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Heterodiene Cycloadditions: Preparation and Transformations of Some Substituted Pyrano[4,3-*b*][1]benzopyrans

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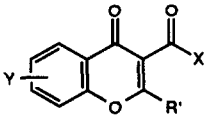
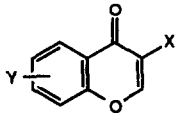
Abstract: Heterodiene cycloadditions of 4-oxo-4*H*-1-benzopyrans with formyl, acetyl, or carboxyl substituents at C-3 to 1-alkoxy- or 1,1-dialkoxyalkenes produce 3-alkoxy- or 3,3-dialkoxy-4,4a-dihydropyrano[4,3-*b*][1]benzopyran-10-ones which are capable of a variety of selective transformations, including acid-induced epimerisation and/or retro-cycloaddition, reduction, hydrolysis and alcoholysis, in some cases under very mild conditions.

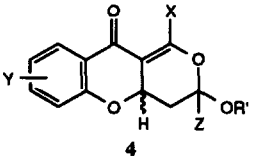
4-Oxo-4*H*-1-benzopyrans (chromones) **1–3** with electron-withdrawing substituents at C-3 are highly versatile molecules. Their reactivity towards nucleophiles can lead to a variety of alkylated,[1,2] heteroannulated[3] and spiroannulated[4] chroman-4-one derivatives, or rearrangement products.[5] They also function as dienophiles in [4π + 2π] cycloadditions of electron-rich dienes,[6] or as heterodienes in inverse electron demand Diels-Alder reactions of enol ethers.[7–9] The latter process offers a direct route to pyrano[4,3-*b*][1]benzopyrans **4**, whose heterocyclic nucleus occurs naturally in the fungal metabolite fulvic acid **5**,[10] and our interest in this and related natural products led us to undertake a study of the chemistry of **4** which we herein describe in detail.



1
X = H, R, OR, Ar, *etc.*



2 X = CHO, COR
3 X = S(O)Ar, CO_2R



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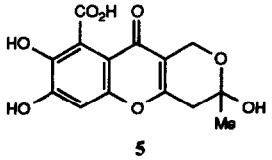

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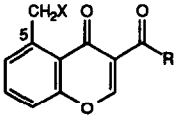

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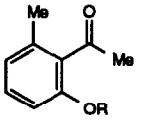
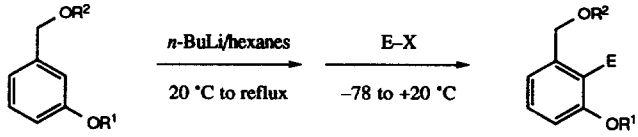


7a R = H
7b R = Me

Starting Materials. The chromone-3-carbaldehydes **2** (X = CHO) used in this work are accessible *via* Vilsmeier formylation of appropriate *o*-hydroxyacetophenones.[11,12] In order to include in our study materials with substitution patterns typical of the polyketide biosynthetic pathway (*cf.* **5**), we sought chromones of the form **6**. Attempts to obtain these by modifying the benzylic methyl group of the acetophenones **7**[13] met with no

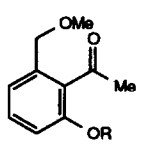
success, so we turned our attention to applying directed lithiation/trapping techniques to the ethers **8**–**13** derived from *m*-hydroxybenzyl alcohol (Table 1).[14–16] The direct acetylation of the 3-(methoxymethyl)phenol derivatives **8** and **9** by this method was moderately effective (entries 1, 2 and 6), whereas the lithiated 3-(methoxymethoxymethyl)arenes **10** and **11** were less amenable to our needs. The dilithiated alcohol **12** gave the *C*-substituted products **22** and **23** on treatment with acetaldehyde and *N*,*N*-dimethylformamide (DMF) respectively, but attempted acetylation yielded only the *O*-acetyl compound **24**. The homologue **25** was obtained from lithiated **13** in modest yield (entry 14). Manganese dioxide oxidation of the diol **22** (which was also available from the lactol **23** *via* treatment with methyllithium) gave the phthalide **26** in high yield.

TABLE 1 Formation of 1,2,3-trisubstituted benzenes *via* lithiation of *m*-hydroxybenzyl alcohol derivatives

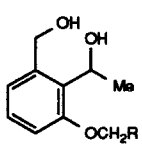


Entry	Substrate	R^1	R^2	E–X	Product	E	Yield (%)†	SM (%)‡
1	**8**	Me	Me	AcCl	**14**	COMe	50	11
2	**8**			Ac_2O	**14**		48	17
3	**8**			CO_2	**15**	CO_2H	62	16
4	**9**	CH_2OMe	Me	MeI	**16**	Me	92	
5	**9**			AcCl	**17**	COMe	18	44
6	**9**			Ac_2O	**17**		44	54
7	**10**	Me	CH_2OMe	MeI	**18**	Me	73	10
8	**10**			Ac_2O	**19**	COMe	13*	50
9	**11**	CH_2OMe	CH_2OMe	MeI	**20**	Me	46	19
10	**11**			Ac_2O	**21**	COMe	25*	
11	**12**	Me	H	MeCHO	**22**	CH(OH)Me	55	27
12	**12**			DMF	**23**		69	
13	**12**			AcCl, Ac_2O	**24**		–	
14¶	**13**	CH_2OMe	H	MeCHO	**25**	CH(OH)Me	39	41

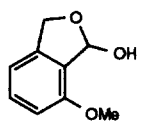
† Refers to isolated chromatographically homogeneous material except where indicated otherwise
‡ Refers to recovered starting material
* Not obtained pure; yield estimated from the ^1H n.m.r. spectrum of the crude product
¶ Benzene used as co-solvent



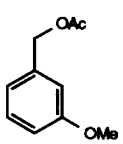
14 R = Me
17 R = CH_2OMe
27 R = H



22 R = H
25 R = OMe



23



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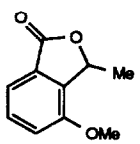
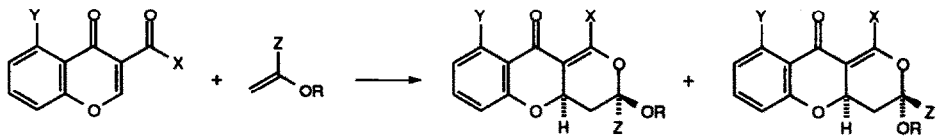


26

Unfortunately most attempts to transform the above products into chromone precursors floundered at the deprotection step. For example, attempted demethylation of the ketone **14** under various conditions[17] led either to the formation of complex mixtures containing none of the desired *o*-hydroxyacetophenone or to recovery of starting material. One notable exception was the ketone **17**, which was smoothly converted into the hydroxy compound **27** *via* treatment with aqueous trifluoroacetic acid.

Cycloadditions. The results of a series of cycloaddition experiments are shown in Table 2, which reveals three significant features of the reaction. Firstly, the anticipated[7] *endo* selectivity (≥3:1) is retained throughout the series, but 5-substituted chromones react much more slowly than their unsubstituted homologues (*cf.* entries 1, 5, 7). This is presumably a result of *peri* interactions, which cause the 4-oxo substituent to be pushed out of the plane of the heterodiene, thereby diminishing its activating effect on it. Secondly, enoic acids can serve as the heterodiene (*cf.* entries 9–12, 16),[18] the 4π system being stabilised in the s-*cis* conformation required for reaction by intramolecular H-bonding between the carboxyl hydrogen and the 4-oxo substituent.

TABLE 2 Heterodiene cycloadditions of 3-substituted chromones to alkoxyalkenes



endo *exo*

Entry	Heterodiene 28	X	Y	Dienophile 34	R	Z	Temp. (°C)	Time (d)	Cycloadducts *endo*	*exo*	Total (%)	Ratio (a:b)
1*	**28**	H	H	**34**	Et	H	20	3	**38a**	**38b**	90	5:1
2*	**29**	Me	H	**34**	Et	H	115	2	**39a**	**39b**	92	3.5:1
3*	**28**	H	H	**35**	Bu^n	H	20	6	**40a**	**40b**	95	8:1
4	**29**	Me	H	**35**	Bu^n	H	95	3.5†	**41a**	**41b**	75	4:1
5	**30**	H	Me	**34**	Et	H	20	21	**42a**	**42b**	77	3:1
6	**30**	H	Me	**34**	Et	H	100	3	**42a**	**42b**	73	2.8:1
7	**31**	H	CH_2OMe	**34**	Et	H	20	10	**43a**	**43b**	85	4:1
8	**31**	H	CH_2OMe	**34**	Et	H	115	1	**43a**	**43b**	74	2.9:1
9	**32**	OH	H	**34**	Et	H	20	7	**44a**	**44b**	77	4:1
10	**32**	OH	H	**35**	Bu^n	H	20	9	**45a**	**45b**	90	7:1‡
11	**32**	OH	H	**36**	Me	Me	20	3	**46a**	**46b**	80	4:1
12	**33**	OH	CH_2Cl	**34**	Et	H	20	5	**47a**	**47b**	100	6:1¶
13	**28**	H	H	**37**	Me	OMe	20	0.01	**48**		100	–
14	**29**	Me	H	**37**	Me	OMe	20	0.2	**49**		100	–
15	**30**	H	Me	**37**	Me	OMe	20	0.1	**50**		99	–
16	**32**	OH	H	**37**	Me	OMe	20	0.01	**51**		95	–

* Results from reference 7 (for comparison)

† Rate enhancement (*ca.* 5-fold) by $Yb(fod)_3$

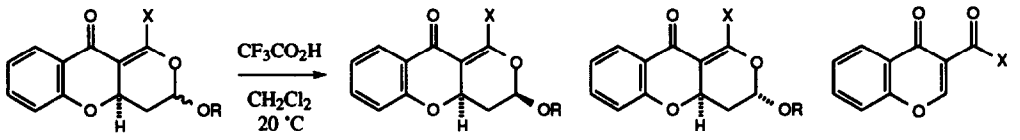
‡ Judged by ^1H n.m.r. spectroscopy; the isolated yield of **45a** was 50%

¶ Judged by ^1H n.m.r. spectroscopy; the isolated yield of **47a** was 56%

Thirdly, cycloadditions involving the highly nucleophilic 1,1-dialkoxyalkenes (ketene acetals) as dienophiles (entries 12–16) are extremely rapid and efficient, and the products possess a variety of synthetically useful properties which are described below.

Acid-induced Equilibration and retro-Cycloaddition Reactions. Although the *endo* cycloadducts are kinetically favoured in the above cycloadditions, the *exo* isomers are thermodynamically more stable due to the anomeric effect,[19] and each of the isomers of **38** gave the same mixture (*exo*:*endo* 6.5:1) on treatment with anhydrous acid for several hours (Table 3). Under similar conditions, the 1-methyl system **39a** was observed to undergo some fragmentation, leading to the formation of 3-acetylchromone **29** in 33% yield, while the cycloadducts **41a** and **52a** reacted almost exclusively through the alternative pathway, a nett retro-cycloaddition.

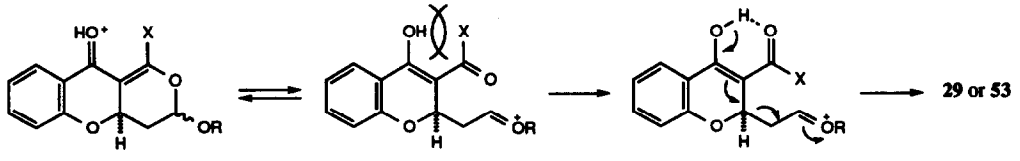
TABLE 3 Acid-induced equilibration and retro-cycloaddition reactions of pyrano[4,3-*b*][1]benzopyrans



a *endo* **b** *exo*

Educt	X	R	Time (h)	Product Composition (%)		
38a	H	Et	3	**38a** (22.8)	**38b** (77.2)	**28** (0)
38a	H	Et	24	**38a** (13.2)	**38b** (86.8)	**28** (0)
38b	H	Et	3	**38a** (9.5)	**38b** (90.5)	**28** (0)
38b	H	Et	24	**38a** (13.4)	**38b** (86.6)	**28** (0)
39a	Me	Et	24	**39a** (11)	**39b** (55)	**29** (33)
41a	Me	Bu^n	24	**41a** (trace)	**41b** (trace)	**29** (100)
52a	Ph	Et	24	**52a** (trace)	**52b** (trace)	**53** (100)

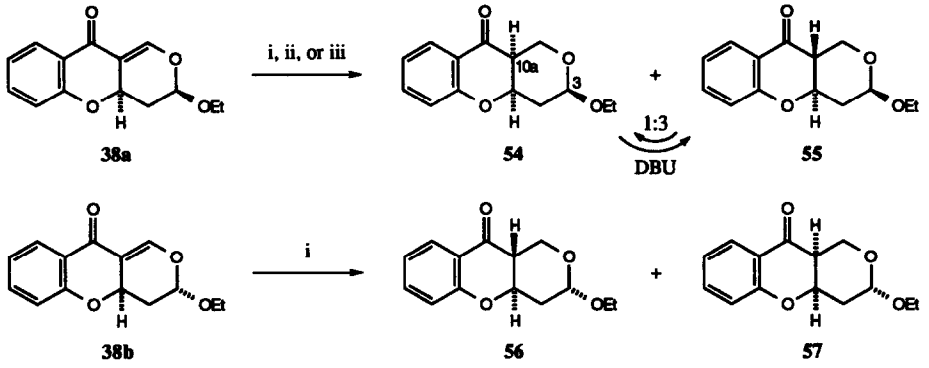
These results are consistent with a mechanism involving initial protonation of the carbonyl group, leading to an oxonium species which can recyclise to give either configuration at C-3 (Scheme 1). With increasing size of X, steric repulsion within the oxonium species inhibits the recyclisation, and the fragmentation becomes dominant.



SCHEME 1

Hydrogenation Studies. Catalytic hydrogenations of the cycloadducts **38a** and **38b** at 1 atm. pressure proved stereoselective but rather capricious, possibly due to variation in the activity of different batches of the catalyst (5% Pd-C). In the respective major products **54** and **56** there was a *trans*-relationship between the new 10a-H and the original 3-OEt substituent (Scheme 2), but treatment of the *cis*-fused system **54** with base produced an equilibrium mixture with the *trans*-fused isomer **55** (in which the saturated ring can adopt a chair

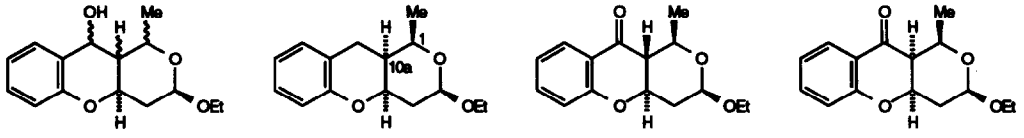
conformation with all substituents equatorial) predominant by a ratio of 3:1. From a synthetic point of view these reductions were more reliable when carried out over two steps, *i.e* reduction to a mixture of chromanols (using either catalytic hydrogenation at 3 atmospheres pressure, or $NaBH_4$) followed by oxidation with MnO_2.



38a **54** **55** **38b** **56** **57**

SCHEME 2 *Reagents:* i, 1 atm. H_2, 5% Pd-C, EtOH; ii, 3 atm. H_2, 5% Pd-C or Raney Ni, EtOH, then MnO_2, CH_2Cl_2; iii, $NaBH_4$, EtOH, then MnO_2, CH_2Cl_2.

Catalytic hydrogenation of the 1-methylated cycloadduct **39a** at the increased pressure of 10 atm. induced a significant amount of hydrogenolysis, the mixture of isomers **58** being accompanied by a comparable amount of the *cis*-fused chroman **59** ($J_{1,10a}$ = 1.7 Hz). Oxidation of the mixed chromanols **58** with MnO_2 gave the corresponding chromanones **60** and **61** (85%, 1:1), the relationship between them being deduced by analysis of their 300 MHz ^1H (including 2-D) n.m.r spectra, in which $J_{1,10a}$ values of 9.5 Hz for **60** and 2.6 Hz for **61** indicated a diaxial arrangement of the 1,10a-hydrogens in the former but not the latter. This was confirmed by the conversion of **61** into the more stable *trans*-isomer **60** upon treatment with a catalytic amount of DBU. The

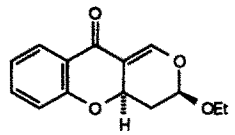


58 **59** **60** **61**

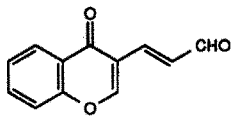
point in the sequence at which the 1α,10aβ-dihydro (1,10a-*trans*) stereochemistry of **60** is established is not yet known, but could be the consequence of some equilibration during the oxidation step. This and other aspects of the reduction sequence are currently under investigation.

Ring-opening Reactions. As a consequence of their dual vinylogous ester and acetal nature, the cycloadducts can react both with nucleophilic and acidic reagents. Treatment of **38a** with methoxide induces rearrangement to the aldehyde **62** in good yield (Table 4). This transformation probably occurs *via* attack of methoxide at C-1 to give **64**, loss of ethoxide then giving **65** and hence **66**, which cyclises either directly or upon (hydrolytic) work-up. The formation of **62** from **38** also occurs under acidic conditions,[9] but we found that an alternative pathway could be promoted by limiting the water content of the reaction medium. Thus treatment of the adduct **38a** with ethanolic or methanolic hydrogen chloride gave the respective acetal **63a** or **63b** in moderate yield. To account for this, we assume that the protonated adduct **67** is transformed by a variety of acetalisation equilibria to intermediates of the form **68** and **69**, but that in the absence of water the concentration of the hemiacetals **68** (R = H) and **69** (R' = H), the precursors of **70** and hence the aldehyde **62**, is minimised.

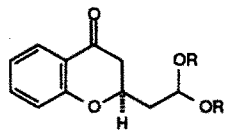
TABLE 4 Ring-opening reactions of 3-ethoxy-4,4a-dihydro-3H,10H-pyrano[4,3-*b*][1]benzopyran-10-one **38a**



38a

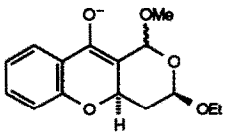


62



63a R = Et
63b R = Me

Educt	Conditions	Products (isolated yields, %)	
38a	NaOMe, MeOH	**62** (70)	–
38a	EtOH, H_2O, H_2SO_4	**62** (49)	–
38a	EtOH, H_2O, *p*-TsOH	**62** (25)	**63a** (36)
38a	EtOH, HCl	–	**63a** (44)
38a	MeOH, HCl	–	**63b** (67)
63a	MeOH, HCl, H_2O	–	**63b** (73)



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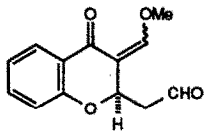

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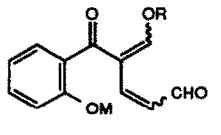
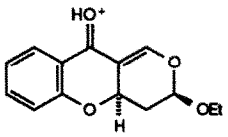


66 M = Na R = Me
70 M = H



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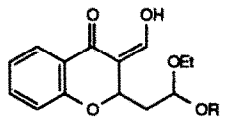

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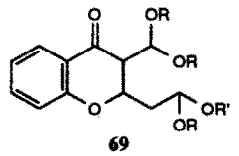
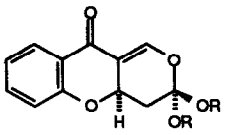


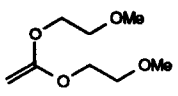
69

The acid-induced loss of the 3-substituent from either a hydroxymethylenechromanone **68** (as alkyl formate) or a fully alkoxylated chromanone **69** (as a trialkyl orthoformate) is essentially a retro-Claisen reaction, analogous to those described by Dean and co-workers.[20]

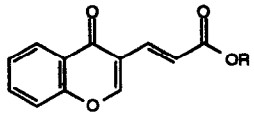
Treatment of the ketene acetal derivatives **48** and **71** (the latter being a convenient type to use due to the ease with which the precursor **72** can be prepared) with aqueous acid (HCl, DMF, water, 80 °C) gave modest yields of the respective rearranged products **73** and **74**. However, similar treatment of **71** but without heating gave a high yield of the 3-(hydroxymethylene)chromanone **75**, which could then be transformed into **74** by subjecting it to the original hot conditions. In contrast, treatment of either of the cycloadducts **48** or **71** with HCl or H_2SO_4 in methanol gave the ester **76** in 60–65% yield, while the alternative use of ethanol and acid gave the corresponding ethyl ester **77** in similar yield. The formation of the esters **76** and **77** is presumed once again to involve the loss of the 3-substituent as formate in a retro-Claisen process. The two-step transformation of the aldehyde **28** into the ester **76** is a potentially useful method for the overall conjugate addition of a two-carbon (acetic ester enolate) unit to an activated enone, and we are currently refining an enantioselective version of this sequence based on the use of a C_2-symmetric recyclable homochiral auxiliary.[21]



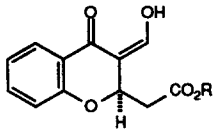
48 R = Me
71 R = CH_2CH_2OMe



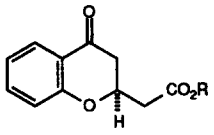
72



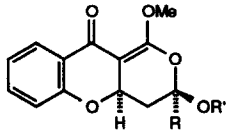
73 R = Me
74 R = CH_2CH_2OMe



75 R = CH_2CH_2OMe



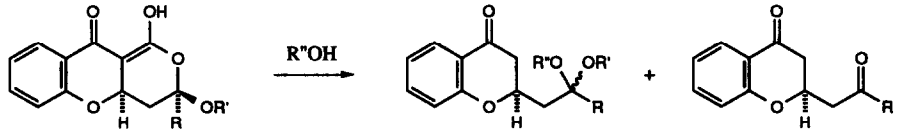
76 R = Me
77 R = Et



78 R = H R' = Et
79 R = OMe R' = Me

The enolic 1-hydroxyl groups of **44a** and **51** reacted cleanly with diazomethane to give the corresponding methoxy compounds **78** and **79**. More interestingly, hydrolysis and alcoholysis reactions of the acid-derived cycloadducts proceeded under very mild conditions, and was accompanied by decarboxylation (Table 5). Thus heating the cycloadduct **44a** in aqueous tetrahydrofuran (THF) gave the unstable aldehyde **80** in almost quantitative yield, while similar treatment of the adduct **46a** gave the dione **81**. The ketene acetal adduct **51** was particularly labile, being transformed into the ester **76** on passage through a column of silica gel. Treatment of **44a** with ethanol cleanly generated the acetal **63a**, while treatment with methanol produced the mixed acetals **82a** and **82b** as a 9:1 mixture of stereoisomers. The butoxy compound **45a** behaved similarly upon methanolysis.

TABLE 5 Ring-opening reactions of cycloadducts derived from chromone-3-carboxylic acid

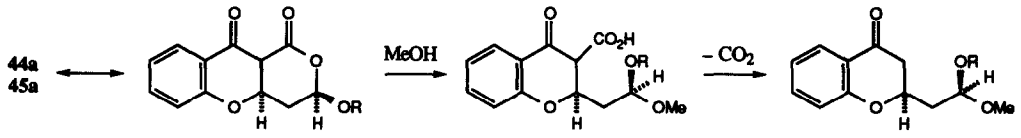


Entry	Educt	R	R'	R"OH		%	Ratio†		%
1	**44a**	H	Et	H_2O	–	–	–	**80**	98
2	**46a**	Me	Me	H_2O	–	–	–	**81**	92
3	**51**	OMe	Me	H_2O‡	–	–	–	**76**	83
4	**44a**	H	Et	EtOH	**63a**	100	–	–	–
5	**44a**	H	Et	MeOH	**82a + b**	100	9:1	–	–
6	**45a**	H	Bu^n	MeOH	**83a + b**	100	8:1	–	–
7	**46a**	Me	Me	MeOH	**84**	90	–	**81**	9

† Ratio a:b as judged by ^1H n.m.r. spectroscopy; for structures see Scheme 3
‡ The formation of **76** was induced by filtration of **51** through silica gel

The susceptibility of the acid-derived cycloadducts to hydrolysis and alcoholysis is unsurprising in view of their acylal character, and the degree of diastereoselectivity in the formation of **82** and **83** is consistent with the majority of the reaction pathway involving concerted bimolecular substitution.[22] Thus attack by methanol on a

cycloadduct **85** with inversion at C-3 will lead to a β-ketoacid **86**, which is readily decarboxylated to give the observed product (Scheme 3). When the attacking species is water the initial product is a hemiacetal, but this decomposes to the corresponding aldehyde **80**.



85 **86** **82a** R = Et
83a R = Bu^n

SCHEME 3

In summary, we have shown that the [4π + 2π] cycloadditions of 4-oxo-4*H*-1-benzopyrans bearing formyl, acetyl, or carboxyl substituents at C-3 to 1-alkoxyalkenes are efficient, *endo*-selective processes, and that the derived cycloadducts are capable of a range of potentially useful transformations. Further investigation of the properties of these cycloadducts, and their synthetic applications, will be described in due course.

EXPERIMENTAL

All compounds are racemic. Melting points were determined using an Electrothermal apparatus and are uncorrected. Unless otherwise stated, i.r. spectra were of liquid paraffin mulls on sodium chloride plates, recorded on Perkin Elmer 297, 1710FT, or Pye-Unicam SP3-100 instruments. ^{1}H N.m.r. spectra were measured for solutions in deuteriochloroform unless otherwise indicated, with tetramethylsilane as the internal standard, on Varian EM 360 (60 MHz), Varian CFT-20 (80 MHz), Perkin-Elmer R32 (90 MHz), Bruker AM250 (250 MHz), or Bruker AC300 (300 MHz) instruments. Deuteriochloroform used for equilibration experiments was freed of HCl by passage through a short plug of alumina (Merck, Art. 1077, 70–230 mesh ASTM). Mass spectra were recorded on a Kratos MS30 instrument with 70 eV electron impact ionisation unless otherwise stated. Data for most of the peaks of intensity <20% of that of the base peak are omitted.

Starting materials and solvents were routinely purified by conventional techniques.[23] Organic solutions were dried over anhydrous magnesium sulphate or anhydrous sodium sulphate and concentrated by rotary evaporation. Analytical thin layer chromatography (t.l.c.) was carried out on Camlab Polygram SIL G/UV$_{254}$ or Kieselgel 60 F$_{254}$ (Art. 5719) plates. Preparative (column) chromatography was carried out using 60H silica gel (Merck 7736 and hand-bellows pressure, or Merck 9385 and the flash technique[24]). Organolithium reactions were performed under an atmosphere of nitrogen dried *via* passage through self-indicating silica gel. Compositions of solvent mixtures are quoted as ratios of volume. Unless otherwise indicated, 'petroleum' refers to light petroleum, b.p. 40–60 °C. 'Ether' refers to diethyl ether.

Starting Materials. – Compounds **7**,[13] **8**,[25] **10**,[15] **13**,[15] **24**,[26] **28**,[11] **29**,[27] **32**,[6] **37**,[28] **38**,[7] **39**,[7] **52a**[7] and **72**[29] were prepared *via* published procedures.

1-(Methoxymethoxy)-3-(methoxymethyl)benzene **9**[30]

To 3-(methoxymethoxy)phenylmethanol **13** (1.60 g, 9.52 mmol) in THF (30 ml) was added sodium hydride (1.2 g of a 60% dispersion on oil - washed three times with petroleum, 30 mmol) and iodomethane (9.09 g, 64.0 mmol). The mixture was fitted with a guard tube and stirred for 16 h at room temperature. The solvent

was then removed to leave a solid residue which was cautiously treated with water (30 ml) and extracted with ether (3 x 30 ml). Evaporation of the ethereal extracts produced an oil which was distilled (Kugelrohr, 102–108 °C, 0.22 mmHg) to afford the *title compound* **9** (1.40 g, 81%) as a colourless oil (Found: C, 65.96, H, 7.87. $C_{10}H_{14}O_3$ requires C, 65.91; H, 7.74%); ν_{max} (neat) 1590 and 1021 cm^{-1}; δ (250 MHz) 3.40 (3 H, s, $ArCH_2OMe$), 3.49 (3 H, s, OCH_2OMe), 4.44 (2 H, s, $ArCH_2OMe$), 5.19 (2 H, s, OCH_2O), 6.92–7.06 (3 H, m, 2-H, 4-H and 6-H), and 7.26 (1 H, t, *J* 7.0 Hz, 5-H); m/z 182 (M^+, 56%), 181 (21), 151 (100), 122 (30), and 91 (21).

1-(Methoxymethoxy)-3-(methoxymethoxymethyl)benzene **11**[31]
To 3-hydroxybenzyl alcohol (1.0 g, 8.06 mmol) in dichloromethane (50 ml) was added dimethoxymethane (6.09 g, 80.0 mmol) and *p*-toluenesulphonic acid (100 mg). A Soxhlet apparatus containing 4Å molecular sieves (12 g) was fitted and the mixture was heated under reflux for 48 h, changing the sieves after 15 and 40 h. The mixture was left to cool, treated with triethylamine (2 ml) and washed with sodium hydroxide (1 M, 2 x 25 ml) and water (25 ml) then concentrated to afford a brown oil. Distillation (Kugelrohr, 135–140 °C, 0.15 mmHg) gave the *title compound* **11** (1.15 g, 67%) as a colourless oil (Found: C, 61.95; H, 7.72. $C_{11}H_{16}O_4$ requires C, 62.24; H, 7.59%); ν_{max} (neat) 1585 and 1020br cm^{-1}; δ (250 MHz) 3.43 (3 H, s, OMe), 3.49 (3 H, s, OMe), 4.58 (2 H, s, benzylic CH_2), 4.72 (2 H, s, CH_2), 5.19 (2 H, s, CH_2), 6.94–7.04 (3 H, m, 2-H, 4-H and 6-H), and 7.27 (1 H, t, *J* 7.0 Hz, 5-H); m/z 212 (M^+, 7%), 152 (51), 151 (100), and 122 (30).

Lithiation of 1-methoxy-3-(methoxymethyl)benzene **8**
To a stirred suspension of the ether **8** (0.50 g, 3.29 mmol) in hexane (25 ml), was added *n*-butyllithium in hexanes (1.5 M; 2.41 ml, 3.62 mmol) at room temperature. The mixture was then heated under reflux for 5 h (forming a red-brown solution), cooled to –78 °C, and treated with an electrophile as below and in Table 1.

2-Methoxy-6-(methoxymethyl)acetophenone **14**
A solution of lithiated **8**, prepared as above, was added *via* cannula to a stirred solution of acetyl chloride (5.20 g, 66.24 mmol) in hexane (20 ml) at –78 °C. The mixture was allowed to warm to room temperature slowly over 0.5 h then quenched cautiously using aqueous sodium hydrogen carbonate and extracted with ethyl acetate (2 x 25 ml). Concentration of the organic phase followed by chromatography (petroleum - ethyl acetate, 4:1) afforded the less polar starting material **8** (55 mg, 11%) and the *title compound* **14** (317 mg, 50%) as a pale yellow oil (M^+, 194.0940. $C_{11}H_{14}O_3$ requires 194.0942); ν_{max} (neat) 1700, 1605, 1595, 1270, and 1100 cm^{-1}; δ (60 MHz) 2.50 (3 H, s, COMe), 3.30 (3 H, s, CH_2OMe), 3.75 (3 H, s, OMe), 4.35 (2 H, s, CH_2), 6.65–6.95 (2 H, m, 3-H and 5-H), and 7.20 (1 H, t, *J* 8.0 Hz, 4-H); m/z 194 (M^+, 90%), 180 (20), 179 (100), 163 (90), 161 (89), 149 (55), 135 (24), 131 (23), 105 (36), 103 (20), 91 (35), 77 (40), 65 (21), and 63 (20). The anion, under the same conditions, was also trapped with acetic anhydride (1.34 g, 13.16 mmol) (*via* dropwise addition from a syringe), and then allowed to warm to room temperature. Sodium hydroxide (2 M, 5 ml) was added and the mixture was stirred for 0.5 h. Water (10 ml) was added then extraction using ether (3 x 10 ml) was performed. Combination and evaporation of the organic extracts, followed by chromatography as above afforded the title compound **14** (304 mg, 48%) and starting material **8** (85 mg, 17%) both identical with authentic samples (i.r., n.m.r., t.l.c.).

2-Methoxy-6-(methoxymethyl)benzoic acid **15**
Carbon dioxide gas (generated from solid CO_2 and dried *via* passage through concentrated sulphuric acid and then solid sodium hydrogen carbonate) was bubbled through a suspension of lithiated **8**, prepared as above, at –78 °C for 15 min with vigorous stirring, while allowing the temperature to increase to room temperature. On addition of the carbon dioxide the red colouration instantly faded producing a white suspension. The mixture was then acidified using hydrochloric acid (4 M, 10 ml) and then extracted with ethyl acetate (3 x 20 ml). The combined organic extracts were then treated with sodium hydrogen carbonate solution (2 x 25 ml). Concentration of the organic phase afforded the starting material **8** (80 mg, 16%). Acidification of the aqueous phase using hydrochloric acid (4 M) followed by extraction using ethyl acetate (2 x 25 ml) and concentration of

the organic extracts afforded the *title compound* **15** (400 mg, 62%) as a yellow oil which solidified on standing under refrigeration (–10 °C) and formed colourless needles, m.p. 57–58 °C (petroleum - dichloromethane) (Found: C, 61.17; H, 6.23. $C_{10}H_{12}O_4$ requires C, 61.21; H, 6.16%); ν_{max} ($CHBr_3$) 3520–3100, 1731, and 1270 cm^{-1}; δ (250 MHz) 3.43 (3 H, s, CH_2OMe), 3.93 (3 H, s, OMe), 4.69 (2 H, s, CH_2), 6.95 (1 H, d, *J* 7.0 Hz, 3-H), 7.14 (1 H, d, *J* 7.0 Hz, 5-H), 7.42 (1 H, t, 7.0 Hz, 4-H), and 10.61 (1 H, s, OH, exchanges with D_2O); m/z 196 (M^+, 20%), 178 (25), and 163 (100).

Lithiation of 1-methoxy-3-(methoxymethoxymethyl)benzene **10**

To the ether **10** (0.50 g, 2.74 mmol) in hexane (30 ml) at room temperature was slowly added *n*-butyllithium in hexanes (0.8 M; 6.86 ml, 5.49 mmol) with stirring. After complete addition the mixture was stirred for 5 h at room temperature during which time a colour change from colourless to dark red occurred. The anion was then cooled to –78 °C, and treated with an electrophile as indicated below and in Table 1.

1-Methoxy-3-(methoxymethoxymethyl)-2-methylbenzene **18**

The lithiated **10**, prepared as above, was treated at –78 °C with iodomethane (1.56 g, 10.99 mmol) in THF (5 ml) dropwise *via* syringe. The mixture was allowed to warm to room temperature and stirred for 1 h, then water (20 ml) was added and the mixture was extracted using ether (2 x 20 ml). Combination and evaporation of the organic extracts afforded the crude products which were isolated *via* chromatography (petroleum - ethyl acetate, 4:1) to afford the less polar *title compound* **18** (393 mg, 73%) as a colourless oil (M^+, 196.1089. $C_{11}H_{16}O_3$ requires 196.1099); ν_{max} (FT, neat) 1589, 1474, 1261, 1150, and 1043 cm^{-1}; δ (60 MHz) 2.20 (3 H, s, Me), 3.40 (3 H, s, CH_2OMe), 3.78 (3 H, s, OMe), 4.57 (2 H, s, CH_2), 4.67 (2 H, s, $OCCH_2O$), and 6.70–7.35 (3 H, m, aromatics); m/z 196 (M^+, 18%), 136 (79), 135 (84), 134 (100), 121 (50), 105 (57), 104 (40), 91 (50), and 77 (24). The chromatography also gave some of the starting material **10** (50 mg, 10%).

Treatment of lithiated **10** *with acetic anhydride*

The lithiated **10**, prepared as above, was treated at –78 °C with acetic anhydride (1.12 g, 10.97 mmol), and then allowed to warm to room temperature. Sodium hydroxide (2 M, 5 ml) was added and the mixture was stirred for 0.5 h. Water (10 ml) was added and the mixture was extracted with ether (3 x 10 ml). The combined extracts were evaporated and the residual oil was distilled (Kugelrohr, 130–140 °C, 1.5 mmHg). The first fraction contained the starting material **10** (215 mg, 43%); a second fraction (b.p. up to 250 °C, 1.5 mmHg) gave a mixture which was further purified by chromatography (hexane - ether, 4:1), giving more starting material **10** (50 mg, 10%) and an impure sample of the acetophenone **19** (*ca.* 80 mg, 13%, by ^1H n.m.r. analysis using dibromomethane as an internal reference) as a pale yellow oil, b.p. 175–180 °C (1 mmHg); ν_{max} ($CHBr_3$) 1695, 1267, 1587, and 1040 cm^{-1}; δ (60 MHz) 2.51 (3 H, s, COMe), 3.37 (3 H, s, CH_2OMe), 3.81 (3 H, s, ArOMe), 4.52 (2 H, s, $ArCH_2O$), 4.60 (2 H, s, OCH_2O), 6.75–7.10 (2 H, m, 4-H and 6-H), 7.15–7.40 (1 H, m, 5-H).

Lithiation of 1-(methoxymethoxy)-3-(methoxymethyl)benzene **9**

To a stirred suspension of the ether **9** (0.50 g, 2.74 mmol) in hexane (30 ml) at room temperature was added *n*-butyllithium in hexanes (0.8 M; 6.86 ml, 5.48 mmol). The mixture was then stirred at room temperature for 1 h, during which time a colour change from colourless to yellow to red occurred. The anion was then cooled to –78 °C, and treated with an electrophile as indicated below and in Table 1.

1-(Methoxymethoxy)-3-(methoxymethyl)-2-methylbenzene **16**

The lithiated **9**, prepared as above, was treated at –78 °C with iodomethane (1.20 g, 8.45 mmol) *via* syringe, slowly with stirring. After complete addition the mixture was left to warm to room temperature, stirred for 15 mins and then water (20 ml) was added. Ether (2 x 20 ml) extraction followed by concentration and chromatography (hexane - ether, 1:1) afforded the *title compound* **16** (493 mg, 92%) as a colourless oil (M^+, 196.1079. $C_{11}H_{16}O_3$ requires 196.1100); ν_{max} (FT, neat) 1587, 1469, 1252, 1153, and 1062 cm^{-1}; δ (250

MHz) 2.23 (3 H, s, ArMe), 3.40 (3 H, s, CH_2OMe), 3.49 (3 H, s, OMe), 4.46 (2 H, s, CH_2OMe), 5.20 (2 H, s, OCH_2O), 7.02 (2 H, t, *J* 7.0 Hz, 4-H and 6-H), and 7.13 (1 H, t, *J* 7.0 Hz, 5-H); m/z 196 (M^+, 29%), 165 (100), 164 (35), 151 (31), 135 (35), 134 (32), 121 (24), 105 (23), 92 (26), 91 (95), 79 (28), 78 (25), 77 (47), 65 (30), 63 (26), and 51 (47).

1-(2-(Methoxymethoxy)-6-(methoxymethyl)phenyl)ethanone **17**

The lithiated **9**, prepared as above, was treated at –78 °C with acetyl chloride (860 mg, 10.96 mmol), *via* syringe, slowly with stirring. After complete addition the mixture was allowed to warm to room temperature then carefully neutralised using saturated sodium hydrogen carbonate solution. Water (10 ml) was added and the mixture was extracted using ether (3 x 10 ml). Concentration and evaporation of the organic extracts gave an oil which was purified by chromatography (hexane - ether, 1:1) to give the more polar *title compound* **17** (111 mg, 18%) as a pale yellow oil, b.p. 180–185 °C (1 mmHg) (M^+, 224.1056. $C_{12}H_{16}O_4$ requires 224.1049); ν_{max} ($CHBr_3$) 1694, 1583, 1460 and 1265 cm^{-1}; δ (250 MHz) 2.55 (3 H, s, COMe), 3.34 (3 H, s, CH_2OMe), 3.47 (3 H, s, OCH_2OMe), 4.41 (2 H, s, benzylic CH_2), 5.20 (2 H, s, OCH_2O), 7.00 (1 H, d, *J* 7.0 Hz, 4-H), 7.10 (1 H, d, *J* 7.0 Hz, 6-H), and 7.26 (1 H, t, *J* 7.0 Hz, 5-H); m/z 224 (M^+, 5%), 193 (26), 179 (100), 164 (22), 163 (97), 162 (34), 161 (80), 149 (21), 105 (27), 91 (23), 77 (21), 45 (91), and 43 (42). The chromatography also gave some of the starting material **9** (220 mg, 44%). The anion, under the same conditions, was also trapped with acetic anhydride (1.12 g, 10.97 mmol), and then allowed to warm to room temperature. Sodium hydroxide (2 M, 5 ml) was added and the mixture was stirred for 0.5 h. Water (10 ml) was added and the mixture was extracted with ether (3 x 10 ml). The combined extracts were evaporated, and the residue purified by chromatography as above, which gave the title compound **17** (272 mg, 44%) and starting material **9** (269 mg, 54%), both identical (i.r., n.m.r., t.l.c.) with authentic samples.

Lithiation of 1-(methoxymethoxy)-3-(methoxymethoxymethyl)benzene **11**

To the ether **11** (0.5 g, 2.36 mmol) in hexane (30 ml) at room temperature, was slowly added *n*-butyllithium in hexanes (1.12 M; 4.21 ml, 4.72 mmol) with stirring. The mixture was then stirred for 5 h at room temperature during which time a colour change from colourless to yellow to red occurred. The anion was then cooled to –78 °C, and treated with an electrophile as indicated below and in Table 1.

1-(Methoxymethoxy)-3-(methoxymethoxymethyl)-2-methylbenzene **20**

The lithiated **11**, prepared as above, was treated at –78 °C with iodomethane (1.34 g, 9.44 mmol) in THF (5 ml) dropwise *via* syringe. The mixture was then allowed to warm to room temperature and stirred for 1 h. Water (20 ml) was added and the products were extracted using ether (2 x 20 ml). Combination and evaporation of the organic extracts gave the crude product which was isolated *via* chromatography (hexane - ethyl acetate, 4:1) to afford the *title compound* **20** (245 mg, 46%) as a colourless oil (M^+, 226.1236. $C_{12}H_{18}O_4$ requires 226.1205); ν_{max} (FT, neat), 1588, 1469, 1253, 1151, and 1043 cm^{-1}; δ (60 MHz) 2.25 (3 H, s, Me), 3.40 (3 H, s, OMe), 3.47 (3 H, s, OMe), 4.57 (2 H, s, CH_2O), 4.68 (2 H, s, OCH_2O), 5.15 (2 H, s, OCH_2O), and 6.90–7.15 (3 H, br. s, aromatics); m/z 226 (M^+, 5%), 165 (38), 164 (22), 151 (24), 86 (28), 84 (46), 51 (48), and 49 (100). The chromatography also gave the starting material **11** (95 mg, 19%).

Treatment of lithiated **11** *with acetic anhydride*

The lithiated **11**, prepared as above, was treated at –78 °C with acetic anhydride (962 mg, *ca.* 0.9 ml, 9.44 mmol) dropwise *via* syringe. The reaction mixture was then allowed to warm to room temperature and sodium hydroxide (2 M, 5 ml) was added and the mixture was stirred for a further 0.5 h. Water (15 ml) was added and the mixture was extracted using ether (3 x 15 ml). Combination and evaporation of the organic extracts afforded the crude product **21** (*ca.* 25% by ^1H n.m.r. analysis using dibromomethane as an internal reference); δ (60 MHz) of the crude product, 2.51 (s) (COMe in product), 3.36 (s), 3.39 (s), 3.45 (s), 4.55 (s), 4.60 (s), 5.15 (s), and 6.70–7.30 (m).

Lithiation of 3-methoxybenzyl alcohol **12**

To 3-methoxybenzyl alcohol **12** (2.0 g, 14.5 mmol) in hexane (150 ml) was added *n*-butyllithium in hexanes (1.6 M; 18.5 ml, 29.6 mmol) at room temperature. The mixture was then heated under reflux for 5 h, cooled to –78 °C, and treated with an electrophile as indicated below and in Table 1.

1-(2-Hydroxymethyl-6-methoxyphenyl)ethanol **22**

Method A: The dianion of 3-methoxybenzyl alcohol **12**, generated as above, was treated at –78 °C with acetaldehyde (2.55 g, 3.24 ml, 58.0 mmol). The mixture thus formed was left to warm to room temperature, then water (50 ml) was added and the organic material was extracted with ether (3 x 40 ml). Combination of the organic extracts followed by evaporation gave the crude product. Isolation, *via* flash chromatography (petroleum - ethyl acetate, 2:1), afforded 3-methoxybenzyl alcohol **12** (540 mg, 27%) and the desired carbinol **22** (1.45 g, 55%), which was identical (i.r., n.m.r., m.p.) to the sample obtained using method B below.

Method B: To the lactol **23** (400 mg, 2.41 mmol) in ether (40 ml) was added methyllithium-lithium bromide complex in ether (1.0 M; 5.04 ml, 5.04 mmol) dropwise at 0 °C. The mixture was then heated under reflux for 0.5 h, left to cool and quenched by careful addition of saturated ammonium chloride solution (5 ml) and water (10 ml). Extraction with ether (3 x 20 ml) followed by evaporation of the organic extracts afforded the *title compound* **22** as a white solid (344 mg, 78%) m.p. 54–55 °C (M^+, 182.0937. $C_{10}H_{14}O_3$ requires 182.0943); ν_{max} (FT, $CDCl_3$) 3350, 2969, 1584, 1256, 1070, and 1015 cm^{-1}; δ (60 MHz) 1.50 (3 H, d, *J* 7.0 Hz, Me), 3.50–4.10 (1 H, br. s, OH, exchanges with D_2O), 3.85 (3 H, s, OMe), 4.25–4.75 (2 H, m, CH_2O), 5.15 (1 H, q, *J* 7.0 Hz, C*H*Me), 6.70–7.00 (2 H, m, aromatics), and 7.00–7.30 (1 H, m, aromatics), other OH not seen; m/z 182 (M^+, 4%), 167 (24), 149 (100), 91 (57), and 77 (24).

7-Methoxy-1(3H)-isobenzofuran-1-ol **23**

The dianion of 3-methoxybenzyl alcohol **12**, generated as above, was treated at –78 °C with a solution of DMF (5 ml, 64 mmol) in THF (20 ml). The mixture was allowed to warm to room temperature, treated with water (50 ml) and extracted with ethyl acetate (3 x 50 ml). Combination of the organic extracts followed by evaporation afforded a residue which could be crystallised with difficulty (petroleum - ether). The mother liquors were concentrated and passed through a short plug of silica gel, eluting with petroleum - ether (1:1), to obtain a further crop of the lactol **23** as a white solid (total 1.65 g, 69%), m.p. 105–106 °C (lit.[32] 99 °C); ν_{max} 3350, 1610, 1605, 1278, and 1048 cm^{-1}; δ (60 MHz) 3.80 (3 H, s, OMe), 4.00–4.30 (1 H, br, s, OH, exchanges with D_2O), 4.75–5.40 (3 H, m, CH_2 and C*H*OH), 6.45–6.90 (2 H, m, 4-H and 6-H), and 7.15–7.50 (1 H, m, 5-H); m/z 166 (M^+, 61%), 165 (68), 149 (100), 148 (46), 121 (29), 79 (22), 78 (21), 77 (67), 76 (21) , 65 (24), 63 (26), and 51 (48).

Treatment of lithiated **12** *with acetyl chloride or acetic anhydride*

Treating the dianion of 3-methoxybenzyl alcohol **12**, generated as above, at –78 °C with acetyl chloride (11.38 g, 10.30 ml, 0.145 mol) by cannelation of the dianion into the electrophile, followed by vigorous stirring at 0 °C, gave after the normal work-up a major product which was identified as 3-methoxybenzyl acetate **24** by comparison with an authentic sample obtained by acetylation of **12**.[26] A similar result was observed with acetic anhydride as the electrophile.

1-(2-Hydroxymethyl-6-(methoxymethoxy)phenyl)ethanol **25**

To 3-(methoxymethoxy)benzyl alcohol **13** (2.45 g, 14.58 mmol) in benzene (70 ml) at room temperature was added *n*-butyllithium in hexanes (1.36 M; 22.1 ml, 30.0 mmol) slowly with stirring. The mixture was then stirred for 1.5 h at room temperature and then cooled to –78 °C and quenched by the addition of acetaldehyde (2.64 g, 3.35 ml, 60 mmol) in THF (10 ml). The reaction was then left to warm to room temperature, stirred for 5 min, and then water (20 ml) was added. The organic material was then extracted using ether (3 x 50 ml). Combination and evaporation of the organic extracts afforded the crude product. Isolation *via* chromatography (petroleum - ethyl acetate, 2:1) afforded the less polar starting material **13** (1.01 g, 41%) and the *title compound* **25** (1.20 g, 39%) as a white solid, m.p. 62–63 °C (M^+, 212.1041. $C_{11}H_{16}O_4$ requires

212.1048); ν_{max} (FT, CH_2Cl_2) 3369, 1584, 1246, 1153, and 1008 cm^{-1}; δ (60 MHz) 1.60 (3 H, d, *J* 7.0 Hz, Me), 3.50 (3 H, s, OMe), 3.65 (1 H, br. s, OH, exchanges with D_2O), 4.40–4.90 (2 H, m, CH_2), 5.20 (2 H, s, OCH_2O), 5.30 (1 H, q, *J* 7.0 Hz, C*H*Me), and 6.90–7.30 (3 H, m, ArH) other OH not observed; m/z 212 (M^+, 2%), 150 (83), 149 (53), 135 (41), 133 (48), 121 (100), 107 (22), 84 (20), and 77 (26).

*4-Methoxy-3-methyl-1(3*H*)-isobenzofuranone* **26**

To the diol **22** (300 mg, 1.65 mmol) in dichloromethane (20 ml) was added manganese dioxide (1.44 g, 16.5 mmol). The mixture was stirred at room temperature for 1 h, filtered, and the solvent evaporated to afford the *title compound* **26** (288 mg, 98%) as a white solid, m.p. 101–102 °C (M^+, 178.0629. $C_{10}H_{10}O_3$ requires 178.0630); ν_{max} (FT, $CDCl_3$) 1759, 1276, 1054, and 1042 cm^{-1}; δ (60 MHz) 1.65 (3 H, d, *J* 7.0 Hz, Me), 3.90 (3 H, s, OMe), 5.55 (1 H, q, *J* 7.0 Hz, 3-H), 7.00–7.30 (1 H, m, 6-H), and 7.30–7.60 (2 H, m, 5-H and 7-H); m/z 178 (M^+, 32%), 163 (92), 135 (100), 107 (20), and 77 (39).

1-(2-Hydroxy-6-(methoxymethyl)phenyl)ethanone **27**

The acetophenone **17** (800 mg, 3.57 mmol) in water (6 ml) and trifluoroacetic acid (2 ml) was stirred at room temperature for 16 h. The reaction mixture was then quenched by cautious addition of saturated aqueous sodium hydrogen carbonate solution and the organic materials were extracted using ether (2 x 10 ml). The organic extracts were combined and concentrated to afford the crude product which was distilled (Kugelrohr, 165–170 °C, 1 mmHg) to afford the *title compound* **27** (597 mg, 93%) as a pale yellow oil (M^+, 180.0810. $C_{10}H_{12}O_3$ requires 180.0797); ν_{max} ($CHBr_3$) 3400–2600 (very broad OH), 1630, 1450 and 1360 cm^{-1}; δ (250 MHz) 2.71 (3 H, s, COMe), 3.35 (3 H, s, OMe), 4.65 (2 H, s, CH_2), 6.88 (1 H, d, *J* 7.5 Hz, 5-H), 6.97 (1 H, d, *J* 7.5 Hz, 3-H), 7.36 (1 H, t, *J* 7.5 Hz, 4-H), and 11.78 (1 H, s, OH, exchanges with D_2O); m/z 188 (M^+, 33%), 165 (50), 149 (100), 147 (55), 105 (20), 91 (37), 77 (24), and 43 (23).

*5-Methyl-4-oxo-4*H*-1-benzopyran-3-carboxaldehyde* **30**

To a stirred solution of the acetophenone **7a** (750 mg, 5.0 mmol) in DMF (10 ml) was added phosphorus oxychloride (1.53 g, 10.0 mmol) dropwise while maintaining the temperature in the range 40–45 °C. After complete addition the solution was stirred at 40–45 °C for 1 h and then poured on to ice (5 g) and water (20 ml) and stirred vigorously for 15 minutes. The precipitate thus formed was filtered under suction and washed with water then crystallised from hexane - ethyl acetate to afford the *title compound* **30** (0.54 g, 57%) as colourless needles, m.p. 123–124 °C (Found: C, 70.17; H, 4.31. $C_{11}H_8O_3$ requires C, 70.20; H, 4.28%); ν_{max} 1695, 1640, 1610, and 1595 cm^{-1}; δ (90 MHz) 2.87 (3 H, s, Me), 7.15–7.70 (3 H, m, aromatics), 8.42 (1 H, s, 2-H), and 10.35 (1 H, s, CHO); m/z 188 (M^+, 10%), 160 (100), 132 (29), 101 (35), and 114 (49).

*5-(Methoxymethyl)-4-oxo-4*H*-1-benzopyran-3-carboxaldehyde* **31**

To a stirred solution of the acetophenone **27** (500 mg, 2.78 mmol) in DMF (8 ml) was added phosphorus oxychloride (853 mg, 5.56 mmol) dropwise while maintaining the temperature between 40–45 °C. After complete addition the solution was stirred at 40–45 °C for 1 h then poured on to ice (4 g) and water (16 ml) and stirred vigorously for 15 minutes. The precipitate thus formed was filtered under suction and washed with water, then crystallised (petroleum - ether) to afford the *title compound* **31** (310 mg, 51%) as colourless needles, m.p. 159–160 °C (Found: C, 65.90; H, 4.53. $C_{12}H_{10}O_4$ requires C, 66.05; H, 4.62%); ν_{max} ($CHBr_3$) 1700, 1650, and 1611 cm^{-1}; δ (250 MHz) 3.59 (3 H, s, OMe), 5.19 (2 H, s, CH_2O), 7.44 (1 H, br. d, *J* 7.5 Hz, 6-H), 7.67–7.80 (2 H, m, 7-H and 8-H), 8.49 (1 H, s, 2-H), and 10.34 (1 H, s, CHO); m/z 218 (M^+, 10%), 203 (100).

*5-(Chloromethyl)-4-oxo-4*H*-1-benzopyran-3-carboxylic acid* **33**

To the aldehyde **30** (1.10 g, 5.85 mmol) in carbon tetrachloride (50 ml) was added sulphuryl chloride (1.0 ml, 1.68 g, 12.44 mmol) and a catalytic amount of AIBN. The mixture was then heated under reflux for 3 h after which time the solvent was removed. The residue thus produced was treated with water (50 ml) and stirred for

30 mins at room temperature. Filtration afforded the *title compound* **33** (610 mg, 44 %) as a white powder contaminated with about 10% starting material. The material was crystallised from ethyl acetate - petroleum, b.p. 80–100 °C; ν_{max} (FT, $CDCl_3$) 3500, 1750 (C=O of acid), 1625 (C=O), 907 and 732 cm^{-1}; δ (300 MHz) 5.30 (2 H, s, CH_2), 7.61 (1 H, dd, *J* 1.2, 8.4 Hz, 6-H), 7.68 (1 H, dd, *J* 1.2, 7.7 Hz, 8-H), 7.81 (1 H, overlapping dd, *J* 7.7, 8.4 Hz, 7-H), 8.95 (1 H, s, 2-H), and 13.36 (1 H, broad s, OH); m/z 240 (M^+, ^{37}Cl, 5%), 238 (M^+, ^{35}Cl, 24%) 222 (15), 220 (38), 194 (54), 192 (100), 164 (28), 158 (39), 157 (25), 102 (25), 77 (20), 53 (30), and 51 (30).

Reactions of the acid were carried out on material which was contaminated with the aldehyde **30**.

*3-Butoxy-4,4a-dihydro-1-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-ones* **41**

To 3-acetylchromone **29** (500 mg, 2.66 mmol) was added *n*-butoxyethene (13 g, 0.13 mol), and the mixture heated under reflux for 3.5 days. Evaporation and chromatography of the residue, eluting with petroleum - ethyl acetate (19:1), afforded trans-*3-butoxy-4,4a-dihydro-1-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **41b** (115 mg, 15%) as a colourless non-distillable oil (M^+, 288.1351. $C_{17}H_{20}O_4$ requires 288.1361); ν_{max} (neat) 1670, 1600, 1460 and 1380 cm^{-1}; δ (90 MHz) 0.95 (3 H, t, *J* 7.0 Hz, Me), 1.10–1.40 (4 H, m, 2 x CH_2), 2.00–2.50 [2 H, m, 4α-H and 4β-H; the characteristic 3.0 Hz coupling ($^3J_{3,4\beta}$) is visible at δ 2.05], 2.32 (3 H, d, *J* 2.0 Hz, 1-Me), 3.35–4.20 (2 H, m, OCH_2), 4.90–5.20 (2 H, m, 3-H and 4a-H), 6.75–7.05 (2 H, m, 6-H and 8-H), 7.35 (1 H, overlapping ddd, *J* 2.0, 7.5, 8.5 Hz, 7-H), and 7.91 (1 H, dd, *J* 2.0, 7.7 Hz, 9-H); m/z 288 (M^+, 12%), 215 (21), 214 (43), 189 (86), 188 (39), 173 (70), 172 (21), 171 (73), 100 (84), 93 (24), 92 (30), 85 (86), 65 (38), 63 (22), 57 (93), 56 (100), 55 (39), 53 (21), and 45 (25).

cis-*3-Butoxy-4,4a-dihydro-1-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **41a** (460 mg, 60%) was obtained from a more polar fraction, and formed colourless platelets, m.p. 77–78 °C (petroleum - ether) (Found: C, 70.94; H, 7.09. $C_{17}H_{20}O_4$ requires C, 70.81; H, 6.99%); ν_{max} 1660, 1600, 1300 and 1000 cm^{-1}; δ (90 MHz) 0.85 (3 H, t, *J* 7.0 Hz, CH_2*Me*), 1.10–1.70 (4 H, m, 2 x CH_2), 2.00–2.65 [2 H, m, 4α-H and 4β-H; the characteristic 9.5 Hz coupling ($^3J_{3,4\beta}$) is visible at δ 2.05], 2.29 (3 H, d, *J* 2.0 Hz, 1-Me), 3.35–3.65 and 3.70–4.00 (each 1 H, m, OCH_2), 4.88–5.15 (2 H, m, 4a-H and 3-H), 6.75–7.02 (2 H, m, 6-H and 8-H), 7.31 (1 H, overlapping ddd, *J* 1.8, 7.5, 8.5 Hz, 7-H), and 7.88 (1 H, dd, *J* 1.8, 7.2 Hz, 9-H); m/z (peaks > 25%) 288 (M^+, 37%), 245 (54), 214 (57), 189 (45), and 75 (100).

*3-Ethoxy-4,4a-dihydro-9-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-ones* **42**

Method A: To 5-methylchromone-3-carboxaldehyde **30** (300 mg, 1.60 mmol) in dichloromethane (6.4 ml) was added ethoxyethene (2.3 g, 32.94 mmol), and the solution was stirred at room temperature for 21 days. The solvent was removed and the residue was separated by chromatography, eluting with petroleum - ethyl acetate (9:1), to afford the less polar trans-*3-ethoxy-4,4a-dihydro-9-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **42b** (80 mg, 19%) as a non-distillable pale yellow oil (M^+, 260.1055. $C_{15}H_{16}O_4$ requires 260.1049); ν_{max} (neat) 1685, 1600, 1465 and 1200 cm^{-1}; δ (300 MHz) 1.14 (3 H, t, *J* 7.0 Hz, CH_2*Me*), 2.08, (1 H, ddd, *J* 2.9, 10.4, 13.0 Hz, 4β-H), 2.47 (1 H, ddd, *J* 2.1, 6.6, 13.0 Hz, 4α-H), 2.63 (3 H, s, 9-Me), 3.50–3.60 (1 H, m, OCH_2), 3.74–3.84 (1 H, m, OCH_2), 5.04 (1 H, ddd, *J* 1.3, 6.6, 10.4 Hz), 5.25 (1 H, apparent t, *J* 2.5 Hz, 3-H), 6.75–6.78 (2 H, m, 6-H and 8-H), 7.22 (1 H, apparent t, *J* 7.8 Hz, 7-H), and 7.44 (1 H, d, *J* 1.3 Hz, 1-H); m/z 260 (M^+, 27%), 160 (83), 135 (25), 114 (22), 77 (23), 73 (32), 72 (100), and 57 (23).

Another fraction gave the more polar cis-*3-ethoxy-4,4a-dihydro-9-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **42a** (240 mg, 58%) as colourless needles, m.p. 127.5–128.5 °C (ethyl acetate - petroleum, b.p. 80–100 °C) (Found: C, 69.05; H, 6.19. $C_{15}H_{16}O_4$ requires C, 69.20; H, 6.12%); ν_{max} 1680, 1620, 1480 and 1160 cm^{-1}; δ (300 MHz) 1.26 (3 H, t, *J* 7.1 Hz, CH_2*Me*), 2.23 (1 H, dt, *J* 10.0, 10.0, 13.0 Hz, 4β-H), 2.53 (1 H, ddd, *J* 2.1, 6.7, 13.0 Hz, 4α-H), 2.64 (3 H, s, 9-Me), 3.59–3.69 and 3.95–4.05 (each 1 H, m, OCH_2Me), 5.05 (1 H, ddd, *J* 1.0, 6.7, 10.0 Hz, 4a-H), 5.14 (1 H, dd, *J* 2.1, 10.0 Hz, 3-H), 6.77–6.81 (2 H, m, 6-H and 8-H), 7.24 (1 H, t, *J* 7.8 Hz, 7-H), and 7.49 (1 H, d, *J* 1.0 Hz, 1-H); m/z 260 (M^+, 74%), 261 (42), 231 (47), 189 (98), 188 (53), 187 (23), 185 (24), 161 (21), 160 (93), 135 (44), 132 (42), 131 (32), 114 (42), 78 (27), 77 (43), 73 (58), 72 (100), 53 (24), 51 (26), 45 (24), and 44 (96).

Method B: To the aldehyde **30** (280 mg, 1.49 mmol) was added ethoxyethene (2.16 g, 30.0 mmol). The mixture was heated at 100 °C in a sealed tube under a nitrogen atmosphere for 3 days. Removal of the solvent and chromatography (as in method A) gave the desired products **42a** (210 mg, 54%) and **42b** (75 mg, 19%) identical by i.r., n.m.r., and t.l.c. to the samples obtained *via* method A.

3-Ethoxy-4,4a-dihydro-9-(methoxymethyl)-3H,10H-pyrano[4,3-b][1]benzopyran-10-ones **43**

Method A: To the aldehyde **31** (400 mg, 1.83 mmol) in dichloromethane (7.3 ml) was added ethoxyethene (2.64 g, 36.67 mmol), and the solution stirred at room temperature for 10 days. The solvent was removed and the residue was crystallised from ethyl acetate - petroleum, b.p. 60–80 °C, to obtain cis-*3-ethoxy-4,4a-dihydro-9-(methoxymethyl)-3H,10H-pyrano[4,3-b][1]benzopyran-10-one* **43a** (260 mg, 49%) as colourless needles, m.p. 108.5–109.5 °C (Found: C, 66.50; H, 6.28. $C_{16}H_{18}O_5$ requires C, 66.19; H, 6.25%); ν_{max} ($CHBr_3$) 1665, 1600, and 1050 cm^{-1}; δ (300 MHz) 1.25 (3 H, t, *J* 7.0 Hz, Me), 2.23 (1 H, dt, *J* 10.0, 10.0, 13.0 Hz, 4β-H), 2.54 (1 H, ddd, *J* 2.0, 6.7, 13.0 Hz, 4α-H), 3.46 (3 H, s, OMe), 3.59–3.69 and 3.94–4.04 (each 1 H, m, OCH_2Me), 4.87 and 4.95 (each 1 H, d, *J* 15.6 Hz, CH_2OMe), 5.06 (1 H, ddd, *J* 1.0, 6.7, 10.0 Hz, 4a-H), 5.14 (1 H, dd, *J* 2.0, 10.0 Hz, 3-H), 6.85 (1 H, d, *J* 8.0 Hz, 8-H), 7.29 (1 H, br. d, *J* 8.0 Hz, 6-H), 7.39 (1 H, t, *J* 8.0 Hz, 7-H), and 7.47 (1 H, d, *J* 1.0 Hz, 1-H); m/z 290 (M^+, 3%), 218 (24), 203 (55), 86 (21), 84 (38), 51 (31), and 49 (100).

Concentration of the mother liquors from crystallisation followed by chromatography, eluting with ethyl acetate - petroleum (9:1), gave the less polar trans-*3-ethoxy-4,4a-dihydro-9-(methoxymethyl)-3H,10H-pyrano[4,3-b][1]benzopyran-10-one* **43b** (90 mg, 17%) as colourless needles, m.p. 66–67 °C (petroleum - ether) (Found: C, 65.91; H, 6.06. $C_{16}H_{18}O_5$ requires C, 66.19; H, 6.25%); ν_{max} (FT, $CDCl_3$) 1669, 1602, and 1111 cm^{-1}; δ (300 MHz) 1.16 (3 H, t, *J* 7.0 Hz, Me), 2.10 (1 H, ddd, *J* 3.0, 10.5, 13.0 Hz, 4β-H), 2.50 (1 H, ddd, *J* 2.0, 6.5, 13.0 Hz, 4α-H), 3.47 (3 H, s, OMe), 3.51–3.62 and 3.76–3.86 (each 1 H, m, OCH_2Me), 4.88 and 4.93 (each 1 H, d, *J* 15.6 Hz, CH_2OMe), 5.07 (1 H, ddd, *J* 1.2, 6.5, 10.5 Hz, 4a-H), 5.27 (1 H, t, *J* 2.5 Hz, 3-H), 6.85 (1 H, d, *J* 8.0 Hz, 8-H), 7.28 (1 H, d, *J* 7.2 Hz, 6-H), 7.35 (1 H, t, *J* 8.0 Hz, 7-H), and 7.44 (1 H, d, *J* 1.2 Hz, 1-H); m/z (methane CI) 291 (M^+ + 1, 49%), 259 (19), 247 (23), 220 (18), 219 (100), 218 (14), and 217 (11). The chromatography also yielded a further quantity (100 mg, 19%) of **43a**. The ratio of *endo*:*exo* isomers was thus about 4:1.

Method B: To the aldehyde **31** (660 mg, 3.03 mmol) in dichloromethane (5.4 ml) was added ethoxyethene (454 mg, 6.31 mmol). The mixture was heated at 115 °C in a sealed tube under a nitrogen atmosphere for 24 h. The solvent was removed and flash chromatography of the residue, eluting with petroleum - ethyl acetate (9:1), afforded the *exo*-cycloadduct **43b** (166 mg, 19%) and the more polar *endo*-isomer **43a** (482 mg, 55%) in a ratio of about 1:3. These products were identical (i.r, n.m.r., t.l.c.) to those obtained using method A.

3-Ethoxy-4,4a-dihydro-1-hydroxy-3H,10H-pyrano[4,3-b][1]benzopyran-10-ones **44**

To the acid **32** (1.0 g, 5.26 mmol) in dichloromethane (21 ml) was added ethoxyethene (7.62 g, 0.106 mol), the mixture was stirred at room temperature for 7 days, and the solvent was then removed. The 300 MHz ^1H n.m.r. spectrum of the crude mixture indicated a *cis*:*trans* ratio of at least 3:1 [δ 5.13 (1 H, dd, *J* 5.7, 10.8 Hz, 4a-H) of *cis*-adduct, δ 5.44 (1 H, t, *J* 2.4 Hz, 3-H) of *trans*-adduct]. Crystallisation gave cis-*3-ethoxy-4,4a-dihydro-1-hydroxy-3H,10H-pyrano[4,3-b][1]benzopyran-10-one* **44a** (855 mg, 62%), m.p. 104–105 °C (petroleum - ether) (Found: C, 64.39; H, 5.35. $C_{14}H_{14}O_5$ requires C, 64.11; H, 5.38%); ν_{max} ($CHBr_3$) 1660, 1625, and 1565 cm^{-1} (OH not visible due to broadening); δ (300 MHz) 1.25 (3 H, t, *J* 7.1 Hz, Me), 2.28 (1 H, ddd, *J* 9.8, 10.8, 13.0 Hz, 4β-H), 2.63 (1 H, ddd, *J* 2.3, 5.7, 13.0 Hz, 4α-H), 3.59–3.69 and 4.01–4.11 (each 1H, m, OCH_2), 5.13 (1 H, dd, *J* 5.7, 10.8 Hz, 4a-H), 5.28 (1 H, dd, *J* 2.3, 9.8 Hz, 3-H), 6.88 (1 H, dd, *J* 0.7, 8.2 Hz, 6-H), 7.02 (1 H, overlapping ddd, *J* 0.7, 7.3, 7.8 Hz, 8-H), 7.35 (1 H, overlapping ddd, *J* 1.7, 7.3, 8.2 Hz, 7-H), 7.65 (1 H, dd, *J* 1.7, 7.8 Hz, 9-H), and 12.48 (1 H, s, exchanges with D_2O, OH); m/z 262 (M^+, 7%), 146 (45), 121 (31), 92 (20), and 72 (100).

Concentration of the mother liquors from crystallisation followed by flash chromatography, eluting with

petroleum - ethyl acetate (9:1), gave an enriched sample of trans-*3-ethoxy-4,4a-dihydro-1-hydroxy-3H,10H-pyrano[4,3-b][1]benzopyran-10-one* **44b** (207 mg, 15%), m.p. 121–122 °C (M^+, 262.0826. $C_{14}H_{14}O_5$ requires 262.0841); ν_{max} (FT, $CDCl_3$) 1660, 1626, and 1407 cm^{-1} (OH not seen due to broadening); δ (300 MHz) 1.16 (3 H, t, *J* 7.0 Hz, Me), 2.23 (1 H, ddd, *J* 2.4, 11.3, 13.0 Hz, 4β-H), 2.58 (1 H, ddd, *J* 2.4, 5.8, 13.0 Hz, 4α-H), 3.55–3.97 (2 H, m, OCH_2), 5.30 (1 H, dd, *J* 5.8, 11.3 Hz, 4a-H), 5.44 (1 H, t, *J* 2.4 Hz, 3-H), 6.87 (1 H, br. d, *J* 8.3 Hz, 6-H), 7.01 (1 H, overlapping dd, *J* 7.4, 8.0 Hz, 8-H), 7.33 (1 H, overlapping ddd, *J* 1.2, 7.4, 8.3 Hz, 7-H), 7.65 (1 H, dd, *J* 1.2, 8.0 Hz, 9-H), and 12.50 (1 H, s, exchanges with D_2O, OH); m/z 262 (M^+, 33%), 217 (23), 216 (52), 191 (52), 173 (55), 171 (40), 146 (35), 121 (85), 120 (30), 92 (40), 77 (25), 72 (100), 65 (28), 63 (28), 58 (46), and 53 (24).

3-Butoxy-4,4a-dihydro-1-hydroxy-3H,10H-pyrano[4,3-b][1]benzopyran-10-ones **45**

To the acid **32** (2.0 g, 10.53 mmol) in dichloromethane (42 ml) was added *n*-butoxyethene **35** (21.0 g, 0.210 mol). The mixture was stirred at room temperature for 9 days, then the solvent was removed. The 300 MHz ^1H n.m.r. spectrum of the crude mixture indicated a *cis:trans* ratio of at least 7:1 [δ 5.27 (1 H, dd, *J* 2.3, 9.9 Hz, 3-H) of *cis*-adduct, δ 5.41 (1 H, t, 3-H) of *trans*-adduct]. Crystallisation of the crude product gave the *title compound* **45a** (1.54 g, 50%) as colourless needles, m.p. 95–97 °C (petroleum - ether) (Found: C, 66.49; H, 6.18. $C_{16}H_{18}O_5$ requires C, 66.19; H, 6.25%); ν_{max} (FT, $CDCl_3$) 3500–3100 (very broad OH), 1659, 1625, and 909 cm^{-1}; δ (300 MHz) 0.90 (3 H, t, *J* 7.0 Hz, Me), 1.37 (2 H, sextet, *J* 7.4 Hz, CH_2Me), 1.60 (2 H, m, CH_2CH_2Me), 2.28 (1 H, ddd, *J* 9.9, 10.7, 13.0 Hz, 4β-H), 2.63 (1 H, ddd, *J* 2.3, 5.7, 13.0 Hz, 4α-H), 3.56 (1 H, dt, *J* 6.7, 9.3 Hz, OCH), 4.01 (1 H, dt, *J* 6.7, 9.3 Hz, OCH), 5.13 (1 H, dd, *J* 5.7, 10.7 Hz, 4a-H), 5.27 (1 H, dd, *J* 2.3, 9.9 Hz, 3-H), 6.87 (1 H, br. d, *J* 8.5 Hz, 6-H), 7.02 (1 H, overlapping ddd, *J* 1.1, 7.4, 7.7 Hz, 8-H), 7.30 (1 H, overlapping ddd, *J* 1.7, 7.7, 9.5 Hz, 7-H), 7.45 (1 H, dd, *J* 1.7, 7.7 Hz, 9-H), and 12.48 (1 H, s, exchanges with D_2O, OH); m/z 290 (M^+, 3%), 173 (24), 146 (50), 122 (23), 85 (33), 57 (57), and 56 (100).

Concentration of the mother liquors from crystallisation, followed by flash chromatography, afforded only 3,4-dihydro-4-oxo-2*H*-1-benzopyran-2-acetaldehyde **80** (see later) and a mixture of **45a** and **45b**. Ratios of products varied with chromatography time. The total yield was greater than 90% when based on all isolated materials, as indicated by the n.m.r. of the crude reaction mixture.

4,4a-Dihydro-1-hydroxy-3-methoxy-3-methyl-3H,10H-pyrano[4,3-b][1]benzopyran-10-ones **46**

To the acid **32** (2.0 g, 10.53 mmol) in dichloromethane (42 ml) was added 2-methoxypropene **36** (15.12 g, 0.210 mol, stabilised with 0.5% potassium carbonate). The mixture was stirred at room temperature for 3 days, then the solvent was removed. The 300 MHz ^1H n.m.r. spectrum of the crude mixture indicated a *cis:trans* ratio of at least 4:1 [δ 5.08 (1 H, dd, *J* 7.0, 9.0 Hz, 4a-H) of *cis*-adduct, δ 5.21 (1 H, dd, *J* 5.9, 11.1 Hz, 4a-H) of *trans*-adduct]. Crystallisation of the crude product gave cis-*4,4a-dihydro-1-hydroxy-3-methoxy-3-methyl-3H,10H-pyrano[4,3-b][1]benzopyran-10-one* **46a** (1.9 g, 69%, two crops) as colourless needles, m.p. 96.5–97.5 °C (petroleum - ether) (Found: C, 64.51; H, 5.36. $C_{14}H_{14}O_5$ requires C, 64.11; H, 5.38%); ν_{max} (FT, CH_2Cl_2) 3430 (OH, very broad), 1652, 1626, and 1399 cm^{-1}; δ (300 MHz) 1.49 (3 H, s, 3-Me), 2.42 (1 H, dd, *J* 7.0, 13.5 Hz, 4β-H), 2.46 (1 H, dd, *J* 8.7, 13.5 Hz, 4α-H), 3.43 (3 H, s, OMe), 5.08 (1 H, dd, *J* 7.0, 8.7 Hz, 4a-H), 6.89 (1 H, dd, *J* 1.2, 8.2 Hz, 6-H), 7.02 (1 H, overlapping ddd, *J* 1.2, 7.2, 7.9 Hz, 8-H), 7.35 (1 H, overlapping ddd, *J* 1.5, 7.2, 8.2 Hz, 7-H), 7.65 (1 H, dd, *J* 1.5, 7.9 Hz, 9-H), and 12.46 (1 H, s, exchanges with D_2O, OH); m/z (peaks ≥ 10%) 262 (M^+, 3%), 230 (11), 191 (17), 173 (15), 146 (41), 121 (19), 120 (14), 104 (14), 92 (17), and 72 (100).

Concentration of the mother liquors from crystallisation, followed by flash chromatography, eluting with petroleum - ethyl acetate (9:1), afforded an enriched sample of trans-*4,4a-dihydro-1-hydroxy-3-methoxy-3-methyl-3H,10H-pyrano[4,3-b][1]benzopyran-10-one* **46b** (105 mg, 4%), m.p. 117–122 °C (M^+, 262.0853. $C_{14}H_{14}O_5$ requires 262.0841); ν_{max} (FT, CH_2Cl_2) 3694 (OH, br.), 1660, 1626, and 1226 cm^{-1}; δ (300 MHz) 1.58 (3 H, s, 3-Me), 2.12 (1 H, dd, *J* 11.1, 12.9 Hz, 4β-H), 2.59 (1 H, dd, *J* 5.9, 12.9 Hz, 4α-H), 3.32 (3 H, s, OMe), 5.21 (1 H, dd, *J* 5.9, 11.1 Hz, 4a-H), 6.85 (1 H, br. d, *J* 8.3 Hz, 6-H), 6.99 (1 H, overlapping dd, *J* 7.6, 7.8 Hz, 8-H), 7.32 (1 H, overlapping ddd, *J* 1.5, 7.6, 8.3 Hz, 7-H), 7.64 (1

H, dd, *J* 1.5, 7.8 Hz, 9-H), and 12.52 (1 H, s, exchanges with D_2O, OH); m/z 262 (M^+, 50%), 261 (75), 231 (31), 230 (79), 229 (34), 192 (22), 191 (100), 185 (20), 173 (21), 73 (24), and 72 (46).
Another fraction contained a mixture of *cis*- and *trans*-isomers **46a** and **46b** (total 200 mg, 7%) and 2,3-dihydro-2-(2-oxopropyl)-4*H*-1-benzopyran-4-one **81** (170 mg, 8%), identical by n.m.r. and t.l.c. with an authentic sample (see later).

*9-Chloromethyl-3-ethoxy-4,4a-dihydro-1-hydroxy-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-ones* **47**
To the acid **33** (150 mg, 0.63 mmol) in dichloromethane (3 ml) was added ethoxyethene (908 mg, 12.61 mmol), and the mixture stirred at room temperature for 5 days. The 300 MHz ^{1}H n.m.r. spectrum of the crude mixture indicated a *cis*:*trans* ratio of 6:1 [δ 13.25 (1 H, s, OH of *cis*-adduct), δ 13.28 (1 H, s, OH of *trans*-adduct)]. Evaporation of the solvent gave the mixed products **47** (195 mg, 100%), and crystallisation gave cis-*9-chloromethyl-3-ethoxy-4,4a-dihydro-1-hydroxy-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **47a** (110 mg, 56%) as a yellow solid, m.p. 120–121 °C (petroleum - ether) (M^+, 310.0633. $C_{15}H_{15}ClO_5$ requires 310.0608); ν_{max} (FT, CH_2Cl_2) 3500–3400, 1648, 1617, and 1130 cm^{-1}; δ (300 MHz) 1.26 (3 H, t, *J* 7.0 Hz, Me), 2.26 (1 H, ddd, *J* 9.5, 10.2, 13.2 Hz, 4β-H), 2.64 (1 H, ddd, *J* 2.2, 6.1, 13.2 Hz, 4α-H), 3.61–3.71 and 4.01–4.12 (each 1 H, m, OC*H*$_2$Me), 4.72 (1 H, d, *J* 11.7 Hz, CHCl), 5.01 (1 H, dd, *J* 6.1, 10.2 Hz, 4a-H), 5.28 (1 H, dd, *J* 2.2, 9.5 Hz, 3-H), 5.29 (1 H, d, *J* 11.7 Hz, CHCl), 6.91 (1 H, br. d, *J* 8.2 Hz, 6-H), 7.10 (1 H, br. d, *J* 7.5 Hz, 8-H), 7.33 (1 H, br. t, *J* 7.9 Hz, 7-H), and 13.26 (1 H, s, OH); m/z 312 (M^+, ^{37}Cl, 1%), 310 (M^+, ^{35}Cl, 3%), 264 (10), 229 (11), 228 (16), 221 (11), 219 (16), 203 (24), 192 (12), 172 (33), 158 (10), 115 (18), 105 (15), 102 (16), 77 (19), and 71 (100). The *trans*-isomer **47b** was not isolated in a pure form.

*4,4a-Dihydro-3,3-dimethoxy-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **48**
To the aldehyde **28** (1.0 g, 5.75 mmol) in dichloromethane (23 ml) was added 1,1-dimethoxyethene **37** (761 mg, 8.65 mmol). The solution was stirred at room temperature for 20 minutes, then the solvent was removed to afford the *title compound* **48** (1.51 g, 100%) as a pale yellow non-distillable oil (Found: C, 63.55; H, 5.53. $C_{14}H_{14}O_5$ requires C, 64.11; H, 5.38%); (M^+, 262.0853. $C_{14}H_{14}O_5$ requires 262.0841); ν_{max} (FT, neat) 1676, 1615, 1464 and 1222 cm^{-1}; δ (300 MHz) 2.22 (1 H, dd, *J* 10.5, 12.6 Hz, 4β-H), 2.62 (1 H, dd, *J* 6.7, 12.6 Hz, 4α-H), 3.27 (3 H, s, OMe), 3.41 (3 H, s, OMe), 5.09 (1 H, ddd, *J* 1.6, 6.7, 10.5 Hz, 4a-H), 6.88 (1 H, dd, *J* 0.8, 8.6 Hz, 6-H), 6.99 (1 H, overlapping ddd, *J* 0.8, 7.4, 7.8 Hz, 8-H), 7.39 (1 H, overlapping ddd, *J* 1.7, 7.4, 8.6 Hz, 7-H), 7.46 (1 H, d, *J* 1.6 Hz, 1-H), and 7.89 (1 H, dd, *J* 1.7, 7.8 Hz, 9-H); m/z (methane CI) 263 (M^+ + 1, 12%), 231 (24), 223 (26), 175 (100), 89 (93), and 88 (27).

*4,4a-Dihydro-3,3-dimethoxy-1-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **49**
To 3-acetylchromone **29** (1.0 g, 5.32 mmol) in dichloromethane (21 ml) was added **37** (704 mg, 8.00 mmol). The solution was then stirred at room temperature for 5 h, the solvent was removed and the residue was crystallised to afford the *title compound* **49** (1.47 g, 100%) as white crystals, m.p. 75–76 °C (petroleum - ether) (Found: C, 65.15; H, 5.91. $C_{15}H_{16}O_5$ requires C, 65.20; H, 5.84%); ν_{max} (FT, CH_2Cl_2) 1671, 1608, and 1311 cm^{-1}; δ (300 MHz) 2.27 (1 H, dd, *J* 9.8, 13.1 Hz, 4β-H), 2.40 (3 H, d, *J* 1.9 Hz, 1-Me), 2.63 (1 H, dd, *J* 7.0, 13.1 Hz, 4α-H), 3.28 (3 H, s, OMe), 3.41 (3 H, s, OMe), 5.02–5.08 (1 H, m, 4a-H), 6.88 (1 H, br. d, *J* 7.8 Hz, 6-H), 7.00 (1 H, overlapping ddd, *J* 1.1, 7.8, 8.4 Hz, 8-H), 7.39 (1 H, overlapping ddd, *J* 1.7, 7.8, 8.6 Hz, 7-H), and 7.92 (1 H, dd, *J* 1.7, 7.8 Hz, 9-H); m/z (methane CI) 277 (M^+ + 1, 9%), 245 (42), 189 (100), 89 (46), and 88 (26).

*4,4a-Dihydro-3,3-dimethoxy-9-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **50**
To the aldehyde **30** (500 mg, 2.66 mmol) in dichloromethane (10 ml) was added **37** (352 mg, 4.00 mmol). The solution was stirred at room temperature for 2·5 h, then the solvent was removed to afford the *title compound* **50** (726 mg, 99%) as a pale yellow non-distillable oil (M^+, 276.0985. $C_{15}H_{16}O_5$ requires 276.0997); ν_{max} (FT, $CDCl_3$) 1673 (C=O), 1604 (C=C), 1044 (C-O), and 910 cm^{-1}; δ (300 MHz) 2.18 (1 H, dd, *J* 10.4, 12.6 Hz, 4β-H), 2.60 (1 H, dd, *J* 6.8, 12.6, 4α-H), 2.63 (3 H, s, 9-Me), 3.27 (3 H, s, OMe),

3.41 (3 H, s, OMe), 5.00 (1 H, ddd, *J* 1.5, 6.8, 10.4 Hz, 4a-H), 6.77 (2 H, apparent t, *J* 7.9 Hz, 6-H and 8-H), 7.23 (1 H, apparent t, *J* 7.9 Hz, 7-H), and 7.42 (1 H, d, *J* 1.5 Hz, 1-H); m/z 276 (M^+, 6%), 261 (15), 246 (14), 245 (73), 213 (22), 203 (24), 190 (24), 189 (86), 188 (20), 187 (21), 185 (27), 174 (15), 173 (12), 172 (22), 161 (33), 160 (82), 145 (11), 135 (44), 134 (16), 132 (39), 131 (44), 115 (21), 114 (48), 106 (16), 105 (23), 103 (13), 91 (11), 90 (20), 89 (96), 88 (100), 85 (16), 83 (23), 79 (11), 78 (23), 77 (29), 63 (13), 59 (10), 58 (55), 53 (13), and 51 (16).

4,4a-Dihydro-1-hydroxy-3,3-dimethoxy-3H,10H-pyrano[4,3-b][1]benzopyran-10-one **51**

To a stirred solution of 4-oxo-4*H*-1-benzopyran-3-carboxylic acid **32** (2.0 g, 10.53 mmol) in dichloromethane (42 ml) at room temperature was added **37** (1.36 g, 15.45 mmol). The resulting exothermic reaction was complete within 15 minutes. Isolation by evaporation and crystallisation gave the *title compound* **51** (2.78 g, 95%) as a pinkish powder, m.p. 92–94 °C (petroleum - ether) (Found: C, 60.95; H, 4.90. $C_{14}H_{14}O_6$ requires C, 60.43; H, 5.07%); ν_{max} (FT, $CDCl_3$) 3200–2400 (OH), 1736 (C=O of decomposition product), 1661, 1626, 1564, 1400, 1292, 1050, 911, 763, and 735 cm^{-1}; δ (300 MHz) 2.33 (1 H, dd, *J* 10.9, 12.7 Hz, 4β-H), 2.70 (1 H, dd, *J* 6.0, 12.7 Hz, 4α-H), 3.35 (3 H, s, OMe), 3.47 (3 H, s, OMe), 5.11 (1 H, dd, *J* 6.0, 10.9 Hz, 4a-H), 6.88 (1 H, d, *J* 8.3 Hz, 6-H), 7.03 (1 H, t, *J* 7.7 Hz, 8-H), 7.36 (1 H, ddd, *J* 1.5, 7.7, 8.3 Hz, 7-H), 7.67 (1 H, dd, *J* 1.5, 7.7 Hz, 9-H), and 12.35 (1 H, s, exchanges with D_2O, OH); m/z (peaks > 10%) 278 (M^+, 0.1%), 221 (12), 219 (10), 192 (13), 191 (100), 174 (10), 173 (79), 147 (13), 89 (73), 80 (12), 59 (27), and 57 (29).

Equilibration Experiments (cf. *Table 3*)

Method 1:[33] Solutions of **38a** and **38b** (0.10 g, 0.4 mmol) were treated with 5% trifluoroacetic acid in chloroform (10 ml) at 20±3 °C. Four samples (1 ml) of each were withdrawn at the periods indicated below, filtered through a short plug of anhydrous sodium carbonate and magnesium sulphate, and then analysed using the h.p.l.c. conditions previously described.[7]

	RUN 1		RUN 2	
Time (h)	**38a** (%)	**38b** (%)	**38a** (%)	**38b** (%)
0	100	0	0	100
3	22.8±0.5	77.2±0.5	9.5±0.2	90.5±0.2
24	13.2±0.3	86.8±0.3	13.4±0.3	86.6±0.3
48	12.9±0.3	87.1±0.3	13.0±0.3	87.0±0.3
72	13.3±0.3	86.7±0.3	12.6±0.3	87.4±0.3

Method 2: To the pyranobenzopyran **39a**, **41a**, or **52a** (200 mg, *ca.* 0.8 mmol) in dichloromethane (25 ml) was added trifluoroacetic acid (1.2 ml). The solution was then stirred for 24 h at room temperature, carefully neutralised using saturated aqueous sodium hydrogen carbonate, and the organic phase isolated. Evaporation followed by chromatography, eluting with petroleum - ethyl acetate (9:1), gave the products described in Table 3. All were identical (i.r., n.m.r., t.l.c.) to previously prepared samples.

Hydrogenation of 4,4a-Dihydro-3H,10H-pyrano[4,3-b][1]benzopyran-10-ones

Method A: To the pyranobenzopyran (1 mmol) in ethanol (25 ml) was added 5% Pd-C (*ca.* 10 mg). The suspension was then shaken under 1 atm. H_2 at room temperature until the starting material was no longer detectable by t.l.c. The catalyst was then filtered off and the filtrate concentrated to obtain the mixture of isomeric ketones.

Method B: To the pyranobenzopyran (4 mmol) in ethanol (100 ml) was added either 5% Pd-C or freshly prepared Raney nickel[34] (*ca.* 25 mg), and the suspension then shaken under 3 atm. H_2 (Cooke hydrogenator) at room temperature until the starting material was no longer detectable by t.l.c. The catalyst was then filtered off and the filtrate concentrated to obtain a mixture of isomeric alcohols, which was dissolved in dichloromethane (50 ml) and stirred with manganese dioxide (3.5 g, 40 mmol) at room temperature for 4 h. Filtration followed by evaporation of the filtrate gave the mixture of isomeric ketones.

Method C: To a stirred solution of the pyranobenzopyran (4 mmol) in ethanol (100 ml) at 0–5 °C was slowly added sodium borohydride (1.5 g, 40 mmol), and the stirring at 0–5 °C continued for 5 h. The solvent was then evaporated off and the residue treated with water (50 ml) followed by hydrochloric acid (4 M, 5 ml). The organic products were extracted into dichloromethane (2 x 50 ml), and the extract dried over $MgSO_4$, filtered, and stirred with manganese dioxide (3.5 g, 40 mmol) for 4 h at room temperature. Filtration followed by evaporation of the filtrate gave the mixture of isomeric ketones.

The results obtained with Method A were difficult to reproduce. Over-reduction was sometimes observed, depending on the age and quantity of the catalyst used. The ketone ratios were determined by 300 MHz ^{1}H-n.m.r. spectroscopy.

Reduction of the Cycloadduct **38a**

Method A: The *cis*-fused isomer **54** predominated (**54**:**55** ratio *ca.* 5:1). Chromatography eluting with petroleum - ethyl acetate (4:1) gave the less polar *3β-ethoxy-1,4,4aα,10aβ-tetrahydro-3*H,*10*H-*pyrano[4,3-b][1]benzopyran-10-one* **55** (35 mg, 14%) as colourless needles, m.p. 148–150 °C (ethyl acetate-petroleum, b.p 80–100 °C) (Found: C, 67.48, H, 6.46. $C_{14}H_{16}O_4$ requires C, 67.72, H, 6.49%); ν_{max} 1690, 1605, 1120, and 1045 cm^{-1}; δ (300 MHz) 1.23 (3 H, t, *J* 7.0 Hz, OCH_2Me), 1.95 (1 H, ddd, *J* 9.6, 11.6, 12.1 Hz, 4β-H), 2.42 (1 H, ddd, *J* 2.1, 4.7, 12.1 Hz, 4α-H), 2.81 (1 H, ddd, *J* 5.0, 10.4, 13.1 Hz, 10a-H), 3.43 (1 H, dd, *J* 10.4, 12.6 Hz, 1α-H), 3.50–3.60 and 3.89–4.00 (each 1 H, m, OCH_2Me), 4.31 (1 H, ddd, *J* 4.7, 11.6, 13.1 Hz, 4a-H), 4.45 (1 H, dd, *J* 2.1, 9.6 Hz, 3-H), 4.52 (1 H, dd, *J* 5.0, 12.6 Hz, 1β-H), 6.96 (1 H, br. d, *J* 8.6 Hz, 6-H), 7.00 (1 H, ddd, *J* 0.9, 7.3, 7.8 Hz, 8-H), 7.46 (1 H, ddd, *J* 1.8, 7.3, 8.6 Hz, 7-H), and 7.82 (1 H, dd, *J* 1.8, 7.8 Hz, 9-H); m/z 248 (M^+, 64%), 203 (21), 175 (30), 174 (83), 170 (42), 147 (50), 146 (62), 131 (25), 121 (89), 120 (100), 92 (54), and 65 (27).

The more polar *3β-ethoxy-1,4,4aα,10aα-tetrahydro-3*H,*10*H-*pyrano[4,3-b][1]benzopyran-10-one* **54** (177 mg, 71%) was obtained as colourless needles, m.p. 108 °C (ethyl acetate - petroleum, b.p. 80–100 °C) (Found: C, 67.52, H, 6.45. $C_{14}H_{16}O_4$ requires C, 67.72, H, 6.49%); ν_{max} 1672, 1608, 1230, 1152, and 1120 cm^{-1}; δ (300 MHz) 1.17 (3 H, t, *J* 7.0 Hz, Me), 2.02–2.15 (2 H, m, 4α-H and 4β-H), 2.89 (1 H, overlapping ddd, *J* 4.2, 4.2, 8.2 Hz, 10a-H), 3.43–3.52 (2 H, m, OCH_2 and 1α-H), 3.72–3.82 (1 H, m, OCH_2), 4.38 (1 H, dd, *J* 7.9, 11.5 Hz, 1β-H), 4.71 (1 H, t, *J* 4.0 Hz, 3-H), 4.75–4.80 (1 H, m, 4a-H), 6.95–7.02 (2 H, m, 6-H and 8-H), 7.46 (1 H, overlapping ddd, *J* 1.8, 7.2, 8.6 Hz, 7-H), and 7.85 (1 H, dd, *J* 1.8, 7.8 Hz, 9-H); m/z 248 (M^+, 23%), 174 (24), 147 (50), 146 (23), 121 (75), 120 (100), 92 (26), 85 (32), and 83 (52).

Method B: The mixture of **54** and **55** was obtained in an overall yield of 80%.

Method C: The mixture of **54** and **55** was obtained in an overall yield of 50% (ratio not determined).

Treating either **54** or **55** (5 mg) with a catalytic amount of DBU in acid-free $CDCl_3$ produced similar mixtures in which the ratio **54**:**55** was *ca.* 1:3.

Reduction of the cycloadduct **38b**

Method A: The *trans*- and *cis*-fused products **56** and **57** were formed (ratio *ca.* 3:1), but only the former was isolated in sufficient quantity for characterisation. Chromatography eluting with petroleum - ethyl acetate (4:1) gave the less polar *3α-ethoxy-1,4,4aα,10aβ-tetrahydro-3*H,*10*H-*pyrano[4,3-b][1]benzopyran-10-one* **56** (187 mg, 74%) as colourless needles, m.p. 101.5–102.5 °C (ethyl acetate - petroleum, b.p. 80–100 °C) (Found: C, 67.66, H, 6.61. $C_{14}H_{16}O_4$ requires C, 67.73, H, 6.49%); ν_{max} 1680, 1600, 1220, 1115 cm^{-1}; δ (300 MHz) 1.16 (3 H, t, *J* 7.0 Hz, CH_2Me), 2.05 (1 H, ddd, *J* 3.6, 11.5, 12.4 Hz, 4β-H), 2.31 (1 H, ddd, *J* 1.3, 4.8, 12.4 Hz, 4α-H), 2.84 (1 H, ddd, *J* 5.2, 10.9, 13.2 Hz, 10a-H), 3.35–3.45 and 3.64–3.74 (each 1H, m, OCH_2Me), 3.79 (1 H, t, *J* 11.3 Hz, 1α-H), 4.17 (1 H, dd, *J* 5.2, 11.9 Hz, 1β-H), 4.67 (1 H, ddd, *J* 4.8, 11.5, 13.2 Hz, 4a-H), 4.99 (1 H, br. d, *J* 3.3 Hz, 3-H), 6.94 (1 H, dd, *J* 0.8, 8.6 Hz, 6-H), 6.98 (1 H, overlapping ddd, *J* 0.8, 7.4, 8.0 Hz, 8-H), 7.44 (1 H, overlapping ddd, *J* 1.7, 7.4, 8.6 Hz, 7-H), and 7.82 (1 H, dd, *J* 1.7, 8.0 Hz, 9-H); m/z 248 (M^+, 35%), 203 (27), 174 (34), 173 (21), 147 (24), 146 (21), 121 (82), 120 (100), and 92 (24).

Reduction of the Cycloadduct **39a**

To the pyranobenzopyran **39a** (1.0 g, 3.85 mmol) in ethanol (100 ml) was added a catalytic amount of 5% Pd-C. The mixture was placed in a Cooke low pressure hydrogenator under 10 atmospheres of hydrogen and rocked at room temperature for 5 h. Filtration followed by evaporation of the solvent afforded the crude product. Chromatography eluting with petroleum - ethyl acetate (9:1) afforded the less polar *3β-ethoxy-1,4,4aα,10aα-tetrahydro-1β-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran* **59** (468 mg, 49%) as a pale yellow oil, (M^+, 248.1388. $C_{15}H_{20}O_3$ requires 248.1412); ν_{max} (FT, $CDCl_3$) 2980, 1611, 1584, 1243, and 1046 cm^{-1}; δ (300 MHz) 1.20 (3 H, t, *J* 7.0 Hz, CH_2Me), 1.28 (3 H, d, *J* 6.5 Hz, 1-Me), 1.65 (1 H, overlapping ddd, *J* 9.8, 12.4, 12.4 Hz, 4β-H), 1.91–1.98 (1 H, m, 4α-H), 2.02–2.09 (1 H, m, 10a-H), 2.57 (1 H, dd, *J* 6.1, 16.8 Hz, 10α-H), 2.93 (1 H, dd, *J* 12.1, 16.8 Hz, 10β-H), 3.45–3.55 (1 H, m, OCH_2), 3.66 (1 H, dd, *J* 1.7, 6.5 Hz, 1-H), 3.87–3.97 (1 H, m, OCH_2), 4.33–4.39 (1 H, m, 4a-H), 4.43 (1 H, dd, *J* 2.2, 9.8 Hz, 3-H), 6.76–6.83 (2 H, m, 6-H and 8-H), and 7.01–7.07 (2 H, m, 7-H and 9-H); m/z (methane CI) 249 ($M^+ + 1$, 2%), 203 (100), 202 (24), and 159 (20).

The chromatography also gave a mixture of the isomeric alcohols **58** (490 mg, 48%), of which a portion (120 mg, 0.45 mmol) in dichloromethane (5 ml) was stirred with manganese dioxide (196 mg, 2.25 mmol) at room temperature for 48 h. Filtration followed by evaporation of the solvent afforded two products which were isolated by chromatography, eluting with petroleum - ethyl acetate (9:1), which gave the less polar *3β-ethoxy-1,4,4aα,10aβ-tetrahydro-1β-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **60** (54 mg, 45%) as a white powder, m.p. 102–103 °C (M^+, 262.1194. $C_{15}H_{18}O_4$ requires 262.1205); ν_{max} (FT) 1682, 1605, 1464, 1154, and 1072 cm^{-1}; δ (300 MHz) 1.23 (3 H, t, *J* 7.0 Hz, CH_2Me), 1.60 (3 H, d, *J* 6.0 Hz, 1-Me), 1.96 (1 H, overlapping ddd, *J* 9.8, 11.8, 12.0 Hz, 4β-H), 2.39 (1 H, ddd, *J* 1.9, 5.0, 12.0 Hz, 4α-H), 2.47 (1 H, dd, *J* 9.5, 13.0 Hz, 10a-H), 3.48–3.58 (1 H, m, OCH_2), 3.68 (1 H, dq, *J* 6.0, 9.5 Hz, 1-H), 3.91–4.01 (1 H, m, OCH_2), 4.33 (1 H, ddd, *J* 5.0, 11.8, 13.0 Hz, 4a-H), 4.46 (1 H, dd, *J* 1.9, 9.8 Hz, 3-H), 6.93 (1 H, br.d, *J* 8.3 Hz, 6-H), 6.96 (1 H, overlapping ddd, *J* 0.9, 7.9, 8.3 Hz, 8-H), 7.43 (1 H, overlapping ddd, *J* 1.7, 7.5, 8.5 Hz, 7-H), and 7.77 (1 H, dd, *J* 1.7, 7.9 Hz, 9-H); m/z 262 (M^+, 16%), 189 (30), 188 (21), 173 (78), 147 (42), 121 (91), 120 (100), 92 (44), 72 (26), 68 (27), and 65 (22).

The *3β-ethoxy-1,4,4aα,10aα-tetrahydro-1β-methyl-3*H,*10*H-*pyrano[4,3-*b*][1]benzopyran-10-one* **61** (48 mg, 40%) was isolated as a white powder, m.p. 108–109 °C (M^+, 262.1174. $C_{15}H_{18}O_4$ requires 262.1205); ν_{max} (FT) 1686, 1606, 1583, 1463, 1219, 1067 and 1049 cm^{-1}; δ (300 MHz), 1.14 (3 H, t, *J* 7.0 Hz, CH_2Me), 1.72 (3 H, d, *J* 6.8 Hz, 1-Me), 1.92 (1 H, ddd, *J* 8.5, 11.5, 13.0 Hz, 4β-H), 2.00–2.06 (1 H, m, ddd with a W-coupling, 4α-H), 2.88–2.91 (1 H, m, dd with a W-coupling, 10a-H), 3.42–3.52 (1 H, m, OCH_2), 3.59 (1 H, dq, *J* 2.6, 6.8 Hz, 1-H), 3.86–3.96 (1 H, m, OCH_2) 4.52 (1 H, dd, *J* 2.8, 8.5 Hz, 3-H), 4.68–4.75 (1 H, m, 4a-H), 6.88 (1 H, br. d, *J* 8.5 Hz, 6-H), 6.94 (1 H, dt, *J* 0.9, 8.0, 8.0 Hz, 8-H), 7.40 (1 H, ddd, *J* 1.7, 8.0, 8.5 Hz, 7-H), and 7.81 (1 H, dd, *J* 1.7, 8.0 Hz, 9-H); m/z 262 (M^+, 7%), 173 (40), 147 (50), 121 (100), 120 (97), 92 (40), 72 (99), and 65 (20).

Treatment of **60** or **61** (5 mg) with a catalytic amount of DBU in acid-free $CDCl_3$ produced a solution in which only the *trans*-isomer **60** was detectable.

*(E)-3-(4-Oxo-4*H*-1-benzopyran-3-yl)propenal* **62**

Method A: A mixture of the pyranobenzopyran **38a** (120 mg, 0.5 mmol) and sodium methoxide (27 mg, 0.5 mmol) in methanol (10 ml) was heated under reflux for 3 h. The cooled mixture was then poured into ice-water (50 ml) and acidified with 10% aqueous HCl (10 ml). The resulting precipitate was collected on a filter, washed with water, and dried by suction. The crude product (68 mg, 70%) was crystallised (ether - dichloromethane) to give the title compound **62** (51 mg, 52%), m.p. 151–152 °C (lit.[9] 150 °C); ν_{max} ($CHCl_3$) 1685, 1655, 1610 cm^{-1}; δ (60 MHz) 7.3–7.9 (5 H, m, 2-H, 3-H, 6'-H, 7'-H, and 8'-H), 8.30 (1 H, s, 2'-H), 8.37 (1 H, dd, *J* 2.0, 8.0 Hz, 5'-H), and 9.73 (1 H, m, 1-H).

Method B: To the pyranobenzopyran **38a** (246 mg, 1.0 mmol) in ethanol (9 ml) and water (1 ml) was added conc. sulphuric acid (1 ml), and the solution heated under reflux for 16 h. The solution was then reduced to

ca. one-half of the original volume by rotary evaporation, diluted with water (10 ml), and cooled. The resulting precipitate was collected on a filter, washed well with water, dried by suction, and crystallised (ether - dichloromethane) to afford the aldehyde **62** (98 mg, 49%), with m.p., i.r. and n.m.r. spectra identical with those of the sample prepared by method A.

*2-(2,2-Diethoxyethyl)-2,3-dihydro-4*H*-1-benzopyran-4-one* **63a**

Method A: To the pyranobenzopyran **38a** (1.0 g, 4.07 mmol) in ethanol (100 ml) was added *p*-toluenesulphonic acid (9.12 g, 48 mmol) and water (2 ml). The mixture was then heated under reflux for 48 h cooled and quenched with saturated aqueous sodium bicarbonate solution. The organic material was extracted with ether (3 x 50 ml) and the ethereal extracts combined and concentrated. Chromatography of the residue, eluting with petroleum - ethyl acetate (4:1), gave the aldehyde **62** (206 mg, 25%) and the acetal **63a** (388 mg, 36%). Both samples were identical (i.r., n.m.r., t.l.c.) to materials prepared by the alternative methods described.

Method B: To the pyranobenzopyran **38a** (1.0 g, 4.07 mmol) was added ethanolic hydrogen chloride (prepared from 50 ml of ethanol and 2.5 ml of acetyl chloride). The yellow solution was then fitted with a guard tube and heated to between 55–60 °C for 16 h. The reaction was then left to cool and quenched cautiously using saturated aqueous sodium hydrogen carbonate solution. Extraction with ether (3 x 25 ml) followed by concentration and chromatography, eluting with petroleum - ether (4:1), gave the acetal **63a** (448 mg, 44%), identical (i.r., n.m.r., t.l.c.) to the sample prepared by method C.

Method C: To the pyranobenzopyran **44a** (250 mg, 0.95 mmol) was added absolute ethanol (10 ml). The mixture was then fitted with a guard tube and heated under reflux for 16 h, cooled and the solvent removed to afford the *title compound* **63a** (252 mg, 100%) as a pale yellow non-distillable oil (Found: C, 68.33; H, 7.79. $C_{15}H_{20}O_4$ requires C, 68.16; H, 7.63%); ν_{max} (neat) 1690, 1605 and 1580 cm^{-1}; δ (300 MHz) 1.15 (3 H, t, *J* 7.0 Hz, Me), 1.18 (3 H, t, *J* 6.8 Hz, Me), 1.95 (1 H, ddd, *J* 4.4, 7.4, 14.3 Hz, 1'-H), 2.16 (1 H, ddd, *J* 4.0, 8.4, 14.3 Hz, 1'-H), 2.681 (1 H, d, *J* 7.4 Hz, 3-H), 2.682 (1 H, d, *J* 8.3 Hz, 3-H), 3.45–3.72 (4 H, m, 2 x OCH_2), 4.58 (1 H, overlapping dddd, *J* 4.4, 7.4, 8.3, 8.4 Hz, 2-H), 4.80 (1 H, dd, *J* 4.0, 7.4 Hz, 2'-H), 6.92 (1 H, dd, *J* 1.2, 8.6 Hz, 8-H), 6.96 (1 H, overlapping ddd, *J* 1.2, 7.2, 8.0 Hz, 6-H), 7.42 (1 H, overlapping ddd, *J* 1.7, 7.2, 8.6 Hz, 7-H), and 7.83 (1 H, dd, *J* 1.7, 8.0 Hz, 5-H); m/z 264 (M^+, 9%), 218 (25), 172 (37), 147 (100), 131 (98), 103 (43), 75 (98), 73 (29), 65 (20), 51 (30), and 49 (83).

*2-(2,2-Dimethoxyethyl)-2,3-dihydro-4*H*-1-benzopyran-4-one* **63b**

Method A: To the pyranobenzopyran **38a** (1.0 g, 4.07 mmol) was added 3% hydrogen chloride in methanol (50 ml).[35] The resulting yellow solution was fitted with a guard tube and heated under reflux for 16 h. The reaction was then left to cool, quenched cautiously using saturated aqueous sodium hydrogen carbonate solution, and extracted with ether (2 x 30 ml). Combination and evaporation of the organic extracts gave an oil which was purified by chromatography, eluting with petroleum - ethyl acetate (4:1), giving the *title compound* **63b** (650 mg, 67%) as a non-distillable pale yellow oil (M^+, 236.1065. $C_{13}H_{16}O_4$ requires 236.1048); ν_{max} ($CHBr_3$) 1685, 1601, 1469 and 1460 cm^{-1}; δ (250 MHz) 2.00 (1 H, ddd, *J* 4.5, 7.0, 14.0 Hz, 1'-H), 2.19 (1 H, ddd, *J* 4.0, 8.0, 14.0 Hz, 1'-H), 2.75 (2 H, d, *J* 8.0 Hz, 3-H), 3.37 (3 H, s, OMe), 3.39 (3 H, s, OMe), 4.63 (1 H, overlapping ddd, *J* 4.5, 8.0, 8.0 Hz, 2-H), 4.74 (1 H, dd, *J* 4.0, 7.0 Hz, 2'-H), 6.90–7.05 (2 H, m, 6-H and 8-H), 7.48 (1 H, dt, *J* 2.0, 8.0, 8.0 Hz, 7-H), and 7.89 (1 H, dd, *J* 2.0, 8.0 Hz, 5-H); m/z 237 ($M^+ + 1$, 10%), 147 (42), 131 (59), 75 (100), and 47 (32).

Method B: To the acetal **63a** (70 mg, 0.27 mmol) in methanol (3 ml) was added hydrochloric acid (4 M, one drop). The solution was then fitted with a guard tube and heated under reflux for 16 h, cooled, quenched with aqueous saturated sodium hydrogen carbonate, and extracted with ether (2 x 5 ml). Evaporation of the organic extracts gave the title compound **63b** (46 mg, 73%) as a pale yellow oil identical to the authentic sample (i.r., n.m.r., t.l.c.).

*(E)-Methyl 3-(4-oxo-4*H*-1-benzopyran-3-yl)propenoate* **73**

To the pyranobenzopyran **48** (500 mg, 1.91 mmol) in DMF (25 ml) was added water (8 ml) and conc. HCl (10

drops). The solution was heated to 80 °C for 16 h, then allowed to cool and poured on to ice (10 g) and water (25 ml). The resulting precipitate was collected on a filter, washed well with water and crystallised (petroleum - dichloromethane) to afford the *title compound* **73** (198 mg, 45%) as colourless needles, m.p. 146.5–147.5 °C (Found: C, 67.77; H, 4.38. $C_{13}H_{10}O_4$ requires C, 67.82; H, 4.38%); ν_{max} 1720, 1640, 1610, and 1230 cm^{-1}; δ (60 MHz) 3.76 (3 H, s, OMe), 7.20–7.75 (5 H, m, 2-H, 3-H, 6'-H, 7'-H, and 8'-H), 8.15 (1 H, s, 2'-H), and 8.30 (1 H, dd, *J* 2.0, 8.0 Hz, 5'-H); m/z 230 (M^+, 7%), 171 (100).

2-Methoxyethyl 3,4-dihydro-4-oxo-2H-1-benzopyran-2-acetate **74**

Method A: A solution of **71** (prepared[33] in the usual way from the aldehyde **28** and the ketene acetal **72**) (0.23 g, 0.66 mmol) in DMF (3 ml) and water (1 ml) containing 5 drops of conc. HCl was stirred at 80 °C for 20 h. The cooled solution was poured into ice-water (50 ml) and allowed to stand overnight. The resulting precipitate was collected, washed with water, and dried by suction. Recrystallisation from dichloromethane - petroleum gave the *title compound* **74** (73 mg, 41%) as colourless needles, m.p. 102–103 °C (Found: C, 65.47; H, 5.23. $C_{15}H_{14}O_5$ requires C, 65.69; H, 5.14%); ν_{max} 1700, 1640 and 1610 cm^{-1}; δ (60 MHz) 3.42 (3 H, s, OMe), 3.65 and 4.34 (each 2 H, m, OCH_2CH_2O), 7.30–7.90 (5 H, m, 2-H, 3-H, 6'-H, 7'-H, 8'-H), 8.10 (1 H, s, 2'-H), and 8.25 (1 H, dd, *J* 2, 8 Hz, 5'-H); m/z 274 (M^+, 3.5%), 199 (28) and 171 (100).

Method B: A solution of **75** (0.15 g, 0.52 mmol) in DMF (3 ml) and water (1 ml) containing 5 drops of conc. HCl was stirred at 80 °C for 20 h. Isolation as before gave the title compound **74** (30 mg, 21%).

2-Methoxyethyl 3,4-dihydro-3-(hydroxymethylene)-4-oxo-2H-1-benzopyran-2-acetate **75**

A solution of **71** (0.175 g, 0.5 mmol) in DMF (4.5 ml) and water (0.5 ml) containing 5 drops of conc. HCl was stirred at 20 °C for 20 h. The solution was poured into water (50 ml) and extracted with ether - petroleum (1:1; 3 x 30 ml). The combined extracts were washed with water and brine, dried and evaporated. Distillation of the crude product (0.134 g) under reduced pressure gave the *title compound* **75** (0.12 g, 82%) as a yellow oil, b.p. 160–165 °C (0.13 mmHg) (M^+, 292.0959; $C_{15}H_{16}O_6$ requires 292.0947); ν_{max} (neat) 3200, 1740, 1650, and 1620 cm^{-1}; δ (60 MHz) 2.85 (1 H, d, *J* 7 Hz, 2-H), 2.90 (1 H, d, *J* 7 Hz, 2-H), 3.40 (3 H, s, OMe), 3.56 and 4.24 (each 2 H, m, OCH_2CH_2O), 5.45 (1 H, t, *J* 7 Hz, 2'-H), 6.70–7.55 (3 H, m, 6'-H, 7'-H, 8'-H), 7.80 (1 H, dd, *J* 2, 8 Hz, 5'-H), and 8.00 (1 H, s, =C*H*OH); m/z 292 (M^+, 1%), 199 (22), 175 (22), and 171 (100).

Methyl 3,4-dihydro-4-oxo-2H-1-benzopyran-2-acetate **76**

Method A: To the pyranobenzopyran **71** (700 mg, 2.0 mmol) in absolute methanol (18 ml) and water (2 ml) was added concentrated sulphuric acid (2 ml). The solution was then heated under reflux for 16 h, cooled, and evaporated to one-half of the original volume to remove the ethanol. Water (20 ml) was added and the resulting oil was extracted using ether (3 x 20 ml). The combined organic extracts were dried and evaporated, and flash chromatography of the residue, eluting with petroleum - ethyl acetate (2:1), afforded the *title compound* **76** (270 mg, 61%) as a pale yellow oil (Found: C, 65.78, H, 5.69. $C_{12}H_{12}O_4$ requires C, 65.44, H, 5.49%. M^+, 220.0730. $C_{12}H_{12}O_4$ requires 220.0735); ν_{max} (neat) 1740, 1690, 1610, and 1210 cm^{-1}; δ (300 MHz) 2.72 (1 H, dd, *J* 5.5, 15.9 Hz, 2-H), 2.768 (1 H, d, *J* 8.7 Hz, 3'-H), 2.771 (1 H, d, *J* 7.1 Hz, 3'-H), 2.86 (1 H, dd, *J* 7.3, 15.9 Hz, 2-H), 3.73 (3 H, s, OMe), 4.90 (1 H, m, 2'-H), 6.95 (1 H, dd, *J* 1.0, 8.5 Hz, 8'-H), 7.01 (1 H, ddd, *J* 1.0, 7.2, 7.9 Hz, 6'-H), 7.46 (1 H, ddd, *J* 1.7, 7.2, 8.5 Hz, 7'-H), and 7.86 (1 H, dd, *J* 1.7, 7.9 Hz, 5'-H); m/z 220 (M^+, 33%), 147 (100), 121 (33), 120 (94), and 92 (51).

Method B: The hydroxy compound **51** (215 mg, 0.77 mmol) was passed through a short plug of silica gel eluting with dichloromethane to afford the ester **76** (141 mg, 83%), identical to the authentic sample (n.m.r. and t.l.c.). A similar result was observed when the adduct **51** was heated in THF - water (14:1), as described for the preparation of **81**.

Method C: To the pyranobenzopyran **48** (524 mg, 2.0 mmol) was added 3% methanolic hydrogen chloride (50 ml).[35] The mixture was heated under reflux for 16 h and the resulting solution was cooled and quenched cautiously with saturated aqueous sodium hydrogen carbonate solution. Ether extraction (3 x 20 ml) followed

by concentration and chromatography (see Method A) afforded the title compound **76** (277 mg, 63%) identical (i.r., n.m.r., t.l.c.) to the samples prepared previously.

*Ethyl 3,4-dihydro-4-oxo-2*H*-1-benzopyran-2-acetate* **77**

Method A: To the pyranobenzopyran **48** (524 mg, 2.0 mmol) in absolute ethanol (9 ml) and water (1 ml) was added concentrated sulphuric acid (1 ml). The solution was then heated under reflux for 16 h, cooled, and evaporated to one-half of the original volume to remove the ethanol. Water (10 ml) was added and the resulting oil was extracted with ether (3 x 20 ml). The combined organic extracts were dried and evaporated, and flash chromatography of the residue, eluting with petroleum - ethyl acetate (4:1), gave the *title compound* **77** (253 mg, 54%) as a pale yellow waxy solid (M^+, 234.0891. $C_{13}H_{14}O_4$ requires 234.0892); ν_{max} (neat) 1737, 1695, 1605, 1460 and 1305 cm^{-1}; δ (300 MHz) 1.27 (3 H, t, *J* 7.0 Hz, Me), 2.70 (1 H, dd, *J* 5.6, 15.8 Hz, 2-H), 2.763 (1 H, d, *J* 8.7 Hz, 3'-H), 2.766 (1 H, d, *J* 6.9 Hz, 3'-H), 2.90 (1 H, dd, *J* 7.3, 15.8 Hz, 2-H), 4.19 (2 H, q, *J* 7.0 Hz, OCH_2), 4.92 (1 H, m, 2'-H), 6.94 (1 H, d, *J* 8.3 Hz, 8'-H), 7.00 (1 H, dd, *J* 7.3, 7.9 Hz, 6'-H), 7.45 (1 H, ddd, *J* 1.7, 7.3, 8.3 Hz, 7'-H), and 7.86 (1 H, dd, *J* 1.7, 7.9 Hz, 5'-H); m/z 234 (M^+, 16%), 147 (77), 121 (29), 120 (69), 92 (40), 88 (34), 86 (78), 83 (84), 51 (78), and 49 (100).

Method B: The pyranobenzopyran **71** (700 mg, 2.00 mmol) was treated as in method A. The title compound **77** (285 mg, 61%) so obtained was identical (i.r., n.m.r., t.l.c.) to the authentic sample.

cis-*3-Ethoxy-4,4a-dihydro-1-methoxy-3*H*,10*H*-pyrano[4,3-*b*][1]benzopyran-10-one* **78**

To the hydroxy compound **44a** (1.0 g, 3.82 mmol) in ether (25 ml) was added diazomethane (4.56 mmol based on the theoretical yield).[36] The solution was then left to evaporate to dryness in the fume cupboard (16 h). Crystallisation of the residue from ethyl acetate - petroleum, b.p. 80–100 °C, gave the *title compound* **78** (750 mg, 72%) as colourless plates. Concentration of the mother liquors and chromatography of the residue, eluting with dichloromethane, afforded a further crop of **78** (250 mg, 24%), m.p. 126–128 °C (Found: C, 64.99; H, 5.83. $C_{15}H_{16}O_5$ requires C, 65.20; H, 5.83%); ν_{max} 1690, 1610, and 1335 cm^{-1}; δ (300 MHz) 1.23 (3 H, t, *J* 7.0 Hz, CH_2*Me*), 2.30 (1 H, ddd, *J* 8.5, 9.0, 13.6 Hz, 4β-H), 2.58 (1 H, ddd, *J* 2.3, 6.7, 13.6 Hz, 4α-H), 3.59–3.65 and 3.97–4.05 (each 1H, m, OCH_2), 4.035 (3 H, s, OMe), 5.01 (1 H, dd, *J* 6.7, 9.0 Hz, 4a-H), 5.22 (1 H, dd, *J* 2.3, 8.5 Hz, 3-H), 6.89 (1 H, dd, *J* 0.8, 8.2 Hz, 6-H), 7.00 (1 H, overlapping ddd, *J* 0.8, 7.4, 7.8 Hz, 8-H), 7.32 (1 H, overlapping ddd, *J* 1.6, 7.4, 8.2 Hz, 7-H), and 7.60 (1 H, dd, *J* 1.6, 7.8 Hz, 9-H); m/z 276 (M^+, 13%), 230 (22), 205 (100), 203 (22), 174 (70), 173 (30), 159 (21), 146 (23), 131 (35), 130 (42), and 121 (26).

*4,4a-Dihydro-1,3,3-trimethoxy-3*H*,10*H*-pyrano[4,3-*b*][1]benzopyran-10-one* **79**

To the hydroxy compound **51** (1.0 g, 3.60 mmol) in ether (25 ml) was added diazomethane (4.30 mmol based on the theoretical yield).[36] The solution was then left to evaporate to dryness in the fume cupboard (16 h). Crystallisation of the residue from ethyl acetate - petroleum, b.p. 80–100 °C, gave the *title compound* **79** (700 mg, 67%) as colourless needles, m.p. 128–129 °C (Found: C, 62.18; H, 5.10. $C_{15}H_{16}O_6$ requires C, 61.64; H, 5.51%); ν_{max} (FT, $CDCl_3$) 1710, 1596, 1265, and 1052 cm^{-1}; δ (300 MHz) 2.36 (1 H, dd, *J* 10.5, 13.3 Hz, 4β-H), 2.71 (1 H, dd, *J* 6.7, 13.3 Hz, 4α-H), 3.33 (3 H, s, 3-OMe), 3.45 (3 H, s, 3-OMe), 4.07 (3 H, s, 1-OMe), 5.00 (1 H, dd, *J* 6.7, 10.5 Hz), 6.89 (1 H, dd, *J* 1.0, 8.2 Hz, 6-H), 7.01 (1 H, overlapping ddd, *J* 1.0, 7.8, 8.5 Hz, 8-H), 7.33 (1H overlapping ddd, *J* 1.6, 8.2, 8.5 Hz, 7-H), and 7.64 (1 H, dd, *J* 1.6, 7.8 Hz, 9-H); m/z (methane CI) 293 (M^+ + 1, 11%), 261 (46), 233 (25), 219 (27), 206 (20), and 205 (100).

*3,4-Dihydro-4-oxo-2*H*-1-benzopyran-2-acetaldehyde* **80**

The hydroxy compound **44a** (290 mg, 1.11 mmol) in THF (14 ml) and water (1 ml) was heated under reflux for 16 h, allowed to cool, and treated with magnesium sulphate. Filtration, evaporation, and rapid flash chromatography, eluting with ether - petroleum (1:1), afforded the *title compound* **80** (206 mg, 98%) as a pale yellow oil (non-distillable) (M^+, 190.0642. $C_{11}H_{10}O_3$ requires 190.0630); ν_{max} (neat) 1729, 1691, 1609, 1227, and 1121 cm^{-1}; δ (300 MHz) 2.74–2.76 (2 H, m, 3'-H_2), 2.79 (1 H, ddd, *J* 1.0, 4.9, 17.3 Hz, 1-H), 3.04 (1 H, ddd, *J* 2.0, 7.6, 17.3 Hz, 1-H), 5.00 (1 H, overlapping dddd, *J* 4.9, 6.7, 7.6, 9.1 Hz, 2'-H),

6.93 (1 H, dd, *J* 0.9, 8.5 Hz, 8-H), 7.01 (1 H, overlapping ddd, *J* 0.9, 7.2, 7.9 Hz, 6-H), 7.45 (1 H, overlapping ddd, *J* 1.7, 7.2, 8.5 Hz, 7-H), 7.86 (1 H, dd, *J* 1.7, 7.9 Hz, 5-H), and 9.85 (1 H, dd, *J* 1.0, 2.0 Hz, CHO); m/z 190 (M^+, 4%), 189 (32), 146 (26), 120 (44), 119 (100), 92 (71), 64 (23), and 63 (23).

2,3-Dihydro-2-(2-oxopropyl)-4H-1-benzopyran-4-one **81**

Method A: To the pyranobenzopyran **46a** (330 mg, 1.26 mmol) was added THF (12 ml) and water (0.5 ml). The solution was then heated under reflux for 16 h, cooled, and treated with magnesium sulphate. Filtration, evaporation, and chromatography, eluting with petroleum - ethyl acetate (7:3), gave the *title compound* **81** (236 mg, 92%) as colourless needles (156 mg, 61%), m.p. 52–53 °C (petroleum - ether) (Found: C, 70.33; H, 5.91. $C_{12}H_{12}O_3$ requires C, 70.57; H, 5.92%. M^+, 204.0771. $C_{12}H_{12}O_3$ requires 204.0786); ν_{max} (FT, $CDCl_3$); 1719, 1692 and 1609 cm^{-1}; δ (300 MHz) 2.22 (3 H, s, Me), 2.66 (1 H, dd, *J* 11.4, 16.7 Hz, 3'-H), 2.73 (1 H, dd, *J* 5.2, 16.9 Hz, 1-H), 2.74 (1 H, dd, *J* 4.3, 16.7 Hz, 3'-H), 3.05 (1 H, dd, *J* 7.2, 16.9 Hz, 1-H), 4.91 (1 H, overlapping dddd, *J* 4.3, 5.2, 7.2, 11.4 Hz, 2'-H), 6.89 (1 H, dd, *J* 1.0, 8.1 Hz, 8-H), 6.97 (1 H, overlapping ddd, *J* 1.0, 7.2, 7.9 Hz, 6-H), 7.42 (1 H, overlapping ddd, J 1.0, 7.2, 8.1 Hz, 7-H) and 7.83 (1 H, dd, *J* 1.7, 7.9 Hz, 5-H); m/z 204 (M^+, 18%), 147 (100), 121 (90), 120 (71) and 92 (43).

Method B: To the hydroxy compound **46a** (150 mg, 0.57 mmol) was added absolute ethanol (12 ml). The mixture was then heated under reflux for 16 h, cooled and the solvent was removed. Flash chromatography of the residue, eluting with petroleum - ether (1:1), gave the title compound **81** (91 mg, 78%) identical (i.r., n.m.r., t.l.c., m.p.) to the sample prepared using method A.

2-[(2-Ethoxy-2-methoxy)ethyl]-2,3-dihydro-4H-1-benzopyran-4-one **82**

To the pyranobenzopyran **44a** (250 mg, 1.02 mmol) was added absolute methanol (10 ml). The mixture was then fitted with a guard tube and heated under reflux for 16 h, cooled, and the solvent removed to afford the *title compounds* **82** (238 mg, 100%) as a pale yellow non-distillable oil (h.p.l.c. purity >97%), the ^1H n.m.r. spectrum (300 MHz) indicating a diastereoisomer ratio of 9:1 (Found: C, 66.75, 66.66; H, 7.35, 7.34. $C_{14}H_{18}O_4$ requires C, 67.18; H, 7.25%); (M^+, 250.1223. $C_{14}H_{18}O_4$ requires 250.1205); ν_{max} ($CHBr_3$) 1690, 1610, and 1475 cm^{-1}; δ (300 MHz) 1.17 (3 H, t, *J* 7.0 Hz, CH_2*Me* of **82a**), 1.195 (t, *J* 6.8 Hz, CH_2*Me* of **82b**), 1.95 (1 H, ddd, *J* 4.3, 7.5, 14.2 Hz, 1'-H), 2.15 (1 H, ddd, *J* 4.0, 8.4, 14.2 Hz, 1'-H), 2.689 (1 H, d, *J* 7.1 Hz, 3-H), 2.692 (1 H, d, *J* 8.5 Hz, 3-H), 3.325 (3 H, s, OMe of **82a**), 3.335 (s, OMe of **82b**), 3.46–3.73 (2 H, m, OCH_2), 4.58 (1 H, overlapping dddd, *J* 4.3, 7.1, 8.4, 8.5 Hz, 2-H), 4.76 (1 H, dd, *J* 4.0, 7.5 Hz, 2'-H), 6.93 (1 H, dd, *J* 0.9, 8.4 Hz, 8-H), 6.98 (1 H, overlapping ddd, *J* 0.9, 7.2, 7.9 Hz, 6-H), 7.44 (1 H, overlapping ddd, *J* 1.8, 7.2, 8.4 Hz, 7-H), and 7.84 (1 H, dd, *J* 1.8, 7.9 Hz, 5-H); m/z 250 (M^+, 10%), 172 (21), 147 (73), 131 (81), 121 (25), 120 (95), 92 (31), 89 (94), and 61 (100).

2-[(2-Butoxy-2-methoxy)ethyl]-2,3-dihydro-4H-1-benzopyran-4-one **83**

To the hydroxy compound **45a** (200 mg, 0.69 mmol) was added absolute methanol (10 ml). The mixture was then fitted with a guard tube and heated under reflux for 16 h, cooled, and the solvent removed to afford the *title compound* **83** (192 mg, 100%), the ^1H n.m.r. spectrum (300 MHz) indicating a diastereoisomer ratio of 8:1 (M^+, 278.1519. $C_{16}H_{22}O_4$ requires 278.1518); ν_{max} (FT, neat) 1695, 1607, 1303, 1229, and 1118 cm^{-1}; δ (300 MHz) 0.81 (3 H, t, *J* 7.3 Hz, Me of **83a**), 0.85 (t, *J* 7.3 Hz, Me of **83b**), 1.26 (2 H, sextet, *J* 7.3 Hz, CH_2Me), 1.43–1.52 (2 H, m, C$H_2$$CH_2$Me), 1.91 (1 H, ddd, *J* 4.4, 7.5, 14.1 Hz, 1'-H), 2.09 (1 H, ddd, *J* 4.0, 8.4, 14.1 Hz, 1'-H), 2.63 (2 H, d, *J* 8.0 Hz, 3-H), 3.27 (3 H, s, OMe of **83a**) 3.28 (s, OMe of **83b**), 3.35–3.43 and 3.53–3.61 (1H each, m, OCH_2), 4.53 (1 H, ddd, *J* 4.4, 8.0, 8.4 Hz, 2-H), 4.71 (1 H, dd, *J* 4.0, 7.5 Hz, 2'-H), 6.86–6.94 (2 H, m, 6-H and 8-H), 7.37 (1 H, overlapping ddd, *J* 1.7, 7.6, 8.6 Hz, 7-H), and 7.78 (1 H, dd, *J* 1.6, 7.8 Hz, 5-H); m/z (methane CI) 279 (M^+ + 1, 1%), 175 (31), 132 (31), 131 (100), and 117 (20).

Methanolysis of the Cycloadduct **46a**

The pyranobenzopyran **46a** (100 mg, 0.38 mmol) in absolute methanol (10 ml) was heated under reflux for 16 h, cooled and the solvent removed. Flash chromatography, eluting with petroleum - ether (1:1), gave 2-(2,2-

dimethoxypropyl)-2,3-dihydro-4*H*-1-benzopyran-4-one **84** (86 mg, 90%) as an unstable pale yellow oil, ν_{max} (neat) 1682, 1602, 1461, 1300 and 1222 cm^{-1}; δ (300 MHz) 1.39 (3 H, s, Me), 2.02 (1 H, dd, *J* 4.3, 14.8 Hz, 1'-H), 2.13 (1 H, dd, *J* 7.1, 14.8 Hz, 1'-H), 2.69–2.72 (2 H, m, 3-H_2), 3.13 (3 H, s, OMe), 3.17 (3 H, s, OMe), 4.58 (1 H, overlapping dddd, *J* 4.3, 6.6, 7.1, 9.0 Hz, 2-H), 6.91 (1 H, dd, *J* 1.0, 8.3 Hz, 8-H), 6.96 (1 H, overlapping ddd, *J* 1.0, 7.3, 7.9 Hz, 6-H), 7.42 (1 H, overlapping ddd, *J* 1.7, 7.3, 8.3 Hz, 7-H), and 7.83 (1 H, dd, *J* 1.7, 7.9 Hz, 5-H); m/z (methane CI) 251 (M^+ + 1, 1%), 219 (43), 175 (31), 146 (20), 145 (100), and 89 (28). Also isolated was the more polar dione **81** (7 mg, 9%), identical (i.r., n.m.r., t.l.c.) to an authentic sample. The constitution of **84** was confirmed by hydrolysis (aq. HCl, THF), which gave the dione **81**.

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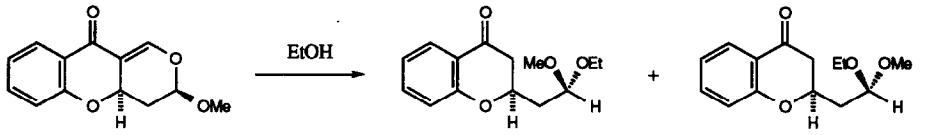

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