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ALKYLIDENE LACTONE SYNTHESIS

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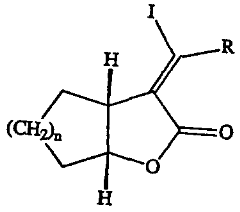
ABSTRACT - *The iodoalkylidene lactones formed by reaction of alkenes with acetylenic acids in the presence of N-iodosuccinimide and subsequent free radical cyclisation, can be de-iodinated photochemically or alkylated with lithium diorganocuprate reagents to yield a variety of α-alkylidene lactones.*

INTRODUCTION

The iodoalkylidene lactones whose synthesis we have described[1] (e.g (1)), combine the structural features of an unsaturated lactone with a halide which provides potential for further structural modification. In this paper we discuss two methods for removal of the iodine to produce simple α-alkylidene lactones. The first of these involves a direct replacement of iodine by a hydrogen atom[2] and the second an alkylation[1].



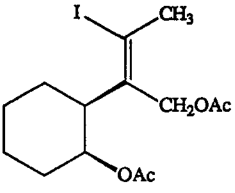
(1) n = 1
(2) n = 2

Used throughout :

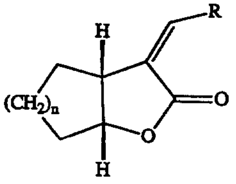
(a) R = H
(b) R = CH_3
(c) R = CH_3CH_2
(d) R = $(CH_3)_2CH$
(e) R = $(CH_3)_3C$
(f) R = $(CH_3)_3Si$
(g) R = Ph

DE-IODINATION OF IODOVINYLIDENE LACTONES

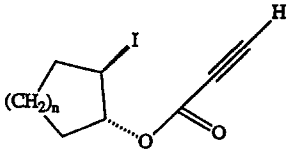
While the iodovinylidene lactones represent a new and interesting class of compounds, it was nonetheless desirable to find a route to the alkylidene lactones. Several reductive chemical methods were investigated. Neither tributyltin hydride with azoisobutyronitrile[3] nor a complex copper hydride reagent[4] gave any reaction. Previous studies of the sodium borohydride reduction of unsaturated esters suggested that attack of the soft hydride nucleophile should occur at the β-position[5,6]. However, sodium borohydride reduction of iodoethylidene lactone (2b) gave a diol which was characterised as its diacetate (3). In this case, reduction had occurred at the carbonyl carbon.



(3)

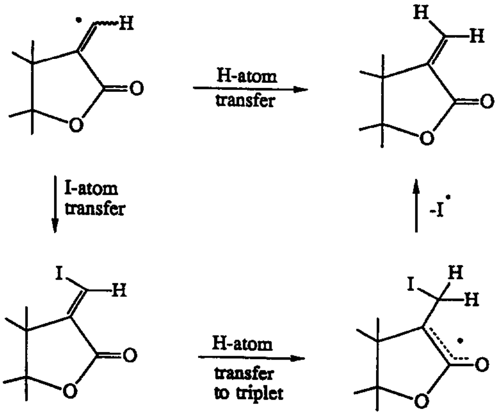


(4) n = 1
(5) n = 2



(6) n = 1
(7) n = 2

Production of small quantities of the methylene lactone (5a) during the photolysis of the iodo acetylenic ester (7)[1] suggested the possibility of adapting the photolysis to produce the iodine-free lactones specifically. The alkylidene radical produced on cyclisation (Scheme 1) can abstract iodine from another iodo ester molecule to give the iodomethylene lactone, or remove hydrogen from a donor such as the solvent to give the methylene lactone. Suppression of the former process might be achieved by conducting the reaction under conditions of low substrate concentration and/or by provision of a good hydrogen atom donor. Reactions carried out on the cyclopentyl iodo ester (6) showed that the success of this transformation depended strongly on the solvent used (Table 1). Of those tested, acetonitrile proved the best.



Scheme 1. Routes from the alkenyl radical to the methylene lactone.

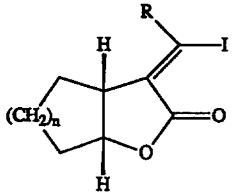
Although dilution did improve the yield of iodine-free methylene lactone up to a point (Table 2), addition of the hydrogen atom donor, cumene, had no effect.

Table 1. Solvent Effects on Photolysis of Iodo Acetylenic Ester (6)[a]

Solvent	Products[b] (*E*)-Iodomethylene Lactone (1a)	 (*Z*)-Iodomethylene Lactone (8a)	 Methylene Lactone (4a)
CH_3CN	8 min (20%)	10 min (10%)	20 min (42%)
EtOAc	6 min (18%)	15 min (10%)	15 min (19%)
C_6H_6	25 min (10%)	25 min (3%)	80 min (19%)
Me_2CO	16 min (9%)	20 min (6%)	50 min (17%)
Bu^tOH	15 min (8%)	15 min (6%)	25 min (16%)

[a] Photolysis at 254 nm with zinc dust. Concentration 0.009 mol L^{-1}. Reactions monitored by GLC.

[b] Time to reach maximum concentration (% of total starting material at maximum).



(8) n = 1
(9) n = 2

Table 2. Concentration Effects on Photolysis of Iodo Acetylenic Ester (6)[a]

Conc. (mol L^{-1})	Products[b] Methylene Lactone (4a)	 Iodomethylene Lactones (1a)/(8a)	 Iodo Acetylenic Ester (6)
0.018	10	32	7
0.009	41	-	-
0.009[c]	39	-	-
0.006	34	-	-

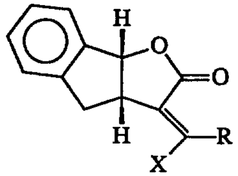
[a] Photolysis at 254 nm for 25 min in CH_3CN with zinc dust.

[b] Percentage yield as determined by GLC.

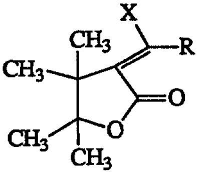
[c] With cumene.

The detailed gas chromatographic analyses of the reaction in acetonitrile showed that, even under relatively dilute conditions, the iodine-atom transfer process was occurring more rapidl

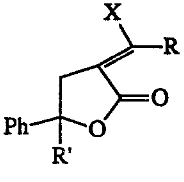
than hydrogen atom transfer. The levels of the iodomethylene lactone isomers reached maxima after 5 - 10 minutes. By this stage, the methylene lactone concentration was less than half its maximum value. After 20 minutes, when the methylene lactone concentration had attained its peak, the iodomethylene lactone levels were barely discernable. Thus the most significant source of methylene lactone was not hydrogen atom capture by the vinylidene radical formed upon cyclisation, but hydrogen atom capture by an excited state of the iodomethylene lactone. Photolysis of iodomethylene lactone (1a) as a source of methylene lactone (4a) was therefore investigated. This process did not require zinc powder and proceeded in high yield. Gas chromatography showed a smooth conversion of the iodinated material into the iodine-free lactone with the only complication being a little *(E)/(Z)* isomerisation of the reactant as a non-destructive bypath. A variety of iodovinylidene lactones were dehalogenated in this way (Table 3).



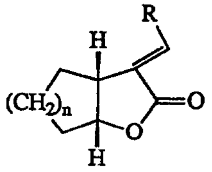
(10) X = I
(16) X = H



(11) X = I
(17) X = H



(12) X = I, R' = H
(13) X = I, R' = CH_3
(18) X = H, R' = H
(19) X = H, R' = CH_3



(14) n = 1
(15) n = 2

Table 3. Photo-deiodination of Iodoalkylidene Lactones[a]

Iodoalkylidene Lactone	Reaction Time (min)	% Yield of Alkylidene Lactone(s)[b]	Product distribution
(1a)	30	80 (88)	(4a)
(1b)	30	77	4:3 ratio of (4b):(14b)
(1c)	40	64	1:1 ratio of (4c):(14c)
(1d)	40	71	4:3 ratio of (4d):(14d)
(1e)	55	70	5:2 ratio of (4e):(14e)
(2a)	30	79	(5a)
(2b)	30	70	4:3 ratio of (5b):(15b)
(2f)	30	0	Mixture of (2f) and (9f)
(2g)	30	0	Mixture of (2g) and (9g)
(10a)	30	63	(16a)
(11a)	30	77 (84)	(17a)
(12a)	30	73	(18a)
(12b)	30	54	(18b), *(E):(Z)* = 7:4
(13a)	100	64	(19a)

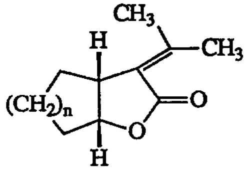
[a] Photolyses were conducted on solutions in tetrahydrofuran at 254 nm.
[b] Isolated yields. Figures in parentheses are yields from flow experiments.

Mixtures of geometric isomers were obtained for the alkyl substituted compounds. The reaction was readily adaptable to large scale as the photolyses could be conducted by flowing the solution through the photoreactor. De-iodination was not successful for the trimethylsilyl substituted iodoalkylidene lactone (2f) nor for the phenyl derivative (2g). Both of these compounds were merely isomerised to *(E)/(Z)*-mixtures.

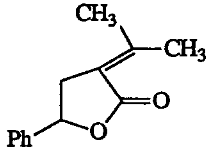
ALKYLATION OF IODOVINYLIDENE LACTONES

Substitution reactions of organocuprates with α,β-unsaturated carbonyl compounds containing a good leaving group at the β-carbon atom have received attention as versatile procedures for the synthesis of β-alkyl substituted α,β-enones or enoates. Leaving groups such as acetates[7], phosphates[8], alkoxides[9], thioalkoxides[10], tosylates[11], and halides[12] have been used. The reactions usually proceed with conservation of stereochemistry. Analogous replacement of the iodine of an iodoalkylidene lactone by an alkyl group in an addition-elimination process was investigated as an alternative route to alkylidene lactones.

Reaction of the iodoalkylidene lactones with lithium dimethylcuprate proceeded generally in reasonable yield (Table 4).



(20) n = 1
(21) n = 2



(22)

Table 4. Reaction of Iodoalkylidene Lactones with Organocuprates

Reactant	Cuprate	Products (Isolated Yield)
(1a)	Me_2CuLi	(14b) (72%)
(1b)	Me_2CuLi	(20) (97%)
(2a)	Me_2CuLi	(15b) (74%)
(2a)	Ph_2CuLi	(15g) (18%)
(2b)	Me_2CuLi	(21) (73%)
(2f)	Me_2CuLi	(5f) (58%); (15f) (17%)
(9a)	Me_2CuLi	(5b) (15%); (15b) (23%)
(12b)	Me_2CuLi	(22) (71%)

With the exception of the trimethylsilyl derivative (2f), the *(E)* isomers reacted with retention of configuration. The *(Z)*-iodoethylidene lactone (9a) gave a low yield of a mixture of the *(E)* and *(Z)*-derivatives with the *(E)*-form predominating. Thus, stereospecificity may be poor for *(Z)*-lactones or for those *(E)*-lactones which already bear bulky substituents on the double bond. Substitution of the iodine atom of (2a) by a phenyl group, using lithium diphenylcuprate, was stereospecific, but gave an unsatisfactory yield. Even though CuBr was used in the production of the cuprate, a considerable amount of biphenyl was produced. The reaction of iodolactone (2a) with phenylmagnesium bromide in the presence of CuBr gave a product containing an alcohol function (IR) which was not investigated further.

CONCLUSIONS

The iodovinylidene lactones, which are readily formed from alkenes by reaction with acetylenic acids and N-iodosuccinimide followed by free radical cyclisation, may be further transformed into iodine-free alkylidene lactones by photolysis in tetrahydrofuran. This process is conveniently conducted on a preparative scale by flowing the solution through the photoreactor. Yields of methylene lactones are high. With alkylidene lactones both geometric isomers are produced but overall yields remain high. Addition of cuprate species to the iodoalkylidene lactones provides a good route to more highly alkylated species such as (20) and, in cases where the attached groupings are not too bulky, allows for alkylation of (E)-iodomethylidene lactones with a high degree of retention of stereochemistry.

EXPERIMENTAL

Infra-red spectra were recorded on a Perkin-Elmer 357 double-beam spectrophotometer, or on a Nicolet 5MX Fourier transform spectrophotometer. High resolution solution spectra were run on a Digilab FTS-60 Fourier transform spectrophotometer using spectroscopic grade chloroform as solvent. Frequencies (ν_{max}) are reported as cm^{-1}.

Mass spectra were recorded using a Varian MAT CH-7 mass spectrometer.

Ultra-violet spectra were recorded on a Shimadzu UV 240 uv-visible recording spectrometer as methanol solutions.

Preparative layer chromatography (PLC) was performed on glass plates (20 cm x 20 cm) coated with a 1.25 mm layer of Merck silica gel $PF_{254+366}$.

Radial chromatography was performed using a 'Chromatotron' model 7924 (Harrison Research, Palo Alto, U.S.A.) preparative centrifugal thin layer chromatograph. 1 mm, 2 mm and 4 mm silica gel layers were prepared and used according to the manufacturer's instructions. The eluting solvents were delivered by gravity feed. Samples were pre-treated by passage through a short column of alumina. Bands were observed under ultra-violet light (254 nm).

Gas chromatography was carried out on a Perkin-Elmer 8420 Capillary Gas Chromatograph fitted with a flame ionisation detector. Peak areas were measured by using the internal integrator and have been corrected to accommodate different detector response factors. A 10m DB-1 column supplied by J&W Scientific was used and the oven temperature was programmed from 60° to 160° at a linear rate of 5° min^{-1} except for the photolyses experiments conducted on (2f) and (2g) where the final oven temperature was 280° and the ramp rate 25° min^{-1}.

Nuclear magnetic resonance spectra were obtained on a Varian VXR 300 instrument operating at 299.9 MHz for ^1H and at 75.4 MHz for ^{13}C. Spectra were recorded as dilute deuterochloroform solutions and chemical shifts are quoted in p.p.m. downfield from tetramethylsilane. Carbon types were determined either by DEPT or APT pulse sequences.

Photolytic reactions were carried out in a Rayonet photochemical reactor at 254 nm using quartz vessels fitted with a nitrogen inlet. In all irradiations, the solutions were degassed by passage of nitrogen gas for 5 min. A steady stream of nitrogen bubbles was continuously passed through the solution and the mixture was stirred with a teflon-coated, magnetic stirrer bar. Flow photolyses were performed with a Fluid Metering Inc. pump model RPSY.

Zinc powder was prepared from commercial zinc powder by washing with dilute HCl (3 x 0.08 M) with vigorous stirring with a contact time of 2 min for each wash. The metal was collected by suction filtration, washed successively with water, acetone and ether and then air dried. The metal was stirred vigorously in the solvent to be used for the photolysis for 2 min and then allowed to settle for 1 min. The supernatant suspension was collected by decantation. Evaporation of the solvent gave the desired grade of zinc powder.

(1'RS-1'α,2'α,2Z)-2-(2'-acetoxycyclohexyl)-3-iodo-2-buten-1-yl acetate (3)

A solution of iodoalkylidene lactone (2b) (0.040g, 0.14 mmol) in ethanol (4 ml) was stirred at room temperature with $NaBH_4$ (0.075 g, 1.98 mmol) for 48 h. The reaction mixture was poured into 4 M H_2SO_4 (10 ml) and extracted with ether (3 x 10 ml). The combined ethereal extracts were dried over $MgSO_4$ and evaporated. The crude mixture was treated with acetic anhydride (5 ml) and pyridine (5 ml) at room temperature for 48 h. Water (30 ml) was added and the mixture was extracted with ether (3 x 15 ml). The ethereal extracts were washed with 2 M HCl (3 x 15 ml) and sat. $NaHCO_3$, dried over $MgSO_4$ and evaporated. PLC (25% Et_2O/hexane) gave (3) as an oil (0.024 g, 50%); distilled 65° (block)/0.04 mm; IR (neat) : 1740, 1285 (ester); ^1H NMR : 2.04 (s, 6H); 2.62 (s, 3H); 2.83 (ddd, J 2.7, 2.7, 11.1 Hz, 1H); 4.63 (d, J 10.73 Hz, 1H); 4.66 (d, J 10.73 Hz, 1H); 5.07 (m, $W_{b/2}$ 7.6 Hz, 1H); ^{13}C NMR : 19.92 (t); 20.93 (q); 21.43 (q); 24.63 (t); 25.56 (t); 30.36 (t); 31.09 (q); 52.61 (d); 58.40 (t); 73.05 (d); 108.59 (s); 139.30 (s); 170.39 (s); 170.82 (s); Anal. Found : C, 48.4; H, 6.0; Calc. for $C_{14}H_{21}IO_2$: C, 48.3; H, 6.2%.

Photolyses of Iodo Acetylenic Ester (1a) - Solvent Studies

A mixture of (1a) (0.050 g, 0.020 mmol), tetradecane (0.020 g, 0.101 mmol) and zinc powder (0.200 g, 3.06 mmol) in the solvent (20 ml) was photolysed at 254 nm. Aliquots were removed at intervals, filtered and analysed by GC. Results are summarised in Table 1.

Photolyses of Iodo Acetylenic Ester (1a) - Concentration Studies

A mixture of (1a) (0.030 g, 0.118 mmol or 0.050 g, 0.197 mmol or 0.100 g, 0.394 mmol), tetradecane (0.020 g, 0.101 mmol) and zinc powder (0.200 g, 3.06 mmol) in acetonitrile (20 ml) was photolysed at 254 nm for 25 min. The mixture was filtered and the filtrate was analysed by GC. In a further experiment with 0.100 g of (1a), cumene (0.480 g, 4 mmol) was also added. Results are summarised in Table 2.

Photolyses of Iodovinylidene Lactones - GC Studies

A solution of the iodovinylidene lactone (0.050 g) and tetradecane (0.020 g, 0.101 mmol) in freshly distilled tetrahydrofuran (20 ml) was irradiated at 254 nm for the specified time. Product mixtures were analysed by GC. Results are summarised in Table 3.

Preparative Photo-deiodinations

A solution of the iodoalkylidene lactone in tetrahydrofuran was irradiated at 254 nm under N_2 for the specified time. Products were isolated by removal of the solvent followed by dissolution in CH_2Cl_2, washing with aqueous $Na_2S_2O_3$ (10% w/v), drying over $MgSO_4$, and evaporation. Purification was by PLC.

Preparations are reported according to the convention : starting iodoalkylidene lactone (mass, mmol), volume of solvent, reaction time, experimental data.

(3aα,6aα)-Hexahydro-3-methylene-2H-cyclopenta[b]furan-2-one (4a)[13,14]

(1a) (0.052 g, 0.197 mmol), 20 ml, 0.5 h, PLC (30% $CHCl_3$/benzene) gave methylene lactone (4a) (0.021 g, 80%); IR ($CHCl_3$) 1755.2 (C=O), 1660.6 (C=C); ^1H NMR : 3.42 (m, $W_{h/2}$ 18 Hz, 1H); 4.99 (br dd, *J* 5, 5 Hz, 1H); 5.65 (d, *J* 2.3 Hz, 1H); 6.25 (d, *J* 2.3 Hz, 1H); ^{13}C NMR : 23.11 (t); 33.90 (t); 35.72 (t); 43.04 (d); 83.34 (d); 122.85 (t); 140.50 (s); 171.25 (s).

(3E,3aα,6aα) and (3Z,3aα,6aα)-Hexahydro-3-ethylidene-2H-cyclopenta[b]furan-2-one (14b) and (4b)

(1b) (0.044 g, 0.160 mmol), 20 ml, 0.5 h, PLC (40% Et_2O/hexane) gave : (i) (Z)-ethylidene lactone (4b) (0.008 g, 34%); IR ($CHCl_3$) 1743.6 (C=O), 1678.1 (C=C); ^1H NMR : 2.19 (dd, *J* 2.1, 7.3 Hz, 3H); 3.33 (m, $W_{h/2}$ 20 Hz, 1H); 4.92 (m, $W_{h/2}$ 15 Hz, 1H); 6.30 (dq, *J* 2.1, 7.3 Hz, 1H); ^{13}C NMR : 14.13 (q); 23.04 (t), 34.13 (t); 36.06 (t); 44.30 (d); 82.72 (d); 131.14 (d); 139.88 (s); 173.11 (s); MS, m/z 152.0839; Calc. for $C_9H_{12}O_2$: 152.0837; and (ii) (E)-ethylidene lactone (14b) (0.010 g, 43%); IR ($CHCl_3$) 1739.8 (C=O), 1666.5 (C=C); ^1H NMR : 1.90 (dd, *J* 1.6, 7.2 Hz, 3H); 3.42 (m, $W_{h/2}$ 18.5 Hz, 1H); 4.97 (ddd, *J* 1.3, 6.6, 6.6 Hz, 1H); 6.77 (dq, *J* 2.5, 7.2 Hz, 1H); ^{13}C NMR : 15.38 (q); 23.38 (t); 34.13 (t); 33.34 (t); 41.09 (d); 83.53 (d); 132.38 (d); 136.26 (s); 171.65 (s); Anal. Found: C, 71.4; H, 8.1; Calc. for $C_9H_{12}O_2$: C, 71.0; H, 8.0%.

(3E,3aα,6aα) and (3Z,3aα,6aα)-Hexahydro-3-propylidene-2H-cyclopenta[b]furan-2-one (14c) and (4c)

(1c) (0.050 g, 0.170 mmol), 20 ml, 0.67 h, PLC (40% Et_2O/hexane) gave : (i) (Z)-propylidene lactone (4c) (0.009 g, 32%); IR ($CHCl_3$) 1739.8 (C=O), 1666.5 (C=C); ^1H NMR : 1.05 (t, *J* 7.6 Hz, 3H); 2.74 (m, $W_{h/2}$ 43 Hz, 2H); 3.32 (m, $W_{h/2}$ 17 Hz, 1H); 4.92 (m, $W_{h/2}$ 15 Hz, 1H); 6.19 (dt, J, 2.0, 7.6 Hz, 1H); ^{13}C NMR : 13.64 (q); 21.07 (t); 23.02 (t); 34.14 (t); 36.18 (t); 44.23 (d); 82.73 (d); 129.82 (s); 146.84 (d); 170.74 (s); MS, m/z 166.1029; Calc. for $C_{10}H_{14}O_2$: 166.0994; and (ii) (E)-propylidene lactone (14c) (0.009 g, 32%); IR ($CHCl_3$) 1739.8 (C=O), 1674.2 (C=C); ^1H NMR : 1.11 (t, *J* 7.6 Hz, 3H); 2.26 (dq, *J* 7.6, 7.6 Hz, 2H); 3.42 (m, $W_{h/2}$ 21 Hz, 1H); 4.96 (m, $W_{h/2}$ 15 Hz, 1H); 6.68 (dt, *J* 2.5, 7.6 Hz, 1H); ^{13}C NMR : 12.98 (q); 23.24 (t); 23.39 (t); 33.90 (t); 34.08 (t); 41.16 (d); 83.52 (d); 131.23 (s); 142.78 (d); 171.92 (s); MS, m/z 166.1018; Calc. for $C_{10}H_{14}O_2$: 166.0994.

(3E,3aα,6aα) and (3Z,3aα,6aα)-Hexahydro-3-(2-methylpropylidene)-2H-cyclopenta[b]furan-2-one (14d) and (4d)

(1d) (0.049 g, 0.160 mmol), 20 ml, 0.67 h, PLC (40% Et_2O/hexane) gave : (i) (Z)-alkylidene lactone (4d) (0.009 g, 32%); IR ($CHCl_3$) 1739.8 (C=O), 1662.7 (C=C); ^1H NMR : 0.99 (d, *J* 6.6 Hz, 3H); 1.00 (d, *J* 6.6 Hz, 3H); 3.29 (m, $W_{h/2}$ 18 Hz, 1H); 3.79 (dsept, *J* 6.6, 10 Hz, 1H); 4.91 (m, $W_{h/2}$ 14 Hz, 1H); 5.98 (dd, *J* 2.0, 10.0 Hz, 1H); ^{13}C NMR : 22.48 (2 x q); 23.02 (t); 26.15 (d); 34.16 (t);

36.28 (t); 44.18 (d); 82.70 (d); 128.24 (s); 152.02 (d); 175.72 (s); MS, m/z 180.1148; Calc. for $C_{11}H_{16}O_2$: 180.1150; and (ii) (E)-alkylidene lactone (14d) (0.011 g, 39%); IR ($CHCl_3$) 1743.8 (C=O), 1674.2 (C=C); ^{1}H NMR : 1.07 (d, *J* 6.6 Hz, 3H); 1.09 (d, *J* 6.6 Hz, 3H); 2.61 (dsept, *J* 6.6, 10 Hz, 1H); 3.42 (m, $W_{b/2}$ 18 Hz, 1H); 4.96 (m, $W_{b/2}$ 14 Hz, 1H); 6.52 (dd, *J* 2.5, 10.0 Hz, 1H); ^{13}C NMR : 21.79 (q); 22.06 (q); 23.43 (t); 29.57 (d); 34.02 (t); 34.41 (t); 41.10 (d); 83.55 (d); 129.41 (s); 147.56 (d); 173.17 (s); MS, m/z 180.1098; Calc. for $C_{11}H_{16}O_2$: 180.1150.

(3E,3aα,6aα) and (3Z,3aα,6aα)-Hexahydro-3-(2,2-dimethylpropylidene)-2H-cyclopenta[b]furan-2-one (14e) and (4e)

(1e) (0.051 g, 0.159 mmol), 20 ml, 0.92 h, PLC (25% Et_2O/hexane) gave : (i) (Z)-alkylidene lactone (4e) (0.006 g, 19%); IR ($CHCl_3$) 1747.5 (C=O), 1650.0 (C=C); ^{1}H NMR : 1.27 (s, 9H); 3.29 (m, $W_{b/2}$ 17 Hz, 1H); 4.91 (m, $W_{b/2}$ 14 Hz, 1H); 6.25 (d, *J* 2.0 Hz, 1H); ^{13}C NMR : 22.89 (t), 29.77 (q), 33.40 (s), 34.09 (t), 36.62 (t), 45.95 (d), 82.27 (d), 130.49 (s), 155.41 (d), 168.90 (s); MS, m/z 194.1303; Calc. for $C_{12}H_{18}O_2$: 194.1307; and (ii) (E)-alkylidene lactone (14e) (0.051 g, 52%); IR ($CHCl_3$) 1743.6 (C=O), 1662.6 (C=C); ^{1}H NMR : 1.20 (s, 9H); 3.60 (m, $W_{b/2}$ 20 Hz, 1H); 4.89 (m, $W_{b/2}$ 12 Hz, 1H); 6.66 (d, *J* 2.0 Hz 1H); ^{13}C NMR : 23.40 (t); 29.69 (q); 33.72 (t); 34.33 (s); 35.72 (t); 41.17 (d); 83.50 (d); 128.00 (s); 150.01 (d); 173.35 (s); MS, m/z 194.1290; Calc. for $C_{12}H_{18}O_2$: 194.1307.

(3aα,7aα)-Hexahydro-3-methylene-2(3H)-benzofuranone (5a)[13,15]

(2a) (0.052 g, 0.188 mmol), 20 ml, 0.5 h, PLC (40% Et_2O/hexane) gave methylene lactone (5a) (0.022 g, 79%); IR ($CHCl_3$) 1755.2 (C=O), 1681.9 (C=C); ^{1}H NMR : 3.03 (m, $W_{b/2}$ 12 Hz, 1H); 4.55 (ddd, *J* 6, 6, 6 Hz, 1H); 5.52 (d, *J* 2.4 Hz, 1H); 6.20 (d, *J* 2.4 Hz, 1H); ^{13}C NMR : 20.58 (t); 21.22 (t); 26.37 (t); 28.95 (t); 39.65 (d); 77.01 (d); 119.83 (t); 139.97 (s); 171.05 (s).

(3E,3aα,7aα) and (3Z,3aα,7aα)-Hexahydro-3-ethylidene-2(3H)-benzofuranone (15b) and (5b)

(2b) (0.044 g, 0.150 mmol), 20 ml, 0.5 h, PLC (40% Et_2O/hexane) gave (i) (Z)-ethylidene lactone (5b) (0.008 g, 33%); IR ($CHCl_3$) 1743.6 (C=O), 1678.1 (C=C); ^{1}H NMR : 1.86 (dd, *J* 7.2, 0.6 Hz, 3H), 2.20 (m, $W_{b/2}$ = 15 Hz), 2.96 (m, $W_{b/2}$ = 15 Hz, 1H), 4.42 (m, $W_{b/2}$ = 11 Hz, 1H), 6.66 (dq, *J* 7.2, 1.5 Hz, 1H); ^{13}C NMR : 14.93 (q), 19.26 (t), 22.64 (t); 26.90 (t), 27.21 (t), 37.15 (d), 76.46 (d), 133.46 (d), 135.14 (s), 171.55 (s); MS, m/z : 166 (M^+); Anal. Found : C, 72.0; H,8.9 ; Calc. for $C_{10}H_{14}O_2$: C, 72.3; H, 8.5%; and (ii) (E)-ethylidene lactone (15b) (0.009 g, 37%); IR ($CHCl_3$) 1747.5 (C=O), 1665.8 (C=C); ^{1}H NMR : 2.16 (dd, *J* 7.3, 1.8 Hz, 3H); 2.87 (m, $W_{b/2}$ = 12 Hz, 1H); 4.45 (ddd, *J* 6, 6, 6 Hz, 1H); 6.13 (dq, *J* 7.3, 1.9 Hz, 1H); ^{13}C NMR : 13.96 (q), 20.46 (t), 21.54 (t), 27.01 (t), 28.55 (t), 40.79 (d), 76.49 (d), 131.17 (s), 136.13 (d), 170.75 (s); MS, m/z : 152 (M^+); Anal. Found : C, 72.6; H, 8.7; Calc. for $C_{10}H_{14}O_2$: C, 72.3; H, 8.5%.

(3bα,8bα)-3b,8b-Dihydro-3-methylene-2H-indeno[1,2b]furan-2-one (16a)

(10a) (0.064 g, 0.205 mmol), 20 ml, 0.5 h, PLC (40% $CHCl_3$/benzene) gave methylene lactone (16a) (0.024 g, 63%); IR ($CHCl_3$) 1759.1 (C=O), 1663.7 (C=C); ^{1}H NMR : 3.04 (dd, *J* 2.7, 16.5 Hz, 1H); 3.55 (dd, *J* 9.0, 16.5, 1H); 3.88 (ddd, *J* 2.7, 7.8, 9.0 Hz, 1H); 5.77 (d, *J* 2.7 Hz, 1H); 5.97 (d, *J* 7.8 Hz, 1H); 6.32 (d, *J* 2.7 Hz, 1H); 7.2-7.4 (m, 3H); 7.51 (d, *J* 7.2 Hz, 1H); ^{13}C NMR : 39.27 (t); 41.40 (d); 85.28 (d); 123.57 (t); 125.23 (d); 126.48 (d); 127.68 (d); 130.07 (d); 138.90 (s); 140.01 (s); 142.18 (s); 170.48 (s); Anal. Found: C, 77.1; H, 5.6; Calc. for $C_{12}H_{10}O_2$: C, 77.4; H, 5.4%.

Dihydro-3-methylene-4,4,5,5-tetramethyl-2(3H)-furanone (17a)[16]

(11a) (0.044 g, 0.160 mmol), 20 ml, 0.5 h, PLC (40% Et_2O/hexane) gave methylene lactone (17a) (0.019 g, 77%); IR ($CHCl_3$) 1751.4 (C=O); ^{1}H NMR : 1.15 (s, 6H); 1.31 (s, 6H); 5.45 (s, 1H); 6.14 (s, 1H); ^{13}C NMR : 23.30 (2 x q); 23.49 (2 x q); 45.17 (s); 87.09 (s); 118.82 (t); 146.98 (s); 169.98 (s); Anal. Found: C, 69.9; H, 9.2; Calc. for $C_9H_{14}O_2$: C, 70.1; H, 9.2%.

Dihydro-3-methylene-5-phenyl-2(3H)-furanone (18a)[13,17]

(12a) (0.050 g, 0.160 mmol), 20 ml, 0.5 h, PLC (50% Et_2O/hexane) gave the methylene lactone (18a) (0.021 g, 73%); IR ($CHCl_3$) 1759.1 (C=O), 1666.5 (C=C); ^{1}H NMR : 2.91 (dddd, *J* 3, 3, 7, 17 Hz, 1H); 3.41 (dddd, *J* 3, 3, 8, 17 Hz, 1H); 5.52 (dd, *J* 7, 8 Hz, 1H); 5.69 (dd, *J* 3, 3 Hz, 1H); 6.31 (dd, *J* 3, 3 Hz,1H); 7.2-7.5 (m, 5H); ^{13}C NMR : 36.35 (t); 78.04 (d); 122.51 (t); 125.45 (2 x d); 128.64 (d); 128.91 (2 x d); 134.26 (s); 139.87 (s); 170.22 (s).

(3E) and (3Z)-Dihydro-3-ethylidene-5-phenyl-2(3H)-furanone (18b)

(12b) (0.050 g, 0.160 mmol), 20 ml, 0.6 h, PLC (40% Et_2O/hexane) gave : (i) the (Z) ethylidene lactone (18b) (0.006 g, 20%); IR ($CHCl_3$) 1751.4 (C=O), 1674.2 (C=C); ^{1}H NMR : 2.22 (ddd, *J* 2, 2, 7 Hz, 3H); 2.86 (m, $W_{h/2}$ 28 Hz, 1H); 3.31 (m, $W_{h/2}$ 28 Hz, 1H); 5.47 (dd, 7, 7 Hz, 1H); 6.33 (ddq, *J* 2, 2, 7 Hz, 1H); 7.2-7.5 (m, 5H) ; ^{13}C NMR : 14.19 (q); 38.01 (t); 125.05 (s); 125.46 (d); 128.43 (d); 128.81 (d); 139.07 (d); 140.23 (s); 169.79 (s); MS, m/z 188.0838; Calc. for $C_{12}H_{12}O_2$: 188.0837; and (ii) the (E)-ethylidene lactone (18b) (0.010 g, 34%); IR ($CHCl_3$) 1751.4 (C=O), 1681.9 (C=C); ^{1}H NMR : 1.86 (ddd, 2, 2, 7 Hz, 3H); 2.78 (m, $W_{h/2}$ 28 Hz, 1H); 3.33 (m, $W_{h/2}$ 30 Hz, 1H); 5.47 (dd, *J* 6, 8 Hz, 1H); 6.32 (ddq, *J* 2, 2, 7 Hz, 1H); 7.2-7.5 (m, 5H); ^{13}C NMR : 15.90 (q); 34.07 (t); 78.07 (d); 125.42 (2 x d); 126.97 (s); 128.50 (2 x d); 128.90 (d); 136.26 (d); 140.55 (s); 170.71 (s); MS, m/z 188.0809; Calc. for $C_{12}H_{12}O_2$: 188.0837.

Dihydro-3-methylene-5-methyl-5-phenyl-2(3H)-furanone (19a)[13,17]

(13a) (0.024 g, 0.076 mmol), 20 ml, 1.6 h, PLC (20% Et_2O/hexane) gave (19a) (0.092 g, 64%); IR ($CHCl_3$) 1755 (C=O), 1635 (C=C); UV (MeOH) : λ_{max} 225 nm (ε 1386); ^{1}H NMR : 1.73 (s, 3H); 3.16 (m, 2H); 5.64, (dd, *J* 2.4, 2.5 Hz, 1H); 6.27 (dd, *J* 2.5, 3.0, 1H); 7.3-7.4 (m, 5H); ^{13}C NMR : 30.16 (q); 42.69 (t); 83.98 (s); 122.66 (t); 124.18 (2 x d); 127.73 (d); 128.68 (2 x d); 135.09 (s); 144.61 (s); 176.17 (s); MS, m/z 188.0879 (M^+); Calc. for $C_{12}H_{12}O_2$: 188.0837.

Flow Photolyses

Tetrahydrofuran (10 ml), followed by a solution of the iodoalkylidene lactone in tetrahydrofuran (concentration 0.01 M), then by tetrahydrofuran (10 ml) was pumped through a quartz tube (length 335 mm, internal diameter 2 mm, flow rate 0.25 ml min^{-1}) mounted in the photochemical reactor with irradiation at 254 mm. Evaporation of the solvent was followed by PLC.

Lithium Dimethylcuprate Preparation

An ethereal solution of methyllithium (1.5 ml, 1.4 M, 2.1 mmol) was added dropwise to a stirred suspension of copper (I) iodide (0.200 g, 1.1 mmol) in Et_2O (12 ml) in a flamed Schlenck tube under a nitrogen atmosphere at 0°. On addition of one equivalent of methyllithium, a yellow slurry of methylcopper was formed which dissolved on addition of the second equivalent of methyllithium, to form a pale yellow solution.

Reaction of Lithium Dimethylcuprate With Iodovinylidene Lactones

A solution of the iodolactone in dry Et_2O was added to the lithium dimethylcuprate solution prepared as described above at the specified temperature. The resulting dark-coloured solution was kept for the specified time at this temperature. The reaction mixture was poured into 2M NH_4Cl solution, extracted with Et_2O (3 x). The combined ethereal extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure.

The cuprate additions are reported according to the convention : lactone (mass, amount), solvent (volume), cuprate (volume, amount), temperature, reaction time, experimental data.

(3E,3aα,6aα)-Hexahydro-3-ethylidene-2H-cyclopenta[b]furan-2-one (14b)

(1a) (0.116 g, 0.44 mmol) in Et$_2$O (2 ml), Me$_2$CuLi (4 ml, 0.66 mmol), -35°, 2 h. Radial chromatography (80% Et$_2$O/hexane) gave (14b) as an oil (0.048 g, 72%).

(3aα,6aα)-Hexahydro-3-(1-methylethylidene)-2H-cyclopenta[b]furan-2-one (20)

(1b) (0.269 g, 0.97 mmol) in Et$_2$O (3 ml), Me$_2$CuLi (12 ml, 1.05 mmol), 0°, 2 h. PLC (25% Et$_2$O/hexane) gave (20) as an oil (0.156 g, 97%); distilled 60° (block)/0.08 mm; IR (neat) : 1740, 1190 (lactone), 1660 (C=C); ^{1}H NMR : 1.93 (s, 3H); 2.26 (d, *J* 1.2 Hz, 3H), 3.40 (dd, *J* 7.6, 7.6 Hz, 1H); 4.86 (ddd, *J* 1.4, 4.5, 5.7 Hz, 1H); ^{13}C NMR : 19.94 (q), 23.27 (t), 24.36 (q), 33.89 (t), 34.21 (t), 43.34 (d), 81.74 (d), 125.33 (s), 150.69 (s), 171.03 (s); MS, m/z : 166 (M$^+$); Anal. Found : C, 72.0; H, 8.2; Calc for C$_{10}$H$_{14}$O$_2$: C, 72.3; H, 8.5%.

(3E,3aα,7aα)-Hexahydro-3-ethylidene-2(3H)-benzofuranone (15b)

(2a) (0.178 g, 0.64 mmol) in Et$_2$O (2 ml), Me$_2$CuLi (4 ml, 0.68 mmol), -35°, 2 h. Radial chromatography (50% Et$_2$O/hexane) gave (15b) as an oil (0.079 g, 74%).

(3E,3aα,7aα)-Hexahydro-3-benzylidene-2(3H)-benzofuranone (15g)

(2a) (0.115 g, 0.41 mmol) in Et$_2$O (3 ml), Ph$_2$CuLi (0.99 mmol, 4 ml) (prepared from phenyllithium (0.99 mmol) and copper (I) iodide (0.095 g, 0.5 mmol), at 0°), -35° - room temperature, 15 h. PLC (50% Et$_2$O/hexane) gave (15g) as an oil (0.017 g, 18%); distilled 70° (block)/0.04 mm ; IR (neat) : 1750, 1195, 1175 (lactone), 1650 (C=C); ^{1}H NMR : 2.08 (m, W$_{h/2}$ 18 Hz, 1H); 2.30 (m, W$_{h/2}$ 18 Hz), 3.35 (m, W$_{h/2}$ 21 Hz, 1H); 4.48 (m, W$_{h/2}$ 11 Hz, 1H); 7.41 (m, 3H); 7.51 (dd, *J* 8.2, 1.9 Hz, 2H); ^{13}C NMR : 19.29 (t), 22.98 (t), 26.12 (t), 27.13 (t), 38.85 (d), 76.66 (d), 129.03 (2 x d), 129.63 (2 x d), 129.73 (d), 133.22 (s), 134.40 (s), 134.73 (d), 172.90 (s); Anal. Found: C, 78.9; H, 7.4; Calc. for C$_{15}$H$_{16}$O$_2$: C, 78.9; H, 7.1%.

(3aα,6aα)-Hexahydro-3-(1-methylethylidene)-2(3H)-benzofuranone (21)

(2b) (0.156 g, 0.53 mmol) in Et$_2$O (2 ml), Me$_2$CuLi (2 ml, 0.58 mmol), 0°, 1h. PLC (25% Et$_2$O/hexane) gave (21) as an oil (0.070 g, 73%); distilled 61° (block)/0.04 mm; IR (neat) : 1750, 1200, 1185 (lactone), 1680 (C=C); ^{1}H NMR : 1.89 (s, 3H); 2.20 (s, 3H), 2.88 (m, W$_{h/2}$ = 15, 1H), 4.35 (m, W$_{h/2}$ = 10 Hz, 1H); ^{13}C NMR : 19.44 (t), 19.89 (q), 22.97 (t), 23.26 (q), 27.05 (t), 27.26 (t), 39.45 (d), 75.22 (d), 128.13 (s), 147.59 (s), 171.03 (s); MS, m/z : 180 (M$^+$); Anal. Found: C, 73.2; H, 9.2; Calc. for C$_{11}$H$_{16}$O$_2$: C, 73.3; H, 9.0%.

(3E,3aα,7aα) and (3Z,3aα,7aα)-hexahydro-3-[iodo(trimethylsilyl)methylene]-2(3H)- benzofuranone (15f) and (5f)

(2f) (0.635 g, 1.81 mmol) in Et$_2$O (7 ml), Me$_2$CuLi (15 ml, 2.2 mmol), -35°, 1 h (followed by 3 h at room temperature). PLC (20% Et$_2$O/hexane) gave : (i) The (Z)-isomer (5f) (0.251 g, 58%), distilled 100° (block)/0.05 mm; IR (neat) : 1755, 1235 (lactone), 1622 (C=C); ^{1}H NMR : 0.21 (s, 9H), 1.95 (s, 3H), 2.22 (m, W$_{h/2}$ 20 Hz, 2H), 2.97 (ddd, *J* 6.4, 6.4, 5.1 Hz, 1H), 4.41 (m, W$_{h/2}$ 10 Hz, 1H); ^{13}C NMR : -0.72 (3 x q), 19.43 (t), 21.22 (q), 23.10 (t), 26.63 (t), 27.40 (t), 39.83 (d), 75.99 (d), 142.44 (s), 152.29 (s), 170.69 (s); MS, m/z: Anal. Found: C, 65.7; H, 9.6; Calc. for C$_{13}$H$_{22}$O$_2$Si: C, 65.5; H, 9.3%; (ii) The (E)-isomer (15f) (0.074 g, 17%), distilled 90° (block)/0.05 mm; IR (neat) : 1753, 1250, 1213, 1161, 1127 (lactone), 1622 (C=C); ^{1}H NMR : 0.21 (s, 9H), 2.19 (m, W$_{h/2}$ 9 Hz, 1H), 2.24 (s, 3H), 2.82 (ddd, *J* 10.4, 4.6, 4.6 Hz, 1H), 4.36 (m, W$_{h/2}$ 8 Hz, 1H); ^{13}C NMR : -0.40 (3 x q), 17.72 (q), 19.39 (t), 23.35 (t), 27.38 (t), 28.48 (t), 41.59 (d), 75.67 (d), 140.19 (s), 150.73 (s), 170.34 (s); MS, m/z: 238 (M$^+$); Anal. Found: C, 65.8; H, 9.6; Calc. for C$_{13}$H$_{22}$O$_2$Si: C, 65.5; H, 9.3%.

(3Z,3aα,7aα)-Hexahydro-3-ethylidene-2(3H)-benzofuranone (5b)

(9a) (0.160 g, 0.58 mmol) in Et_2O (3 ml), Me_2CuLi (4 ml, 0.86 mmol), -30°, 2 h. PLC (50% Et_2O/hexane) gave : (i) (E)-ethylidene lactone (15b) (0.022 g, 23%); (ii) (Z)-ethylidene lactone (5b) as an oil (0.014 g, 15%).

Dihydro-3-(1-methylethylidene)-5-phenyl-2(3H)-furanone (22)

(12b) (0.100 g, 0.32 mmol) in Et_2O (4 ml), Me_2CuLi (1 ml, 0.37 mmol), 0°, 2 h. Radial chromatography (25% E /H) gave (22) as an oil (0.046 g, 71%); distilled 80° (block)/0.08 mm; IR (neat) : 1750, 1195 (lactone), 1670 (C=C); ^{1}H NMR : 1.88 (s, 3H); 2.31 (br. s, 3H); 2.79 (m, W = 21 Hz, 1H); 3.33 (dd, *J* 15.7, 7.8 Hz, 1H); 5.45 (dd, *J* 7.8, 7.1 Hz, 1H); 7.36 (m, 5H); ^{13}C NMR : 19.97 (q), 24.62 (q), 36.63 (t), 76.65 (d), 118.99 (s), 125.36 (2 x d), 128.25 (d), 128.76 (2 x d), 140.93 (s), 150.82 (s), 170.07 (s); MS, m/z : 202 (M^+); Anal. Found: C, 77.1; H, 7.3; Calc. for $C_{13}H_{14}O_2$: C, 77.2; H, 7.0%.

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