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A NEW ROUTE TO γ-SUBSTITUTED γ-LACTONES AND δ-SUBSTITUTED δ-LACTONES BASED ON THE REGIOSELECTIVE β-SCISSION OF ALKOXYL RADICALS GENERATED FROM TRANSANNULAR HEMIACETALS[1]

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Key Words γ-Lactones, δ-Lactones, Mercury(II) Oxide-Iodine Reagent, Photolysis, β-Scission of Alkoxyl Radicals

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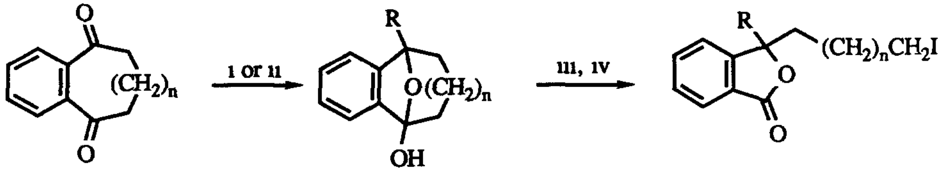
Abstract - A new general synthesis of γ-substituted γ-lactones and δ-substituted δ-lactones including dihydro-5-octyl-2(3*H*)-furanone, a natural pheromone, is described The synthesis involves the regioselective β-scission of alkoxyl radicals generated from transannular hemiacetals as the key step

Substituted γ- and δ-lactones have recently attracted considerable attention, mainly because molecules of this class include many natural products that reveal significant biological activity [2] A variety of methods for synthesizing this class of molecules have recently been developed [3,4]

In our previous papers,[5] we reported on a new short-step general synthesis of isobenzofuran-1(3*H*)-ones (phthalides) and its 3-substituted derivatives based on a double β-scission of alkoxyl radicals generated from 1-ethyl-1, 2-dihydrobenzocyclobuten-1-ols and 1,2-catacondensed 1,2-dihydrocyclobuten-1-ols, respectively

The mechanistic considerations regarding the route from 1,2-catacondensed 1,2-dihydrocyclobuten-1-ols to the phthalides led us to develop a second new method for the general synthesis of 3-substituted phthalides, which is outlined in Scheme 1 Thus, the phtolysis of the hypoiodites of 1,3-dihydro-1,3-alkanoisobenzofuran-1-ols (**2**), obtainable from acyclic and cyclic 1,4-diones (**1**) and alkylmagnesium halides, in benzene containing mercury(II) oxide and iodine gives 3-(3-iodopropyl)phthalides (**3**)

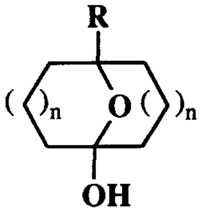


1 n=1 or 2 **2** n=1 or 2 , R=H or alkyl **3**

Reagents and conditions· i, Zn, AcOH, ii, RMgX, Et$_2$O, -78 °C, iii, HgO-I$_2$, benzene, iv, hν

Scheme 1

This paper describes a new general synthesis of γ-substituted γ-lactones and δ-substituted δ-lactones based on the regioselective β-scission of alkoxyl radicals generated from 8- or 9-oxabicycloalkan-1-ols of type A (n=1 or 2, R=H or C_6H_5 or alkyl)



(A)

An application of the method to synthesize a racemic form of a pheromone is also described

Results and Discussions

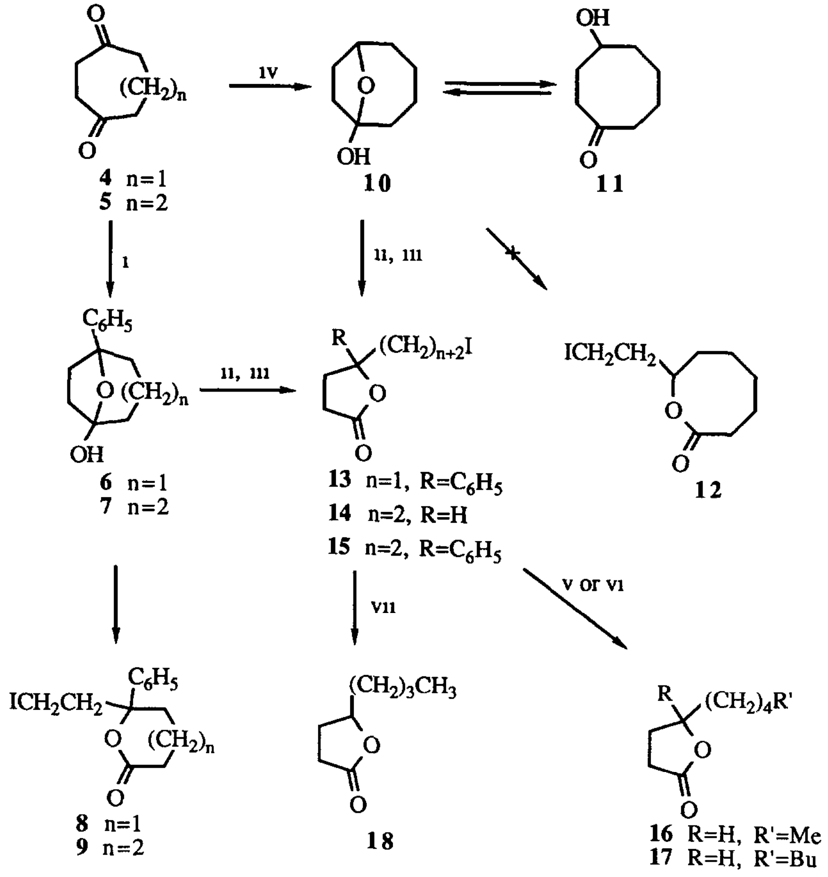
Preparations of γ-(ω-iodoalkyl)-γ-lactones

5-Alkyl or aryl-substituted 8-oxabicyclo[3 2 1]octan-1-ols and 6-alkyl or aryl-substituted 9-oxabicyclo [4 2 1]nonan-1-ols can be prepared by the reaction of 1,4-cycloheptanedione or 1,4-cyclooctanedione with alkyl or phenyllithium

Thus, the reaction of 1,4-cycloheptanedione (4),[6] prepared by oxidation of 1,4-cycloheptanediol[7] with PCC, with phenyllithium under standard conditions gave 5-phenyl-8-oxabicyclo[3 2 1]octan-1-ol (6)[8] in 74%

yield Similarly, the reaction of 1,4-cyclooctanedione (**5**)[9] with phenyllithium gave 6-phenyl-9-oxabicyclo[4 2 1] nonan-1-ol (**7**) in 71% yield. Irradiation of the hypoiodite of transannular hemiacetal (**6**) in benzene containing mercury(II) oxide and iodine (each 3 equivalents) in a nitrogen atmosphere for 4 h gave dihydro-5-(3-iodopropyl)-5-phenyl-2(3*H*)-furanone (**13**) in 76% yield A similar photolysis of the hypoiodite of transannular hemiacetal (**7**) in benzene gave dihydro-5-(4-iodobutyl)-5-phenyl-2(3*H*)-furanone (**15**)[10] in 99% yield.

The reduction of 1,4-cyclooctanedione (**5**) with sodium borohydride in ethanol according to the reported procedure[11] gave a tautomeric mixture of 8-oxabicyclo[4 2 1]octan-1-ol (**10**) and 4-hydroxycyclooctanone (**11**)



Reagents and conditions i, C_6H_5Li, Et_2O, -78 °C, ii, HgO-I_2, benzene, iii, hv, 25 °C, iv, $NaBH_4$, EtOH, r t , v, $Me_2Cu(CN)Li_2$, THF, -78 °C for **16**, vi, $Bu_2Cu(CN)Li_2$, THF, -78 °C for **17**, vii, $NaCNBH_3$, HMPA, r t

Scheme 2

as an oil. Irradiation of the tautomeric mixture in benzene containing mercury(II) oxide and iodine (as mentioned above) gave dihydro-5-(4-iodobutyl)-2(3*H*)-furanone (**14**) in 71% yield This furanone was identical to the product[12] obtained by the photolysis of cyclooctanol under the same conditions as in the present experiment No 7-membered lactone (**12**) was formed in this β-scission It is noteworthy that no products arising from the cleavage of the 5-membered ring of oxabicycloalkanols (**6**) and (**7**) were formed in the above-mentioned β-scission

Preparations of δ-(ω-iodoalkyl)-δ-lactones

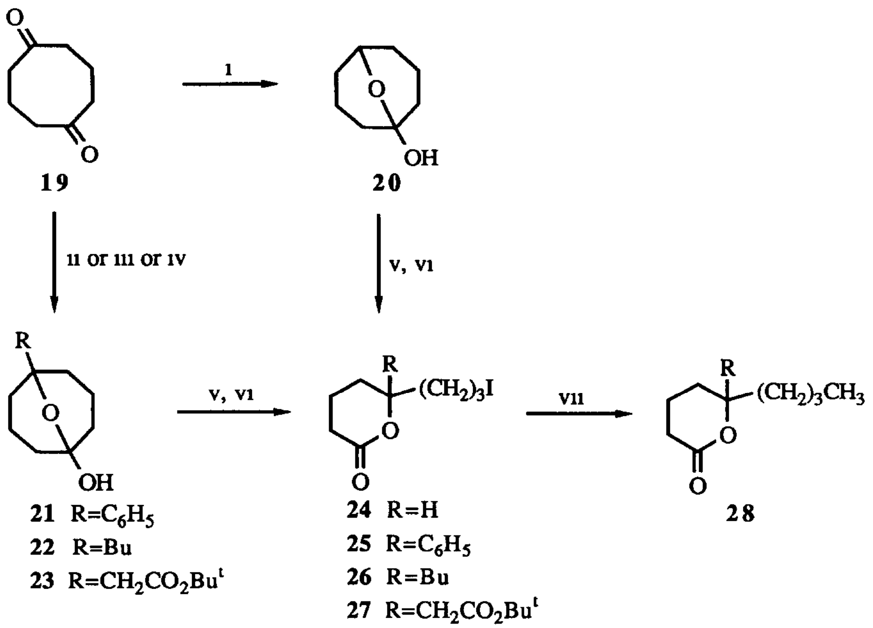
The reduction of cyclooctane-1,5-dione (**19**)[13] with sodium borohydride in ethanol (as described for the preparation of 8-oxabicyclo[4 2 1]octan-1-ol (**10**)) gave 9-oxabicyclo[3 3 1]nonan-1-ol (**20**) in 92 % yield In contrast to transannular hemiacetal (**10**), the ^{1}HNMR spectrum of hemiacetal (**20**) indicated that it existed completely in the transannular hemiacetal form (**20**) in solution, as has already been reported [13]

The reaction of cyclooctane-1,5-dione (**19**) with phenyllithium in diethyl ether gave 5-phenyl-9-oxabicyclo[3 3 1]nonan-1-ol (**21**)[14] in 73% yield Similarly, the reaction of cyclooctane-1,5-dione (**19**) with butyllithium in diethyl ether gave 5-butyl-9-oxabicyclo[3 3 1]nonan-1-ol (**22**) in 43% yield Moreover, the reaction of cyclooctane-1,5-dione (**19**) with *t*-butyl acetate and lithiumdiisopropylamide in tetrahydrofuran gave 1,1-dimethylethyl-5-hydroxy-9-oxabicyclo[3 3 1]nonane 1-acetate (**23**) in 52% yield

Irradiation of the hypoiodite of 9-oxabicyclo[3 3 1]nonan-1-ol (**20**), prepared *in situ* in benzene with mercury(II) oxide and iodine, gave tetrahydro-6-(3-iodopropyl)-2*H*-pyran-2-one (**24**) in 84% yield Irradiation of the hypoiodites of 5-substituted 9-oxabicyclo[3 3 1]nonan-1-ols (**21**), (**22**), and (**23**) prepared similarly gave tetrahydro-6-(3-iodopropyl)-6-phenyl-2*H*-pyran-2-one (**25**) (74%), 6-butyltetrahydro-6-(3-iodopropyl)-2*H*-pyran-2-one (**26**) (73%), and 1,1-dimethylethyl tetrahydro-2-(3-iodopropyl)-6-oxo-6*H*-pyran-2-acetate (**27**) (81%), respectively

Transformations of γ-(ω-iodoalkyl)-γ-lactones into γ-alkyl-γ-lactones and of δ-(ω-iodoalkyl)-δ-lactone into δ-alkyl-δ-lactone

The iodo substituent of the ω-iodoalkyl group of the γ- or δ-lactones obtained above can be either removed by an appropriate reducing reagent to the corresponding alkyl or displaced by appropriate alkyl metals to the longer alkyl chain



Reagents and conditions i, $NaBH_4$, EtOH, r t, ii, C_6H_5Li, Et_2O, -78 °C for **21**, iii, BuLi, Et_2O, -78 °C for **22**, iv, $CH_3CO_2Bu^t$, $LiN(Pr^i)_2$, Et_2O, 0 °C for **23**, v, HgO-I_2, benzene, vi, hν, 25 °C, vii, $Me_2Cu(CN)Li_2$,THF, -78 °C

Scheme 3

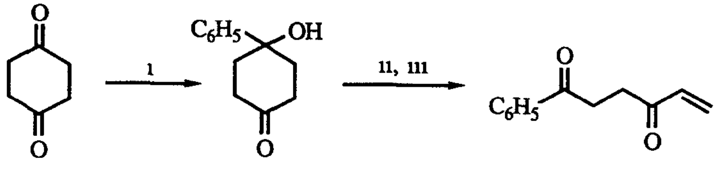
Thus, the reduction of furanone (**14**) in hexamethyl phosphoric triamide with sodium cyanohydride[15] at room temperature gave 5-butyldihydro-2(3*H*)-furanone (**18**) in excellent yield The reaction of furanone (**14**) with dilithium cyanodimethylcuprate in THF gave dihydro-5-pentyl-2(3*H*)-furanone (**16**) in 61% yield

Dihydro-5-octyl-2(3*H*)-furanone (**17**), a racemic form of sex pheromone from the *rove* beetle, was then prepared by treatment of furanone (**14**) with dilithiumdibutylcyanocuprate[16] prepared from the reaction of cuprous cyanide and butyllithium The spectral data were identical to those of optically active pheromone[17] or its synthetic racemate [18]

Finally, the reaction of δ-(ω-iodopropyl)pyranone (**24**) in tetrahydrofuran with dilithium cyanodimethylcuprate, as described for the preparation of γ-lactone (**16**), gave tetrahydro-4-butyl-2*H*-pyran-2-one (**28**)[19] in 35% yield

The β-scission of alkoxyl radical generated from 4-hydroxy-4-phenylcyclohexanone

The reaction of cyclohexane 1,4-dione with phenyllithium gave 4-hydroxy-4-phenylcyclohexanone (**30**) in 34 % yield



29 **30** **31**

Reagents and conditions i, C_6H_5Li, Et_2O, -78 °C, ii, HgO-I_2, benzene, iii, hv, 25 °C
Scheme 4.

The ^{1}HNMR spectrum of 4-hydroxycyclohexanone indicated that there was no hemiacetal form in the solution Irradiation of the hypoiodite of hydroxycyclohexanone (**30**), as mentioned above, gave 1-phenyl-5-hexene-1,4-dione (**31**) in 13% yield The vinyl diketone (**31**) has previously been prepared in 20 % yield by the addition of an aldehyde with a vinyldiketone catalysed by thiazolium salt by Stetter and landscheidt Vinyl diketones, such as (**31**), were used by them to synthesize a number of unsymmetrical 1,4,7-triketones by a thiazolium salt-catalysed condensation with aldehydes [20]

EXPERIMENTAL

General Method

Regarding the instruments used and a description of the general photolysis procedure, see the previous paper[5] of this series

1,4-Cycloheptanedione (**4**).——This dione was prepared by the treatment of 1,4-cycloheptanediol[7] with pyridinium chlorochromate (PCC) and Celite 545 in dichloromethane at room temperature (82%) The spectral data were identical to those reported in the literature [6]

1,4-Cyclooctanedione (**5**).[9] ——This dione was prepared from commercially available *cis*-1,4-cyclooctanediol by the same procedure used for the preparation of 1,5-cyclooctanedione, described above Mp 45~46°C (lit[9] 46 8°C)

1,5-Cyclooctanedione **(18)**.[13,14] ——Commercially available *cis*-1,5-cyclooctanedione (1 44 g, 10 mmol), PCC (12 9 g, 60 mmol), Celite 545 (10g) in dichloromethane (500 ml) was stirred at room temperature for 24h in a nitrogen atmosphere. The mixture was filtered and the filtrate washed with 5% hydrochloric acid and then dried over anhydrous magnesium sulphate Removing the solvent gave a product which was purified by PLC on silica gel (1 3 ethyl acetate - hexane) to give 1,5-cyclooctanedione (980 mg, 70%) Mp 69~71°C (diethyl ether - hexane) (lit [13] Mp 71~72°C)

5-Phenyl-8-oxabicyclo[3 2 1]octan-1-ol **(6)**.[8] ———To a stirrd solution of 1,4-cycloheptanedione **(4)** (11mg, 0 086 mmol) in diethyl ether (5 ml) at -78°C in an argon atmosphere was added dropwise phenyllithium (0 86 mmol, 1 8 M solution in cyclohexane) The solution was stirred for 1 h The reaction was quenched by adding aq ammonium chloride The two layers were separated and the aqueous layer extracted with diethyl ether The combined organic layers were washed with brine and dried over anhydrous magnesium sulphate After removing the solvent under reduced presure, the product was purified by PLC (silica gel - 1 3 ethyl acetate hexane) to give hemiacetal **(6)** (13 mg, 74%) IR (neat) 3350 cm^{-1}(OH), ^{1}HNMR (90 MHz) δ 1 4~2 25 (10H, m, methylenes), 2 89 (1H, s, OH), 7 2~7 45 (5H, m, aromatic H), MS (rel, intensty) *m/z* 204 (M^+, 42), 105(100)

6-Phenyl-9-oxabicyclo[4 2 1]nonan-1-ol **(7)**. ———This hemiacetal **(7)** was prepared by the same procedure used for the synthesis of hemiacetal **(6)** The reaction of 1 4-dione **(5)** (50 mg, 0 36 mmol) with phenyllithium (0 36 mmol) at -78°C for 30 min gave hemiacetal **(6)** (56 mg, 71%) Mp 80~81°C (diethyl ether-hexane) IR (Nujol) 3290 cm^{-1} (OH), ^{1}HNMR (90MHz) δ 1 2~2 9 (12H, m, methylenes), 2 59 (1H, s, OH), 7 0~7 7 (5H, m, aromatic H), MS (rel, intensity) *m/z* 218 (M^+, 13), 105 (100), (Found M^+, 218 1320 $C_{14}H_{18}O_2$ requires *M*, 218 1307)

8-Oxabicyclo[4 2 1]octan-1-ol **(10)**.——1,4-Cyclooctanedione **(5)** (397 mg, 2 80 mmol) and sodium borohydride (25 mg, 0 70 mmol) in ethanol (10 ml) was stirred for 4 h in a nitrogen atmosphere After removing the solvent, water was added to the residue The mixture was then extracted with diethyl ether The organic layer was washed with brine and dried over anhydrous magnesium sulphate Evaporation of the solvent gave a product which was purified by PLC (silica gel - 2 1 ethyl acetate and hexane) to give a tautomeric mixture of hemiacetal **(10)** and 4-hydroxycyclooctanone **(11)** as an oil Bp 98~103°C (bath temp)/0 3mm Hg (lit [11]

100~102°C/0 4mm Hg) IR (neat) 3375 and 1702 cm^{-1}, ^{1}HNMR (270 MHz) δ 1 3~2 7 [12 33 H, m, -CH$_2$- of (**10**) and (**11**) and OH of (**11**)], 3 66 [0 67 H, s, OH of (**11**)], 3 8~3 9 [0 33H, m CH-O- of (**11**)] and 4 45~4 55 [0.67H, m, CH-O of (**10**)]

9-Oxabicyclo[3 3 1]nonan-1-ol (**20**).——This hemiacetal (**20**) was prepared by the same procedure as described for hemiacetal (**10**) The treatment of 1,5-dione (**19**) (210 mg, 1 5 mol) with sodium borohydride (14 mg, 0 38 mmol, in ethanol (7 ml) for 3h gave a crude product Purification by PLC gave hemiacetal (**20**) (196 mg, 92%) Mp 101~102°C (diethyl ether-hexane) (lit [13] mp 100~102°C)

5-Phenyl-9-oxabicyclo[3 3 1]nonan-1-ol (**21**).——To a stirred solution of dione (**19**) (100 mg 0 70 mmol) in diethyl ether (20 ml) in an argon atmosphere at -78°C was added dropwise phenyllithium (0 70 mmol, 1M solution in cyclohexane) The solution was stirred for 1 h The reaction was then quenced by adding ammonium chloride The aq layer was extracted with diethyl ether The combined organic layers were washed with brine and dried over anhydrous magnesium sulphate Removing the solvent gave a product which was purified by PLC (silica gel -1 3 ethyl acetate and hexane) to give hemiacetal (**15**) (111 mg, 73%) Mp 135~137°C (diethyl ether-hexane) (lit [14] tan crystals with no description of m p)

5-Butyl-9-oxabicyclo[3 3 1]nonan-1-ol (**22**).——To a stirred solution of 1 5-cyclooctanedione (**19**) (100 mg, 0 70 mmol) in diethyl ether (20 ml) in a nitrogen atmosphere at -78°C was added dropwise butyllithium (0 70 mmol, 1 6 M in hexane) and the mixture was stirred for 2h at that temperature The solution was worked up as described above The crude product was purified by PLC (silica gel - 1 2 ethyl acetate - hexane) to give hemiacetal (**22**) (60 mg, 43%) Mp 86~88°C (diethyl ether-hexane) IR (Nujol) 3336 cm^{-1} (OH), ^{1}HNMR (90MHz) δ 0 90 (3H, distorted t Me), 1 2~2 2 (18H, m, methylenes), 2 40 (1H, s, OH), MS (rel intensity) *m/z* 198 (M^{+}, 14), 141 [(M-Bu)$^{+}$, 22], 128 (100) (Found M^{+}, 198 1593 $C_{12}H_{22}O_2$ requires M, 198 1620)

1,1-Dimethylethyl-5-hydroxy-9-oxabicyclo[3 3 1]nonane-1-acetate (**23**).——To a stirred solution of lithium diisopropylamide (1mmol) in tetrahydrofuran (10 ml) at -78°C prepared by the usual method was added *t*-butyl acetate (116 mg, 1 mmol) The mixture was stirred for 30 min To this solution was added a solution of 1 5-dione

(19) (132 mg, 0.94 mmol) in tetrahydrofuran (10 ml), the resulting solution was stirred for 1h The reaction was then quenched by adding aq ammonium chloride The mixture was worked up in a similar manner as mentioned above The crude product was purified by PLC (silica gel-1 1 ethyl acetate and hexane) to give hemiacetal **(23)** (124 mg, 52%) Mp 124~125°C (diethyl ether-hexane) IR (Nujol) 3356 cm^{-1} (OH), ^{1}HNMR (90MHz) δ 1 1~2 2 and 1 44 (11H, m and s, methylenes and t-Bu), 2 42 (2H, s, CH_2CO_2), 2 50 (1H, s, OH), MS (rel intensity) *m/z* 200[$(M-CH_2CMe_2)^+$, 22], 182 [$(M - CH_2CMe_2 - H_2O - CO)^+$, 78], 57 ($CMe_3^+$, 100), [Found $(M-CH_2CMe_2)^+$, 200.1029 $C_{10}H_{16}O_4$ requires (M - CH_2CMe_2), 200 1049]

Preparation of γ- Lactones by β-Scission of Alkoxyl Radicals generated from Cyclic Hemiacetals.

(a) *Preparation of Dihydro-5-(3-iodopropyl)-5-phenyl-2(3H)-furanone* **(13)** *(General procedure)* —A stirred solution of 5-phenyl-8-oxabicyclo[3 2 1]octan-1-ol **(6)** (12 mg, 0 059 mmol) in benzene (5 ml) containing mercury(II) oxide (39 mg, 0 18 mmol) and iodine (46 mg, 0 18 mmol) was irradiated through a Pyrex filter with a 100-W high pressure Hg arc in an atmosphere of nitrogen for 4h at room temperature The resulting mixture was filtered through a Celite pad and the filtrate was washed with 5% aq sodium thiosulphate and then brine The solution was then dried over anhydrous magnesium sulphate Evaporation of the solvent gave a residue which was subjected to PLC (silica gel - 1 1 ethyl acetate and hexane) to afford g-lactone **(13)** (15 mg, 76%) Rf 0 32 IR (neat) 1776 cm^{-1} (C=O), ^{1}HNMR (270 MHz) δ 1 45~1 65(1H, m), 1 75~2 2 (3H, m), 2 4~2 65 (4H, m), 3 09 (2H, t, *J*=6 59 Hz, CH_2I), 7 25~7 4 (5H, m, aromatic H), MS (rel intensity) *m/z* 330 (M^+, 0 2), 203 [$(M - I)^+$, 27], 161 [$(M - C_3H_6I)^+$, 100] (Found M^+, 330 0101 $C_{13}H_{15}IO_2$ requires *M*, 330 0117)

(b) *Dihydro-5-(4-iodobutyl)-2(3H)-furanone* **(14)**.[12]———The photolysis of hemiacetal **(10)** (32 mg, 0 23 mmol) in benzene (15 ml) containing mercury(II) oxide (151 mg, 0 70 mmol) and iodine (177 mg, 0 70 mmol) for 2h, carried out as mentioned above, gave furanone **(14)** (43 mg, 71%) identical to the sample described in the previous paper [12]

(c) *Dihydro-5-(4-iodobutyl)-5-phenyl-2(3H)-furanone* **(15)**.[10]—The photolysis of 6-phenyl-9-oxabicyclo[4 2 1]nonan-1-ol **(7)** (47 mg, 0 22 mmol) in benzene (15 ml) containing mercury(II) oxide (142 mg, 0 66 mmol) and iodine (167 mg, 0.66 mmol) for 4h as described above gave furanone (**15**) (75 mg, 99%) R^f 0.41 (1 3 ethyl acetate-hexane) IR (neat) 1772 cm^{-1} (C=O), ^{1}HNMR (270MHz) δ 1 1~1 25 (1H, m), 1 35~1 55 (1H, m), 1 65~2 1 (4H, m), 2 4~2 65 (4H, m), 3 08 (2H, t, *J* 6 96 Hz, CH_2I), 7 25~7 4 (5H, m, aromatic H), MS (rel intensity) *m/z* 344 (M^+, 0 21), 217 [$(M - I)^+$, 6.8], 161 [$(M - C_3H_6I)^+$,100] (Found M^+, 344 0256 $C_{14}H_{17}IO_2$ requires *M*, 344.0273).

(**d**) *Tetrahydro-6-(3-iodopropyl)-2H-pyran-2-one* (**24**). —— Irradiation of a solution of hemiacetal (**20**) (515 mg, 3 6 mmol) in benzene (72 ml) containing mercury(II) oxide (2 3 g, 10 8 mmol) and iodine (2 7g, 10 8 mmol) for 2 h, as described above, gave a product which was purified by PLC to give pyranone (**23**) (806 mg, 84%) Rf 0 33 (2 3 ethyl acetate -hexane) IR (neat) 1731 cm^{-1} (C=O), ^{1}HNMR (270 MHz) δ 1 4~2 1 (8H, m), 2.25~2 7 (2H, m, CH_2CO) 3 1~3 3 (2H, m, CH_2I), 4.2~4 4 (1H, m, -CHOCO), MS (rel intensity) *m/z* 269 [$(M+I)^+$, 14], 268 (M^+, 0 29) 141 [$(M - I)^+$, 100] (Found M^+, 267 9990 $C_8H_{13}IO$, requires *M*, 267 9960)

(**e**) *Tetrahydro-6-(3-iodopropyl)-6-phenyl-2H-pyran-2-one* (**25**). —— The photoreaction of hemiacetal (**21**) (100 mg, 0 47 mmol) in benzene (24 ml) containing mercury(II) oxide (310 mg, 1 4 mmol) and iodine (260 mg, 1 4 mmol) for 5.5h, carried out as mentioned above, gave pyranone (**25**) (119 mg, 74%) Rf 0 21 (1 3 ethyl acetate -hexane). IR (neat) 1730 cm^{-1} (C=O) , ^{1}HNMR (270 MHz) δ 1 45~1 85 (3H, m), 1 9~2 1 (4H, m), 2 25~2 35 (1H, m), 2 4~2 5 (2H, m, CH_2CO), 3.08 (2H, t, *J* 6.59 Hz, CH_2I) 7 2~7 4 (5H, m, aromatic H), MS (rel intensity) *m/z* 345 [$(M+I)^+$, 2 0], 344 (M^+, 0 5), 217 [$(M - I)^+$, 47], 175 (100) (Found M^+, 344 0275 $C_{14}H_{17}IO_2$ requires, *M*, 344 0273)

(**f**) *6-Butyltetrahydro-6-(3-iodopropyl)-2H-pyran-2-one* (**26**).——The photolysis of hemiacetal (**22**) (60 mg, 0 30 mmol) in benzene (15 ml) containing mercury(II) oxide (194 mg, 0 90 mmol) and iodine (228 mg, 0 90 mmol) for 1 5h executed by the same procedure as mentioned above gave pyranone (**26**) (71 mg, 73 %) Rf 0 30 (1 1 ethyl acetate-hexane) IR (neat) 1722 cm^{-1} (C=O), ^{1}HNMR (270 MHz) δ 0 92 (3H, t, *J* 6 78 Hz, Me), 1 2~1 4 (4H, m), 1 55~2 05 (10H, m), 2 48 (2H, t, *J* 6 96 Hz, CH_2CO), 3 1~3 25 (2H, m, CH_2I), MS (rel intensity) *m/z* 325 [$(M+I)^+$, 1 2], 324 (M^+, 0 17), 267 [$(M - I)^+$, 100] (Found M^+, 324 0608 $C_{12}H_{21}IO_2$ requires M, 324 0587)

(g) *1,1-Dimethylethyl Tetrahydro-2-(3-iodopropyl)-6-oxo-6H-pyran-2-acetate* **(27)**. —— The photoreaction of hemiacetal **(23)** (114 mg, 0 45 mol) in benzene (23 ml) containing mercury(II) oxide (292 mg, 1 35 mmol) for 4h, as described above, gave pyranone **(27)** (139 mg, 81 %) Rf 0 42 (1 1 ethyl acetate-hexane) IR (neat) 1730 cm^{-1} (C=O), ^{1}HNMR (270 MHz) δ 1 46 (9H, s, t-Bu), 1 75~2 15 (8H, m), 2 45~2 55 (2H, m CH$_2$CO), 2 62 (2H, m, CH$_2$CO), 2 62 (2H, s, C*H*$_2$CO$_2$Bu^t), 3 15~3 25 (2H, m, CH$_2$I), MS (rel intensity) *m/z* 326 [(M - CH$_2$COOBu^t)$^+$, 7 0], 309 [(M - OBu^t)$^+$, 8 4], 267 [(M - CH$_2$CMe$_2$ - C$_3$H$_6$I)$^+$, 58], 57 (t - Bu$^+$, 100], [Found (M-CH$_2$CMe$_2$)$^+$, 326 0016 $C_{10}H_{15}IO_4$(M - CH$_2$CMe$_2$) requires *M*, 326 0015]

Preparations of Dihydro-5-alkyl-2(3*H*)-furanones and Tetrahydro-6-alkyl-2*H*-Pyran-2-ones.

(a) *Dihydro-5-pentyl-2(3H)-furanone* **(16)**. —— To a stirred solution of cuprous cyanide (90 mg, 1 mmol) in tetrahydrofuran (10 ml) at -78°C in an atmosphere of argon was added methyllithium (2 mmol, 1M in diethyl ether) dropwise After stirring for 30 min a solution of furanone **(14)** (208 mg, 0 78 mmol) in tetrahydrofuran (5ml) was added and the resulting mixture stirred for an additional 2h at that temperature The reaction was then quenched by adding aq ammonium chloride and extracted with diethyl ether The organic layer was washed with water and dried over anhydrous magnesium sulphate Evaporation of the solvent gave a residue which was subjected to PLC on silica gel (Rf 0 32 1 3 ethyl acetate-hexane) to give 5-pentylfuranone **(16)** (74 mg, 61%) This product was identical to an anthentic sample commercially available (Aldrich)

(b) *Dihydro-5-octyl-2(3H)-furanone* **(17)**. —— The treatment of furanone **(14)** (160 mg, 0 60 mmol) in tetrahydrofuran (15 ml) with dilithiumdibutylcyanocuprate (0 97 mmol), prepared from the reaction of cuprous cyanide (87 mg, 0 97 mmol) with butyllithium (1 94 mol, 1 6 M in hexane), in a same manner as described for 5-pentylfuranone **(16)**, gave octyl furanone **(17)** (72 mg, 61%) Rf 0 32 (1 3 ethyl acetate-hexane) The spectral data were identical to those of the optically active natural product[17] and the synthetic racemate [18]

(c) *5-Butyldihydro-2(3H)-furanone* **(18)**. —— Furanone **(14)** (46 mg, 0 17 mmol) and sodium cyanoborohydride (43 mg, 0 68 mmol) in hexamethylphosphoric triamide (2 ml) was stirred overnight at room temperature The mixture was then poured into brine and the solution extracted with diethyl ether The usual work-up gave a product which was subjected to PLC on silica gel (Rf 0.26, 1 4 ethyl acetate-hexane) to give butylfuranone (**18**) identical to a commercially available sample (Aldrich)

(**d**) *4-Butyltetrahydro-2H-pyran-2-one* (**28**). ——— The treatment of tetrahydro-6-(3-iodopropyl)-2*H*-pyran-2-one (**23**) (138 mg, 0 51 mmol) in tetrahydrofuran (15 ml) with dilithium cyanodimethylcuprate (1 02 mmol) in a same manner as described for the preparation of lactone (**10**) gave δ-lactone (**23**) (28 mg, 35%) The spectral data of this lactone was identical to those of the reported lactone [19]

4-Hydroxy-4-phenylcyclohexanone (**30**). ——— The treatment of 1,4-cyclohexane dione (**29**) commercially obtainable (112 mg, 1 mmol) with phenyllithium (1 mmol 1M solution in cyclohexane) in diethyl ether (30 ml) at -78°C for 2h in a similar manner as for the preparation of hemiacetal (**21**) gave the title cyclohexanone (**30**)[8] (66 mg, 34%) Mp 124~127°C (diethyl ether-hexane)(lit [8] 127~128°C) IR (Nujol) 3446 (OH), 1699 cm^{-1} (C=O), ^{1}HNMR (90 MHz) δ 2 0~2 5 (6H, m), 2 6~3 2 (2H, m), 7 1~7 6 (5H, m aromatic H), MS (rel intensity) *m/z* 190 (M^+, 38), 133 (100)

1-Phenyl-5-hexene-1,4-dione (**31**) *by a Radical Cleavage of 4-Hydroxy-4-Phenylcyclohexane* (**30**). ——— The irradiation of a solution of cyclohexanol (**30**) (38 mg, 0 20 mmol) in benzene (15 ml) containing mercury(II) oxide (194 mg, 0 90 mmol) and iodine (228 mg, 0 9 mmol) for 3 5h in a same manner as for the cleavage of the above hemiacetals gave 1,4-dione (**31**) (5mg, 13%) Rf 0 32 (1 2 ethyl acetate-hexane) The spectral data of this dione was in accord with those of the 1,4-dione in the literature [20]

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