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Bicyclo[3.3.1]nonanes as Synthetic Intermediates. IV.[1] Behavior of Bicyclo[3.*n*.1]alkan-3-ones toward the Baeyer-Villiger Oxidation

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The Baeyer–Villiger oxidation of bicyclo[3.*n*.1]alkan-3-ones and related systems is described. Bicyclo[3.3.1]nonan-2-one (**8**) was oxidized into the corresponding lactone, which was found to be converted into the *cis*-1,3-disubstituted cyclohexane system by the subsequent methanolysis. Meanwhile, the 3-oxo system (**2**) manifested an anomalous inactivity against the oxidation. The "backside steric hindrance" caused by the axial (*endo*) proton at C-7 was postulated as the origin of the inactivity. The differential reactivity of the ketones in the Baeyer–Villiger reaction of the bicyclic systems (**2**, **3**, **4**) enabled the regiospecific lactonization of the bicyclic diketones (**17**, **18**, **19**) into the lactones (**37**, **38**, **39**), which would be important precursors for specifically substituted medium-sized lactones, to be achieved.

Keywords——Baeyer–Villiger Oxidation; bicyclo[3.*n*.1]alkan-3-one; twin-chair conformation; "backside" steric hindrance; "hard acid"; "soft nucleophile"; tricyclo-[5.3.1.$0^{3,8}$]undecan-5-one; tetracyclo[5.4.0.$0^{3,9}$.$0^{6,8}$]undecan-5-one; bridged lactone; *m*-chloroperbenzoic acid

There has been reported the utility of the bridged bicyclic compounds as important synthons[3] for the syntheses of specifically substituted rings. In the course of our exploratory study on applicability of the bicyclo[3.3.1]nonanone system (**1**) to the natural product syntheses, one of us previously examined the Baeyer–Villiger oxidation of **1** ($X=NSO_2Ph$) and discovered an anomalous inactivity of the 3-oxo system.[4] This inactivity was also observed in the case of the carbobicyclic bicyclo[3.3.1]nonan-3-one (**2**) and reported in a preliminary form.[5] The present paper deals with some novel steric factors operating on the Baeyer–Villiger oxidation of various oxo-bicyclic systems involving bicyclo[4.3.1]decan-8-one (**3**), bicyclo[3.2.1]octan-3-one (**4**), and related systems. As for the materials employed in this study, we had already reported the improved synthetic methods in the preceding papers.[1,6]

The Baeyer-Villiger Oxidation of Bicyclo[3.*n*.1]alkan-3-ones

Treatment of bicyclo[4.3.1]decan-8-one (**3**) with *m*-chloroperbenzoic acid (MCPBA) in dichloromethane at room temperature converted **3** into the corresponding bicyclic lactone

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[1] Part III: T. Momose and O. Muraoka, *Chem. Pharm. Bull.* (Tokyo), 26, 2589 (1978).

[2] Location: *133-1, Yamada-kami, Suita, Osaka 565, Japan.*

[3] See, for example; *a*) A. Murai, H. Murase, H. Matsue, and T. Masamune, *Tetrahedron Lett.*, **1977**, 2507; *b*) P.A. Grieco, C.S. Pogonowsk, S.D. Burke, M. Nishizawa, M. Miyashita, Y. Masaki, C.-L.J. Wang, and G. Majetich, *J. Am. Chem. Soc.*, **99**, 4111 (1977); *c*) H.C. Brown and C.D. Pfaffenberger, *Tetrahedron*, **31**, 925 (1975); *d*) H. Tanaka and S. Torii, *J. Org. Chem.*, **40**, 462 (1975); *e*) R.C. Kelly and I. Schletter, *J. Am. Chem. Soc.*, **95**, 7156 (1973); *f*) R.B. Woodward, J. Gosteli, I. Ernest, R.J. Friary, G. Nestler, H. Raman, R. Sitrin, Ch. Suter, and J.K. Whitesell, *ibid.*, **95**, 6853 (1973); *g*) E.J. Corey and G. Moinet, *ibid.*, **95**, 6831 (1973).

[4] T. Momose and C.H. Eugster: unpublished work.

[5] T. Momose, S. Atarashi, and O. Muraoka, *Tetrahedron Lett.*, **1974**, 3697.

[6] *a*) T. Momose and O. Muraoka, *Chem. Pharm. Bull.* (Tokyo), **26**, 288 (1978); *b*) *Idem*, *ibid.*, **26**, 2217 (1978).

(**5**) in good yield, but with markedly slow rate. The structural confirmation was performed on the basis of its spectral evidences. The proton magnetic resonance (^{1}H-NMR) spectrum of **5** shows a two-proton doublet at 4.08 ppm attributing to the methylene protons adjacent to the acyloxyl oxygen of the lactone formed. A strong band at 1739 cm^{-1} in its infrared (IR) spectrum along with the disappearance of the one at 1718 cm^{-1} also indicates the complete lactonization into **5**. Treatment of bicyclo[3.2.1]octan-3-one (**4**) with MCPBA under the same condition also gave the corresponding lactone (**6**) in 81% yield,[7] though somewhat

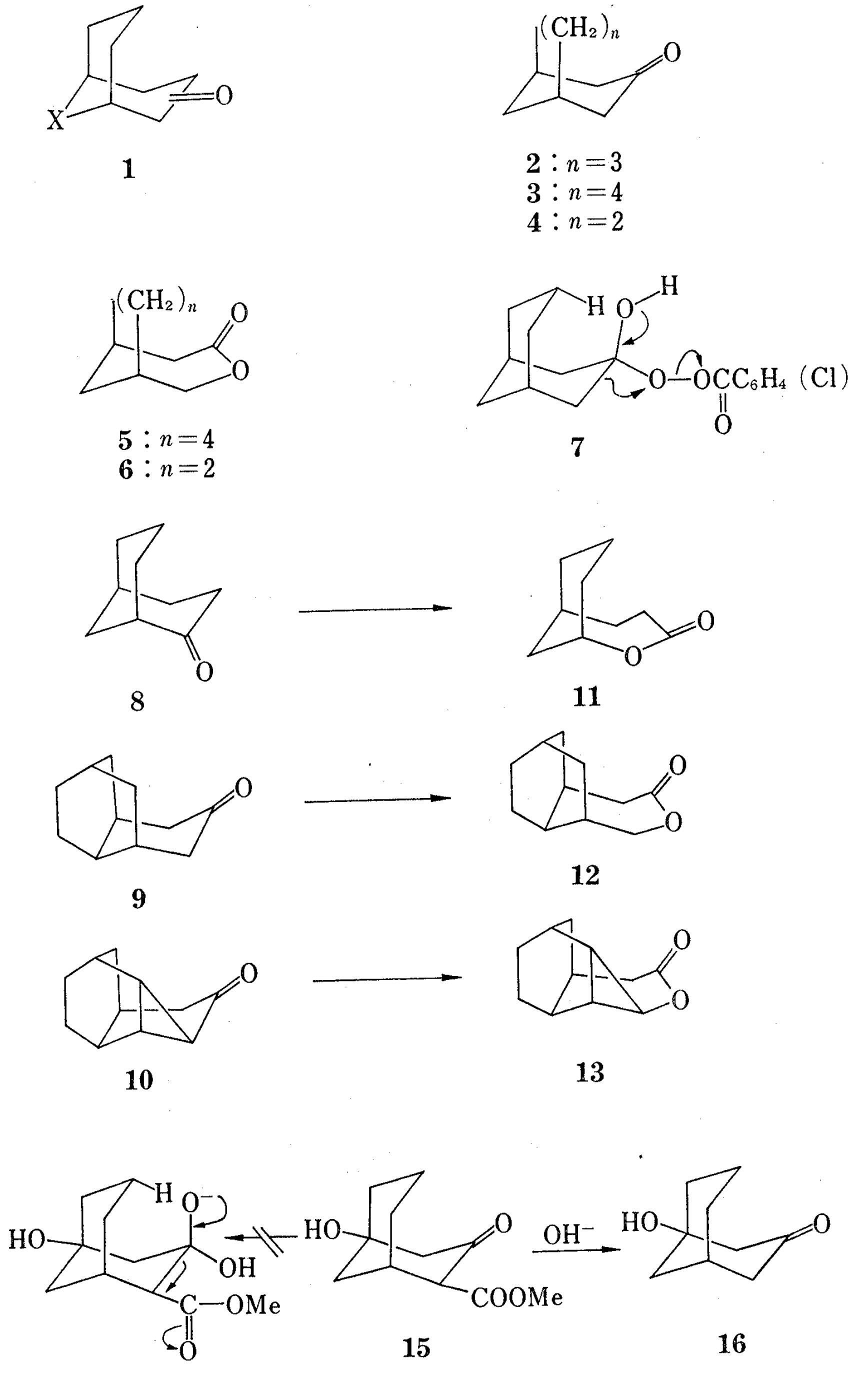

Chart 1

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[7] The reaction has been reported to be furnished by use of a reaction period of a week and with careful control of the vapor pressure in the reaction vessel: [A.J. Playtis and J.D. Fissekis, *J. Org. Chem.*, **40**, 2488 (1975)]. However, in the present experiment, a period of 56 hrs was found sufficient for the reaction to come to completion with no special control of the reaction.

slow in rate as compared to the run upon cyclohexanone, while the same procedure toward its homologue bicyclo[3.3.1]nonan-3-one (**2**) resulted in complete recovery of the starting material. Even in the presence of the catalyst *p*-toluenesulfonic acid or under the condition of gentle reflux, the reaction did not proceed to any extent.

Bicyclo[3.3.1]nonane and some of its derivatives have been reported to exist in a somewhat flattened double chair (cc) conformation.8) For the carbonyl center to be attacked by the bulky MCPBA, the attack by the nucleophile must be from the *exo* side of the carbonyl group in this conformation. So, the anomalous inactivity of **2** against the Baeyer–Villiger oxidation can be explained in terms of the backside steric hindrance by the axial (*endo*) hydrogen atom at C-7, which operates on the stage of formation of the tetragonal Baeyer–Villiger intermediate (**7**). Such a steric constraint over the "hard acid" carbonyl carbon often exert a retarding effect on attack especially by "soft nucleophiles" as encountered at the marked slow rate of the metal hydride reduction of **2**9) or the 7-oxa-ketone.10) In order to justify the validity of this assumption, we examined also the behavior of some of its analogues, bicyclo[3.3.1]nonan-2-one (**8**)11) and tricyclo[5.3.1.0^{3,8}]undecan-5-one (**9**),12) both of which are devoid of such a hindrance as encountered with **2**, and also of tetracyclo[5.4.0.0^{3,9}.0^{6,8}]undecan-5-one (**10**),12) an important precursor for **9**, toward the Baeyer–Villiger oxidation. Each gave the corresponding lactones, **11**, **12**, and **13**, in good yields, respectively. The lactonization of **8** and **10** proceeded specifically to give 2-oxabicyclo[4.3.1]decan-3-one (**11**) and 6-oxatetracyclo[6.4.0.0^{3,10}.0^{7,9}]dodecan-5-one (**13**), respectively, the structural confirmation of which was performed on the basis of their spectral evidences. The ^{1}H-NMR spectrum of **11** displays a one-proton multiplet at 4.45 ppm attributing to the methine proton at C-1, adjacent to the ring oxygen of the lactone formed, the result indicating that the migration occurred at the tertiary carbon C-1, and not at the methylene C-3. The ^{1}H-NMR spectrum of **13** shows a one-proton triplet at 3.84 ppm and a two-proton multiplet in the region of 2.45—2.84, the feature indicating that the migratory group was the methine carbon of the cyclopropane ring.13) Meanwhile, the ^{1}H-NMR spectrum of **12** displays a two-proton doublet, at 4.05 ppm, due to the methylene protons next to the ring oxygen of the lactone, which was in good accord with the corresponding signals for the analogous lactones, **5** and **6**, obtained above. The success in lactonization of these systems proved the validity of the assumption postulated as an origin of the anomalous inactivity of **2** against the Baeyer–Villiger oxidation. And in addition, the lactone (**11**) was transformed into the *cis*-1/3 hydroxy-

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8) W.A.C. Brown, G. Eglinton, J. Martin, W. Parker, and G.A. Sim, *Proc. Chem. Soc.* (London), **1964**, 57; W.A.C. Brown, J. Martin, and G.A. Sim, *J. Chem. Soc.*, **1965**, 1844; M. Dobler and J.D. Dunitz, *Helv. Chim. Acta*, **47**, 695 (1964); I. Laszlo, *Rec. Trav. Chim. Pays-Bas*, **84**, 251 (1965); N.C. Webb and M.R. Becker, *J. Chem. Soc.* (*B*), **1967**, 1317; G.J. Gleicher and P.v.R. Schleyer, *J. Am. Chem. Soc.*, **89**, 582 (1967).

9) The failure of the oxidation of **2** caused by the backside steric constraint would also be attributed to the softness of the perbenzoate anion, because the reduction of **2** by the "soft hydride" conjugate sodium borohydride is retarded [facile conversion of **2** into *endo*-bicyclo[3.3.1]nonan-3-ol has been reported: J.P. Schaefer, J.C. Lark, C.A. Flegal, and L.M. Honig, *J. Org. Chem.*, 32, 1372 (1967), but upon reexamination of the reduction, both rather drastic reaction condition and a long reaction period were found necessary for the reaction to come to completion (see Experimental)] while that by the "hard" conjugate lithium aluminum hydride [the condition of reflux in tetrahydrofuran is needed for the reduction: see M. Fisch, S. Smallcombe, J.C. Gramain, M.A. McKervey, and J.E. Anderson, *J. Org. Chem.*, **35**, 1886 (1970)] or the oxime formation [H.K. Hall, Jr., *J. Org. Chem.*, **28**, 3213 (1963)] is conducted rather smoothly.

10) The inactivity of the 9-aza-3-oxabicyclo[3.3.1]nonan-7-one system against the reduction by sodium borohydride has been reported: see T. Masamune, H. Matsue, H. Murase, and M. Ono, Symposium Papers of 18th Symposium on the Chemistry of Natural Products, Kyoto 1974, p. 148.

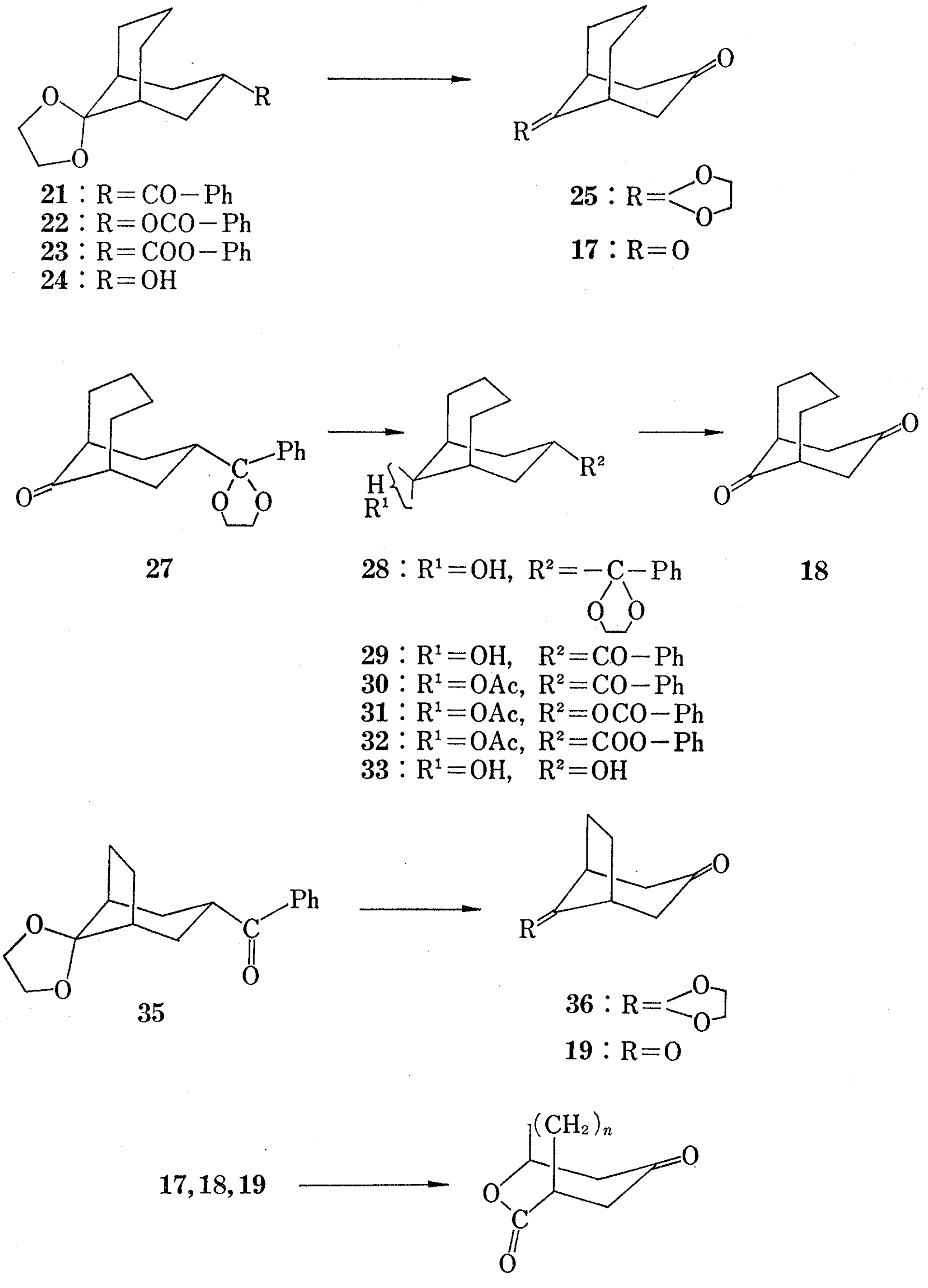
11) M. Hartmann, *Z. Chem.*, **6**, 182 (1966).

12) A. Krantz and C.Y. Lin, *J. Am. Chem. Soc.*, **95**, 5662 (1973).

13) The migratory aptitude is reversed compared to that in the usual Baeyer–Villiger reaction and may be attributed to the uneven ring strain at α- and α′-ketonic carbon in the transition state.

ester (**14**) by methanolysis, the sequence demonstrating an example of a stereoselective conversion of the bicyclo[3.3.1]nonane system into the specifically substituted cyclohexane system.

The steric hindrance caused by the axial proton at the C-7 position was also encountered on the attempted cleavage of methyl 5-hydroxy-3-oxobicyclo[3.3.1]nonane-2-carboxylate (**15**)[6a)] by treatment with 20% aq. KOH, which would be a condition for the acid cleavage. Owing to this effect, the ketonic cleavage predominated to give exclusively 1-hydroxybicyclo-[3.3.1]nonan-3-one (**16**), which could also be obtained by treatment of **15** with 5% ethanolic KOH.[6a)]



21 : R=CO−Ph
22 : R=OCO−Ph
23 : R=COO−Ph
24 : R=OH

25 : R= (dioxolane)
17 : R=O

27

28 : R^1=OH, R^2=−C−Ph (O O)
29 : R^1=OH, R^2=CO−Ph
30 : R^1=OAc, R^2=CO−Ph
31 : R^1=OAc, R^2=OCO−Ph
32 : R^1=OAc, R^2=COO−Ph
33 : R^1=OH, R^2=OH

18

35

36 : R=
19 : R=O

17,18,19

37 : n=3
38 : n=4
39 : n=2

Chart 2

The Selective Oxidation of Bicyclic Diketones

The steric factors operating upon the bicyclo[3.*n*.1]alkan-3-one system, caused either by the C-7 axial hydrogen of **2** or by di- or tetramethylene bridge of **3** or **4**, could be utilized for the regioselective oxidation of the bicyclic diketones, **17**, **18**, and **19**, into the corresponding keto lactones. The lactones would be of importance as precursors for the medium-sized lactones when subjected to methanolysis and subsequent second Baeyer–Villiger lactonization.

The diketones, **17**, **18**, and **19**, were synthesized starting from the corresponding benzoyl ketones[6b,14] as shown in Chart 2.

The Baeyer–Villiger oxidation of 3-benzoylbicyclo[3.3.1]nonan-9-one 9-ethylene ketal (**21**)[6b] gave a mixture of the benzoate (**22**) and alkanoate (**23**) in 96% yield. The ratio of the products was determined to be of *ca.* 10: 1 by the method described in a preceding paper.[1] The lithium aluminum hydride (LAH) reduction and subsequent oxidation of the resulting alcohol (**24**) with chromic acid gave a monoketal (**25**)[14] in 54% overall yield. Hydrolysis of **25** with 1N hydrochloric acid afforded the target diketone (**17**) quantitatively.

As 8-benzoylbicyclo[4.3.1]decan-10-one (**26**) did not exhibit the selectivity in its monoketalization using an equimolar amount of ethylene glycol, another keto ketal (**27**)[6b] was used as a starting material. The reduction and subsequent hydrolysis converted **27** into a benzoyl alcohol (**29**) in good yield. The structure was supported by the absorption bands, at 3490 cm^{-1} and 1688 cm^{-1} in its IR spectrum, due to the bridge hydroxyl and benzoyl, respectively. The Baeyer–Villiger oxidation of its acetate (**30**) followed by LAH reduction gave bicyclo[4.3.1]decane-8,10-diol (**33**) as a main product, which was oxidized into the target diketone (**18**) in good yield. The structural confirmation was performed by its spectral evidences.

Table I. Some Physical and Spectral Properties of the Baeyer–Villiger Products

Compd. No.	Appearance mp or bp	Reaction period (hr)	Yield (%)	Analysis (%) Calcd. (Found)		MS (M$^+$, %)	IR (cm^{-1}) (C=O)	NMR δ:
				C	H			
5	Oil 132—135/0.5	240	78	71.39 (71.01	9.52 9.59)	168(14)	1739[b]	4.08 (2H, d, *J*=3), 1.40, 2.85 (14H, m)[b]
6[d]	—	56	81	—	—	—	—	—
11	Oil 120—125/0.7	3	83	70.10 (69.97	9.15 9.04)	154(11)	1728[b]	4.45 (1H, m), 2.63 (2H, m), 1.32—2.30 (11 H, m)[b]
12	Solid mp 90—91	70	86	73.30 (73.07	8.95 8.90)	180(56)	1745[b]	4.05 (2H, d, *J*=4), 2.27 (1H, dd, *J*=16, 6), 2.50 (1H, dd, *J*=15, 2) 1.10—2.20 (12H, m)[b]
13	Oil 110—113/1.0	48	88	—	—	—	1740[b]	3.84 (1H, t, *J*=8), 2.79 (1H, dd, *J*=18, 7.5), 2.50 (1H, dd, *J*=18, 2), 0.90—2.30 (11H, m)[b]
37	Solid mp 130—131	16	89	64.27 (64.00	7.19 7.26)	168(33)	1731[a] 1705	4.70 (1H, m), 3.24 (1H, m), 2.60—3.00 (4H, m), 1.70—2.20 (6H, m)[c]
38	Oil 120—125/0.1	24	85	65.91 (65.66	7.74 7.85)	184(21)	1735[b] 1705	4.71 (1H, m), 2.48—3.25 (5H, m), 1.55—2.45 (8H, m)[c]
39	Solid mp 99—101	24	86	62.32 (62.21	6.54 6.50)	154(60)	1745[a] 1710	4.74 (1H, m), 2.40—3.20 (5H, m), 1.50—2.40 (4H, m)[c]

The spectra were determined in KBr (*a*), or in CCl_4 (*b*), or in $CDCl_3$ (*c*). *d*) See ref. 7.

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14) H. Stetter, K.-D. Rämsch, and K. Elfert, *Ann. Chem.*, **1974**, 1322.

Bicyclo[3.2.1]octane-3,8-dione (**19**) was obtained by the oxygenation of the benzoyl ketal (**35**)[6b] with molecular oxygen and subsequent hydrolysis of the resulting monoketal (**36**) with 1N HCl.

Treatment of bicyclo[3.3.1]nonane-3,9-dione (**17**) with MCPBA gave exclusively a bridged lactone (**37**) in 89% yield. The structural confirmation of **37** was performed by its spectral evidences. The two strong absorption bands at 1731 cm^{-1} and 1705 cm^{-1} could be attributed to the lactone formed and to the ordinary seven-membered ring carbonyl function left unchanged, respectively. An observed high deshielding shift of the signal of the methine proton at C-1, appearing at 4.70 ppm in its ^{1}H-NMR spectrum, indicates that the lactone formed was at the bridged position. Treatment of **18** and **19** under the same condition also gave the corresponding bridged lactones, **38** and **39**, respectively. The physical and spectral properties were listed in Table I.

These keto lactones obtained by the selective oxidation would serve as important precursors for the particularly substituted medium-sized lactones structurally related to the macrolide antibiotics.

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, d=doublet, t=triplet, m=multiplet, bs=broad singlet, arom=aromatic. 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. All the organic extracts were dried over anhydrous magnesium sulfate prior to evaporation.

Materials——Bicyclo[3.*n*.1]alkan-3-one (**2**, **3**, **4**) and the monoketal of 3-benzoylbicyclo[3.*n*.1]alkanone (**21**, **27**, **35**) employed in this study were prepared by the methods described in the preceding papers.[1,6] Bicyclo[3.3.1]nonan-2-one (**8**), tricyclo[5.3.1.0^{3,8}]undecan-5-one (**9**), and tetracyclo[5.4.0.0^{3,9}.0^{6,8}]undecan-5-one (**10**) were prepared by the methods of Hartman[11] and Krantz,[12] respectively.

The Baeyer-Villiger Oxidation——The typical procedure was carried out as follows: To a solution of **8** (0.276 g, 0.002 mol) in abs. CH_2Cl_2 (8 ml) was added MCPBA (*ca.* 0.003 mol), and the reaction mixture was swirled at intervals and set aside in the dark. After completion of the reaction (3 hr) the reaction mixture was washed with a 5% sodium thiosulfate-$NaHCO_3$ solution (10 ml × 3) to remove *m*-chlorobenzoic acid and excess peracid. The washings were combined and extracted with CH_2Cl_2 (7 ml × 3), and the combined CH_2Cl_2 layer was washed with water. Removal of the solvent gave a colorless oil, which on distillation gave 2-oxabicyclo[4.3.1]decan-3-one (**11**, 0.256 g, 83.1%) as a colorless oil. The physical and spectral properties were listed in Table I.

Methyl 3-Hydroxycyclohexanepropionate (14)——A mixture of **11** (70 mg), *p*-toluenesulfonic acid (7 mg), and dry MeOH (6 ml) was heated under reflux for 3 hr. After removal of most of the MeOH under the reduced pressure, 15 ml of water was added to the residue, and the resulting mixture was extracted with benzene (5 ml × 3). The organic layer was washed with satd. $NaHCO_3$, brine, and evaporated to give an oil, which on distillation gave **14** (78 mg, 91.0%) as a colorless oil, bp 125—130°/1 mmHg. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 1747. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 3.70—3.30 (1H, m, $>C\underline{H}OH$), 3.66 (3H, s, $-COOCH_3$), 1.79 (1H, s, OH). MS *m/e*: 186 (M^+, $<1\%$). *Anal.* Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.29; H, 9.71.

Bicyclo[3.3.1]nonan-3α-ol——The method described by Schaefer, *et al.*[9] was partially modified. To a stirred solution of $NaBH_4$ (1.5 g) in MeOH (5 ml) was added dropwise a solution of **2** (0.6 g) in MeOH (4 ml) at room temperature, and the resulting mixture was heated under reflux for 30 hr, during which time, another 400 mg of $NaBH_4$ was added to the mixture portionwise every 6 hr. After completion of the reaction, the excess hydride was decomposed with water, and the mixture was extracted with ether (10 ml × 3). The extract was washed with brine and evaporated to give a colorless solid, which on sublimation gave bicyclo[3.3.1]nonan-3α-ol (0.493 g, 81.0%) as colorless crystals, mp 120—122.5° (lit.,[9] mp 121.5—124°).

1-Hydroxybicyclo[3.3.1]nonan-3-one (16)[15]——A solution of methyl 5-hydroxy-3-oxobicyclo[3.3.1]nonane-2-carboxylate (**15**,[6a] 0.339 g) and potassium hydroxide (6 g) in 50% aq. EtOH (24 ml) was heated under reflux for 4 hr, and evaporated to remove the ethanol under the reduced pressure. The aqueous residue was thoroughly extracted with CH_2Cl_2 (5 ml × 5), and the extract was washed with brine, and evap-

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[15] W.D.K. Macrosson, J. Martin W. Parker, and A. B. Penrose, *J. Chem*, *Soc*, (*C*), **1968**, 2323.

orated to afford a solid, which on sublimation gave **16** (0.166 g, 71.9%) as colorless crystals, mp 188—190° (lit.,15) 192—193°). This product was homogeneous on GLC, and its IR and ^{1}H-NMR spectra were identical with those of an authentic specimen obtained by an alternative method.6a) From the aqueous alkaline layer was obtained no isolable amount of the dicarboxylic acid after acidification with dil. H_2SO_4 followed by extraction with AcOEt.

3β-Hydroxybicyclo[3.3.1]nonan-9-one Ethylene Ketal (24)——Following the general procedure, the benzoyl ketal (21,6a) 1.43 g) was oxidized with MCPBA to give a mixture of two esters, the bicycloalkyl benzoate (22) and the phenyl carboxylate (23), in 96% yield, which was subjected to the LAH reduction without further purification.

To a stirred suspension of LAH (0.34 g) in abs. ether (50 ml) was added a solution of the Baeyer–Villiger oxidation products (1.470 g) in 10 ml of abs. ether, and the resulting mixture was stirred for 8 hr at room temperature. Work-up in a usual manner and removal of the solvent ($CHCl_3$) gave an oil, which on distillation gave **24**16) (0.538 g, 54.0% from **21**) as a colorless oil, bp 120—122°/3 mmHg. IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 3450, 2925, 1450, 1388, 1120, 1042, 1020, 980. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 4.30 (1H, m, C_3–H), 3.96 (4H, s, $-CH_2O-$), 1.20—2.30 (12H, m, C_1–, C_5–H and ring methylene). *Anal.* Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.28; H, 9.20.

Bicyclo[3.3.1]nonane-3,9-dione 9-Ethylene Ketal (25)——To a stirred solution of **24** (0.396 g) in acetone (5 ml) was added a slight excess of Jones reagent (1.2 ml) below 5°, and the stirring was continued for 15 min at room temperature. After the excess oxidant was decomposed with iso-PrOH, the reaction mixture was made alkaline with satd. $NaHCO_3$ and evaporated to remove the acetone. The aqueous residue was extracted with ether (15 ml×3), and the extract was washed with brine. Removal of the solvent gave a solid, which on recrystallization from petroleum ether afforded **25** (0.370 g, 94.4%) as colorless crystals, mp 50—52° (lit.,14) mp 50—53°).

Bicyclo[3.3.1]nonane-3,9-dione (17)——A mixture of **25** (0.392 g) and 1 N HCl (10 ml) was stirred at room temperature for 24 hr. The mixture was neutralized with satd. $NaHCO_3$ and extracted with ether. The extract was washed with brine and evaporated to give a colorless solid, which on sublimation gave **17** (0.292 g, 96.1%) as colorless crystals, mp 97—99°. IR $\nu_{\max}^{KBr}$ cm^{-1}: 2950, 1720, 1450, 1410, 1308, 1260, 1180, 1159. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 2.76 (2H, bs, C_1–, C_5–H), 1.80—2.10 (4H, m, C_2–, C_4–H), 0.80—1.70 (6H, m, C_6–, C_7–, C_8–H). MS *m/e*: 152 (M^+, 100%). *Anal.* Calcd. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 70.88; H, 8.10.

10-Hydroxybicyclo[4.3.1]dec-8β-yl Phenyl Ketone Ethylene Ketal (28)——A solution of **27**6b) (2.4 g) in 30 ml of MeOH was added dropwise to a stirred solution of 1.5 g of sodium borohydride in 30 ml of MeOH, and the stirring was continued for 8 hr at room temperature. After addition of 80 ml of water, the resulting mixture was neutralized with dil. HCl, and extracted with benzene (20 ml×4). The extract was washed with water and evaporated to give a colorless solid, which on recrystallization from EtOH gave **28** (2.21 g, 91.5%) as colorless crystals, mp 121—122°. IR $\nu_{\max}^{KBr}$ cm^{-1}: 3400, 2929, 1450, 1046, 701. ^{1}H-NMR (90 MHz, $CDCl_3$), 7.15—7.60 (5H, m, arom H), 3.60—4.05 (5H, m, $-CH_2O-$ and C_{10}–H), 1.10—2.50 (16H, m, C_{1-9}–H and OH). MS *m/e*: 242 (2%), 225 (2%), 149 (100%). *Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.23; H, 8.72.

10-Hydroxybicyclo[4.3.1]dec-8β-yl Phenyl Ketone (29)——A mixture of **28** (1.91 g) and 1 N HCl (30 ml) was stirred at room temperature for 6 hr. The solution was made alkaline with satd. $NaHCO_3$ and extracted with benzene (10 ml×3). The combined extract was washed with water and evaporated to give a colorless solid, which on recrystallization from EtOH gave **29** (1.58 g, 96.8%) as colorless crystals, mp 76—77°. IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 3490, 2925, 2855, 1688, 1451, 1205, 1060, 699, 675. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 7.80—8.12 (2H, m, arom H *ortho* position), 7.30—7.70 (3H, m, arom H *meta* and *para* position), 4.04 (1H, t, $J=5$, C_{10}–H), 3.75 (1H, m, C_8–H), 3.22 (1H, s, OH), 1.20—2.70 (14H, m, C_1–, C_5–H, and ring methylene). MS *m/e*: 258 (M^+, 13%), 105 (100%). *Anal.* Calcd. for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.82; H, 8.64.

10-Acetoxybicyclo[4.3.1]dec-8β-yl Phenyl Ketone (30)——A mixture of **29** (1.5 g), acetic anhydride (1.0 g), and pyridine (10 ml) was allowed to stand at room temperature overnight. The reaction mixture was poured into 50 ml of ice-water and extracted with benzene (15 ml×3). The combined extract was washed with dil. HCl and then with water. Removal of the solvent gave a colorless oil, which on distillation gave the acetate (**30**, 1.7 g, 97.4%) as a colorless oil, bp 138—140°/0.6 mmHg. IR $\nu_{\max}^{CCl_4}$ cm^{-1}: 2925, 1738, 1690, 1256, 1242, 1209, 1030, 694. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 7.25—8.00 (5H, m, arom H), 5.02 (1H, t, C_{10}–H), 3.74 (1H, m, C_8–H), 2.50 (2H, bs, C_1–, C_6–H), 1.20—2.30 (12H, m, ring methylene), 2.05 (3H, s, $-OCH_3$). *Anal.* Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 79.82; H, 8.13.

Bicyclo[4.3.1]decane-8β,10-diol (33)——Following the general procedure, the acetoxy ketone (30) was oxidized with MCPBA to give a mixture of two esters, the bicycloalkyl benzoate (31) and the phenyl carboxylate (32), in 92% yield, which was subjected to the LAH reduction without further purification.

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16) Benzyl alcohol and the other minor by-products were found to be readily removed by careful control of the distillation temperature.

To a stirred suspension of LAH (0.5 g) in abs. ether (50 ml) was added dropwise a solution of the Baeyer–Villiger oxidation products (1.5 g) in abs. ether (20 ml), and the resulting reaction mixture was stirred at room temperature for 8 hr. Work-up in a usual manner and removal of the solvent ($CHCl_3$) gave a colorless oil, which on distillation afforded the diol (33,[16] 0.561 g, 52.2% from **30**) as a colorless oil which solidified on standing. mp 168—170°. IR ν_{max}^{KBr} cm^{-1}: 3438, 1982, 1450, 1148. *Anal.* Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.29; H, 10.81.

Bicyclo[4.3.1]decane-8,10-dione (18)——To a stirred solution of the diol (**33**, 0.340 g) in acetone (10 ml) was added a slight excess of Jones reagent (1.2 ml), and the resulting reaction mixture was allowed to be stirred for 15 min and worked up in a manner similar to that for **25** from **24** to give a colorless oil, which on distillation gave **18** (0.300 g, 90.4%) as a colorless oil, bp 122—125°/2 mmHg. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2938, 1720, 1220. ^1H-NMR (90 MHz, CCl_4) δ: 2.68—3.00 (2H, m, C_1–, C_6–H), 1.48—2.60 (12H, m, ring methylene). *Anal.* Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.89; H, 8.62.

Bicyclo[3.2.1]octane-3,8-dione 8-Ethylene Ketal (36)——To a mixture of **35**[6b] (1.35 g), potassium *tert*-butoxide (0.6 g), and *tert*-butanol (0.6 g) were added 7.5 ml of hexamethylphosphoric triamide and 1.4 ml of *tert*-butanol. The resulting mixture was saturated with dry oxygen under stirring at room temperature. After the reaction was completed, 50 ml of water was added, and the mixture was extracted with benzene (15 ml × 3). The extract was washed with water and evaporated to give a pale yellow oil, which on distillation gave **36** (0.473 g, 52.4%) as a colorless oil, bp 120—123°/10 mmHg. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2960, 2883, 1723, 1210, 1111, 1019. ^1H-NMR (90 MHz, $CDCl_3$) δ: 3.97 (4H, s, $-CH_2O-$), 2.65—3.00 (2H, m, C_1–, C_5–H), 1.35—2.40 (8H, m, C_2–, C_4–, C_6–, C_7–H). MS *m/e*: 182 (M^+, 79%), 99 (100%). *Anal.* Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.66; H, 7.75.

Bicyclo[3.2.1]octane-3,8-dione (19)——A mixture of **36** (0.546 g) and 1 N HCl (15 ml) was stirred at room temperature for 24 hr and worked up in a manner similar to that for **17** from **25** to give a colorless solid, which on sublimation gave **19** (0.390 g, 94.2%) as colorless crystals, mp 119—120°. IR ν_{max}^{KBr} cm^{-1}: 2970, 1760, 1720, 1220, 1190, 1120, 1062, 1013. ^1H-NMR (60 MHz, $CDCl_3$) δ: 2.65—3.00 (2H, m, C_1–, C_5–H), 1.50—2.65 (8H, m, ring methylene). *Anal.* Calcd. for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.26; H, 7.36.