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Bicyclo[3.3.1]nonanes as Synthetic Intermediates. II.[1] Synthesis of Bicyclo[3.n.1]alkan-3-one *via* α,α′ Annelation of Cycloalkanone

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Bicyclo[4.3.1]decan-8-one (3) was synthesized from 8-benzoylbicyclo[4.3.1]decan-10-one (4) by making use of regio-selective deketalization of a bisketal (8). Bicyclo-[3.3.1]nonan-3-one (1) and bicyclo[3.2.1]octan-3-one (2) were also prepared from the corresponding 3-benzoylbicyclo[3.n.1]alkanone, but *via* a modified route.

Keywords——bicyclo[3.n.1]alkan-3-one; α,α′-annelation of cycloalkanone; selective deketalization; oxidative removal of benzoyl moiety; steric hindrance; chair/boat conformation; γ-gauche interaction; epimerization; ^{1}H-NMR; ^{13}C-NMR

Although the bicyclo[4.3.1]decane structure as well as the bicyclo[3.3.1]nonane and bicyclo[3.2.1]octane system is a potentially interesting framework for the investigation of structure-reactivity relationships,[3] a detailed study of the chemistry of this system has not yet been reported owing, in part, to the relative inaccessibility of its suitable, simple derivatives. In the course of the exploratory study on applicability of this system to natural product syntheses,[4] we have investigated several synthetic approaches to the parent system, and have developed a practical route *via* α,α′-annelation[5] of cycloheptanone, which is versatile and adaptable to a large scale preparation of this system. Another aim of establishing the general synthetic routes to bicyclo[3.n.1]alkan-3-one has also been achieved by extending this method. Namely, the synthesis of bicyclo[3.3.1]nonan-3-one (**1**)[6] as well as that of bicyclo[3.2.1]octan-3-one (**2**)[7] has been accomplished in excellent yield.

Bicyclo[4.3.1]decan-8-one

The preparation of bicyclo[4.3.1]decan-8-one (**3**) was carried out as shown in Chart 1 starting from 8α-benzoylbicyclo[4.3.1]decan-10-one (**4**)[5a] which was prepared by condensation of *N*-cycloheptenylpyrrolidine with 2-benzoyl-1,3-dichloropropane.[8] The α,α′-annelation of

1) Part I: T. Momose and O. Muraoka, *Chem. Pharm. Bull.* (Tokyo), **26**, 288 (1978).
2) Location: *133-1, Yamada-kami, Suita, Osaka 565, Japan.*
3) A series of studies on bishomotropylium ion have been reported: see, for example, G. Schröder, U. Prange, and J.F.M. Oth, *Chem. Ber.*, **105**, 1854 (1972); P. Ahlberg, D.L. Harris, M. Roberts, P. Warner, P. Seidl, M. Sakai, D. Cook, A. Diaz, J.P. Dirlam, H. Hamberger, and S. Winstein, *J. Am. Chem. Soc.*, **94**, 7063 (1972). Studies in relation to the anti-Bredt compounds have been reported: see, for example, W.D. Dauben and J. Ipaktschi, *J. Am. Chem. Soc.*, **95**, 5088 (1973); K. Taguchi and F.H. Westheimer, *J. Am. Chem. Soc.*, **95**, 7413 (1973); B.G. Cordiner, M.R. Vegar, and R.J. Wells, *Tetrahedron Lett.*, **1970**, 2285.
4) A. sesquiterpene synthesis *via* bicyclo[4.3.1]decane intermediates has been reported: see, for example, J.A. Marshall and J.J. Partridge, *Tetrahedron*, **25**, 2159 (1969); *idem*, *J. Am. Chem. Soc.*, **90**, 1090 (1968).
5) *a*) H. Stetter, K.-D. Rämsch, and K. Elfert, *Ann. Chem.*, **1974**, 1322; *b*) R.P. Nelson, J.M. McEuen, and R.G. Lawton, *J. Org. Chem.*, **34**, 1225 (1969); *c*) R.P. Nelson and R.G. Lawton, *J. Am. Chem. Soc.*, **88**, 3884 (1966); *d*) J.M. McEuen, R.P. Nelson, and R.G. Lawton, *J. Org. Chem.*, **35**, 690 (1970).
6) J.P. Schaefer, J.C. Lark, C.A. Flegal, and L.M. Honig, *J. Org. Chem.*, **32**, 1372 (1967); H.K. Hall, Jr., *J. Org. Chem.*, **28**, 3213 (1963), and ref. 1.
7) W. Kraus, G. Klein, H. Sadlo, and W. Rothenwöhrer, *Synthesis*, **1972**, 485, and references cited therein.
8) *a*) R.C. Fuson, W.E. Ross, and C.H. McKeever, *J. Am. Chem. Soc.*, **60**, 2935 (1938); *b*) A. Terada, *Nippon Kagaku Zasshi*, **81**, 612 (1960). The method described by Terada was found more effective for the preparation of this compound.

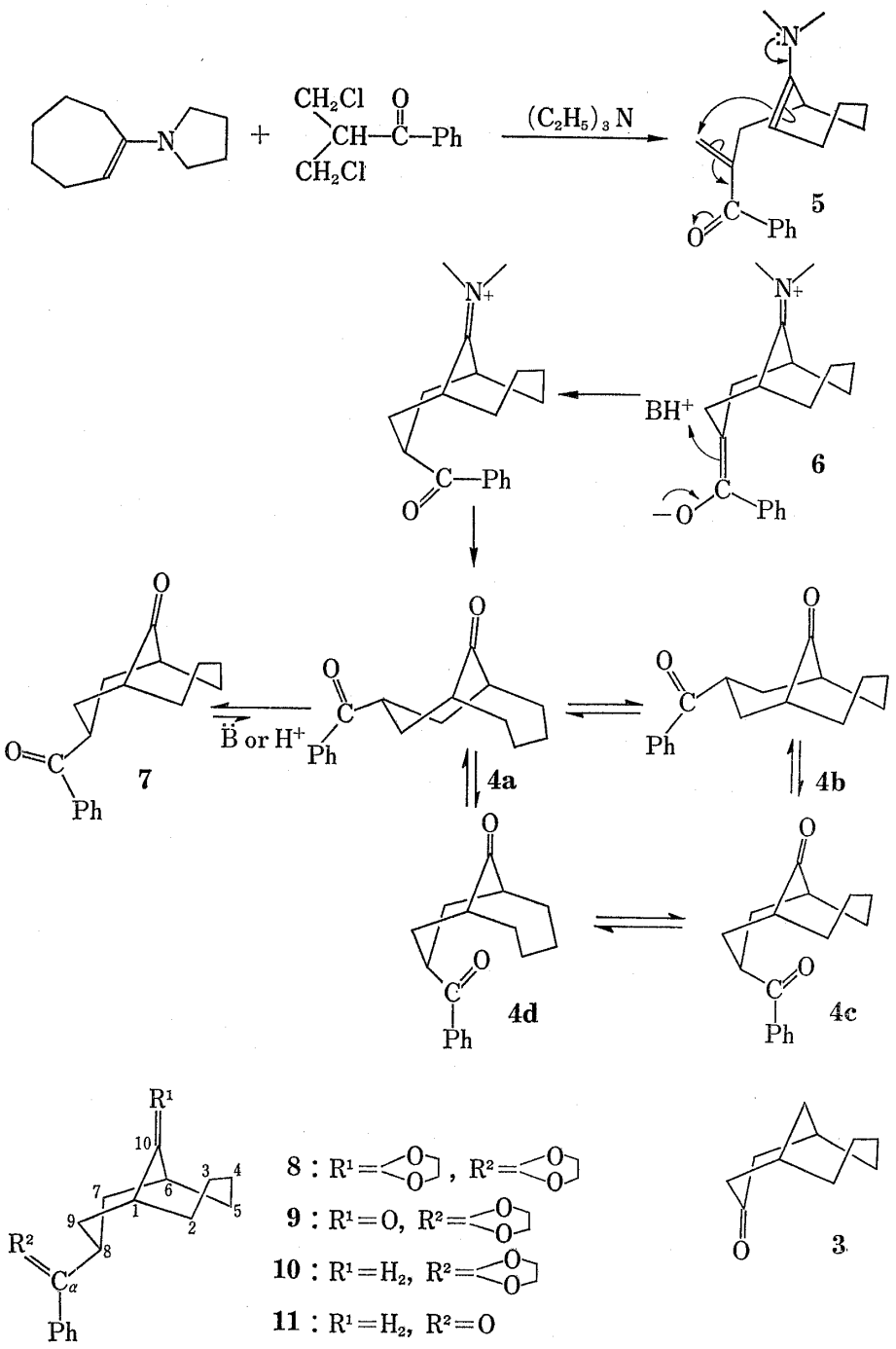

Chart 1

this type had been reported to proceed *via* a C-alkylation-proton transfer-Michael condensation path.[5b,d] For the Michael condensation to take place, it is necessary for the 2-benzoylpropenyl group to be in a quasi-axial position (**5**). Protonation of the Michael reaction product (**6**) from the least hindered side results in the formation of the 8α-benzoyl derivative (**4**) upon hydrolysis. The axial or *endo* configuration of the benzoyl function was also established by its proton magnetic resonance (^{1}H-NMR) spectral evidences for C_8–H conformation and by the facile isomerization of **4** to a more stable *exo*-isomer (**7**) on treatment with base or acid.

The bisketal (**8**) prepared in a usual manner in 95% yield was subjected to ketal exchange reaction with acetone in the presence of *p*-toluenesulfonic acid at room temperature to afford a monoketal (**9**) in 96% yield. The structure was assigned on the basis of its infrared (IR)

and ^{1}H-NMR spectral evidences and of the behavior toward its subsequent reactions. The IR spectrum of **9** displayed a non-conjugated carbonyl band at 1710 cm^{-1}, and the ^{1}H-NMR spectrum displayed a broad signal, at 7.28 ppm, attributing to the aromatic protons bearing no adjacent carbonyl on the ring. One pot synthesis of **9** from **4** was also performed effectively by the addition of acetone directly to the reaction mixture of bisketalization of **4** without isolation of the bisketal (**8**) formed. No careful control was needed for this selective deketalization because of the absence of side products due probably to an extreme steric hindrance over C_8 side chain under these conditions. Reduction of **9** by the Huang-Minlon method and subsequent hydrolysis of the resulting monoketal (**10**) afforded 8-benzoylbicyclo[4.3.1]decane (**11**) in an overall yield of 90%. Oxidation of **11** with molecular oxygen in hexamethylphosphoric triamide/*tert*-butanol containing potassium *tert*-butoxide gave the desired ketone, bicyclo[4.3.1]decan-8-one (**3**), in 52% yield.

Bicyclo[3.3.1]nonan-3-one and Bicyclo[3.2.1]octan-3-one

Bicyclo[3.3.1]nonan-3-one (**1**) was obtained from the corresponding bicyclic diketone, 3-*endo*-benzoylbicyclo[3.3.1]nonan-9-one (**12a**),[5a] in almost the same yield as that for **3** from **4**, but *via* a modified route (Chart 2).

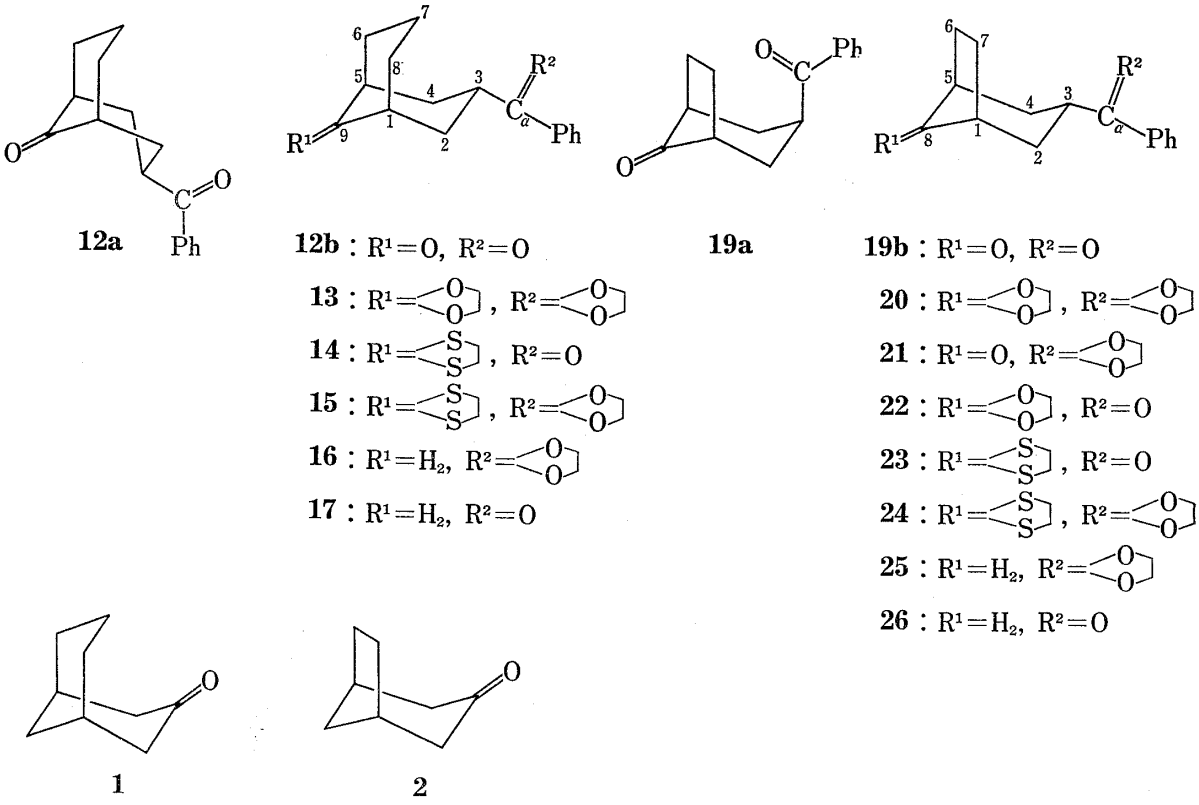

Chart 2

The diketone (**12a**) was bisketalized effectively in a usual manner, but it was found difficult to avoid the formation of the concomitant diketone (**12b**) in the deketalization of the resulting bisketal (**13**). Meanwhile, treatment of **12a** with an equimolar amount of ethanedithiol in the presence of *p*-toluenesulfonic acid at room temperature gave a thioketal (**14**) as a sole product in 93% yield. Direct desulfurization of **14** was unsuccessful, but the second ketalization of **14** with ethylene glycol and subsequent desulfurization with W-2 Raney nickel afforded the desired monoketal (**16**) in 89% yield. Conversion of **16** to the target ketone (**1**) was carried out, in overall 50% yield, in the same manner as that for **3** from **10**. Structural confirmation for **1** was realized by an alternative synthesis.[6]

As for the rigid chair-boat (cb) conformation of **12a**, the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra afforded informations additional to the Stetter's results,[5a] as listed in Table I. Appreciable shielding of the C_7-atom in **12a**, compared to the corresponding carbon in **12b** or bicyclo[3.3.1]nonane (**18**), would be attributed to the *γ-gauche* interaction[9] between the 7-*endo*- and the 2- and 4-*endo*-hydrogens in its cb conformation. Owing to this effect, C_2 and C_4 would also be shielded.

Table I. ^{13}C-NMR Chemical Shifts of α- and β-Benzoylbicyclo[3.n.1]alkanones[a]

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8
4	46.94	29.44[b]	26.13	26.13	29.44[b]	46.94	30.91[b]	40.16
7	46.94	30.98	27.13	27.13	30.98	46.94	35.07	37.30
12a	43.85	32.24	38.79	32.24	43.85	35.75	15.11	35.75
12b	45.65	36.75	39.11	36.75	45.65	34.12	21.31	34.12
19a	43.03	37.83	37.43	37.83	43.03	22.46	22.46	221.34
19b	43.61	38.99	37.37	38.99	43.61	22.81	22.81	219.48
18[c]	27.9	31.6	22.5	31.6	27.9	31.6	22.5	31.6

	C-9	C-10	Benzoyl ketone	Aromatic carbons			
				α	*para*	*ortho*	*meta*
4	30.91[b]	217.33	201.68	135.87	133.02	128.63	128.16
7	35.07	213.47	201.68	136.10	133.02	128.70	128.09
12a	220.02		201.54	135.85	133.15	128.70	128.16
12b	218.48		201.02	136.15	133.04	128.66	128.12
19a			202.60	136.30	132.39	128.55	128.34
19b			200.75	136.09	133.09	128.69	128.16
18[c]	35.1						

a) Chemical shifts in ppm for TMS, in $CDCl_3$.
b) Signals may be reversed.
c) Bicyclo[3.3.1]nonane, literature value; A. Heumann and H. Kolshorn, *Tetrahedron*, **31**, 1571 (1975).

The synthesis of bicyclo[3.2.1]octan-3-one (**2**)[7] was performed starting from 3-*endo*-benzoylbicyclo[3.2.1]octan-8-one (**19a**)[5a] in exactly the same manner as that for **1** from **12a** because of the failure in the desired selective deketalization of the bisketal (**20**) into the monoketal (**21**). The *endo* isomer (**19a**) was easily isomerized to a more stable *exo* isomer (**19b**) by its distillation at 200° as well as by its treatment with acid or base. Ketal exchange reaction of the bisketal (**20**) with acetone under the same condition as that for **9** from **8** afforded an undesired monoketal (**22**) as a sole product in 94% yield, which was readily obtained also by the direct ketalization of **19** using an equimolar amount of ethylene glycol. The contrasting behavior of the deketalization between these two systems would be attributable to both the difference in steric factors derived from 1,3-tetra- and 1,3-dimethylene bridge attached to the cyclohexanone system and that in stability of the tetragonal ketal system between the cycloheptane and cyclopentane system. The suggestion was also supported by the fact that the reaction period needed for the completion of the bisketalization of **4** was about ten times as long as that for **19**. The overall yield from **19** to the target ketone is *ca.* 40%. The structural confirmation of **2** was performed by an alternative synthesis.[7]

9) A chemical shift of the C_7-atom in the cb conformation of the 3-endo-substituted bicyclo[3.3.1]nonane system has been reported to show appreciable shielding: see, for example, J.R. Wiseman and H.O. Krabbenhoft *J. Org. Chem.*, **40**, 3222 (1976); J. A. Peters, J.M. van der Toorn, and H. van Bekkum, *Tetrahedron*, **33**, 349 (1977).

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 in $CDCl_3$ 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, bs=broad singlet, m=multiplet, arom=aromatic. The 22.63 MHz ^{13}C-NMR spectra were measured for the solution in CCl_4 or in $CDCl_3$ 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. Column chromatography was performed on Mallinckrodt silicic acid. All the organic extracts were dried over anhydrous magnesium sulfate prior to evaporation.

The *endo*-benzoylbicyclo[3.n.1]alkanones (**4**,[10] **12a**, **19a**) were synthesized following the procedure of Stetter, *et al.*[5a] starting from the corresponding *N*-cycloalkenylpyrrolidines.

8-*exo*-Benzoylbicyclo[4.3.1]decan-10-one (7)——This compound was prepared by both base- and acid-catalyzed epimerization of the corresponding *endo* compound (**4**).

a) To a solution of sodium (0.05 g) in dry EtOH (50 ml) was added 2.54 g of *endo* compound (**4**). The mixture was heated under reflux for 3 hr, allowed to cool, and neutralized with dil. HCl. The ethanol was removed, and the resulting residue was extracted with benzene (20 ml×3). The combined extract was washed with water and evaporated to give a colorless solid, which was chromatographed on silica gel in $CHCl_3$ to give **7** (2.06 g, 81%) as colorless crystals, mp 67—68°. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2930, 2865, 1718, 1690, 1452, 1268, 1208, 698. ^{1}H-NMR (CCl_4, 90 MHz) δ: 7.28—8.00 (5H, m, arom H), 3.97 (1H, m, >CHCO-), 2.60—2.90 (2H, bs, C_1-, C_6-H), 1.20—2.45 (12H, m, ring methylene). *Anal.* Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.33; H, 7.91.

b) A mixture of **4** (2.54 g), *p*-toluenesulfonic acid (0.15 g), and benzene (50 ml) was heated under reflux for 8 hr, allowed to cool, neutralized with satd. $NaHCO_3$, and washed with water. Removal of the solvent and subsequent purification gave **7** (2.03 g, 80.0%) as colorless crystals, mp 67—68°.

3-*exo*-Benzoylbicyclo[3.3.1]nonan-9-one (12b)——This compound was prepared by epimerization of **12a** in exactly the same methods as those for **7** from **4** as colorless crystals, mp 87° (lit., [5a] 85—86°).

3-*exo*-Benzoylbicyclo[3.2.1]octan-8-one (19b)——This compound was obtained by distillation of **19a** at 200°, as well as by epimerization using base or acid, as colorless crystals, mp 106—107°. IR ν_{max}^{KCl} cm^{-1}: 2960, 2930, 2890, 2870, 1749, 1670, 1595, 1580, 1450, 1376, 1276, 1219, 1187, 1176, 766, 700. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 7.30—8.00 (5H, m, atom H), 4.00 (1H, m, >CHCO-), 1.75—2.90 (10H, m, C_1-, C_5-H and ring methylene). *Anal.* Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.04. Found: C, 79.12; H, 7.30.

8-Benzoylbicyclo[4.3.1]decan-10-one 8α,10-Bisethylene Ketal (8)——A mixture of diketone (**4**, 5.12 g), ethylene glycol (5.0 g), *p*-toluenesulfonic acid (0.5 g), and dry benzene (80 ml) was heated under reflux by use of a Dean-Stark water separator for 72 hr. The cooled solution was washed with satd. $NaHCO_3$ and then with water. Removal of the solvent gave a colorless solid, which on recrystallization from EtOH gave **8** (6.55 g, 95.2%) as colorless crystals, mp 99—100°. IR ν_{max}^{KBr} cm^{-1}: 2930, 2880, 1448, 1223, 1183, 1103, 1049, 1030, 981, 710. MS *m/e*: 344 (M^+, 5%). ^{1}H-NMR (60 MHz, CCl_4) δ: 7.27 (5H, bs, arom H), 3.40—4.10 (8H, m, $-CH_2O-$), 1.00—2.30 (15H, m, C_1-, C_6-, C_8-H and ring methylene). *Anal.* Calcd. for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19. Found: C, 73.22; H, 8.19.

8-Benzoylbicyclo[4.3.1]decan-10-one 8α-Ethylene Ketal (9)——A mixture of bisketal (**8**, 7.5 g), *p*-toluenesulfonic acid (0.2 g), and acetone (50 ml) was stirred at room temperature for 3 hr. To the solution, satd. $NaHCO_3$ (50 ml) was added, and the acetone was removed under reduced pressure. The resulting aqueous residue was extracted with benzene (20 ml×3), and the combined organic extract was washed with water. Removal of the solvent gave a colorless solid, which on recrystallization from EtOH gave **9** (6.30 g, 96.3%) as colorless crystals, mp 89—90°. IR ν_{max}^{KCl} cm^{-1}: 2925, 1710, 1451, 1191, 1039, 1027, 746, 703. ^{1}H-NMR (60 MHz, CCl_4) δ: 7.10—7.50 (5H, m, arom H), 3.55—4.07 (4H, m, $-CH_2O-$), 2.35—2.80 (2H, m, C_1-, C_6-H), 1.10—2.10 (13H, m, C_8-H and ring methylene). MS *m/e*: 300 (M^+, 2%), 149 (base peak). *Anal.* Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 76.11; H, 8.06.

Bicyclo[4.3.1]decan-8-yl Phenyl Ketone Ethylene Ketal (10)——A mixture of **9** (5.4 g), 85% hydrazine hydrate (4 ml), potassium hydroxide (4.0 g), and ethylene glycol (40 ml) was heated at 130° for 3 hr and then at 210° for 4 hr, during which time the water formed and excess hydrazine were removed. To the cooled solution, ice-water (100 ml) was added, and the resulting mixture was extracted with benzene (30 ml×3). The extract was washed with water and evaporated to give a colorless solid, which on recrystallization from

10) The yield of **4** was improved by use of the *N*-cycloheptenylpyrrolidine which was freshly prepared and distilled just before use; 28.5% (lit.,[5a] 11%).

EtOH gave **10** (5.0 g, 97.1%) as colorless crystals, mp 52—53°. IR ν_{max}^{KBr} cm^{-1}: 2902, 2854, 1448, 1209, 1188, 1049, 995, 705. ^{1}H-NMR (60 MHz, CCl_4) δ: 7.20—7.55 (5H, m, arom H), 3.59—3.99 (4H, m, $-CH_2O-$), 1,00—2.40 (17H, m, C_1-, C_6-, C_8-H and ring methylene). MS *m/e*: 286 (M^+, 2%), 149 (base peak). GLC: retn. time, 5.0 min. (column temp., 170°). *Anal.* Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.52; H, 9.13.

Bicyclo[4.3.1]decan-8-yl Phenyl Ketone (11)——A mixture of **10** (2.7 g), *p*-toluenesulfonic acid (0.3 g), and acetone (30 ml) was heated under reflux for 8 hr. To the cooled solution, satd. $NaHCO_3$ was added, and the acetone was removed. The resulting residue was extracted with benzene (15 ml×3), and the combined extract was washed with water. Removal of the solvent gave a pale yellow oil, which on distillation gave **11** (2.12 g, 92.8%) as colorless oil, bp 160°/0.5 mmHg. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2925, 2865, 1675, 1598, 1582, 1450, 1275, 1206, 690. ^{1}H-NMR (90 MHz, CCl_4) δ: 7.31—8.00 (5H, arom H), 3.63 (1H, m, >CHCO–), 2.20 (2H, bs. C_1-, C_6-H), 1.25—2.00 (14H, m, ring methylene). ^{13}C-NMR (CCl_4) δ: 200.93 (benzoyl ketone), 136.52, 131.80, 128.09, 127.89 (arom C; α, *para*, *ortho*, and *meta* position in order), 37.71 (C_8), 35.14 and 34.67 (C_2, C_5, C_7, C_9) 31.10 (C_{10}), 30.15 (C_1, C_6), 27.93 (C_3, C_4). GLC: retn. time, 4.4 min. (column temp., 170°). *Anal.* Calcd. for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.11; H, 9.15.

Bicyclo[4.3.1]decan-8-one (3)——To a mixture of **11** (2.4 g), potassium *tert*-butoxide (1.2 g), and *tert*-butanol (1.2 g), 15 ml of hexamethylphosphoric triamide and 2.7 ml of *tert*-butanol were added. The resulting mixture was saturated with dry oxygen under stirring at room temperature. After the reaction was completed, 80 ml of water was added, and the mixture was extracted with benzene (20 ml×3). The extract was washed with water and evaporated to give a waxy solid, which on sublimation gave **3** (0.79 g, 52.4%) as colorless crystals, mp 26—29°. IR $\nu_{max}^{CCl_4}$ cm^{-1} 2925, 2852, 1718, 1455, 1448, 1216, 909. ^{1}H-NMR (90 MHz, CCl_4) δ: 2.15—2.46 (6H, m, C_1-, C_6-, C_7- C_9-H), 1.30—2.00 (10H, m, C_2-, C_3-, C_4-, C_5, C_{10}-H). *Anal.* Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.51; H, 10.66.

3-Benzoylbicyclo[3.3.1]nonan-9-one 3α,9-Bisethylene Ketal (13)——A mixture of **12a** (24.2 g), ethylene glycol (20 g), *p*-toluenesulfonic acid (0.5 g) and dry benzene (200 ml) was heated under reflux by use of a Dean–Stark water separator for 72 hr. Work-up in a manner similar to that for **8** from **4** gave a colorless solid, which on recrystallization from EtOH gave **13** (31.0 g, 93.9%) as colorless crystals, mp 195°. IR ν_{max}^{KBr}cm^{-1}: 2970, 2930, 2885, 1445, 1212, 1190, 1128, 1110, 1050, 1029, 989, 952, 934, 917, 708. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 7.18—7.52 (5H, m, arom H), 3.55—4.16 (4H, m, $-CH_2O-$), 3.91 (4H, s, $-CH_2O-$ at C_9). *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.80; H, 7.93.

3-Benzoylbicyclo[3.3.1]nonan-9-one 9-Dithioethylene Ketal (14)——A mixture of **12a** (9.7 g), ethanedithiol (5.0 g), *p*-toluenesulfonic acid (0.5 g), and $CHCl_3$ (50 ml) was stirred at room temperature for 24 hr. To the solution, 20% aq. NaOH (100 ml) was added and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (20 ml×3). The combined organic phase was washed with water (10 ml×3) and evaporated to give a colorless solid, which on recrystallization from EtOH gave **14** (11.9 g, 93.3%) as colorless crystals, mp 136—137°. IR ν_{max}^{KCl} cm^{-1}: 2950, 2920, 1860, 1677, 1448, 1245, 1240, 960, 700. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 7.28—8.00 (5H, m, arom H), 4.06 (1H, m, >CHCO–), 3.27 (4H, s, $-CH_2S-$), 1.20—2.80 (12H, m, C_1-, C_5-H and ring methylene). *Anal.* Calcd. for $C_{18}H_{22}OS_2$: C, 67.91; H, 6.97. Found: C, 67.58; H, 7.01.

3-Benzoylbicyclo[3.3.1]nonan-9-one 3α-Ethylene,9-Dithioethylene Ketal (15)——A mixture of **14** (3.18 g), ethylene glycol (1.0 g), *p*-toluenesulfonic acid (0.2 g), and dry benzene (30 ml) was heated under reflux by use of a Dean–Stark water separator for 12 hr. Work-up in a manner similar to that for **8** from **4** gave a colorless solid, which on recrystallization from EtOH gave **15** (3.45 g, 95.3%) as colorless crystals, mp 178—180°. IR ν_{max}^{KCl} cm^{-1}: 2925, 2892, 1448, 1189, 1043, 1030, 1011, 956, 704. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 7.18—7.50 (5H, m, arom H), 3.62—4.10 (4H, m, $-CH_2O-$), 3.18 (4H, s, $-CH_2S-$), 1.30—2.80 (13H, m, C_1-C_3-, C_5-H and ring methylene). *Anal.* Calcd. for $C_{20}H_{26}O_2S_2$: C, 66.28; H, 7.23. Found: C, 66.52; H, 7.25.

Bicyclo[3.3.1]nonan-3-yl Phenyl Ketone Ethylene Ketal (16)——A mixture of **15** (3.0 g), W-2 Raney nickel (2.0 g), and dry EtOH (50 ml) was heated under gentle reflux for 6 hr. The catalyst was filtered off and washed thoroughly with EtOH. Removal of the solvent gave a colorless solid, which on recrystallization from EtOH–H_2O (5:1) gave **16** (2.1 g, 93.2%) as colorless crystals, mp 114—115°. IR ν_{max}^{KCl} cm^{-1}: 2955, 2880, 2850, 1450, 1218, 1190, 1180, 1053, 1045, 1030, 998, 976, 705. ^{1}H-NMR (60 MHz, CCl_4) δ: 7.15—7.50 (5H, bs, arom H), 3.57—4.05 (4H, m, $-CH_2O-$), 1.30—2.78 (15H, m, C_1-, C_3-, C_5- H and ring methylene). *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.24; H, 8.87.

Bicyclo[3.3.1]nonan-3-yl Phenyl Ketone (17)——A mixture of **16** (2.0 g), *p*-toluenesulfonic acid (0.15 g), and acetone (20 ml) was heated under reflux for 8 hr, and worked up in a manner similar to that for **11** from **10** to give a pale yellow oil, which on distillation gave **17** (1.55 g, 92.5%) as colorless oil, bp 140°/0.5 mmHg. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2918, 1685, 1447, 1296, 1240, 1204, 1178, 1008, 950, 693, 664. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 7.31—8.00 (5H, m, atom H), 3.75—4.23 (1H, m, >CHCO–), 1.25—2.70 (14H, m, C_1-, C_5-H, and ring methylene). ^{13}C-NMR ($CDCl_3$) δ: 201.23 (benzoyl ketone), 136.75, 132.58, 128.51, 128.21 (arom C; α, *para*, *ortho*, and *meta* position in order), 41.45 (C_3), 34.28 (C_2, C_4, C_9), 31.09 (C_6, C_8), 27.81 (C_1, C_5), 22.61 (C_7). GLC: retn. time, 10 min. (column temp., 160°). *Anal.* Calcd. for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 83.81; H, 8.76.

Bicyclo[3.3.1]nonan-3-one (1)——To a mixture of **17** (2.3 g), potassium *tert*-butoxide (1.2 g), and *tert*-butanol (1.2 g), 15 ml of hexamethylphosphoric triamide and 2.7 ml of *tert*-butanol were added. The resulting mixture was saturated with dry oxygen under stirring at room temperature. Work-up in a manner similar to that for **3** from **11** gave a waxy solid, which on sublimation gave **1** (1.0 g, 54.2%) as colorless crystals, mp 173—175° (lit.,[6] 170—176°).

3-Benzoylbicyclo[3.2.1]octan-8-one 3α,8-Bisethylene Ketal (20)——A mixture of diketone (**19a**, 24.2 g), ethylene glycol (15 g), *p*-toluenesulfonic acid (0.5 g), and dry benzene (200 ml) was heated under reflux by use of a Dean-Stark water separator for 8 hr. Work-up in a manner similar to that for **8** from **4** gave a colorless solid, which on recrystallization from EtOH gave **20** (30.0 g, 96.6%) as colorless crystals, mp 127°. IR ν_{max}^{KBr} cm^{-1}: 2950, 2885, 1360, 1221, 1193, 1159, 1116, 1099, 1059, 1040, 1022, 972, 947, 758, 715. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 7.15—7.50 (5H, m, arom H), 3.60—4.08 (8H, m, $-CH_2O-$), 1.20—2.30 (11H, m, C_1-, C_3-, C_5-H, and ring methylene). *Anal.* Calcd. for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65. Found: C, 72.31; H, 7.65.

3-Benzoylbicyclo[3.2.1]octan-8-one 8-Ethylene Ketal (22)——a) From **20** by Selective Deketalization: A mixture of the bisketal (**20**, 3.16 g), *p*-toluenesulfonic acid (0.1 g) and acetone (20 ml) was stirred for 6 hr. Work-up in a manner similar to that for **9** from **8** gave a colorless solid, which on recrystallization from EtOH gave **22** (2.62 g, 96.3%) as colorless crystals, mp 118°. IR ν_{max}^{KCl} cm^{-1}: 2925, 1690, 1365, 1212, 1100, 1090, 1020, 1007, 989, 699. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 7.30—8.00 (5H, m, arom H), 3.93 (4H, s, $-CH_2O-$), 3.55 (1H, m, >CHCO-), 1.45—2.45 (10H, m, C_1-, C_5-H, and ring methylene). MS *m/e*: 272 (M^+, 50%). *Anal.* Calcd. for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.88; H, 7.41.

b) From **19a** by Direct Ketalization: A mixture of the diketone (**19a**, 4.56 g), ethylene glycol (1.4 g), *p*-toluenesulfonic acid (0.1 g), and dry benzene (80 ml) was heated under reflux by use of a Dean-Stark water separator for 8 hr. Work-up in a manner similar to that for **8** from **4** gave a colorless solid, which on recrystallization from EtOH gave **22** (5.2 g, 95.6%) as colorless crystals, mp 117—118°

3-Benzoylbicyclo[3.2.1]octan-8-one 8-Dithioethylene Ketal (23)——A mixture of diketone (**19a**, 11.4 g), ethanedithiol (5.6 g), *p*-toluenesulfonic acid (0.5 g), and $CHCl_3$ (50 ml) was stirred at room temperature for 24 hr. Work-up in the same manner as that for **14** from **12a** gave a colorless solid, which on recrystallization from EtOH gave **23** (14.2 g, 93.4%) as colorless crystals, mp 144—145°. IR ν_{max}^{KBr} cm^{-1}: 2960, 2875, 1675, 1450, 1358, 1225, 970, 695. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 7.35—7.85 (5H, m, arom H), 3.23 (4H, s, $-CH_2S-$), 1.55—2.70 (10H, m, C_1-, C_5-H, and ring methylene). *Anal.* Calcd. for $C_{17}H_{20}OS_2$: C, 67.09; H, 6.62. Found. C, 67.08; H, 6.77.

3-Benzoylbicyclo[3.2.1]octan-8-one 3α-Ethylene,8-Dithioethylene Ketal (24)——A mixture of **23** (6.8 g), ethylene glycol (2.0 g), *p*-toluenesulfonic acid (0.3 g), and dry benzene (100 ml) was heated under reflux by use of a Dean-Stark water separator for 12 hr. Work-up in a manner similar to that for **8** from **4** gave a colorless solid, which on recrystallization from EtOH gave **24** (6.6 g, 96.1%) as colorless crystals, mp 107°. IR ν_{max}^{Nujol} cm^{-1}: 2955, 1454, 1371, 1229, 1240, 1159, 1059, 1024, 1018, 988, 968, 752, 716. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 7.15—7.45 (5H, m, arom H), 3.55—4.15 (4H, m, $-CH_2O-$), 3.18 (4H, s, $-CH_2S-$), 1.25—2.35 (11H, m, C_1-, C_3-, C_5-H, and ring methylene). MS *m/e*: 348 (M^+, 2%), 149 (base peak). *Anal.* Calcd. for $C_{19}H_{24}O_2S_2$: C, 65.50; H, 6.94. Found: C, 65.28; H, 7.02.

Bicyclo[3.2.1]octan-3-yl Phenyl Ketone Ethylene Ketal (25)——A mixture of **24** (3.5 g), W-2 Raney nickel (3.0 g), and dry EtOH (50 ml) was heated under gentle reflux for 6 hr. The catalyst was filtered off and washed thoroughly with EtOH. Removal of the solvent gave a colorless solid, which on recrystallization from EtOH gave **25** (2.4 g, 92.5%) as colorless crystals, mp 79—80°. IR ν_{max}^{KBr} cm^{-1}: 2950, 2925, 2878, 1450, 1232, 1184, 1062, 985, 744, 670, 649. MS *m/e*: 258 (M^+, 2%), 149 (base peak). ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 7.15—7.50 (5H, m, arom H), 3.55—4.15 (4H, m, $-CH_2O-$), 1.10—2.50 (13H, C_1-, C_3-, C_5-H, and ring methylene). *Anal.* Calcd. for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.01; H, 8.60.

Bicyclo[3.2.1]octan-3-yl Phenyl Ketone (26)——A mixture of **25** (1.84 g), *p*-toluenesulfonic acid (0.3 g), and acetone (30 ml) was heated under reflux for 8 hr. Work-up in a similar manner to that for **11** from **10** gave a pale yellow oil, which on distillation gave **26** (1.47 g, 96.3%) as colorless crystals, mp 43—43.5° (bp 120°/1 mmHg). IR ν_{max}^{neat} cm^{-1}: 2920, 2855, 1675, 1592, 1578, 1440, 1366, 1280, 1258, 1213, 1177, 985, 977, 766, 684. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 7.30—8.05 (5H, m, arom H), 3.62 (1H, m, >CHCO-), 1.40—2.55 (12H, m, C_1-, C_5-H, and ring methylene). MS *m/e*: 214 (M^+, 5%). GLC: retn. time, 5.8 min. (column temp., 160°). *Anal.* Calcd. for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.09; H, 8.53.

Bicyclo[3.2.1]octan-3-one (2)——To a mixture of **26** (2.1 g), potassium *tert*-butoxide (1.2 g), and *tert*-butanol (1.2 g), 15 ml of hexamethylphosphoric triamide and 2.7 ml of *tert*-butanol were added. The resulting mixture was saturated with dry oxygen under stirring at room temperature. Work-up in a manner similar to that for **3** from **11** gave a waxy solid, which on sublimation gave **2** (0.65 g, 50.3%) as colorless crystals, mp 136—137° (lit.,[7] 135—136°).