Stereoselective Reactions of 2-Oxabicyclo[3.3.0]hept-6-en-3-ones leading to Functionalized α-Methylene-γ-lactones and Δαβ-Butenolides

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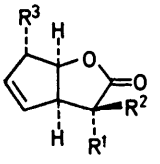
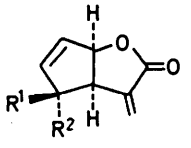
4-Bromo-4-methyl-2-oxabicyclo[3.3.0]oct-6-en-3-ones have been oxidized with peracid. The resulting epoxides suffer regioselective attack by nucleophiles at C-7. In this way, stereospecific pathways to 6-acetoxy-4-methylene-2-oxabicyclo[3.3.0]oct-7-en-3-ones (3) and (4) have been found in which the necessary dehydrobrominations are effected by triethylamine or potassium acetate and 18-crown-6. The latter reagents have been used also to form the $\Delta^{\alpha\beta}$-butenolides (26) and (27) from the bromolactones (28) and (2), respectively.

A WIDE range of biologically active α-methylene-γ-lactones have been described.[1] While it has been shown that the *exo*-methylene function plays a role of paramount importance in the cytotoxic behaviour of these molecules, neighbouring functional groups have been shown to accentuate this biological activity. In particular, an acyloxy group situated in a homoallylic position to the α-methylene moiety is often present in naturally occurring systems and it has been proposed that such a combination can give rise to molecules possessing potent cytotoxic properties.[2] In an effort to mimic such potentially useful properties of the complex natural products, we have synthesized some simple bicyclic α-methylene-γ-lactones possessing an homoallylic ester group close in space to the α-methylene function.[3]

We have described elsewhere the preparation of α-methylenelactones [4] and $\Delta^{\alpha\beta}$-butyrolactones [5] from the bromolactones (1) and (2) respectively. Herein we show that compounds (3) and (4) are readily obtained

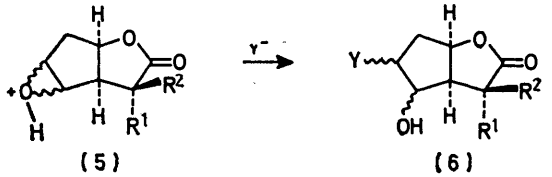


(1) R^1 = Br, R^2 = CH_3, R^3 = H
(2) R^1 = CH_3, R^2 = Br, R^3 = H
(24) R^1 = R^3 = Br, R^2 = CH_3



(3) R^1 = H, R^2 = OCOMe
(4) R^1 = OCOMe, R^2 = H

from (1) by initial electrophilic attack at the olefinic double bond. Functionalization of the olefinic bond is regulated by the adjacent lactone ring such that nucleophilic attack on derived cations, *e.g.* protonated epoxides (5) (Scheme) occurs at C-7 with very high selectivity.[6]

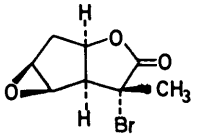


(5) (6)

SCHEME

The configurations of the substituents (OH, Y) in the oxaoctanones (6) so formed were conclusively defined by ^{1}H n.m.r. spectroscopy using double irradiation techniques where necessary.

The epoxides (7) and (8) required for the present study were formed by *m*-chloroperbenzoic acid oxidation of the lactone (1). The ratio of the epoxides formed was solvent dependent, with the *endo*-isomer (7) being formed specifically in non-polar solvents; [7] separation of epoxide mixtures was readily accomplished by chromatography over silica.



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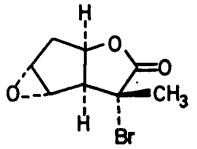
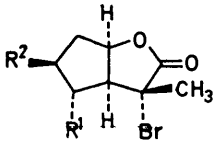


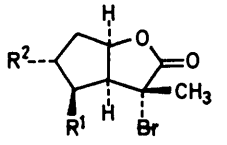
(8)

endo-Epoxy-lactone (7) reacted with a solution of hydrobromic acid in acetic acid to give the bromohydrin (9) and a small amount of the bromo-acetate (10). Purification and acetylation of (9) furnished the acetate (11) which on prolonged treatment with triethylamine in hot benzene formed the required *endo*-acetoxy-α-methylenelactone (4) in good yield.

Cleavage of the epoxide (7) with hydroiodic acid proceeded cleanly and specifically to give the iodohydrin (12). Acetylation furnished the acetoxy-iodo-lactone (13) which on brief treatment with triethylamine in hot benzene gave the dehydroiodinated product (14): longer reaction times under the same basic conditions gave the α-methylene-γ-lactone (4) in excellent yield.



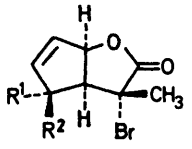
(10) R^1 = Br, R^2 = OCOMe
(17) R^1 = OH, R^2 = Br
(18) R^1 = OH, R^2 = I
(19) R^1 = OCOMe, R^2 = Br
(20) R^1 = OCOMe, R^2 = I



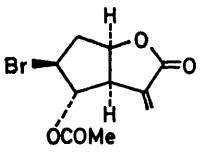
(9) R^1 = OH, R^2 = Br
(11) R^1 = OCOMe, R^2 = Br
(12) R^1 = OH, R^2 = I
(13) R^1 = OCOMe, R^2 = I

A second route to the *endo*-ester (4) was investigated. Sequential treatment of the *endo*-bromo-lactone (2) with alkali, carbon dioxide, and potassium tri-iodide gave the iodohydrin (15) in low yield.[8] Conversion of (15) into the acetate (14) was accomplished in quantitative yield through intermediate formation of the iodo-ester (16).

The *exo*-epoxide (8) was readily attacked by hydrobromic or hydroiodic acid to yield the halogenohydrins (17) and (18) respectively from which the dihalogenoacetates (19) and (20) were formed. Exocyclic double bond formation proceeded preferentially on base treatment of the dibromo-acetate (19) so that the acetoxybromo-α-methylene-γ-lactone (22) could be isolated in



(14) R^1 = H, R^2 = OCOMe
(23) R^1 = OCOMe, R^2 = H



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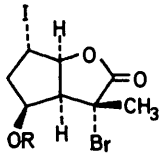
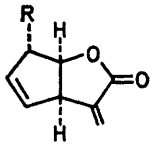


(15) R = H
(16) R = COMe

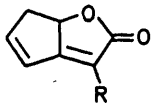
50% yield. On the other hand, elimination of HI occurred rapidly when the lactone (20) was mixed with triethylamine yielding the bromo-acetate (23): the *exo*-acetoxy-α-methylene-γ-lactone (3) was obtained on continuation of the base treatment.

An attempt was made to prepare the bromoacetate (23) from the allyl bromide (24) [obtainable from the lactone (1) and *N*-bromosuccinimide] using potassium acetate in acetonitrile and employing 18-crown ether as catalyst. Unexpectedly, in addition to the isolable bromo-α-methylenelactone (21) the α-methylenelactone (4) was observed as a second component of the multiproduct mixture.

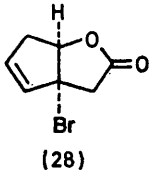
We have found that triethylamine is better suited for the production of the α-methylene-γ-lactones (3), (4), and (22) from the bromomethyl-lactones (23), (14), and (19) than the more strongly basic 1,5-diazabicyclo-[4.3.0]non-5-ene (DBN) despite the necessity of prolonged reaction times. Latterly, we have found that potassium acetate and a catalytic amount of 18-crown-6 in hot acetonitrile (' naked ' acetate) is an excellent reagent for the production of α-methylene-γ-lactones by dehydrohalogenation. For example, loss of HBr from



(21) R = Br
(25) R = H



(26) R = H
(27) R = CH_3



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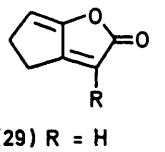

(29) R = H
(30) R = CH_3

the bromolactone (1) to give the α-methylenelactone (25) occurs in over 90% yield using ' naked ' acetate, compared to the 60% yield obtained using DBN.[4,5]

' Naked ' acetate was also used in the synthesis of the unstable γ-butyrolactones (26) and (27), effecting clean dehydrobromination of the bromolactones (28) and (2) respectively. Stronger bases (*e.g.* DBN) caused isomerization of (26) and (27) to the thermodynamically more stable $\Delta^{\alpha\beta}$-butenolides (29) and (30), as adumbrated previously.

EXPERIMENTAL

M.p.s were determined by the capillary tube method. The Buchi Kügelrohr (bulb-to-bulb) system was used for distillations and the b.p.s reported are oven temperatures at distillation. I.r. spectra were recorded on a Perkin-Elmer 257 spectrometer for neat films unless otherwise stated. N.m.r. spectra were recorded on a Varian EM-360 or Perkin Elmer R-32 spectrometer (CCl_4 or $CDCl_3$ solvent). Column chromatography was performed using silica gel MFC; t.l.c. was accomplished using silica gel G (Merck). Anhydrous sodium sulphate was used as a drying agent for solutions in organic solvents. Unless otherwise stated light petroleum refers to the fraction boiling at 60—80°.

4-exo-*Bromo*-4-endo-*methyl*-6,7-*epoxy*-2-*oxabicyclo*[3.3.0]-*octan*-3-*ones* (7) *and* (8).—The lactone (1) (1.0 g) in carbon tetrachloride (30 ml) was treated with *m*-chloroperbenzoic acid (1.6 g) and sodium hydrogencarbonate (1.0 g) and the mixture was stirred at room temperature. Work-up yielded a mixture of the two epoxy-lactones (7) and (8) (1.0 g) in the ratio 4 : 1, from which the endo-*epoxy-lactone* (7) was obtained readily. Column chromatography of the crude mixture furnished the exo-*epoxy-lactone* (8) as needles (0.18 g), m.p. 95—96° (from carbon tetrachloride); $\nu_{max.}$ (Nujol) 1 775 cm^{-1}; δ 4.99 (1 H, m, H-1), 3.6br (2 H, s, H-6 and -7), 3.37 (1 H, d, *J* 6.0 Hz, H-5), 2.3 (2 H, m, 2 × H-8), and 2.05 (3 H, s, Me) (Found: C, 41.2; H, 3.8. $C_8H_9BrO_3$ requires C, 41.2; H, 3.9%).

Preparation of the Acetoxy-halogenolactones (13) *and* (20).—A solution of the appropriate epoxy-lactone (0.005 mol) in glacial acetic acid (5 ml) was treated with hydroiodic acid (5 ml; 32% in water). After 30 min at room temperature the solution was evaporated under reduced pressure and the residue was purified by column chromatography using chloroform as eluant. Acetylation of the isolated halogenohydrins was carried out by using excess of acetic anhydride in the presence of pyridine and the crude product was recrystallized from chloroform–petroleum.

(a) 6-endo-*Acetoxy*-4-exo-*bromo*-7-exo-*iodo*-4-endo-*methyl*-2-*oxabicyclo*[3.3.0]*octan*-3-*one* (13). The *endo*-epoxy-lactone (7) and hydroiodic acid yielded the *iodohydrin* (12) as needles (90%), m.p. 169—170° (from chloroform); $\nu_{max.}$ 3 480 and 1770 cm^{-1} (Found: C, 26.5; H, 2.7. $C_8H_{10}BrIO_3$ requires C, 26.6; H, 2.7%). After acetylation the *lactone* (13) was obtained as cubes (96%), m.p. 156—157°; $\nu_{max.}$ (Nujol) 1 785 and 1 750 cm^{-1} (Found: C, 29.7; H, 2.9. $C_{10}H_{12}BrIO_4$ requires C, 29.7; H, 2.9%).

(b) 6-exo-*Acetoxy*-4-exo-*bromo*-7-endo-*iodo*-4-endo-*methyl*-2-*oxabicyclo*[3.3.0]*octan*-3-*one* (20). From *exo*-epoxy-lactone (8) was obtained the *iodohydrin* (18) as an oil (90%), $\nu_{max.}$ 3 360 and 1 770 cm^{-1} (Found: M^+, 359.884 8. $C_8H_{10}BrIO_3$ requires *M*, 359.886 0). Acetylation of the iodohydrin (18) yielded the required lactone (20) as needles (95%), m.p. 112—114°, $\nu_{max.}$ (Nujol) 1775 and 1 755 cm^{-1} (Found: C, 29.7; H, 2.9. $C_{10}H_{12}BrIO_4$ requires C, 29.7; H, 2.9%).

6-endo-*Acetoxy*-4-exo-*bromo*-8-exo-*iodo*-4-endo-*methyl*-2-

oxabicyclo[3.3.0]*octan*-3-*one* (16).—The bicyclic lactone (2) (1.0 g) was dissolved in a solution of sodium hydroxide (0.3 g) in water (20 ml) and cooled to 0°. Carbon dioxide gas was bubbled through the mixture until the aqueous phase attained pH 7. A solution of potassium iodide (8.0 g) and iodine (4.0 g) in water (15 ml) was added and the mixture was stirred for 24 h at 0—5°. After addition of dichloromethane (50 ml) and sodium sulphite, the aqueous phase was saturated with potassium sodium tartrate. The aqueous layer was extracted with dichloromethane (3 × 30 ml) and the combined organic extracts were washed with saturated brine (2 × 20 ml), dried, and evaporated. Purification by t.l.c. and crystallization from chloroform yielded 4-exo-*bromo*-6-endo-*hydroxy*-8-exo-*iodo*-4-endo-*methyl*-2-*oxabicyclo*[3.3.0]*octan*-3-*one* (15) as cubes (0.08 g, 12% on the basis of the recovered starting material), m.p. 134—135° (decomp.); $\nu_{max.}$ (Nujol) 3 450 and 1 760 cm^{-1}; δ 5.3 (1 H, dd, *J* 5.0 and 2.0 Hz, H-1), 4.5 (1 H, m, H-8), 4.25 (1 H, m, H-6), 3.15 (1 H, dd, *J* 5.0 and 5.0 Hz, H-5), 2.6 (3 H, m, 2 × H-7 and OH), and 2.1 (3 H, s, Me) (Found: M^+, 359.884 8. $C_8H_{10}BrIO_3$ requires *M*, 359.886 0). Acetylation of the iodohydrin (15) yielded the *acetoxy-lactone* (16) as a semi-solid (90%), δ 5.5 (1 H, m, H-6), 5.2 (1 H, m, H-1), 4.4 (1 H, m, H-8), 3.4 (1 H, dd, *J* 5.0 and 5.0 Hz, H-5), 2.5 (2 H, m, 2 × H-7), and 2.1 and 2.0 (2 × 3 H, 2 × s, Me and $OCOCH_3$).

4-exo,8-exo-*Dibromo*-4-endo-*methyl*-2-*oxabicyclo*[3.3.0]-*oct*-6-*en*-3-*one* (24).—To a solution of the lactone (1) (0.7 g) in carbon tetrachloride (25 ml) was added *N*-bromosuccinimide (0.55 g) and the mixture was refluxed for 1 h under irradiation by a 500 W light bulb. Filtration, evaporation of the solvent, and purification by column chromatography yielded the lactone (24) as cubes (0.8 g, 83%), m.p. 110—112° (from $CHCl_3$–petroleum); $\nu_{max.}$ (Nujol) 1 775 cm^{-1}; δ 6.2 (1 H, m, H-6), 5.8 (1 H, m, H-7), 5.25 (1 H, d, *J* 4.0 Hz, H-1), 4.9br (1 H, s, H-8), 4.1 (1 H, m, H-5), and 2.03 (3 H, s, Me) (Found: C, 32.1; H, 2.6. $C_8H_8Br_2O_2$ requires C, 32.4; H, 2.5%).

Dehydrohalogenations using Triethylamine.—(a) 6-endo-*Acetoxy*-4-exo-*bromo*-4-endo-*methyl*-2-*oxabicyclo*[3.3.0]*oct*-7-*en*-3-*one* (14).—A solution of the bicyclic lactone (13) (0.13 g) in dry benzene (5 ml) and triethylamine (3 ml) was refluxed for 10 h. Filtration, evaporation, and crystallization from chloroform–petroleum yielded the lactone (14) as needles (0.075 g, 85%), m.p. 101—102°; $\nu_{max.}$ (Nujol) 1 775 and 1 740 cm^{-1}; δ 6.45 (2 H, m, H-7 and -8), 5.63 (1 H, dd, *J* 6.0 and 2.0 Hz, H-6), 5.33 (1 H, dd, *J* 5.0 and 2.0 Hz, H-1), 3.28 (1 H, dd, *J* 6.0 and 5.0 Hz, H-5), and 2.13 and 2.03 (2 × 3 H, 2 × s, Me and $OCOCH_3$) (Found: C, 43.6; H, 4.1. $C_{10}H_{11}BrO_4$ requires C, 43.6; H, 4.0%).

(b) 6-endo-*Acetoxy*-4-*methylene*-2-*oxabicyclo*[3.3.0]*oct*-7-*en*-3-*one* (4). (i) The bicyclic lactone (14) (0.12 g) and triethylamine (3 ml) in benzene (5 ml) were heated under reflux for 88 h. Work-up as above followed by crystallization from petroleum yielded the required *lactone* (4) as needles (0.068 g, 80%), m.p. 62—64°, $\nu_{max.}$ (Nujol) 1 760, 1 740, and 1 670 cm^{-1}, δ 6.4 and 5.6 (2 H, 2 × d, *J* 2.0 Hz, $=CH_2$), 6.15 (2 H, m, H-7 and -8), 5.85 (1 H, d, *J* 7.0 Hz, H-6), 5.3 (1 H, dd, *J* 7.0 and 2.0 Hz, H-1), 3.9 (1 H, dd, *J* 7.0 and 7.0 Hz, H-5), and 2.1 (3 H, s, Me) (Found: M^+, 194.056 9. $C_{10}H_{10}O_4$ requires *M*, 194.057 9).

(ii) 6-endo-*Acetoxy*-4-exo-*bromo*-8-exo-*iodo*-4-endo-*methyl*-2-*oxabicyclo*[3.3.0]*octan*-3-*one* (16) yielded the lactone (4) (80%), when refluxed in benzene with triethylamine for 66 h after work-up and purification as described above.

(c) 6-exo-*Acetoxy*-4-*methylene*-2-*oxabicyclo*[3.3.0]*oct*-7-*en*-3-*one* (3). Refluxing a solution of the *lactone* (20) (0.12 g) in benzene (5 ml) and triethylamine (5 ml) for 48 h yielded the *lactone* (3) as an oil (0.056 g, 80%), b.p. 110° at 0.01 mmHg; $\nu_{max.}$ 1 765, 1 735, and 1 665 cm^{-1}, δ 6.46 and 6.0 (2 H, 2 × d, *J* 2.0 Hz, $=CH_2$), 6.2 (2 H, m, H-7 and -8), 5.6 (2 H, m, H-1 and -6), 3.5 (1 H, m, H-5), and 2.1 (3 H, s, $OCOCH_3$) (Found: M^+, 194.056 9. $C_{10}H_{10}O_4$ requires *M*, 194.057 9).

Refluxing the above mixture for 15 h only gave a mixture separable into equimolar amounts of the lactone (3) and 6-exo-*acetoxy*-4-exo-*bromo*-4-endo-*methyl*-2-*oxabicyclo*-[3.3.0]*oct*-7-*en*-3-*one* (23), $\nu_{max.}$ 1 780 and 1 740 cm^{-1}, δ 5.6 (2 H, m, H-7 and -8), 5.7 (2 H, m, H-1 and -6), 3.4 (1 H, dd, *J* 5.0 and 5.0 Hz, H-5), and 2.13 and 2.04 (2 × 3 H, 2 × s, Me and $OCOCH_3$) (Found: M^+, 273.983 0. $C_{10}H_{11}BrO_4$ requires *M*, 273.984 0).

(d) 6-exo-*Acetoxy*-7-endo-*bromo*-4-*methylene*-2-*oxabicyclo*-[3.3.0]*octan*-3-*one* (22). A solution of the lactone (19) (0.23 g) in benzene (5 ml) and triethylamine (5 ml) was refluxed for 10 h. Filtration, evaporation of the solvent, and purification by t.l.c. yielded the oily *lactone* (22) (0.89 g, 50%), $\nu_{max.}$ 1 760, 1 740, and 1 665 cm^{-1}, δ 6.4 and 6.0 (2 H, 2 × d, *J* 2.0 Hz, $=CH_2$), 5.35 (1 H, s, H-6), 5.2 (1 H, m, H-1), 4.25 (1 H, m, H-7), 3.6 (1 H, m, H-5), 2.7 (2 H, m, 2 × H-8), and 2.1 (3 H, s, $OCOCH_3$) (Found: M^+, 273.985 1. $C_{10}H_{11}BrO_4$ requires *M*, 273.984 0).

(e) 2-*Oxabicyclo*[3.3.0]*octa*-4,6-*dien*-3-*one* (26). The bicyclic lactone (28) (0.35 g) in tetrahydrofuran (15 ml) was treated with triethylamine (0.25 g) for 24 h at room temperature. After work-up and purification as above, the *lactone* (26) was obtained as an oil (0.17 g, 81%), b.p. 75° at 0.5 mmHg, $\nu_{max.}$ 1 750 and 1 640 cm^{-1}, δ 6.63 (2 H, s, H-6 and -7), 5.54 (1 H, d, *J* 2.0 Hz, H-4), 5.23 (1 H, ddd, *J* 7.0, 5.0, and 2.0 Hz, H-1), 2.92 (1 H, dd, *J* 15.0 and 7.0 Hz, H-8), and 2.32 (1 H, dd, *J* 15.0 and 5.0 Hz, H-8) (Found: M^+, 122.036 7. $C_7H_6O_2$ requires *M*, 122.036 7).

Dehydrohalogenations using Potassium Acetate and 18-*Crown*-6.—(a) 8-exo-*Bromo*-4-*methylene*-2-*oxabicyclo*[3.3.0]-*oct*-6-*en*-3-*one* (21).—18-Crown-6 (0.03 g) and dry potassium acetate (0.20 g) were stirred in dry acetonitrile (15 ml) for 30 min at room temperature. The bromo-lactone (24) (0.20 g) was added and the mixture was refluxed for 10 h. Filtration, evaporation of the solvent, and purification by t.l.c. ($CHCl_3$) yielded the *lactone* (21) as an oil (0.03 g), $\nu_{max.}$ 1 775 and 1 670 cm^{-1}, δ 6.26 and 5.8 (2 H, 2 × d, *J* 2.0 Hz, $=CH_2$), 6.05 (1 H, m, H-6), 5.75 (1 H, m, H-7), 5.25 (1 H, d, *J* 5.0 Hz, H-1), 5.0 (1 H, m, H-8), and 4.3 (1 H, m, H-5) (Found: M^+, 213.963 0. $C_8H_7BrO_2$ requires *M*, 213.962 9). In addition a small amount of impure 6-*endo*-acetoxy-4-methylenelactone (4) was obtained.

(b) 4-*Methyl*-2-*oxabicyclo*[3.3.0]*octa*-4,6-*dien*-3-*one* (27).—Dry potassium acetate (0.1 g) and 18-crown-6 (0.02 g) were stirred in dry acetonitrile (5 ml) for 30 min at room temperature before adding the lactone (2) (0.21 g). The mixture was refluxed for 15 h. Work-up as above yielded the required *lactone* (27) as an oil (0.12 g, 90%), b.p. 75° at 0.08 mmHg; $\nu_{max.}$ 1 750 and 1 685 cm^{-1}; δ 6.6 (2 H, m, H-6 and -7), 5.2 (1 H, m, H-1), 2.9 (1 H, ddd, *J* 14.0, 7.0, and 2.0 Hz, H-8), 2.3 (1 H, dd, *J* 14.0 and 7.0 Hz, H-8), and 1.9 (3 H, s, Me) (Found: M^+, 136.052 8. $C_8H_8O_2$ requires *M*, 136.052 4).

Dehydrohalogenations and Rearrangements involving DBN.—(a) 2-*Oxabicyclo*[3.3.0]*oct*-4,8-*dien*-3-*one* (29). The lactone (26) (0.077 g) and DBN (0.01 g) in benzene (10 ml)

was heated to reflux for 1 h. Work-up and purification as above yielded the *lactone* (29) as an oil (0.075 g, 97%), b.p. 75° at 0.5 mmHg; $\nu_{max.}$ 1 770 and 1 655 cm^{-1}, δ 5.74br and 5.6br (2 H, 2 × s, H-4 and -8), 2.86br (4 H, s, 2 × H-7 and 2 × H-8) (Found: M^+, 122.036 9. $C_7H_6O_2$ requires M, 122.036 7).

4-*Methyl*-2-*oxabicyclo*[3.3.0]*octa*-4,8-*dien*-3-*one* (30).—To a solution of the bicyclic lactone (27) (0.06 g) in benzene (5 ml) was added DBN (0.01 g) and the mixture was refluxed for 30 min. Ether (20 ml) was added to the cooled mixture and the ethereal solution was washed with hydrochloric acid (10%; 2 × 10 ml) and with saturated sodium chloride solution (2 × 10 ml). The ether extract was dried and evaporated to yield the lactone (30) as a semi-solid (0.058 g, 88%).

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REFERENCES

[1] A. T. McPhail, K. D. Onan, K.-H. Lee, T. Ibuka, and H.-C. Huang, *Tetrahedron Letters*, 1974, 3203; K.-H. Lee, T. Ibuka, M. Kozuka, A. T. McPhail, and K. D. Onan, *ibid.*, p. 2287; K.-H. Lee, T. Ibuka, S.-H. Kim, B. R. Vestal, and I. H. Hall, *J. Medicin. Chem.*, 1975, **18**, 812 and references therein.

[2] S. M. Kupchan, M. A. Eakin, and A. M. Thomas, *J. Medicin. Chem.*, 1971, **14**, 1147; A. Rosowsky, N. Papathanasopoulos, H. Lazarus, G. E. Foley, and E. J. Modest, *ibid.*, 1974, **17**, 672; F. E. Ziegler, A. F. Marino, O. A. C. Petroff, and W. L. Studt, *Tetrahedron Letters*, 1974, 2035; K.-H. Lee, R. Meck, C. Piantadosi, and E.-S. Huang, *J. Medicin. Chem.*, 1973, **16**, 299.

[3] Preliminary communication, S. M. Ali and S. M. Roberts, *J.C.S. Chem. Comm.*, 1976, 584.

[4] S. M. Ali and S. M. Roberts, *J.C.S. Chem. Comm.*, 1975, 887.

[5] S. M. Ali and S. M. Roberts, *J.C.S. Perkin I*, 1976, 1934.

[6] S. M. Ali, N. M. Crossland, T. V. Lee, S. M. Roberts, and R. F. Newton, preceding paper.

[7] E. J. Corey and R. Noyori, *Tetrahedron Letters*, 1970, 311.

[8] P. A. Grieco, N. Marinovic, and M. Miyashita, *J. Org. Chem.*, 1975, **40**, 1670.