* the bromide (X). A solution of PBr_3 (7 g) in dry benzene (5 ml) was added over a 30 min period to a cold and stirred solution of IX (8 g) in 20 ml of dry benzene. During the addition, the temperature was maintained below 3°. The mixture was stirred for an additional 5 hr at room temperature, and poured into ice water (30 ml). The benzene layer was separated, and the aqueous layer was extracted with ether (3×20 ml). The combined organic layer was washed with satd. $NaHCO_3$ and brine, and evaporated to give a labile bromide (X, 10.3 g, 91%) as colorless crystals. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1705 (CO). ^{1}H-NMR (90 MHz, CCl_4) δ: 2.95 (2H, s, C_4–H), 2.30 (7H, bs, C_2,C_5,C_6,C_9–H). The bromide decomposed even on standing at room temperature, and was immediately subjected to hydrogenation.

A suspension consisting of X (8.8 g), Raney nickel (5 g), and dry diisopropylamine (200 ml) was hydrogenated at room temperature under atmospheric pressure until absorption of hydrogen ceased. The catalyst was removed, and the mixture was concentrated. The residue was neutralized with dil. HCl and extracted with ether (3×50 ml). The extract was washed with brine and evaporated. Sublimation of the resulting residue afforded IV (5.15 g, 92%) as colorless crystals, mp 173—176° (lit., mp 170—176°,[8a] 180—182°[8b]). This preparation was homogeneous on GLC and identical with an authentic specimen prepared by the method of Schaefer, *et al.*[8a]

b) From XIX by the Huang-Minlon reduction. A mixture of XIX (588 mg), 85% hydrazine hydrate (2.5 ml), potassium hydroxide (2.5 g), and diethylene glycol (25 ml) was heated at 120° for 2 hr, then at 200° for 3 hr. The cooled solution was poured into 100 ml of ice water, acidified with conc. HCl, and extracted with ether. The extract was washed with brine and evaporated. Spontaneous deketalization proceeded during work-up and storage at room temperature. Sublimation of the residue gave IV (322 mg, 77.7%), as colorless crystals, mp 173—176°.

c) From XXII by ozonolysis. A solution of XXII (272 mg) in AcOEt (20 ml) was saturated with

26) Conversion of XXV into XXI was attempted by means of $LiAlH_4$ in ether, or $LiBH_4$ in ether, or $NaBH_4$ in methanol, or (n-Bu)$_3$SnH in ether, or H_2/Raney Ni in ethanol. All the attempts resulted in recovery of the starting material except the reduction by $LiAlH_4$ in ether, which gave the desired hydrocarbon (XXI) in 41% yield only after an extremely long reaction period (*i.e.*, 10 days).

27) T. Norin and L. Westfelt, *Acta Chem. Scand.*, **17**, 1828 (1963).

ozone at −78°, and treated with AcOH (1 ml) and 1.0 g of zinc dust, followed by vigorous stirring for 3 hr. The insoluble solid was removed, and the organic solution was neutralized with satd. $NaHCO_3$ and taken in AcOEt. The AcOEt extract was washed with brine and evaporated to give a colorless solid, which on sublimation gave IV (207 mg, 76%) as colorless crystals, mp 174—176°.

d) From XXII by oxidation with 'purple benzene'. To a mixture of potassium permanganate (0.47 g), dicyclohexyl-18-crown-6 (1.1 g), and benzene (20 ml) was added 0.136 g of the olefin (XXII), and the solution was stirred for 2 hr. Work-up as described above for compound XVIII gave IV (72 mg, 52.2%) as colorless crystals, mp 172−175°.