Photoinduced Molecular Transformations. Part 137.[1] New General Synthesis of 3-Substituted 3,4-Dihydro-1*H*-benzo[2]pyran-1-ones (3,4-Dihydroisocoumarins) *via* Radical and Photochemical Fragmentations as the Key Step

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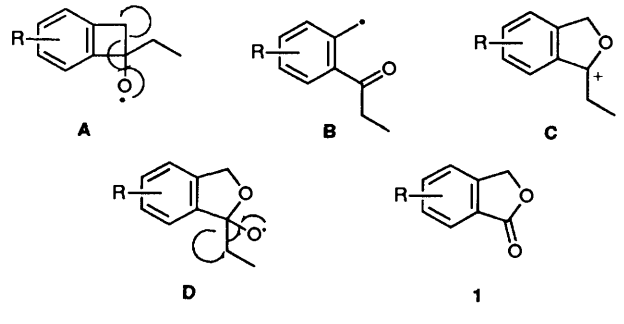
A new general method for a two-step synthesis of 3-substituted 3,4-dihydro-1*H*-benzo[2]pyran-1-ones (3,4-dihydroisocoumarins) is described. This method involves either regioselective alkoxyl radical fragmentation or regioselective photochemical fragmentation as the key step. 2-Hydroxyalkylation of a lithiated *o*-tolyl *tert*-butyl ketone with aromatic and aliphatic aldehydes and ketones gave equilibrated mixtures of 1-*tert*-butyl-3,4-dihydro-1-hydroxy-3-alkyl (or 3-aryl)-1*H*-2-benzopyrans and their ring-opened isomers in 42–94% yield. Photolysis of mixtures in chloroform with Pyrex-filtered light gave 3-alkyl (or 3-aryl)-3,4-dihydro-1*H*-benzo[2]pyran-1-ones (3,4-dihydroisocoumarins) in 27–64% yield as exclusive isolable products. On the other hand, photolysis of hypoiodites of the equilibrated mixture in benzene containing mercury(II) oxide and iodine gave the 3-substituted dihydroisocoumarins in 37—64% yield with an accompanying formation of phthalide, arising from a radical cascade process triggered by β-scission of the alkoxyl radicals generated from the ring-opened isomer of the lactones. The formation mechanisms of all the products are discussed.

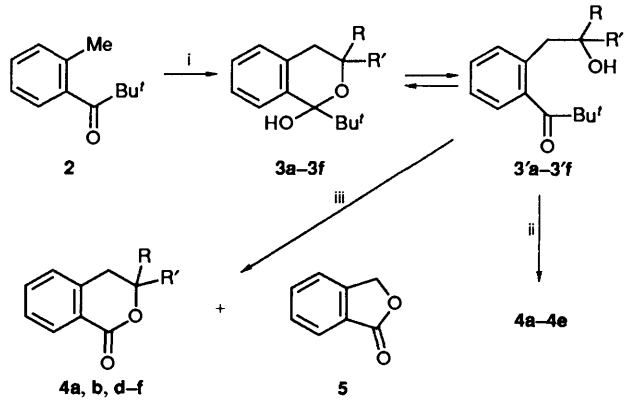
Dihydroisocoumarins (3,4-dihydro-1*H*-benzo[2]pyran-1-one) are a class of naturally occurring lactones, many of which display a wide variety of significant biological activity.[2] They have also been employed as key intermediates for the synthesis of natural products.[3]

A number of methods for synthesizing this class of molecules have been reported. Some of the recently published methods include the following: those *via* π-allylnickel halide and π-olefin–palladium complexes;[4a] *via* the reaction of *o*-tolyloxazoline with arylaldehydes in the presence of a base;[4b] *via* the thermal cyclization of δ-hydroxy amides prepared by the reaction of metalated *N*-methyl-*o*-toluamide with ketones and aldehydes;[4c] *via* the reaction of metalated toluic acids with aryl ketones;[4d,4e] *via* a thermal ring closure of stilbene-2-carboxylic acids;[4f] and *via* an electrocyclic reaction of the α-oxo-*ortho*-quinodimethane generated from *o*-(trimethylsilylmethyl)benzoyl chloride in the presence of aromatic aldehydes.[4g]

We have recently developed methods to synthesize isobenzofuran-1(3*H*)-ones **1** (phthalides),[5,6] including naturally occurring phthalides[5] and phthalide lignans.[6] This method comprises a cascade process involving the β-scission of alkoxyl radicals **A** generated by photolysis of the hypoiodites of 1-ethylbenzocyclobuten-1-ols.[5] Thus, the one-electron oxidation of a stabilized benzyl radical **B**, generated by the β-scission of alkoxyl radical **A**, to the corresponding benzyl cation by a metal ion, followed by its intramolecular combination with the carbonyl oxygen, affords cyclic cation **C**. The second β-scission of the alkoxyl radical **D** generated from a second hypoiodite formed by combination of cation **C** with iodine oxide [generated from mercury(II) oxide and iodine] gives phthalides **1**.



This pathway indicated that the generation of alkoxyl radicals of type **D** from appropriate hypoiodites may give lactones through an expulsion of the alkyl radicals. We herein report in full on a two-step general synthesis of 3-substituted dihydroisocoumarins from the lactols based on this process as the key reaction. We also report on an alternative procedure to form the dihydroisocoumarins from these lactols based on a photochemical fragmentation process which we found during this work. Scheme 1 outlines these methods.



a, R = Me, R^1 = H; **b**, R = *p*-tolyl, R^1 = H; **c**, R = PhCH=CH, R′ = H; **d**, R = R′ = Me; **e**, RR′ = [CH$_2$]$_5$; **f**, R = R′ = Ph

Scheme 1 *Reagents and conditions*: i, RCOR′, LDA, THF, −78 °C; ii, $CHCl_3$, *hν*; iii, HgO, I_2, benzene, *hν*

Results

Preparation of Substrates for the Fragmentations.—*tert*-Butyl *o*-tolyl ketone **2**[7] for the present experiments was prepared by the reaction of pivalaldehyde with *o*-tolylmagnesium bromide, followed by oxidation of the resulting 2,2-dimethyl-1-(*o*-tolyl)propyl alcohol. Treatment of ketone **2** with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −78 °C generated a benzyl anion. This anion reacted with various electrophiles such as aliphatic and aromatic aldehydes (acetaldehyde and *p*-tolualdehyde), an α,β-unsaturated aldehyde (cinnamaldehyde), and aliphatic and aromatic ketones

Table 1 Synthesis of 3,4-dihydro-1*H*-benzol[2]pyran-1-ones

	Lactols 3		Yield of lactols 3 and 3′ (%)[a]	The ratio of lactol to hydroxy ketone in $CDCl_3$[b]	Yields of 4 and 5 (%)[a]			
	R	R′			Method		4a–f	5
a	Me	H	91	67:33	A	4a[c]	62	
					B		57	11
b	*p*-tolyl	H	74	70:30	A	4b[d]	46	
					B		53	
c	PhCH=CH	H	69	56:44	A	4c	27	
d	Me	Me	94	72:28	A	4d[e]	64	
					B		44	26
e	$[CH_2]_5$		64	61:39	A	4e[f]	42	
					B		37	31
f	Ph	Ph	42	75:25	A	4f[f]	*g*	
					B		64	

A: *hv*–$CHCl_3$; B: i, HgO–I_2–benzene; ii, *hv* (> 300 nm).
[a] Isolated yield. [b] Estimated by ^1H NMR spectroscopy. [c] Refs. 4*a* and 8. [d] Ref. 4*b*. [e] Ref. 9. [f] Ref. 4*c*. [g] Olefin **10** is the product.

(acetone, cyclohexanone, and benzophenone) to give the corresponding 6-membered lactols **3a–f** in 42–94% yield (Table 1).

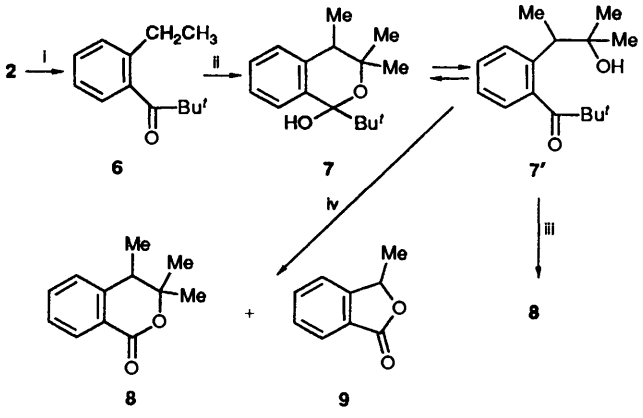
The ^1H NMR spectra of solutions of these lactols in $CDCl_3$ indicated that in solution they exist as an equilibrated mixture of lactols **3a–3f** and their hydroxy ketone forms **3′a–3′f**. The ratio of these two forms in $CDCl_3$, estimated from the signal areas of their *tert*-butyl group in the spectra, is given in Table 1. The results indicated that although the predominant form in the mixtures is the lactol **3** in all cases, the mixtures in solution contain 25–44% of the hydroxy ketone form **3′**.

Preparation of 3-Substituted Dihydroisocoumarins **4a, b, d** *and* **4f** *by β-Scission of the Hypoiodites of Lactols* **3** *in Benzene* (*Scheme* 1).—Irradiation of an equilibrated mixture of lactol **3a** and hydroxy ketone **3′a** in benzene containing mercury(II) oxide and iodine (2 mol equiv. each) with a 100 W high pressure Hg arc through a Pyrex filter at room temperature gave the expected dihydroisocoumarin **4a**[4a,8] in 57% yield along with phthalide **5** in 11% yield.

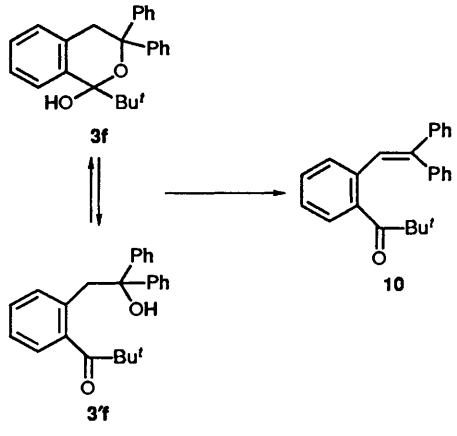
A similar photolysis concerning lactols **3b** and **3d–3f** gave dihydroisocoumarins **4b**,[4b] **4d**,[9] **4e**[4c] and **4f**[4c] as the major products in 37–64% yield along with the accompanying formation of phthalide **5** 26–31% yield. The results are summarized in Table 1.

Preparation of Dihydroisocoumarins **4a–4e** *by Photochemical α-Fission in Chloroform.*—The exclusive formation of dihydroisocoumarins **4a–4e** in better yields can be attained by a simpler procedure: irradiation of an equilibrated mixture of lactol **3a** and hydroxy ketone **3′a** in chloroform produced the dihydroisocoumarin **4a** in 62% yield. No phthalide **5** was formed in this photolysis. Similarly, the photolysis of lactols **3b–3e** in chloroform with Pyrex-filtered light gave the corresponding dihydroisocoumarins **4b–4e** in 46, 27, 64 and 42% yield, respectively. The photolysis of 3,3-diphenyl-3,4-dihydro-1*H*-benzo[2]pyran-1-ol **3f** in chloroform for 40 min, however, resulted in rapid dehydration to give olefin **10** in almost quantitative yield (Scheme 3, see below).

Preparation of 3,3,4-*Trimethyldihydroisocoumarin* **8** (*Scheme* 2).—The present preparation method of 3-substituted dihydroisocoumarins can be extended to the preparation of 3,4-disubstituted dihydroisocoumarins. 3,3,4-Trimethyldihydroisocoumarin **8** was thus prepared as the one simple example. Thus, lithiation of ketone **2** with LDA in THF at −78 °C, followed by treatment with methyl iodide, gave 1-(2-ethylphenyl)-2,2-dimethylpropan-1-one **6** in 72% yield. The hydroxymethylenation of ketone **6** with acetone in the presence of lithium 2,2,6,6-tetramethylpiperidide instead of LDA gave a 3:1 lactol–hydroxy ketone **7–7′** in 42% yield. Photolysis of the hypoiodites of the mixture **7–7′** according to the procedure mentioned above gave 3,3,4-trimethyldihydro isocoumarin **8** (52%) along with 3-methylphthalide **9**[10] (28%). Photolysis of the mixture **7–7′** in chloroform, however, gave the dihydroisocoumarin **8** in 65% yield as the exclusive product.



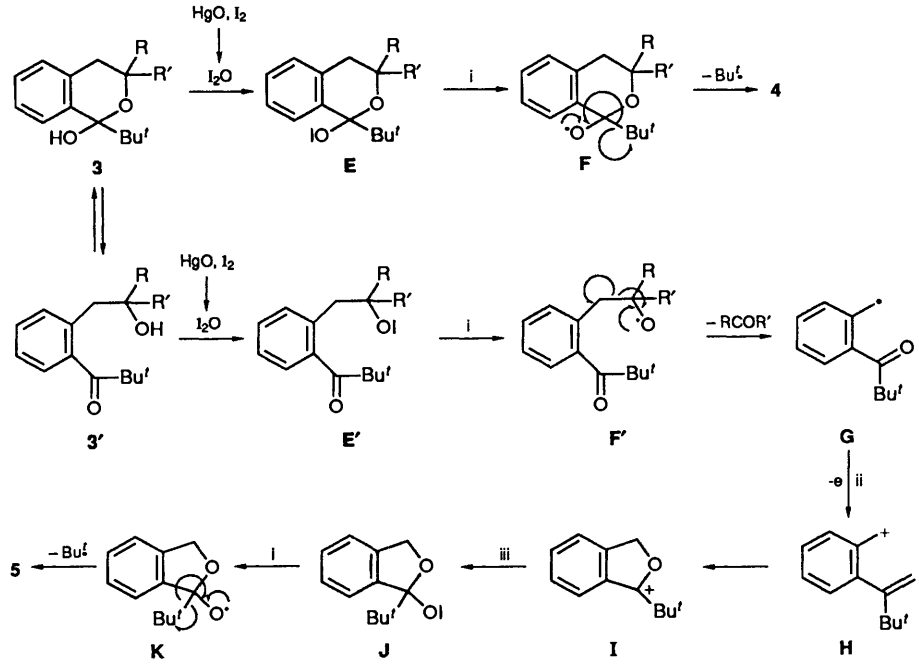
Scheme 2 *Reagents and conditions:* i, LDA, MeI; ii, LDA, acetone; iii, $CHCl_3$, *hv*; iv, HgO, I_2, benzene, *hv*



Scheme 3 *Reagents and conditions:* $CHCl_3$, *hv*, HCl (photogenerated)

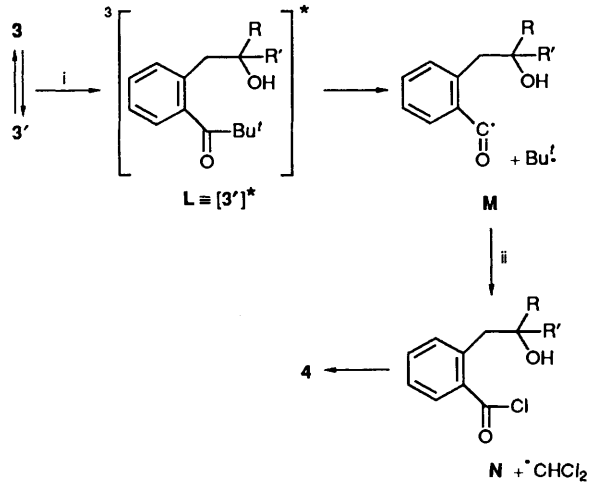
Discussion

Scheme 4 outlines the pathway for the formation of dihydroisocoumarins **4** and **8**, as well as phthalides **5** and **9**, when the hypoiodites of an equilibrated mixture of the lactol–hydroxy



Scheme 4 *Reagents and conditions:* i, *hv*; ii, Hg^{++}; iii, I_2O

ketones **3**–**3′** in benzene containing mercury(II) oxide–iodine are irradiated. Dihydroisocoumarins **4** and **8** are formed from the hypoiodites **E** of lactols **3** and **7** by expulsion of the *tert*-butyl radical from the alkoxyl radicals **F**. Phthalides **5** and **9** are formed from the hypoioites **E′** of hydroxy ketones **3′** through intermediates **F′** and **G**–**K**, as already outlined. The intermediate **G** corresponds to species **B** in the photolysis of the hypoiodites of 1-ethylbenzocyclobuten-1-ols. Species **G** then cascades to phthalides **5** and **9** by following exactly the same pathway as that for radical **B**.



Scheme 5 *Reagents and conditions:* i, $CHCl_3$, *hv*; ii, $CHCl_3$

Scheme 5 outlines the pathway for the formation of dihydroisocoumarins **4** and **8** in the photolysis of lactols **3** and **7** in chloroform; in contrast to the hypoiodite photolysis mentioned above, dihydroisocoumarins **4** and **8** are formed exclusively, with no accompanying formation of phthalides **5** and **9**, when the equilibrated mixtures of the lactol–hydroxy ketones **3**–**3′** and **7**–**7′** in chloroform are irradiated with Pyrex-filtered light. The absence of phthalides **5** and **9** in the products indicates that no alkoxyl radicals are involved in the formation of dihydroisocoumarins **4** and **8**. Irradiation of lactol–hydroxy ketones **3**–**3′** and **7**–**7′** thus generates triplet-excited hydroxy ketones **L** [≡**3′**]*. The type-II cleavage of the excited ketones **L** generates the acyl radicals **M**, which abstract chlorine from chloroform to give acid chlorides **N**. Cyclization of the acid chlorides afforded dihydroisocoumarins **4** and **8**. Exceptionally, irradiation of the lactol–hydroxy ketone **3f**–**3′f** in chloroform gave olefin **10**, arising from dehydration. This highly conjugated olefin **10** is believed to be formed by an acid-catalysed dehydration in which a trace of hydrogen chloride formed during the photolysis must play the role of a catalyst. The formation of olefin **10** in quantitative yield in equilibrium **4f**–**4′f** indicates that the dehydration is a ground-state reaction and that the formation of this olefin **10** should be especially easy due to its highly conjugated nature.

The generation of lithiated *o*-tolyl *tert*-butyl ketone and its application to the synthesis of heterocyclic molecules is unprecedented[11] although the reactions of lithiated α-substituted toluene derivatives with electrophiles have been used for the synthesis of heterocyclic molecules.[12]

It should also be noted that not only aromatic aldehydes and ketones as well as acyclic ketones, but also α,β-unsaturated aldehydes, aliphatic ketones, and aliphatic aldehydes can be used as electrophiles in the present method.

The present new general synthesis of dihydroisocoumarins indicates that a combination of the reaction of lithiated *o*-toluic acid derivatives with electrophiles and photochemical fragmentation is a useful and efficient method for the new annelation.

Experimental

M.p.s were recorded with a Yanagimoto melting-point apparatus and are uncorrected. The IR spectra were determined for Nujol mulls (except where stated otherwise) with a JASCO IR-810 spectrophotometer. The ^1H NMR spectra were determined in $CDCl_3$ ($SiMe_4$ as internal reference) with either a Hitachi R-90H FT NMR spectrometer operating at 90 MHz or a JEOL JNM-GX270 FT NMR spectrometer operating at 270 MHz. *J*-Values are given in Hz. High- and low-resolution mass spectra were recorded with a JEOL JMS-DX 303 spectrometer. TLC was carried out on Merck Kieselgel $60PF_{254}$. Photolysis

was carried out with a 100 W high-pressure Hg arc lamp (EIKOSHA, EHB-WU-100).

2,2-*Dimethyl*-1-(o-*tolyl*)*propyl Alcohol*—To a mixture of magnesium (608 mg, 25 mmol) in refluxing diethyl ether (8 cm^3) was added dropwise a solution of *o*-tolyl bromide (3.97 g, 23.2 mmol) in diethyl ether (8 cm^3) under argon. To this solution at 0 °C was added dropwise a solution of pivalaldehyde (1.35 g, 15.7 mmol) in diethyl ether (8 cm^3). The solution was stirred for 1 h at 0 °C and then neutralized with 0.5 mol dm^{-3} aq. sulfuric acid. The solution was extracted with diethyl ether. The organic layer was washed with brine and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave 2,2-*dimethyl*-1-(o-*tolyl*)*propyl alcohol*, which was purified by distillation (2.4 g, 86%), b.p. 70–73 °C/0.2 mmHg; ν_{max}(neat)/cm^{-1} 3430 (OH); δ(90 MHz) 0.97 (9 H, s, Bu^t), 2.35 (3 H, s, Ar*Me*) and 4.76 (1 H, s, C*H*OH); *m*/*z* 178 (M^+, 4.1%) and 121 [$(M - C_4H_9)^+$, 100] (Found: C, 80.7; H, 10.4. $C_{12}H_{18}O$ requires C, 80.85; H, 10.18%).

tert-*Butyl* o-*Tolyl Ketone* **2**.—To a solution of 2,2-dimethyl-1-(*o*-tolyl)propyl alcohol (2.4 g, 13.5 mmol) in methylene dichloride (30 cm^3) were added Celite and then PCC (8.76 g, 40.8 mmol) gradually. The solution was stirred for 12 h and filtered through Celite. The filtrate was washed with 5% aq. hydrochloric acid and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave an oil, which was distilled to give *tert*-butyl *o*-tolyl ketone **2**[7] (1.79 g, 75%), b.p. 52–57 °C/0.5 mmHg.

1-tert-*Butyl*-3-*methyl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*ol* **3a** *and its Ring-opened Tautomer* **3'a**.—To a stirred solution of LDA (3.0 mmol), generated *in situ* by the standard method, in THF (5 cm^3) at −78 °C under argon was added dropwise ketone **2**[7] (0.26 g, 15 mmol). After 5 min the deep red carbanion was allowed to react with acetaldehyde (132 mg, 3.0 mmol). The red colour disappeared immediately. The reaction mixture was quenched with saturated aq. ammonium chloride and was extracted with diethyl ether. The extract was washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a residue, which was subjected to PLC on silica gel to give *compounds* **3a** and **3'a** (302 mg) (**3a**:**3'a** ~ 2:1 in $CDCl_3$); R_f 0.37 [(1:10) ethyl acetate–hexane]; ν_{max}(neat)/cm^{-1} 3444 (OH), 1686 (C=O) and 1072 (C–O); δ(270 MHz) 0.98 (9 H, s, Bu^t of **3a**), 1.25 (3 H, d, *J* 7.43, Me of **3'a**), 1.27 (9 H, s, Bu^t of **3'a**), 1.34 (3 H, d, *J* 7.43, Me of **3a**), 2.4–2.9 (3 H, m, OH and benzylic H), 3.8–3.9 (1 H, m, CHO of **3a**) and 3.95–4.05 (1 H, m, CHO of **3'a**); *m*/*z* 221 [$(M + 1)^+$, 0.24%], 220 (M^+, 0.03) and 163 [$(M - Bu^t)^+$, 100] (Found: M^+, 220.1483. $C_{14}H_{20}O_2$ requires *M*, 220.1464).

1-tert-*Butyl*-3-(p-*tolyl*)-3,4-*dihydro*-1H-2-*benzopyran*-1-*ol* **3b** *and its Ring-opened Tautomer* **3'b**.—This *equilibrated mixture* was prepared similarly to compound **3a**; R_f 0.34 [(1:10) ethyl acetate–hexane]; ν_{max}(neat)/cm^{-1} 3446 (OH), 1684 (C=O) and 1052 (C–O); δ(270 MHz) 1.08 (9 H, s, Bu^t of **3b**), 4.77 (1 H, dd, *J* 10.99 and 2.20, CHO of **3b**) and 4.86 (1 H, dd, *J* 9.16 and 3.30, CHO of **3'b**); *m*/*z* 296 (M^+, 1.1%), 279 [$(M - OH)^+$, 6.3], 2.39 [$(M - Bu^t)^+$, 44], 221 (95) and 119 (100) (Found: M^+, 296.1801. $C_{20}H_{24}O_2$ requires *M*, 296.1776).

1-tert-*Butyl*-3-*styryl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*ol* **3c** *and its Ring-opened Tautomer* **3'c**.—This *mixture* was prepared by hydroxyalkylation of ketone **2** with cinnamaldehyde as mentioned above. R_f 0.31 [(1:5) ethyl acetate–hexane]; ν_{max}(neat)/cm^{-1} 3420 (OH), 1685 (C=O) and 1069 (C–O); δ(400 MHz) 1.07 (9 H, s, Bu^t of **3c**), 1.28 (9 H, s, Bu^t of **3'c**), 2.65–2.95 (3 H, m, benzylic H of **3c** and **3'c**, OH of **3c**), 3.40 (1 H, d, *J* 4.39, OH of **3'c**), 4.45–4.55 [1 H, m, C*H*(OH)], 6.27 (1 H, dd, *J* 15.62 and 5.86, PhCH=C*H* of **3'c**), 6.31 (0.55 H, dd, *J* 15.62 and 5.86, PhCH=C*H* of **3c**), 6.35 (1 H, d, *J* 15.62, PhCH=C*H* of **3'c**) and 6.39 (1 H, d, *J* 15.62, PhC*H*=CH of **3c**); *m*/*z* 308 (M^+, 0.93%), 291 [$(M - OH)^+$, 5.4], 251 [$(M - Bu^t)^+$, 30] and 119 (100) (Found: M^+, 308.1751. $C_{21}H_{24}O_2$ requires *M*, 308.1776).

1-tert-*Butyl*-3,3-*dimethyl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*ol* **3d** *and its Ring-opened Isomer* **3'd**.—This *equilibrated mixture* was prepared by hydroxyalkylation of ketone **2** with acetone as described for the preparation of compound **3a**; R_f 0.42 [(1:10) ethyl acetate–hexane]; ν_{max}(neat)/cm^{-1} 3478 (OH), 1677 (C=O) and 1059 (C–O); δ(270 MHz) 0.95 (9 H, s, Bu^t of **3d**), 1.04 (3 H, s, Me of **3'd**), 1.24 (3 H, s, Me of **3d**), 1.25 (9 H, s, Bu^t of **3'd**), 1.40 (3 H, s, Me of **3d**), 2.47 (1 H, d, *J* 16.12, benzylic H of **3d**), 2.87 (1 H, d, *J* 16.12, benzylic H of **3d**) and 3.58 (1 H, s, benzylic H of **3'd**); *m*/*z* 235 [$(M + 1)^+$, 0.27%], 234 (M^+, 0.33), 217 [$(M - OH)^+$, 13], 177 [$(M - Bu^t)^+$, 29], 159 (46) and 131 (100) (Found: C, 76.6; H, 9.5. $C_{14}H_{22}O_2$ requires C, 76.88; H, 9.46%).

1-tert-*Butyl*-3,4-*dihydro*-1H-2-*benzopyran*-3-*spirocyclohexan*-1-*ol* **3e** *and its Ring-opened Tautomer* **3'e**.—This *mixture* was prepared by the reaction of ketone **2** with cyclohexanone; R_f 0.54 [(1:5) ethyl acetate–hexane]; ν_{max}(neat)/cm^{-1} 3606 and 3500 (OH), 1677 (C=O), 1059 and 1040 (C–O); δ(90 MHz) 0.97 (9 H, s, Bu^t of **3e**), 1.26 (9 H, s, Bu^t of **3'e**), 1.3–2.0 (10 H, m), 2.60 (2 H, s, benzylic H of **3'e**), 2.63 (1 H, d, *J* 14.94, benzylic H of **3e**) and 2.77 (1 H, s, benzylic H of **3e**); *m*/*z* 274 (M^+, 0.36%), 257 [$(M - OH)^+$, 1.1], 217 [$(M - Bu^t)^+$, 9.1] and 119 (100) (Found: M^+, 294.1904. $C_{18}H_{26}O_2$ requires *M*, 274.1933).

1-tert-*Butyl*-3,3-*diphenyl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*ol* **3f** *and its Ring-opened Tautomer* **3'f**.—This *equilibrated mixture* was prepared from ketone **2** and benzophenone by the procedure as mentioned above. M.p. 143–147 °C (from Et_2O–hexane); ν_{max}/cm^{-1} 3580 and 3370 (OH), 1662 (C=O) and 1051 (C–O); δ(270 MHz), 1.11 (9 H, s, Bu^t of **3f**), 1.27 (9 H, s, Bu^t of **3'f**), 3.29 (1 H, d, *J* 16.12, benzylic H of **3f**), 3.48 (2 H, s, benzylic H of **3'f**) and 3.64 (1 H, d, *J* 16.12, benzylic H of **3f**); *m*/*z* 358 (M^+, 0.5%), 341 [$(M - OH)^+$, 2.4], 30 [$(M - Bu^t)^+$, 7.5), 283 (26) and 183 (100) (Found: C, 83.7; H, 7.3. $C_{25}H_{26}O_2$ requires C, 83.76; H, 7.31%).

1-(2-*Ethylphenyl*)-2,2-*dimethylpropan*-1-*one* **6**.—To a stirred solution of *t*-butyl *o*-lithiomethylphenyl ketone (1 mmol), generated as mentioned above, was added methyl iodide (0.28 g, 2 mmol). After the disappearance of the red colour, the mixture was worked up in a similar manner as mentioned above. Distillation (Kugelrohr) gave *title ketone* **6** (0.14 g, 72%), b.p. 95–100 °C (bath temp.)/0.5 mmHg; ν_{max}(neat)/cm^{-1} 1678 (C=O); δ(90 MHz) 1.21 (3 H, t, *J* 7.47, Me), 1.25 (9 H, s, Bu^t) and 2.50 (2 H, q, *J* 7.47, CH_2); *m*/*z* 190 (M^+, 2.9%) and 133 [$(M - Bu^t)^+$, 100] (Found: M^+, 190.1336. $C_{13}H_{18}O$ requires M, 190.1358).

1-tert-*Butyl*-3,3,4-*trimethyl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*ol* **7** *and its Ring-opened Tautomer* **7'**.—Hydroxyalkylation of ketone **6** with acetone was carried out in a similar way as described for the preparation of lactol **4a**, with the exception of the use of 2,2,6,6-tetramethylpiperidine in place of diisopropylamine as above, to give *lactol* **7** (3:1) in 42% yield. R_f 0.42 [(1:10) EtOAc–hexane]; ν_{max}(neat)/cm^{-1} 3486 (OH), 1681 (C=O) and 1043 (C–O); δ(270 MHz) 0.88 (3 H, s, 3-Me of **7**), 0.96 (9 H, s, Bu^t of **7**), 1.03 (3 H, s, 3-Me of **7'**), 1.19, 1.22, 1.24, 1.26, 1.29, 1.32 and 1.38 (24 H, 6 peaks), 2.57 (1 H, q, *J* 6.96, benzylic H of **7'**) and 2.8–2.9 and 2.86 (2 H, br s and q, *J* 6.96, OH of **7'** and benzylic H of **7**); *m*/*z* 231 [$(M - OH)^+$, 6.2%], 191 [(M −

Bu^t)$^+$, 70] and 133 (100) (Found: C, 77.3; H, 9.8. $C_{16}H_{24}O_2$ requires C, 77.37; H, 9.74%).

3-*Methyl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*one* **4a**.—(a) *By photochemical fragmentation in chloroform.* A solution of lactol **3a** (100 mg, 0.452 mmol) in chloroform (20 cm^3) was irradiated for 6 h under nitrogen through a Pyrex filter with a 100 W high-pressure mercury arc. The removal of the solvent gave a residue, which was subjected to PLC on silica gel [(1:10) ethyl acetate–hexane] to afford the dihydroisocoumarin **4a**[9] as an oil (45 mg).

(b) *By the photolysis of the hypoiodite in benzene.* A stirred solution of lactol **3a** (199 mg, 0.54 mmol) in benzene (20 cm^3) containing red HgO (234 mg, 1.08 mmol) and iodine (274 mg, 1.08 mmol) was irradiated through a Pyrex filter for 5 h. The solution was then filtered through a Celite pad. The filtered solution was washed successively with 5% aq. sodium thiosulfate and brine, and dried over anhydrous $MgSO_4$. After removal of the solvent, followed by PLC on SiO_2 [(1:10) ethyl acetate–hexane] of the resulting product mixture gave compound **4a**[9] (50 mg) and *phthalide* **5** (8.0 mg).

3-(p-*Tolyl*)-3,4-*dihydro*-1H-2-*benzopyran*-1-*one* **4b**.[4b]—(a) *By photochemical fragmentation.* Photolysis of a solution of lactol **3b** in chloroform as described for the preparation of the isocoumarin **4a** for 24 h gave the isocoumarin **4b**, m.p. 93–95 °C (from hexane–methylene dichloride) (lit.,[4b] 95–96 °C).

(b) *By photolysis of the hypoiodite in benzene.* Photolysis of a solution of lactol–hydroxy ketone in benzene containing red mercury(II) oxide and iodine gave the isocoumarin **4b**.

3-[(Z)-*Styryl*]-3,4-*dihydro*-1H-2-*benzopyran*-1-*one* **4c**.—Irradiation of lactol **3c** in chloroform for 3.5 h gave *compound* **4c** as an oil; R_f 0.40 [(1:5) ethyl acetate–hexane]; ν_{max}(neat)/cm^{-1} 1724 (C=O) and 1606 (C=C); δ(400 MHz) 3.11 (1 H, dd, *J* 16.12 and 3.90, 4-H), 3.19 (1 H, dd, *J* 16.12 and 10.25, 4-H′), 5.22 (1 H, dddd, *J* 10.25, 6.34, 3.90 and 1.46, 3-H), 6.34 (1 H, dd, *J* 15.62 and 6.34, PhCH=C*H*) and 6.79 (1 H, dd, *J* 15.62 and 1.46, PhC*H*=CH); *m*/*z* 250 (M$^+$, 34%) and 118 [(M − $C_6H_5CHCHCHO$)$^+$, 100] (Found: M$^+$, 250.1010. $C_{17}H_{14}O_2$ requires *M*, 250.0994).

3,3-*Dimethyl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*one* **4d**.[9]—(a) *By photochemical fragmentation.* Irradiation of lactol **3d** in chloroform for 52 h gave compound **4d**; b.p. 150 °C (bath temp.)/0.1 mmHg [lit.,[9] 190 °C (bath temp.)/2.5 mmHg].

(b) *By photolysis of the hypoiodite of lactol* **3d** *in benzene.* Irradiation of lactol **3d** in benzene containing red mercury(II) oxide and iodine for 3 h gave the isocoumarin **4d** along with phthalide **5**.

3,4-*Dihydro*-1H-2-*benzopyran*-3-*spirocyclohexan*-1-*one* **4e**.[4c] (a) *By photochemical fragmentation.* Irradiation of lactol **3e** in chloroform for 7 h gave compound **4e**; b.p. 112–115 °C (bath temp.)/0.1 mmHg (lit.,[4c] 142–144 °C/0.35 mmHg).

(b) *By photolysis of the hypoiodite of lactol.* The photolysis of lactol **3e** for 6 h gave compound **4e** along with phthalide **5**.

1-[2-(2,2-*Diphenylethenyl*)*phenyl*]-2,2-*dimethylpropan*-1-*one* **10**.—Irradiation of lactol **3f** in chloroform for 40 h gave compound **10** (99%); m.p. 106–108 °C (from hexane–Et_2O); ν_{max}/cm^{-1} 1678 (C=O); δ(90 MHz) 1.27 (9 H, s, Bu^t) and 6.75–7.35 (15 H, m); *m*/*z* 340 (M$^+$, 30%) and 233 [(M − Bu^t)$^+$, 100] (Found: C, 88.2; H, 7.1. $C_{25}H_{24}O$ requires C, 88.19; H, 7.11%).

3,3-*Diphenyl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*one* **4f**.—Irradiation of lactol **3f** in benzene containing red mercury(II) oxide and iodine for 5 h gave the isocoumarin **4f**; m.p. 145–146 °C (from hexane–ethanol) (lit.[4c] 144–144.5 °C).

3,3,4-*Trimethyl*-3,4-*dihydro*-1H-2-*benzopyran*-1-*one* **8**.—*Irradiation of lactol* **7** in chloroform for 23 h gave *compound* **8** (65%); R_f 0.19 [(1:5) EtOAc–hexane]; ν_{max}(neat)/cm^{-1} 1716 (C=O); δ(90 MHz) 1.32 (3 H, d, *J* 7.26, 4-Me), 1.38 (s, 3-Me), 1.43 (s, 3 H, 3′-Me) and 2.98 (1 H, q, *J* 7.26, 4-H); *m*/*z* 190 (M$^+$, 2.2%), 175 [(M − Me)$^+$, 4.2], 147 (4.3) and 132 [(M − Me_2CO)$^+$, 100] (Found: M$^+$, 190.1004. $C_{21}H_{14}O_2$ requires *M*, 190.0993).

Irradiation of the hypoiodite of compound **7** in benzene containing red mercury(II) oxide and iodine for 8 h gave compound **8** in 52% yield along with 3-methylphthalide **9**[10] in 28% yield.

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