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Expeditious Synthesis of Dihydronaphthofurans Utilising 1,2-Dioxines and Stabilised Phosphorus Ylides

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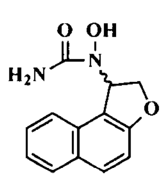
Abstract: A new practical synthesis of functionalised 1,2-dihydronaphtho[2,1-*b*]furans from substituted 2,4*a*-dihydronaphtho[2,1-*c*][1,2]dioxines and stabilised phosphorus ylides is described. Functionalised γ-hydroxy enones and their isomeric hemiacetals are key intermediates. © 1999 Elsevier Science Ltd. All rights reserved.

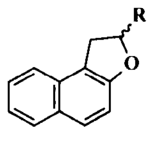
Keywords: Furans, Peroxides, Phosphoranes, Ylides and Cyclisation.

INTRODUCTION

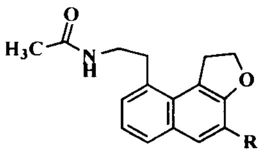
As part of an overall synthetic program directed towards the development of new chemical transformations utilising 1,2-dioxines and stabilised phosphorus ylides we have now focused attention on the synthesis of bio-active dihydronaphthofurans and related analogues.[1] Dihydronaphthofuran containing natural and non-natural products are receiving considerable attention as synthetic targets since the incorporation of the rigidified naphthofuran skeleton into bio-active analogues leads to conformationally constrained molecules. Such modifications often have significant effects on bio-activities with concomitant medical implications. A number of known biologically-active dihydronaphthofurans are depicted below along with their biological property / action.[2-4] Others have found application in the construction of molecular assemblies,[5] in theoretical NMR studies[6] and to evaluate the Neophyl radical rearrangement.[7] Thus, compounds of this type have found direct application in the fields of chemistry, biochemistry and medicine.



5-Lipoxygenase Inhibitors



R = $COCH_2Br$ Inhibitor of α-Chymotrypsin
R = CO_2Me Resolved by α-Chymotrypsin



R = H, F
Melatonin Receptor Ligands

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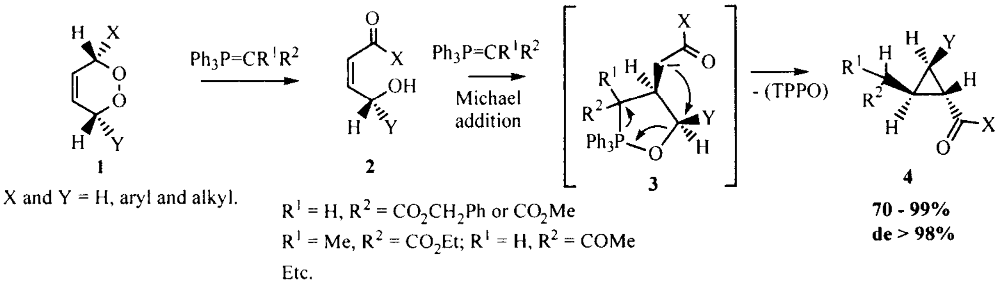
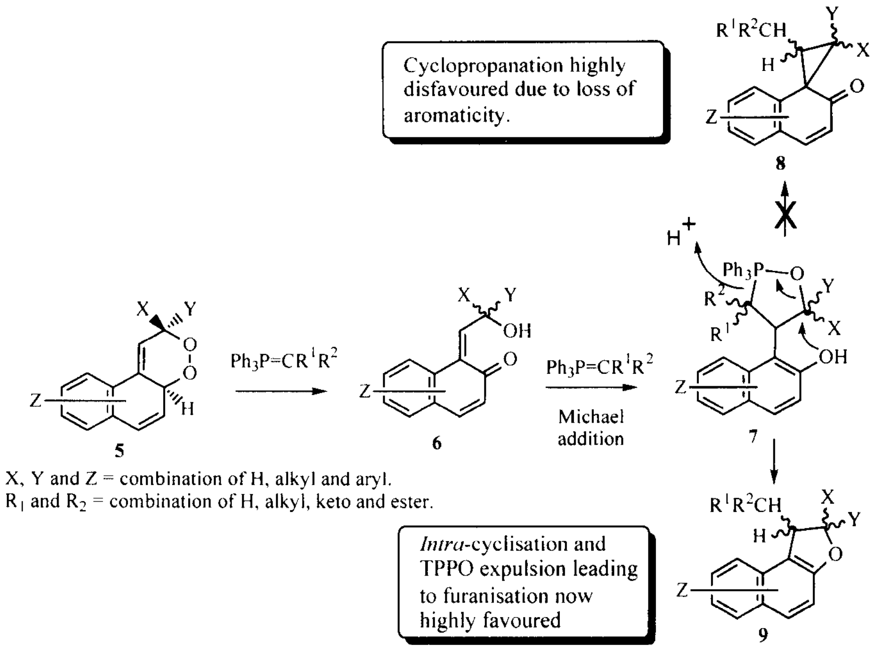
We recently reported new synthetic methodology for the synthesis of diastereomerically-pure cyclopropanes **4** in high yield by the interaction of stabilised phosphoranes and various 3,6-disubstituted-1,2-dioxines **1**, Scheme 1.[1] A key mechanistic finding was the observation of the intermediacy of the *cis* γ-hydroxy enones **2**. The initial acid-base isomerisation of the 1,2-dioxines **1** to the *cis* γ-hydroxy enones **2** was a direct consequence of the ylide acting as a weak base[8] in a catalytic manner. Michael-type addition of the ylide to the γ-hydroxy enone, cyclisation and loss of triphenylphosphine oxide (TPPO) from the intermediate 1-2λ^5-oxaphospholane **3** afforded the observed cyclopropanes.



Scheme 1

Given the above findings, we speculated that most, if not all, 1,2-dioxines containing an acidic proton α to the O-O linkage will undergo initial isomerisation to functionalised *cis* γ-hydroxy enones. These γ-hydroxy enones should then be 'captured' by the ylide and lead to cyclopropanation (but not always!). It occurred to us that the enol (or enolate) of the intermediate 1-2λ^5-oxaphospholane **3** has two possible nucleophilic reactive centres. The first being the nucleophilic carbon pole which leads to carbon-carbon bond formation in our new cyclopropanation reaction, while the second nucleophilic centre is the nucleophilic oxygen pole which should lead to oxygen-carbon bond formation. Therefore, if we could in some way 'stabilise' the resultant enol (or enolate) formed during the Michael addition stage so that the reactivity through the nucleophilic oxygen pole becomes dominant then we should be able to perturb the cyclopropanation pathway in favour of furanisation. The solution to this rationale was obvious! If the resultant enol (or enolate) formed during Michael addition becomes part of an aromatic ring system (compare **7** and **3**) then reactivity through the nucleophilic oxygen pole would be 'expected' as reactivity through the carbon pole would be highly disfavoured energetically due to the necessity for loss of aromaticity. This argument is highlighted in Scheme 2 and should represent a new general synthetic strategy for the construction of diversely functionalised dihydronaphthofurans and related analogues **9**.



Cyclopropanation highly disfavoured due to loss of aromaticity.

X, Y and Z = combination of H, alkyl and aryl.
R$_1$ and R$_2$ = combination of H, alkyl, keto and ester.

Intra-cyclisation and TPPO expulsion leading to furanisation now highly favoured

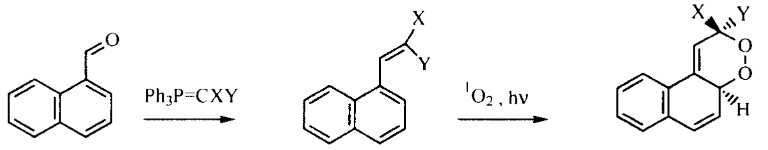
Scheme 2

This contribution therefore reports in full our extensive mechanistic findings and highlights further the scope of our new furanisation methodology utilising dihydronaphtho[1,2]dioxines and stabilised phosphorus ylides for the construction of substituted dihydronaphthofurans.

RESULTS AND DISCUSSION

Construction of the requisite dihydronaphtho[1,2]dioxines

In order to accumulate widespread mechanistic information whilst limiting the study to a practical size we decided to investigate the furanisation utilising three distinctly different 2-substituted-2,4*a*-dihydronaphtho[2,1-*c*][1,2]dioxines (**12-14**)[9] and six stabilised phosphorus ylides (**15a-f**), Scheme 4. The substituents on the stabilised phosphorus ylides evaluated contained a combination of keto- and / or ester-functionality and were either mono- or disubstituted. The dioxines (**12-14**) were prepared according to the simple synthetic sequence outlined in Scheme 3 *via* the Rose Bengal, *bis*(triethylammonium)salt sensitised [4π + 2π] cycloaddition of singlet oxygen and the corresponding substituted vinylic naphthalenes **11**.



12 X = Y = H
13 X = H, Y = Me
14 X = Me, Y = Me

Scheme 3

Treatment of 1,2-dioxine (12) with stabilised phosphorus ylides

The dioxine (**12**) was allowed to interact with ylides (**15a-e**) under a variety of conditions, the results of which are summarised in Table 1 and depicted in Scheme 4. Thus, treatment of 1,2-dioxine (**12**) with *ca.* one equivalent of ylide (**15a**) resulted in the 'expected' formation of dihydronaphthofuran **16a** in 34% yield along with the 'unexpected' formation of the opposite regioisomer **20a** in 64% yield, entry 1. The remaining material was found to be the parent furan (dehydration of **23**). Furthermore, following the reaction by ^{1}H NMR clearly revealed the intermediacy of the *E* and *Z*-butenoates **19a** which cyclised under the reaction conditions to dihydronaphthofuran **20a**. In addition, a small amount of the *E* and *Z*-butenoates **19a** were isolated from the reaction mixture after 24 hours and were found to slowly cyclise to the dihydronaphthofuran **20a** both in the absence and presence of ylide. Thus, formation of **20a** results from the cyclisation of butenoates **19a**. Performing the reaction at elevated temperatures (entry 2) lead to an increase in reaction rate but failed to change the product ratios. Conducting the experiment under the same conditions, however this time utilising four equivalents of ylide (**15a**) elevated the yield of the desired dihydronaphthofuran **16a** to 65% with the remaining material once again being the opposite regioisomer **20a** in 33% yield, entry 3. Thus, these results clearly suggest that there is a competition for formation of these two regioisomers from a common intermediate. Treatment of 1,2-dioxine (**12**) with ylides (**15b** and **15c**) resulted in the formation of the 'unexpected' regioisomer in excellent yield even if excess ylide was utilised. X-ray analysis of **20b** confirmed structural connectivity, Figure 1. Finally, treatment of the same dioxine (**12**) with the disubstituted ylide (**15d**) resulted in the formation of *E* and *Z*-butenoates **19d** in 96% which failed to further cyclise to furan **20d**, entry 6, while the strongly stabilised ylide (**15e**) afforded the hemiacetal **18** which failed to further react, entry 8.

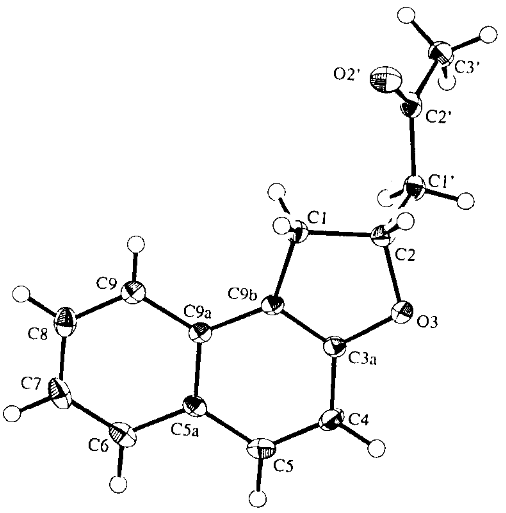


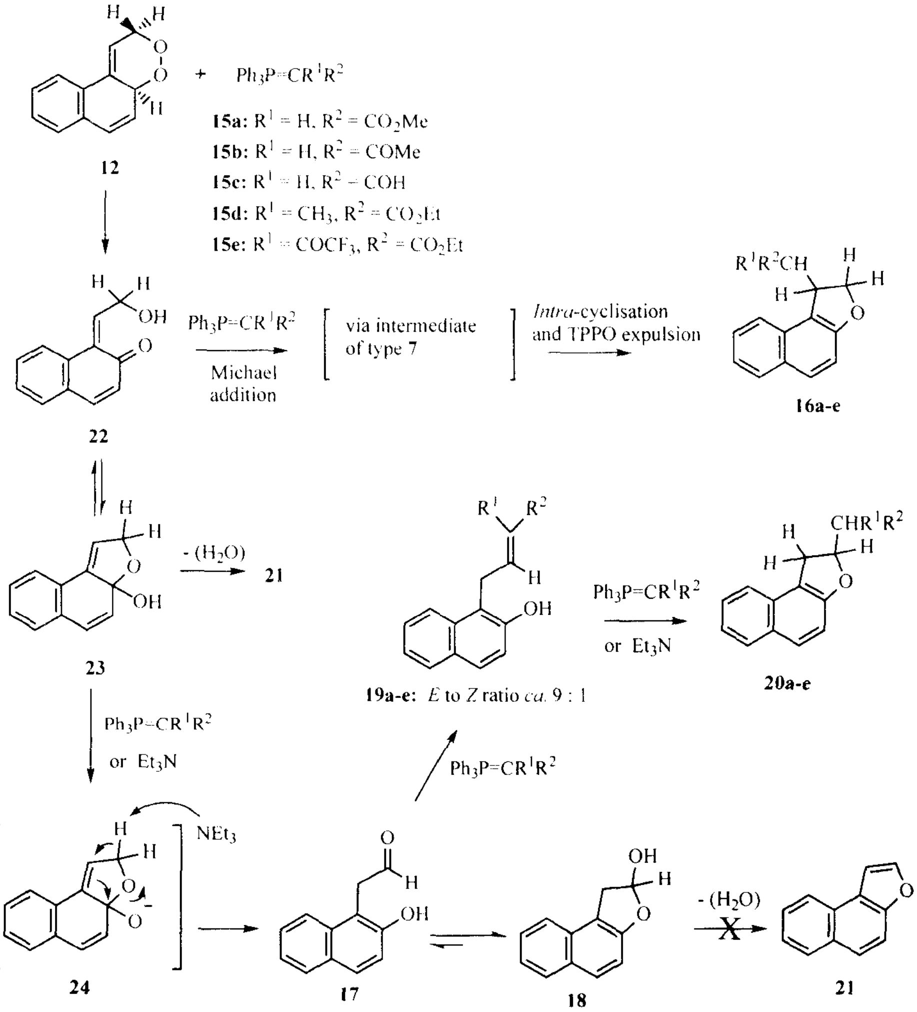
Fig. 1. Molecular structure of dihydronaphthofuran **20b**.

Table 1. Treatment of 1,2-dioxine (12) and hemiacetal 18 with ylides (15a-e).[a]

entry	precursor	ylide	solvent	temp. (°C)	Time (hr)	product(s) (%)
1	**12**	**15a**	$CDCl_3$		24	**12a** (26), *E*-**19a** (38), *Z*-**19a** (7), **16a** (25), **20a** (3)
					48	*E*-**19a** (36), *Z*-**19a** (6), **16a** (34), **20a** (23), **21** (1)
					96	**16a** (34), **20a** (64), **21** (2)
2			$CDCl_3$	60	24	*E*-**19a** (40), *Z*-**19a** (10), **16a** (23), **20a** (16), **21** (5)
3[b]		**15a**	$CDCl_3$		96	**16a** (65), **20a** (33), **21** (2)
4		**15b**	$CDCl_3$		48	**20b** (85), **21** (15)
5		**15c**	$CDCl_3$		48	**20c** (98), **21** (2)[c]
6		**15d**	$CDCl_3$		62	*E*-**19d** (88), *Z*-**19d** (8), **21** (4)
7		**15e**	$CDCl_3$		96	no reaction
8			benzene	80	48	**18** (95), **21** (5)
9[d]		—	$CDCl_3$	5	20	**18** (95)
10	**18**	**15a**	$CDCl_3$		0.5	*E*-**19a** (75), *Z*-**19a** (17)
11			$CDCl_3$	60	24	**20a** (90)
12		**15b**	$CDCl_3$		2	**20b** (93)
13		**15c**	$CDCl_3$		2	**20c** (79)[e]
14		**15d**	$CDCl_3$		0.5	*E*-**19d** (88), *Z*-**19d** (9)
15			$CDCl_3$	60	24	*E*-**19d** (88), *Z*-**19d** (9)
16			benzene	80	24	*E*-**19d** (88), *Z*-**19d** (9)
17		**15e**	$CDCl_3$		0.5	no reaction
18			benzene	80	96	no reaction

[a] All reactions resulted in 100% conversion unless otherwise specified. All reactions performed at ambient temperature unless otherwise specified. Entries 1-8 refer to ^1H NMR yields as determined at the time indicated and were performed under identical reaction volumes and concentrations. i.e., 1,2-dioxine (**12**) (30 mg, 0.16 mmol), phosphorane (1.05 equiv.) in the appropriate solvent (0.7 mL). Entries 9-18 refer to isolated yields, see Experimental Section; [b] 1,2-dioxine (**12**) (30 mg, 0.16 mmol), phosphorane (4.0 equiv.) in the appropriate solvent (0.7 mL). See experimental section for a typical large scale reaction for entry 3; [c] Formation of a minor amount (*ca.* 10%) of (*E*) and (*Z*)-4-(1,2-dihydronaphtho[2,1-*b*]furan-2-yl)-2-butenal was also observed and is not included in this ratio; [d] Triethylamine (0.05 equiv.) added, see Experimental Section; [e] A minor amount (6%) of (*E*) and (*Z*)-4-(1,2-dihydronaphtho[2,1-*b*]furan-2-yl)-2-butenal was also isolated as an inseparable mixture.

We were extremely interested to understand at this stage why it was that the ester ylide (**15a**) lead to the 'expected' dihydronaphthofuran while the other ylides lead to the 'unexpected' regiochemical series. Based on our detailed understanding of our cyclopropanation methodology we suspected the answer rested with subtle differences in ylide basicity / nucleophilicity.[1,8] It is known that while ester ylide (**15a**) is not only a slightly stronger base than keto-ylide (**15b**), it is also a superior nucleophile for Michael additions. Thus, while the basicity strength of both ylides is high enough to effect isomerisation of the 1,2-dioxine (**12**) to the requisite γ-hydroxy enone (**22**, may be in equilibrium with hemiacetal **23**), only the ester ylide (**15a**) which is a superior nucleophile, can compete in Michael addition to lead to the desired dihydronaphthofuran. In the case of the keto-ylide (**15b**) competitive rearrangement of γ-hydroxy enone **22** to the fully aromatised aldehyde (**17**) *via* intermediate **24** occurs. It should be noted that the proposed base induced rearrangement of hemiacetal **23** to aldehyde **17** *via* intermediate **24** is simply a special example of a Kornblum-De La Mare rearrangement.[10] If this rationale was true then we should be able to utilise a non-nucleophilic base to isomerise the 1,2-dioxine (**12**) to the isomeric aldehyde **17**. Indeed, addition of a catalytic amount of triethylamine to (**12**) resulted in the rapid quantitative formation of aldehyde **17**, which existed solely as the cyclised hemiacetal **18**. Treatment of this crystalline hemiacetal **18** with ylides (**15a** - **15c**) resulted in quantitative formation of the opposite regiochemical dihydronaphthofuran series **20**, while ylide (**15d**) yielded the uncyclised *E* and *Z*-butenoates **19**, entries 9-18. Finally, we were unable to detect the formation of furan (**21**) during these latter reactions suggesting that formation of (**21**) results from the dehydration of **23** and not hemiacetal **18** when entering the reaction manifold from dioxine (**12**). Scheme 4 depicted below summarises the above findings.



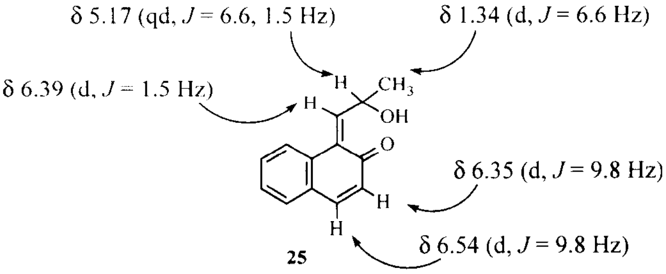
Scheme 4

The question could now be asked, why was the yield of the dihydronaphthofuran **16a** substantially elevated at the expense of the opposite regioisomer **20a** when excess ylide was utilised given that this situation would not alter the ylide basicity / nucleophilicity? The most plausible explanation appears to be that while the ylide (**15a**) is effecting the base catalysed isomerisation of the dioxine (**12**) to **22**, there is a lag time before the γ-hydroxy enone **22** / hemiacetal **23** equilibria is established.[11] If this was true then an increase in ylide concentration would be expected to result in an increase in **16a** formation at the expense of **20a**.

Treatment of 1,2-dioxine (13) with stabilised phosphorus ylides

Anticipating that treatment of dioxine (**13**) with ylides (**15a-f**) may well lead to a mixture of the dihydronaphthofuran regioisomers (**33a-f** and / or **32a-f**) and in order to facilitate product identification, we first analysed the base induced rearrangement of (**13**) to ketone (**28**) and / or hemiacetal (**29**) which upon addition of ylide should give the dihydronaphthofuran series **32a-f**. Thus, treatment of dioxine (**13**) with DABCO (20 mol%) led to the rapid formation of ketone (**28**), which existed in equilibrium with hemiacetal (**29**). Purification by column chromatography afforded crystalline (**28** / **29**) in 76% yield which displayed physical and chemical properties consistent with those reported previously.[12]

Monitoring this isomerisation by ^1H NMR showed the presence of a short-lived intermediate, which could be assigned as γ-hydroxy enone **25**, Figure 2. Interestingly, no cyclic hemiacetal **26** could be detected suggesting that the extra steric bulk of the methyl group disfavours cyclisation or that under basic conditions the equilibrium is shifted to favour **25**. Support for the latter comes from the observation that while the pair (**28**) and (**29**) exist in a 3 : 2 ratio in deuterochloroform at ambient temperature, addition of a small amount of ylide or base results in a complete shifting of the equilibrium in favour of the ketone (**28**). Naturally, although **26** could not be detected, there must be a trace amount present in order for the base induced rearrangement of **26** to (**28** / **29**) to occur. Indeed, **25** is completely rearranged to ketone (**28**) in less than ten minutes at 10°C.



25

Fig. 2. Proton assignments for γ-hydroxy enone **25** (600 MHz).

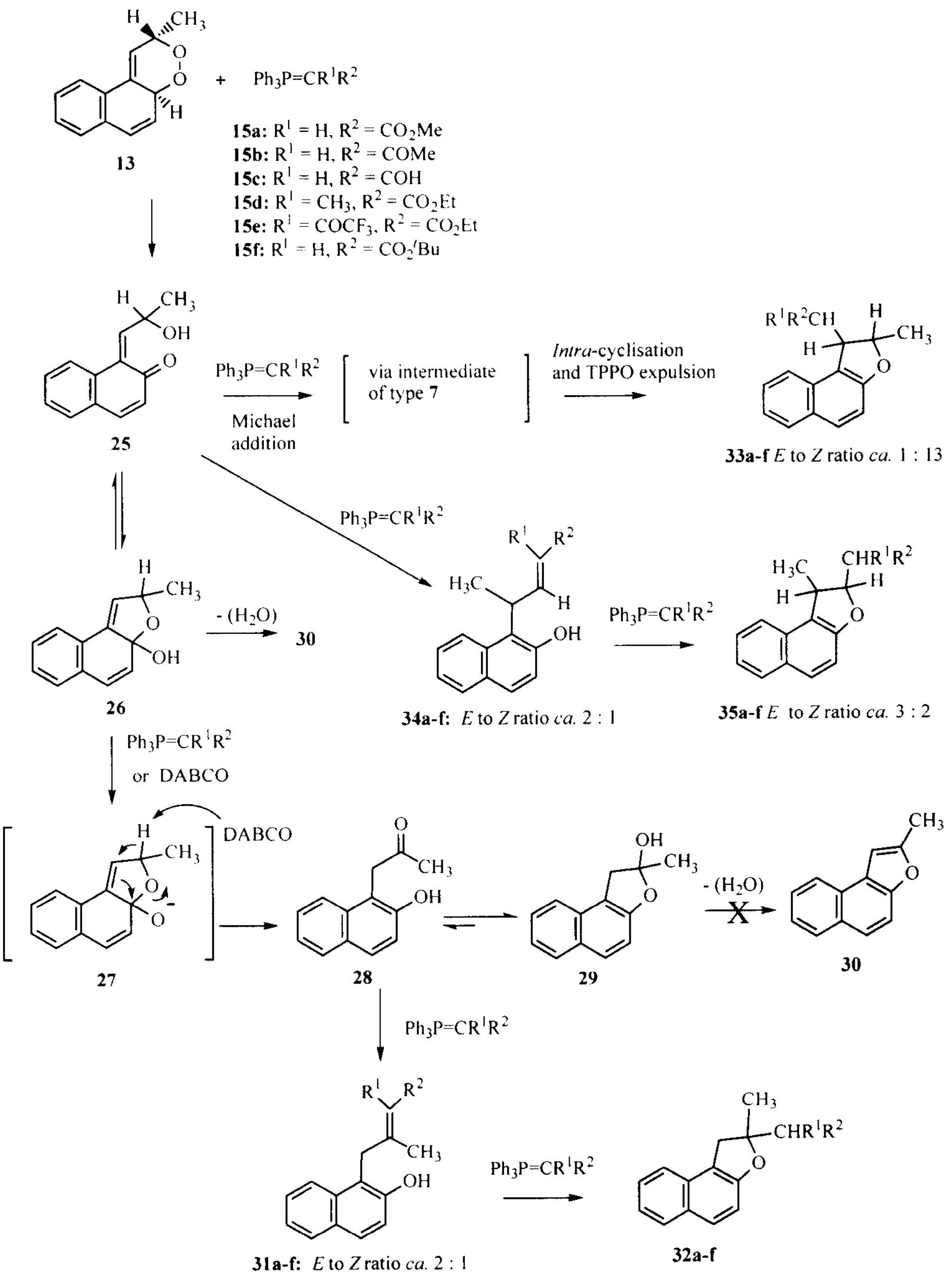
With (**28** / **29**) now in hand we investigated the formation of the dihydronaphthofuran series **32a-f**, the results of which are collated in Table 2. While ylides (**15a, b and f**) all afforded the 'expected' dihydronaphthofurans (**32a, b** and **f**) *via* the intermediacy of the 2-butenoates, utilisation of the aldo-ylide (**15c**) resulted in multiple addition products which were left uncharacterised. The highly stabilised ylide (**15e**) failed to effect addition even at elevated temperatures, entry 5. Its also worth mentioning that while the stabilised ylides utilised in this study do not normally effect facile addition to 'normal' ketones, the presence of the extra hydroxyl grouping within ketone (**28**) clearly enhances the addition process. ^{1}H NMR monitoring of these reactions revealed that ketone (**28**) is rapidly consumed at ambient temperature while elevated temperatures and extended reaction times are necessary to induce cyclisation. This rate enhancement is presumably due to intramolecular hydrogen bonding enhancing the electrophilicity of the carbon atom of the ketone functionality and as a consequence would aid in the reduction of possible multiple addition products.

Table 2. Treatment of ketone (28) with phosphoranes (15a-c,e and f).[a]

entry	ylide	temp. (°C)	time (hr)	product(s) (%)
1	**15a**		1.0	*E*-**31a** (45), *Z*-**31a** (21), **28** (34)
			48	*E*-**31a** (59), *Z*-**31a** (31)
			96	*E*-**31a** (61), *Z*-**31a** (31)
2		60	24	**32a** (94)
3	**15b**		24	**32b** (50)[b]
4	**15c**		48	—[c]
5	**15e**	60	48	no reaction
6	**15f**	60	24	*E*-**31f** (50), *Z*-**31f** (38), **32f** (7)

[a] All reactions resulted in 100% conversion unless otherwise specified while yields refer to isolated yields, except for entry 1. All reactions performed in chloroform (5 mL) at ambient temperature unless otherwise specified, see Experimental Section; [b] Recovered ketone (**28**) 40% [c] Complex mixture of products resulted due to further addition of ylide to aldehyde **31c** and / or **32c** at 80°C while there was no reaction at 60°C.

We next investigated the reaction of dioxine (**13**) with ylides (**15a-c** and **e**) under a variety of conditions, the results of which are summarised in Table 3 and depicted in Scheme 5. Thus, treatment of 1,2-dioxine (**13**) with *ca.* one equivalent of ylide (**15a**) resulted in the 'expected' formation of dihydronaphthofuran **33a** in 65% overall yield (*E* and *Z* ratio *ca.* 1 : 13) along with the 'unexpected' formation of regioisomer **35a** in 19% overall yield (*E* and *Z* ratio *ca.* 3 : 2) in which the methyl group had undergone migration, entry 1. Mechanistically important was the observation that none of the series **31a-f** or **32a-f** could be detected by ^{1}H NMR indicating that (**28**) / (**29**) are not present and further suggesting that the methyl migration must occur spontaneously from the intermediate γ-hydroxy enone **25** or during ylide addition to **25**. Moreover, monitoring this reaction by ^{1}H NMR clearly showed the presence of pentenoates (**34**, *E* : *Z* ratio *ca.* 2 : 1) which cyclised under the reaction conditions to dihydronaphthofuran **35**. Thus, given this latter fact coupled with the aforementioned observation that no methyl migrated material could be detected during the base catalysed rearrangement of dioxine (**13**) through γ-hydroxy enone **25** to (**28** / **29**) suggests that this methyl migration occurs during ylide addition to **25**. Additionally, a modest amount of furan (**30**, 16%) was detected indicating that parent furan formation originates from hemiacetal **26** and not from (**28** / **29**) as no furan was detectable when (**28** / **29**) was treated with a variety of ylides, see Table 2.


13
+ Ph3P=CR1R2
15a: R1 = H, R2 = CO2Me
15b: R1 = H, R2 = COMe
15c: R1 = H, R2 = COH
15d: R1 = CH3, R2 = CO2Et
15e: R1 = COCF3, R2 = CO2Et
15f: R1 = H, R2 = CO2tBu
25
Ph3P=CR1R2
Michael addition
via intermediate of type 7
Intra-cyclisation and TPPO expulsion
33a-f E to Z ratio ca. 1 : 13
Ph3P=CR1R2
34a-f: E to Z ratio ca. 2 : 1
Ph3P=CR1R2
35a-f E to Z ratio ca. 3 : 2
26
- (H2O)
30
Ph3P=CR1R2
or DABCO
DABCO
27
28
29
- (H2O)
X
30
Ph3P=CR1R2
31a-f: E to Z ratio ca. 2 : 1
Ph3P=CR1R2
32a-f

Scheme 5

Table 3. Treatment of 1,2-dioxine (13) with phosphoranes (15a-e).[a]

entry	ylide	Equiv.[b]	time (hr)	product(s) (%)
1	**15a**		72	*E*-**33a** (3), *Z*-**33a** (62), *E*-**35a** (11), *Z*-**35a** (8), **30** (16)
		2	72	*E*-**33a** (4), *Z*-**33a** (66), *E*-**35a** (13), *Z*-**35a** (9), **30** (8)
		4	72	*E*-**33a** (5), *Z*-**33a** (69), *E*-**35a** (15), *Z*-**35a** (10), **30** (1)
2	**15b**			**28** / **29** (100)
3	**15c**		0.1	**28** / **29** (100)
4[c]	**15e**		24	No reaction

[a] All reactions resulted in 100% conversion. All entries refer to ^{1}H NMR yields as determined at the time indicated and were performed under identical reaction volumes and concentrations at ambient temperature. i.e., 1,2-dioxine (**13**) (30 mg, 0.16 mmol), phosphorane (1-4 equiv.) in the $CDCl_3$ (0.7 mL), see Experimental Section; [b] One equivalent of ylide utilised unless otherwise specified; [c] Performed at 60°C.

Hydrolysis of **33a** followed by recrystalisation allowed for the isolation of the parent acid of ***Z*-33a**, the ORTEP diagram of which is displayed in Figure 3 and clearly shows the *cis* stereochemistry about the dihydronaphthofuran ring.

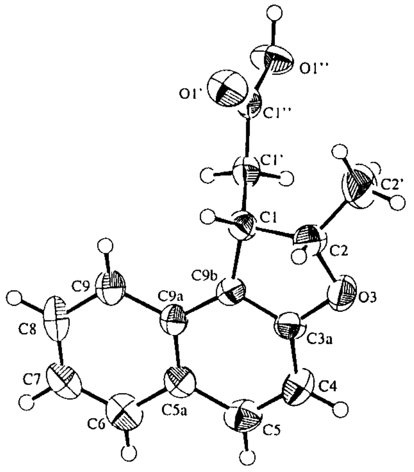
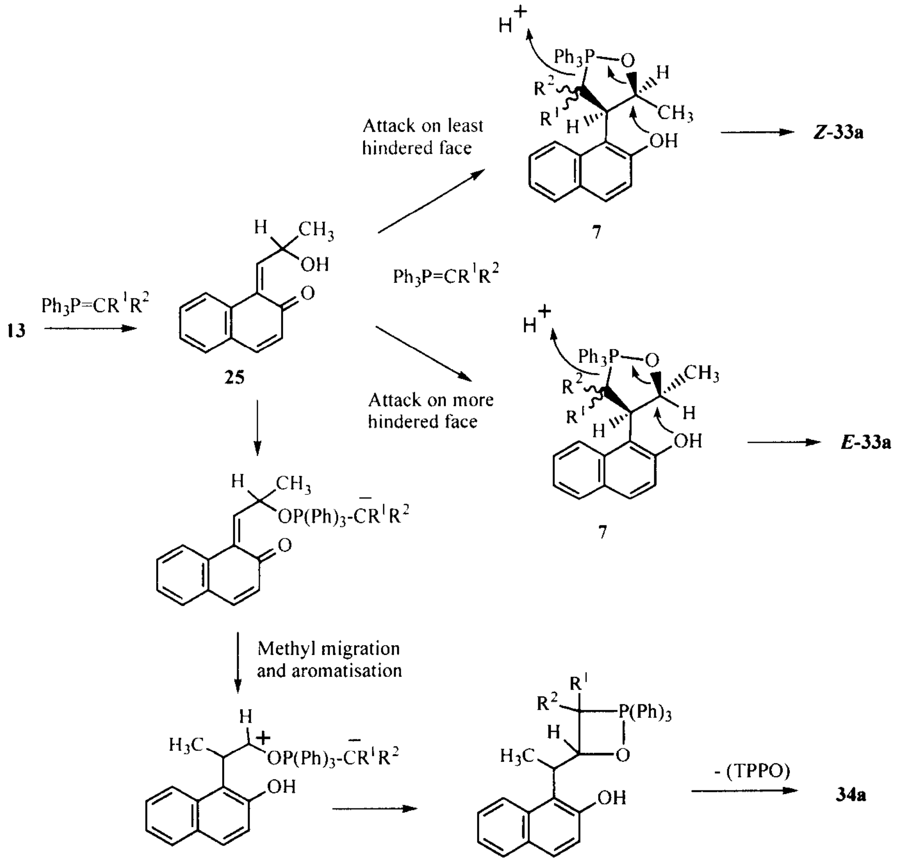


Fig.3. Molecular structure of the parent acid of ***Z*-33a**.

The connectivity of *E* and *Z*-**35a** was verified by gCOSY, gHSQC and gHMBC NMR techniques while the assignment of (*E* and *Z*) stereochemistry was based on analysis of the two isomers by the ROESY NMR technique. Thus, while H_α (adjacent to furan oxygen) of the *Z*-isomer showed strong correlations with the adjacent *beta* proton of the furan moiety and the methylene group within the side chain, there was only a very weak correlation to the methyl group. However, H_α (adjacent to furan oxygen) of the *E*-isomer displayed strong correlations to H_β the methylene grouping and the methyl moiety. Furthermore, the observed $^3J_{H\alpha\text{-}\beta}$ coupling of 7 Hz for the *Z*-isomer is greater than the found for the *E*-isomer (3 Hz) and is consistent with trends already cited in the literature.[6]

In an attempt to increase the yield of the 'desired' dihydronaphthofuran (**33a**) and / or the diastereoslectivities we investigated the reaction of dioxine (**13**) with excess ylide. As can been seen from the data collated within entries 2 and 3, Table 3, addition of excess ylide failed to change the regioisomer ratio or the diastereomeric ratio within each regioisomer series. A slight increase in overall dihydronaphthofuran yield, at the expense of parent furan (**30**) formation, was seen indicating that the quicker the γ-hydroxy enone **25** is 'trapped' by ylide the less likely dehydration of **26** will occur. Thus, the ratio of the dihydronaphthofuran regioisomers (**33a** and **35a**) is independent of ylide concentration and further suggests that methyl migration occurs during ylide 'attack' on **25**.

The formation of the *Z*-isomer of **33a** as the major diastereomer is consistent with our proposed mechanism *via* the intermediacy of **7** in which ylide undergoes synchronous *syn* addition on the least hindered face of the γ-hydroxy enone as depicted below, Scheme 6. Attachment of the ylide to the sterically more hindered face is energetically less favourable and results in the formation of the *E*-diastereomer of **33a**.



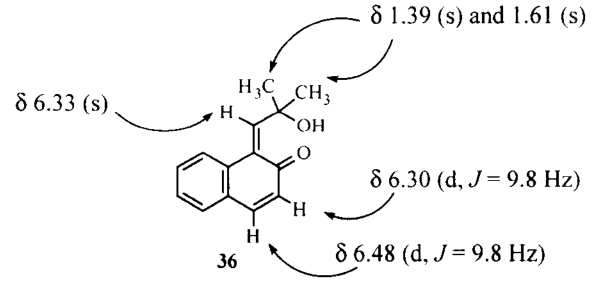
Scheme 6

The formation of the methyl migrated material **34a** is inconsistent with a synchronous addition of the ylide to the γ-hydroxy enone, as it is extremely difficult to envisage what the driving force for methyl migration would be after carbon-carbon formation and aromatisation has occurred. Hence, in order to explain the formation of **34a** / **35a** coupled with the fact that the amount is unaltered with increasing ylide concentration we speculate that the positive phosphorus pole of the ylide becomes attached to the hydroxyl moiety (oxygen atom) of the γ-hydroxy enone prior to C-C bond formation as depicted above. This situation would allow for methyl migration and aromatisation to occur in a synchronous manner followed by capture of the resultant carbocation by the nucleophilic carbon pole of the ylide and finally collapse of the betaine intermediate to afford the observed alkene **34a**.

Finally, the reactions between dioxine (**13**) and ylides (**15b, c and e**) were investigated, the results of which are summarised in Table 3. Both ylides (**15b** and **c**) simply induced quantitative rearrangement to the ketone (**28**) at ambient temperature with no methyl migrated material being detected while the highly stabilised ylide (**15e**) failed to effect the isomerisation of dioxine (**13**) even at elevated temperatures.

Treatment of 1,2-dioxine (14) with stabilised phosphorus ylides

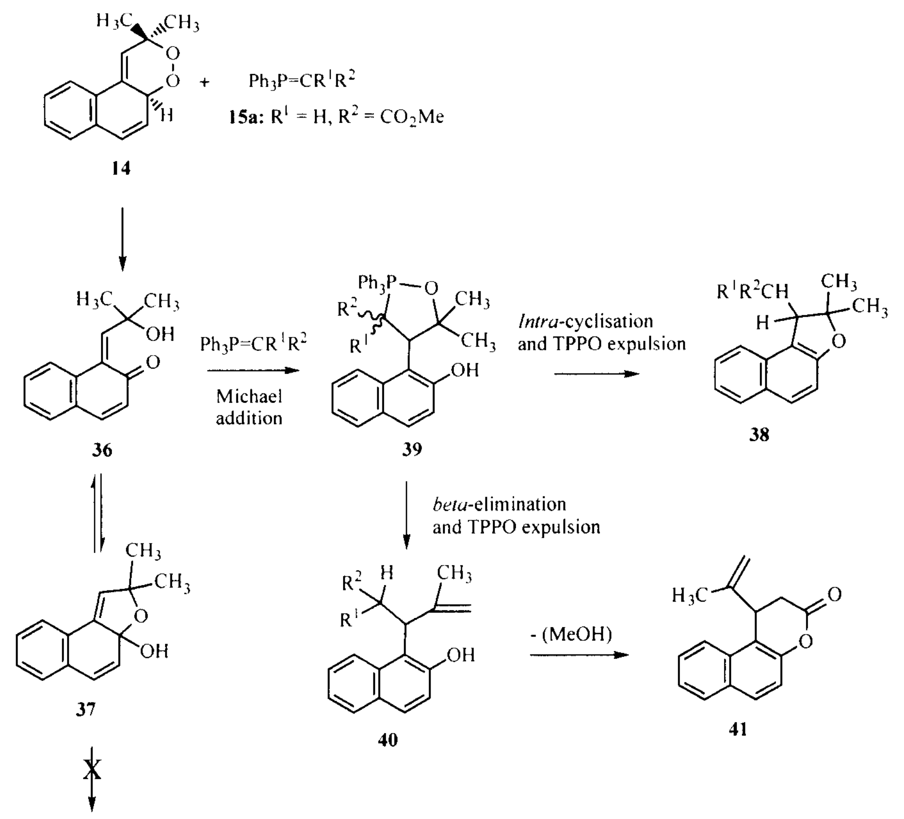
The 1,2-dioxine (**14**) was chosen as our final example to be analysed as the dimethyl substitution α to the O-O peroxide linkage precludes both the base induced rearrangement of hemiacetal **37** and dehydration to the parent furan. Thus, exposure of (**14**) to a catalytic amount of DABCO and monitoring the isomerisation by ^{1}H NMR allowed for the detection of the key γ-hydroxy enone **36**, Figure 4, with none of the cyclic hemiacetal **37** being detected.



36

Fig. 4. Proton assignments for γ-hydroxy enone **36** (600 MHz).

Treatment of dioxine (**14**) with ylide (**15a**) only resulted in a minor amount of the desired dihydronaphthofuran **38** with the major product being that of elimination **40**, or its cyclised form **41**. Presumably the poor yield of **38** is the result of unfavorable steric interactions preventing intramolecular 'attack' by the enolate on the intermediate oxaphospholane **39** and as such elimination now becomes dominant.



Both base induced rearrangement
and dehydration pruculded.

Scheme 7

CONCLUSIONS

We have presented here new synthetic methodology for the construction of the dihydronaphthofuran framework, that allows for the incorporation of a diverse range of substituents utilising 1,2-dioxines and stabilised phosphorus ylides as the key synthons. Mechanistically, the transformations elucidated here conforms to our overall mechanistic picture which is that the ylide acts as a weak base removing the most acidic hydrogen α to the O-O linkage, thus effecting isomerisation of the dioxines (**12-14**) to their isomeric γ-hydroxy enones. Synchronous capture of these latter intermediates by the ester stabilised ylides leads to our proposed dihydronaphthofurans while exposure to bases of higher basicity (or ylides of lower basicity, e.g. methyl-ketone ylide) leads to further isomerisation of the intermediate hemiacetals of the γ-hydroxy enones to the fully aromatised hemiacetals. Ylide addition to these aromatised hemiacetals allows access to the opposite dihydronaphthofuran regiochemical series in excellent yield. Ylide basicity / nucleophilicity is extremely important in determining the outcomes of these reactions. We are currently investigating the formation of dihydrofurans from a variety of 1,2-dioxines derived from a variety of aromatic systems, the results of which will be reported in due course.

EXPERIMENTAL SECTION

General. Solvents were dried by appropriate methods wherever needed. All organic extracts were dried over anhydrous magnesium sulphate. All hemiacetals were purified by column chromatography utilising silica gel (40-63 υm) or florisil (60-100 U.S. mesh) as adsorbent purchased from Merck. Thin-layer chromatography (TLC) used aluminum sheets silica gel 60 F_{254} (40 x 80 mm) from Merck. Melting points were taken on a Reichert Thermovar Kofler apparatus and are uncorrected. Infrared spectra were recorded on a ATI Mattson Genesis Series FTIR spectrophotometer as nujol mulls unless otherwise stated. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a Varian INOVA (600 MHz) or on a Varian Gemini 2000 instrument, TMS (0 ppm) and $CDCl_3$ (77.0 ppm) as internal standards unless otherwise specified. All yields reported refer to isolated material judged to be homogeneous by TLC and NMR spectroscopy unless otherwise specified. The following materials were purchased from Aldrich and used without further purification; Triphenylalkyidenephosphoranes (**15a-f**), 1-naphthaldehyde, Rose Bengal, *bis*(triethylammonium)salt.

General Procedure for the Preparation of 1,2-Dioxines (12-15). All 1,2-dioxines were prepared by the Rose Bengal, *bis*(triethylammonium)salt sensitised [4π + 2π] cycloaddition of singlet oxygen and the corresponding substituted vinylic naphthalenes. The requisite vinylic naphthalenes were acquired as follows: 1-vinylnaphthalene was prepared in 71% yield from the action of methylene(triphenyl)phosphorane on 1-naphthaldehyde; 1-(1-propenyl)naphthalene (*E* : *Z*; 75 : 25) was prepared in 65% yield from the action of ethylene(triphenyl)phosphorane on 1-naphthaldehyde; 1-(2-methyl-1-propenyl)naphthalene was prepared in 52% yield from the action of isopropylene(triphenyl)phosphorane on 1-naphthaldehyde. The appropriate vinylic naphthalene (3.0 g) and rose bengal, *bis*(triethylammonium)salt (30 mg) were dissolved in dry dichloromethane (100 mL) and the reaction vessel semi-immersed in an ice bath so that the reaction mixture maintained a temperature *ca.* 5-10 °C. A stream of oxygen was then passed through the solution, whilst irradiating with two tungsten halogen lamps (500 W) at a distance of 10 cm from the reaction vessel for *ca.* 5 hr. The volatiles were then removed *in vacuo* and the residue subjected to column chromatography. All 1,2-dioxines prepared in this work were manipulated with teflon coated spatulas to prevent premature decomposition. **2,4*a*-Dihydronaphtho[2,1-*c*][1,2]dioxine (12).** 50% yield based on recovered 1-vinylnaphthalene, R_f 0.45 (9 : 1 hexane / ethyl acetate); Mp: 79-79.5 °C, (Lit.[9] Mp: 67-68 °C); **2-Methyl-2,4*a*-dihydronaphtho[2,1-*c*][1,2]dioxine (13).**[9] 84% yield based on recovered 1-(1-propenyl)naphthalene, R_f 0.36 (15 : 1 hexane / ethyl acetate); **2,2-Dimethyl-2,4*a*-dihydronaphtho[2,1-*c*][1,2]dioxine (14).**[9] 30% yield based on recovered 1-(2-methyl-1-propenyl)naphthalene, R_f 0.43 (16 : 1 hexane / ethyl acetate).

Reaction of Dioxine (12) with ylide (15a). A Typical Procedure. To a solution of the dioxine (**12**) (375 mg, 2.02 mmol) in anhydrous chloroform (10 mL) under a nitrogen gas atmosphere was added ylide (**15a**) (2.70 g, 8.08 mmol). The mixture was warmed at a temperature of 60 °C for 3 days after which time the volatiles were removed and the residue subjected to silica gel chromatography. Elution with a mixture of hexane / ethylacetate (6 : 1) afforded the desired dihydronaphthofuran (**16a**) (0.30 g, 61 %) as a colourless oil, the opposite dihydronaphthofuran regeoisomer (**20a**) (0.14 g, 28 %) as a crystalline solid and a small amount of the known furan (**21**) (4 mg, 1 %) as a crystalline solid, Mp: 62-62.5 °C, (Lit.[13] Mp: 60-61 °C); R_f 0.72 (6 : 1 hexane / ethylacetate); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 105.60, 112.54, 122.68, 123.45, 124.52, 125.21, 126.32, 127.89, 128.77, 130.40, 144.25, 152.62.

Methyl 2-(1,2-dihydronaphtho[2,1-*b*]furan-1-yl)acetate (16a). R_f 0.42 (6 : 1 hexane / ethylacetate); IR (CH_2Cl_2) 3055, 2955, 1735, 1631, 1598, 1521, 1172, 814.2 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.59 (1H, dd, J = 16.5, 11.0 Hz), 3.01 (1H, ddd, J = 16.5, 3.3, 1.1 Hz), 3.73 (3H, s), 4.22 (1H, dddd, J = 11.0, 8.4, 3.3, 2.9 Hz), 4.58 (1H, dd, J = 9.5, 2.9 Hz), 4.80 (1H, ddd, J = 9.5, 8.4, 1.1 Hz), 7.09-7.84 (6H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 38.19, 38.36, 51.84, 77.21, 112.30, 120.22, 121.86, 122.93, 126.99, 129.14, 129.58, 129.97, 130.20, 157.52, 172.61; MS *m/z* (%): 242 (M^+, 21), 169 (100), 141 (41), 115 (12); Anal. Calcd for $C_{15}H_{14}O_3$ (242.2): C, 74.36; H, 5.82. Found: C, 74.12; H, 5.99.

1,2-Dihydronaphtho[2,1-*b*]furan-2-ol (18). To a solution of dioxine (**12**) (0.4 g, 2.15 mmol) in chloroform (15 mL) at 5 °C was added triethylamine (11 mg, 0.05 equiv. in chloroform, 2 mL) and the mixture kept at this temperature overnight. The volatiles were then removed *in vacuo* and the residue subjected to flash chromatography on florisil (R_f 0.23, 6 : 1, hexane / ethylacetate) to afford pure **18** as a crystalline white solid (0.38 g, 95%). Mp: 115-116 °C; IR 3462, 1633, 1601, 1576, 1518, 1248, 1086, 910, 808 cm^{-1}; ^1H NMR ($CDCl_3$ + 1 drop D_2O, 300 MHz) δ 3.32 (1H, dd, J = 16.4, 2.3 Hz), 3.43 (1H, s, exch. D_2O), 3.63 (1H, dd, J = 16.7, 6.9 Hz), 6.23 (1H, dd, J = 6.9, 2.3 Hz), 7.14-7.83 (6H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 36.86, 101.54, 112.06, 116.64, 122.80, 123.20, 126.80, 128.76, 129.22, 129.59, 130.72, 155.17; MS *m/z* (%): 186 (M^+, 100), 157 (51), 130 (48); Anal. Calcd for $C_{12}H_{10}O_2$ (186.1): C, 77.40; H, 5.41. Found: C, 77.56; H, 5.60. A minor amount (15 mg) of furan (**21**) was also isolated.

Reaction of hemiacetal (18) with phosphoranes (15a-e). A Typical Procedure. The hemiacetal **18** (100 mg, 0.54 mmol) and the appropriate phosphorus ylide (**15a-e**)(1.05 equiv.) were allowed to react under the conditions specified in Table 1. After cessation of the reaction, the volatiles were then evaporated *in vacuo* and the residue further purified by flash chromatography to afford the following products. Yields are collated in Table 1 and refer to isolated yields.

Methyl (*E*)-4-(2-hydroxy-1-naphthyl)-2-butenoate (*E*-19a). Decomposes over several days. R$_f$ 0.35 (20 : 1 dichloromethane / ethyl acetate); IR (CH_2Cl_2) 3300, 1680, 1620, 1600, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.68 (3H, s), 3.95 (2H, dd, *J* = 6.3, 1.6), 5.76 (1H, dt, *J* = 15.7, 1.6 Hz), 6.18 (1H, bs, exch. D_2O), 7.00-7.04 (1H, m), 7.23 (1H, dt, *J* = 15.7, 6.3 Hz), 7.29-7.79 (5H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 27.69, 51.42, 115.53, 117.61, 121.57, 122.79, 123.37, 126.92, 128.74, 128.84, 129.45, 133.24, 147.07, 151.00, 167.38; MS *m/z* (%): 242 (M$^+$, 68), 214 (26), 181 (100), 156 (35), 115 (23); HRMS of (***E*-19a**), $C_{15}H_{14}O_3$: calcd, 242.0943; found, 242.0933.

Methyl (*Z*)-4-(2-hydroxy-1-naphthyl)-2-butenoate (*Z*-19a). Decomposes over several days. R$_f$ 0.73 (20 : 1 dichloromethane / ethyl acetate); Mp: 87-89 °C; IR (CH_2Cl_2) 3327, 1695, 1641, 1622, 1601, 1215 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.85 (3H, s), 4.31 (2H, dd, *J* = 8.7, 1.2), 5.89 (1H, dt, *J* = 11.4, 1.2 Hz), 6.54 (1H, dt, *J* = 11.4, 8.7 Hz), 7.16-7.94 (6H, m), 8.47 (1H, s, exch. D_2O); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 25.11, 52.13, 113.25, 118.77, 119.34, 121.91, 122.88, 126.78, 128.91, 128.94, 129.26, 133.02, 146.53, 153.54, 169.77; MS *m/z* (%): 242 (M$^+$, 55), 210 (12), 181 (100), 168 (80), 152 (22); HRMS of (***Z*-19a**), $C_{15}H_{14}O_3$: calcd, 242.0943; found, 242.0934.

Methyl 2-(1,2-dihydronaphtho[2,1-*b*]furan-2-yl)acetate (20a). R$_f$ 0.35 (6 : 1 hexane / ethylacetate); Mp: 76-76.5 °C; IR (CH_2Cl_2) 1737, 1632, 1602, 1522, 1465, 1245 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.76 (1H, dd, *J* = 15.0, 6.3 Hz), 2.95 (1H, dd, *J* = 15.0, 7.2), 3.20 (1H, dd, *J* = 15.3, 6.9 Hz), 3.70 (1H, dd, *J* = 15.3, 9.6 Hz), 3.75 (3H, s), 5.36 (1H, dddd, *J* = 9.6, 7.2, 6.9, 6.3 Hz), 7.08-7.78 (6H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 34.29, 40.84, 51.85, 79.45, 112.11, 117.65, 122.63, 122.94, 126.71, 128.69, 129.13, 129.30, 130.76, 156.54, 170.92; MS *m/z* (%): 242 (M$^+$, 55), 181 (12), 168 (100), 141 (8); HRMS of (**20a**), $C_{15}H_{14}O_3$: calcd, 242.0943; found, 242.0941.

Ethyl (*E*)-4-(2-hydroxy-1-naphthyl)-2-methyl-2-butenoate (*E*-19d). R$_f$ 0.13 (dichloromethane); Mp: 128.5-129.5 °C; IR 3390, 1674, 1630, 1599, 1513, 1281, 1263 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.23 (3H, t, *J* = 7.2 Hz), 2.13 (3H, d, *J* = 1.2), 3.94 (2H, d, *J* = 6.8 Hz), 4.14 (2H, q, *J* = 7.2 Hz), 5.17 (1H, s, exch. D_2O), 6.80 (1H, dt, *J* = 6.8, 1.2 Hz), 7.02-7.84 (6H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 12.75, 14.23, 24.82, 60.52, 117.31, 117.68, 122.87, 123.29, 126.77, 128.22, 128.38, 128.68, 129.45, 133.30, 140.20, 150.70, 168.15; MS *m/z* (%): 270 (M$^+$, 32), 224 (53), 195 (62), 181 (100), 169 (14); Anal. Calcd for $C_{17}H_{18}O_3$ (270.2): C, 75.53; H, 6.71. Found: C,75.53; H, 6.50.

Ethyl (*Z*)-4-(2-hydroxy-1-naphthyl)-2-methyl-2-butenoate (*Z*-19d). R$_f$ 0.71 (dichloromethane); IR (CH_2Cl_2) 3294, 1685, 1643, 1622, 1599, 1520, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37 (3H, t, *J* = 6.9

Hz), 1.88 (3H, d, J = 1.2), 4.15 (2H, d, J = 8.9 Hz), 4.34 (2H, q, J = 7.5 Hz), 6.18 (1H, dt, J = 8.9, 1.2), 7.17-7.95 (6H, m), 8.83 (1H, s, exch. D_2O); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.14, 20.31, 25.56, 61.51, 113.91, 119.27, 121.89, 122.65, 126.55, 126.89, 128.57, 128.84, 129.14, 132.98, 139.69, 153.61, 170.50; MS *m/z* (%): 270 (M^+, 69), 225 (72), 224 (72), 196 (82), 183 (100), 168 (41); HRMS of (***E*-19d**), $C_{17}H_{18}O_3$: calcd, 270.1256; found, 270.1249.

1-(1,2-Dihydronaphtho[2,1-*b*]furan-2-yl)acetone (20b). R_f 0.31 (6 : 1 hexane / ethylacetate); Mp: 69-69.5 °C; IR 1703, 1630, 1599, 1464, 1244, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.26 (3H, s), 2.85 (1H, dd, J = 16.8, 6.5 Hz), 3.11 (1H, dd, J = 15.7, 6.6 Hz), 3.14 (1H, dd, J = 16.8, 7.0 Hz), 3.72 (1H, dd, J = 15.7, 9.4 Hz), 5.38 (1H, dddd, J = 9.4, 7.0, 6.6, 6.5 Hz), 7.07-7.78 (6H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.72, 34.51, 49.82, 79.25, 112.11, 117.89, 122.70, 123.00, 126.79, 128.75, 129.17, 129.34, 130.86, 156.66, 206.30; MS *m/z* (%): 226 (M^+, 8), 181 (24), 168 (100), 139 (24), 115 (10), 69 (21); Anal. Calcd for $C_{15}H_{14}O_2$ (226.2): C, 79.66; H, 6.19. Found: C, 79.40; H, 6.35.

2-(1,2-Dihydronaphtho[2,1-*b*]furan-2-yl)acetaldehyde (20c). R_f 0.47 (dichloromethane); IR (CH_2Cl_2) 1726, 1631, 1602, 1581, 1466 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.89 (1H, ddd, J = 17.5, 5.7, 1.2 Hz), 3.09 (1H, dd, J = 17.5, 7.2, 1.5 Hz), 3.16 (1H, dd, J = 15.6, 6.9 Hz), 3.74 (1H, dd, J = 15.6, 9.6 Hz), 5.43 (1H, dddd, J = 9.6, 7.2, 6.9, 5.7 Hz), 7.08-7.82 (6H, m), 9.91 (1H, d, J = 0.9 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 34.56, 50.06, 81.39, 111.96, 117.57, 122.63, 123.07, 126.83, 128.73, 129.29, 129.37, 130.74, 156.49, 199.70; MS *m/z* (%): 212 (M^+, 100), 181 (28), 168 (52), 141 (16), 115 (15); Anal. Calcd for $C_{14}H_{12}O_2$ (212.2): C, 79.26; H, 5.66. Found: C, 79.12; H, 5.61.

Equilibrium mixture of 1-(2-Hydroxy-1-naphthyl)acetone (28) and 2-methyl-1,2-dihydronaphtho[2,1-b]furan-2-ol (29). To a solution of dioxine (**13**) (0.5 g, 2.5 mmol) in anhydrous dichloromethane (60 mL) under nitrogen at 5°C was added DABCO (56 mg, 0.5 mmol). After 10 hours the volatiles were removed *in vacuo* and the residue subjected to flash chromatography R_f 0.28 (20 : 1 dichloromethane / ethyl acetate) to afford pure (**28** / **29**) (0.38 g, 76 %) as a crystalline white solid. Mp: 149.5-151 °C (Lit.[12] Mp: 151-152 °C); IR 3412, 3236, 1694, 1659, 1630, 1583, 1512, 1274, 1175, 1048, 816, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.84 (3H, s), 2.26 (3H, s), 3.24 (1H, s, exch. D_2O), 3.48 (2H, s), 4.14 (2H, s), 6.88 (1H, s, exch. D_2O), 7.10-7.14 (1H, m), 7.31-7.38 (1H, m), 7.46-7.67 (1H, m), 7.69-7.72 (1H, m), 7.77-7.82 (1H, m), 7.83-7.88 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 27.41, 29.71, 40.67, 41.63, 77.20, 109.95, 112.12, 112.68, 117.25, 118.63, 122.18, 122.70, 123.07, 123.32, 126.76, 127.06, 128.77, 128.81, 129.20, 129.33, 129.39, 130.75, 133.05, 152.60, 155.04, 209.56; Anal. Calcd for $C_{13}H_{12}O_2$ (200.2, mixture): C, 77.98; H, 6.04. Found: C, 77.99; H, 6.28.

Interestingly, while the ratio of (**28** : **29**) was 3 : 2 in $CDCl_3$ addition of a small quantity of ylide (**15a**) resulted in a shifting of the equilibrium to entirely (**28**).

Reaction of ketone (28) with phosphoranes (15a-f). A Typical Procedure. The ketone (**28**) (100 mg, 0.50 mmol) and the appropriate phosphorus ylide (**15a-f**)(1.1 equiv.) were allowed to react under the conditions specified in Table 2. After cessation of the reaction, the volatiles were then evaporated *in vacuo* and the residue further purified by flash chromatography to afford the following products. Yields are collated in Table 2 and refer to isolated yields.

Methyl (*E*)-4-(2-hydroxy-1-naphthyl)-3-methyl-2-butenoate (*E*-31a). R_f 0.40 (4 : 1 hexane / ethyl acetate); Mp: 96-97 °C; IR (CH_2Cl_2) 3579, 3405, 1714, 1649, 1630, 1602, 1585, 1566, 1437, 1065, 810 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.33 (3H, s), 3.60 (3H, s), 3.91 (2H, s), 5.05 (1H, s, exch. D_2O), 5.43 (1H, s), 7.05-7.08 (1H, m), 7.33-7.36 (1H, m), 7.41-7.47 (1H, m), 7.68-7.79 (3H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 19.28, 35.73, 50.71, 108.1, 115.68, 117.68, 123.08, 123.42, 126.91, 128.65, 129.03, 129.49, 133.72, 151.36, 158.22, 167.28; MS *m/z* (%): 256 (M^+, 36), 224 (16), 195 (61), 182 (100), 181 (95), 152 (12), 129 (11); HRMS of (***E*-31a**), $C_{16}H_{16}O_3$: calcd, 256.1099; found, 256.1096.

Methyl (*Z*)-4-(2-hydroxy-1-naphthyl)-3-methyl-2-butenoate (*Z*-31a). R_f 0.49 (4 : 1 hexane / ethyl acetate); Mp: 93-93.5 °C; IR (CH_2Cl_2) 3290, 1689, 1641, 1601, 1581, 1195, 1064, 1027, 818 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.79 (3H, s), 3.84 (3H, s), 4.33 (2H, s), 5.85 (1H, s), 7.15-7.18 (1H, m), 7.29-7.34 (1H, m), 7.47-7.53 (1H, m), 7.67-7.70 (1H, m), 7.77-7.80 (1H, m), 8.01-8.04 (1H, m), 8.67 (1H, s, exch. D_2O); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 24.74, 28.18, 52.02, 113.19, 116.19, 118.94, 122.52, 122.77, 126.41, 128.87, 129.01, 129.21, 133.74, 154.04, 158.46, 170.25; MS *m/z* (%): 256 (M^+, 40), 224 (15), 195 (62), 182 (100), 181 (92), 152 (12); HRMS of (***Z*-31a**), $C_{16}H_{16}O_3$: calcd, 256.1099; found, 256.1103.

Methyl 2-(2-methyl-1,2-dihydronaphtho[2,1-*b*]furan-2-yl)acetate (32a). R_f 0.53 (4 : 1 hexane / ethyl acetate); IR (neat) 1753, 1631, 1599, 1522, 1353, 1054, 881, 768 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.64 (3H, s), 2.83 and 2.85 (2H, AB_q, J_{AB} = 15.0 Hz), 3.29 and 3.60 (2H, AB_q, J_{AB} = 15.6 Hz), 3.63 (3H, s), 7.06-7.07 (1H, m), 7.26-7.29 (1H, m), 7.42-7.45 (1H, m), 7.53-7.55 (1H, m), 7.64-7.66 (1H, m), 7.76-7.78 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 26.65, 40.15, 45.00, 51.54, 86.90, 112.15, 117.89, 122.60, 122.75, 126.57, 128.62, 129.01, 129.16, 130.91, 155.66, 170.54; MS *m/z* (%): 256 (M^+, 60), 195 (12), 182 (100), 181 (30), 153 (7); HRMS of (**32a**), $C_{16}H_{16}O_3$: calcd, 256.1099; found, 256.1089.

1-(2-Methyl-1,2-dihydronaphtho[2,1-*b*]furan-2-yl)acetone (32b). R_f 0.60 (dichloromethane); Mp: 80-81 °C; IR (CH_2Cl_2) 1714, 1631, 1598, 1579, 1522, 773 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.62 (3H, s), 2.21 (3H, s), 2.98 and 3.02 (2H, AB_q, J_{AB} = 15.6 Hz), 3.35 and 3.47 (2H, AB_q, J_{AB} = 15.6 Hz), 7.06-7.08 (1H, m), 7.29-7.32 (1H, m), 7.44-7.47 (1H, m), 7.55-7.56 (1H, m), 7.68-7.70 (1H, m), 7.79-7.80 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 26.72, 31.66, 40.39, 53.69, 87.38, 112.15, 118.17, 122.69, 122.87, 126.71, 128.68, 129.12, 129.21, 152.02, 155.53, 206.52; MS *m/z* (%): 240 (M$^+$, 12), 182 (100), 165 (6), 129 (5); HRMS (**32b**), $C_{16}H_{16}O_2$: calcd, 240.1150; found, 240.1136.

***tert*-Butyl (*E*)-4-(2-hydroxy-1-naphthyl)-3-methyl-2-butenoate (*E*-31f).** R_f 0.73 (dichloromethane); IR 3263, 1676, 1641, 1599, 1583, 1520, 1271, 1155, 910, 734 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.41 (9H, s), 2.27 (3H, s), 3.87 (3H, s), 5.32 (1H, s), 5.39 (1H, s, exch. D_2O) 7.03-7.06 (1H, m), 7.34-7.37 (1H, m), 7.47-7.50 (1H, m), 7.64-7.67 (1H, m), 7.74-7.80 (2H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 24.48, 28.00, 28.19, 82.01, 113.36, 118.28, 119.00, 122.40, 122.76, 126.30, 128.83, 128.91, 129.14, 133.81, 154.15, 156.24, 169.56; MS *m/z* (%): 298 (M$^+$, 5), 242 (68), 225 (26), 195 (58), 182 (97), 181 (100), 157 (10), 129 (21), 69 (43), 57 (64); Anal. Calcd for $C_{19}H_{22}O_3$ (298.4): C, 76.48; H, 7.43. Found: C, 76.62; H, 7.45.

***tert*-Butyl (*Z*)-4-(2-hydroxy-1-naphthyl)-3-methyl-2-butenoate (*Z*-31f).** R_f 0.36 (dichloromethane); Mp: 184.5-185.5 °C; IR 3336, 3257, 1675, 1645, 1630, 1516, 1144, 806 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.56 (9H, s), 1.73 (3H, s), 4.28 (3H, s), 5.76 (1H, s), 7.15-7.18 (1H, m), 7.27-7.32 (1H, m), 7.45-7.50 (1H, m), 7.66-7.69 (1H, m), 7.75-7.78 (1H, m), 8.00-8.03 (1H, m), 9.10 (1H, s, exch. D_2O); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 19.15, 28.24, 35.82, 79.85, 115.71, 117.75, 117.85, 123.16, 123.26, 126.74, 128.53, 128.85, 129.38, 133.72, 151.49, 155.92, 166.57; MS *m/z* (%): 298 (M$^+$, 13), 242 (89), 225 (26), 195 (62), 182 (98), 181 (100), 152 (7), 57 (31); HRMS (*Z*-**32f**), $C_{19}H_{22}O_3$: calcd, 298.1569; found, 298.1569.

***tert*-Butyl 2-(2-methyl-1,2-dihydronaphtho[2,1-*b*]furan-2-yl)acetate (32f).** R_f 0.85 (dichloromethane); IR (CH_2Cl_2) 1722, 1631, 1601, 1521, 1466, 1157, 812 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.35 (9H, s), 1.64 (3H, s), 2.73 and 2.80 (2H, AB_q, J_{AB} = 14.4 Hz), 3.29 and 3.69 (2H, AB_q, J_{AB} = 15.6 Hz), 7.06-7.07 (1H, m), 7.28-7.30 (1H, m), 7.44-7.47 (1H, m), 7.55-7.57 (1H, m), 7.66-7.68 (1H, m), 7.78-7.80 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 27.22, 27.93, 40.02, 46.90, 80.91, 87.21, 112.22, 118.12, 122.63, 122.72, 126.61, 128.68, 128.99, 129.18, 131.02, 155.93, 169.48; MS *m/z* (%): 298 (M$^+$, 35), 241 (54), 195 (82), 182 (100); HRMS (**32f**), $C_{19}H_{22}O_3$: calcd, 298.1569; found, 298.1567.

Reaction of Dioxine (13) with ylide (15a). A Typical Procedure. To a solution of the dioxine (**13**) (0.5 g, 1.67 mmol) in anhydrous chloroform (10 mL) under a nitrogen gas atmosphere was added ylide (**15a**) (0.56 g, 1.67 mmol). The mixture was allowed to stir at ambient temperature for 3 days after which time the volatiles were removed and the residue subjected to silica gel chromatography. Elution with a mixture of hexane / ethylacetate (10 : 1) afforded the desired dihydronaphthofuran (***E*** and ***Z*-33a**) (0.26 g, 60 %) as a colourless oil, the methyl migrated dihydronaphthofuran regeoisomer (***E*** and ***Z*-35a**) (64 mg, 15 %) as a colourless oil and a small amount of the known furan (**30**) (42 mg, 14 %) as a crystalline solid, Mp: 57-57.5 °C, (Lit.[12] Mp: 57 °C); R_f 0.68 (10 : 1 hexane / ethylacetate); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.16, 101.72, 112.06, 123.43, 123.78, 124.16, 124.22, 125.91, 127.44, 128.67, 130.29, 151.98, 154.71. See Table 3 for further variations of this procedure.

Diastereomeric mixture of Methyl (*E and Z*)-2-(2-methyl-1,2-dihydronaphtho[2,1-*b*]furan-1-yl)acetate (*E*- and *Z*-33a). Anal. Calcd for $C_{16}H_{16}O_3$ (256.3, mixture): C, 74.98; H, 6.29. Found: C, 74.97; H, 6.42. **(*Z*-33a)**: R_f 0.39 (10 : 1 hexane / ethyl acetate); ^1H NMR ($CDCl_3$, 600 MHz) δ 1.55 (3H, d, J = 7.0 Hz), 2.63 (1H, dd, J = 17.0, 3.6 Hz), 2.69 (1H, dd, J = 17.0, 9.6 Hz), 3.70 (3H, s), 4.20 (1H, ddd, J = 9.6, 7.0, 3.6 Hz), 5.03 (1H, dq, J = 7.0, 7.0 Hz), 7.08-7.09 (1H, m), 7.29-7.31 (1H, m), 7.45-7.48 (1H, m) 7.64-7.70 (2H, m), 7.80-7.82 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.95, 33.60, 40.60, 51.90, 83.15, 112.14, 122.01, 122.23, 122.90, 126.93, 129.11, 129.60, 129.69, 130.09, 156.79, 173.00. **(*E*-33a)**: R_f 0.39 (10 : 1 hexane / ethyl acetate); ^1H NMR ($CDCl_3$, 600 MHz) δ 1.45 (3H, d, J = 6.5 Hz), 2.57 (1H, dd, J = 16.8, 11.2 Hz), 3.02 (1H, dd, J = 16.8, 3.1 Hz), 3.74 (3H, s), 3.82 (1H, ddd, J = 11.2, 3.1, 2.6 Hz), 4.81 (1H, dq, J = 6.5, 2.6 Hz), 7.08-7.10 (1H, m), 7.28-7.30 (1H, m), 7.43-7.46 (1H, m) 7.65-7.69 (2H, m), 7.78-7.80 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 21.46, 30.89, 38.42, 51.73, 85.93, 112.65, 121.79, 122.20, 122.76, 126.90, 129.10, 129.48, 130.01, 130.62, 151.14, 173.17.

Parent acid of (*Z*-33a), (*Z*)-2-(2-methyl-1,2-dihydronaphtho[2,1-*b*]furan-1-yl)acetic acid. To a mixture of (***E*** and ***Z*-33a**; ratio 9 : 1) (40 mg, 0.16 mmol) in water / methanol (10 : 1, 5 mL) was added sodium hydroxide (25 mg, 4 equiv.) at ambient temperature. After 1 hour the mixture was acidified and extracted with chloroform (4 x 10 mL). The combined organic extracts were then evaporated to dryness and the residue recrystallised trice from a mixture of hexane and chloroform (ratio, 3 : 1) to afford the title compound (25 mg, 66%) as colourless needles. Mp: 175.5-176.5 °C; IR (CH_2Cl_2) 3200-2600, 1710, 1630, 1599, 1581, 815 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.61 (3H, d, J = 6.6 Hz), 2.74-2.77 (2H, AB portion of ABX), 4.16-4.24 (1H, X portion of ABX), 5.06 (1H, dq, J = 6.6, 6.6 Hz), 7.08-7.11 (1H, m), 7.30-7.35 (1H, m), 7.46-7.51 (1H, m), 7.68-7.72 (1H, m), 7.81-7.84 (1H, m), 11.60 (1H, bs, exch. D_2O); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 15.06, 33.40, 40.34, 83.04, 112.17, 121.82, 122.99, 127.06, 129.20, 129.67, 129.85, 130.00, 156.81, 177.98, one carbon masked; MS *m/z*

(%): 242 (M^+, 36), 183 (100), 155 (37), 115 (10); Anal. Calcd for $C_{15}H_{14}O_3$ (242.3): C, 74.36; H, 5.82. Found: C, 74.47; H, 5.83.

Diastereomeric mixture of Methyl (*E* and *Z*)-2-(1-methyl-1,2-dihydronaphtho[2,1-*b*]furan-2-yl)acetate (*E*- and *Z*-35a). Anal. Calcd for $C_{16}H_{16}O_3$ (256.3, mixture): C, 74.98; H, 6.29. Found: C, 74.93; H, 6.14. R_f 0.32 (10 : 1 hexane / ethyl acetate); ^{13}C NMR ($CDCl_3$, mixture, 150 MHz) δ 14.49, 20.42, 35.02, 38.15, 39.94, 41.87, 51.83, 52.02, 82.90, 86.75, 112.23, 112.49, 122.02, 122.18, 122.26, 122.84, 122.87, 124.51, 126.66, 126.69, 129.02, 129.03, 129.16, 129.52, 129.70, 129.71, 130.22, 130.59, 155.71, 155.78, 171.07, 171.38; **(*E*-35a).** ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.49 (3H, d, *J* = 6.9 Hz), 2.65 (1H, dd, *J* = 16.0, 6.5 Hz), 2.81 (1H, dd, *J* = 16.0, 7.2 Hz), 3.58 (1H, dq, *J* = 6.9, 3.5 Hz), 3.73 (3H, s), 4.90 (1H, ddd, *J* = 7.2, 6.5, 3.5 Hz), 7.08-7.10 (1H, m), 7.28-7.30 (1H, m), 7.43-7.46 (1H, m) 7.65-7.69 (2H, m), 7.78-7.80 (1H, m); **(*Z*-35a)**: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.23 (3H, d, *J* = 6.9 Hz), 2.89 (1H, dd, *J* = 16.2, 6.9 Hz), 3.04 (1H, dd, *J* = 16.2, 6.9 Hz), 3.79 (3H, s), 3.86 (1H, dq, *J* = 6.9, 6.9 Hz), 5.21 (1H, ddd, *J* = 6.9, 6.9, 6.9 Hz), 7.08-7.10 (1H, m), 7.28-7.30 (1H, m), 7.43-7.46 (1H, m) 7.65-7.69 (2H, m), 7.78-7.80 (1H, m).

Reaction of Dioxine (14) with ylide (15a). A Typical Procedure. To a solution of the dioxine (**14**) (0.13 g, 0.61 mmol) in anhydrous dichloromethane (5 mL) under a nitrogen gas atmosphere was added ylide (**15a**) (0.25 mg, 0.75 mmol). The mixture was allowed to stir at ambient temperature for 5 days after which time the volatiles were removed and the residue subjected to silica gel chromatography. Elution with a mixture of hexane / ethylacetate (9 : 1) afforded the desired dihydronaphthofuran (**38**) (9 mg) as a crystalline solid, the alkene (**40**) (46 mg) as a colourless oil and the chromenone (**41**) (45 mg) as a crystalline solid.

Methyl 2-(2,2-dimethyl-1,2-dihydronaphtho[2,1-*b*]furan-1-yl)acetate (38). Mp: 76.5-78.5 °C; R_f 0.40 (9 : 1 hexane / ethyl acetate); IR (CH_2Cl_2) 1736, 1630, 1599, 1581, 1466, 814 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.47 (3H, s), 1.52 (3H, s), 2.65 (1H, dd, *J* = 17.5, 10.3 Hz), 2.79 (1H, dd, *J* = 17.5, 3.3 Hz), 3.73 (3H, s), 3.98 (1H, dd, *J* = 10.3, 3.3 Hz), 7.05-7.08 (1H, m), 7.27-7.33 (1H, m), 7.44-7.50 (1H, m), 7.64-7.71 (1H, m), 7.80-7.83 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 22.16, 28.50, 35.31, 46.03, 51.83, 89.28, 112.69, 121.16, 121.88, 122.71, 126.90, 129.24, 129.56, 129.82, 130.62, 155.56, 173.24; MS *m/z* (%): 270 (M^+, 38), 197 (100), 181 (12), 169 (9), 141 (15); Anal. Calcd for $C_{17}H_{18}O_3$ (270.3): C, 75.53; H, 6.71. Found: C, 75.67; H, 6.72.

Methyl 3-(2-hydroxy-1-naphthyl)-4-methyl-4-pentenoate (40). R_f 0.34 (9 : 1 hexane / ethyl acetate); IR (CH_2Cl_2) 3446, 1736, 1641, 1621, 1600, 1211, 1155, 820 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.66 (3H, m), 2.95 (1H, dd, *J* = 16.2, 7.1 Hz), 3.24 (1H, dd, *J* = 16.2, 7.1 Hz), 3.60 (3H, m), 4.70 (1H, dd, *J* = 7.1, 7.1 Hz), 5.21 (1H, s), 7.09-7.12 (1H, m), 7.34-7.36 (1H, m), 7.44-7.48 (1H, m), 7.66-7.69 (1H, m), 7.76-7.78 (1H, m), 8.09-8.12 (1H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 22.72, 36.05, 39.57, 51.91, 111.15, 118.19, 119.82, 122.45, 123.23, 126.53, 128.93, 129.41, 129.86, 132.96, 148.25, 153.45, 173.73; MS *m/z* (%): 270 (M^+, 42), 138 (20), 197 (100), 181 (56), 169 (21), 141 (22); HRMS (**40**), $C_{17}H_{18}O_3$: calcd, 270.1256; found, 270.1262.

1-Isopropenyl-2,3-dihydro-1*H*-benzo[*f*]chromen-3-one (41). Mp: 155-156 °C; R_f 0.20 (9 : 1 hexane / ethyl acetate); IR (CH_2Cl_2) 1765, 1647, 1626, 1601, 1218, 1156, 817 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.87 (3H, s), 2.94 (1H, dd, J = 15.9, 7.0 Hz), 3.10 (1H, dd, J = 15.9, 1.8 Hz), 4.24 (1H, dd, J = 7.0, 1.8 Hz), 4.54 (1H, d, J = 0.7 Hz), 4.88 (1H, d, J = 0.7 Hz), 7.24-7.28 (1H, m), 7.46-7.48 (1H, m), 7.52-7.55 (1H, m), 7.80-7.87 (3H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 20.52, 34.02, 39.08, 106.89, 114.09, 117.48, 123.08, 125.19, 127.32, 128.80, 129.68, 131.10, 131.19, 143.30, 149.64, 167.70; MS *m/z* (%): 238 (M^+, 100), 223 (8), 195 (72), 181 (78), 165 (22), 141 (33), 115 (35); Anal. Calcd for $C_{16}H_{14}O_2$ (238.3): C, 80.65; H, 5.92. Found: C, 80.73; H, 5.91.

Crystal Structure Data for 20b: Crystals of **20b** were grown from the slow evaporation of an *n*-heptane solution. Data were measured for a colourless plate (0.05 x 0.18 x 0.29 mm) at 123 K using the ω:2θ scan technique and graphite-monochromatised MoKα radiation on a Nonius Kappa CCD such that θ_{max} was 60.0 °. The structure was solved by direct-methods[14] and refined on F[15] using 1936 data with $I \geq 3.0\sigma(I)$. Non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were included in the model at their calculated positions (C-H 0.97 Å). A weighting scheme of the form $w = 1/[\sigma^2(F)]$ was employed and refinement was continued until convergence when R = 0.050 and R_w = 0.042. The molecular structure is shown in Fig. 1 which was drawn with ORTEP[16] at 40 % displacement ellipsoids. Crystal data: $C_{15}H_{14}O_2$, M = 226.3, monoclinic, space group $P2_1/c$, a = 15.5195(6), b = 4.9504(1), c = 15.0575(5) Å, β = 98.203(1)°, V = 1145.00(5) Å^3, Z = 4, D_c = 1.313 g cm^{-3}, F(000) = 480, μ = 0.86 cm^{-1}, CCDC deposition number: 133089.

Crystal Structure Data for parent acid of Z-33a: Crystals of parent acid of Z-**33a** were grown from the slow evaporation of an deuterochloroform / *n*-heptane (1 : 4) solution. Data were collected as described above but at 293 K, on a Rigaku AFC6R diffractometer and with θ_{max} of 55.2°. Structure solution was by direct methods[17] and refinement was as above: $w = 1/[\sigma^2(F) + 0.00001|F^2|]$, R = 0.076 and R_w = 0.073 for 1059 data. Molecular structure is shown in Fig. 2, drawn at the 40 % probability level.[16] Crystal data: $C_{15}H_{14}O_3$, M = 242.3, monoclinic, space group $C2/c$, a = 40.38(3), b = 4.927(2), c = 12.670(7) Å, β = 102.00(5)°, V = 2466(2) Å^3, Z = 8, D_c = 1.305 g cm^{-3}, F(000) = 1024, μ = 0.90 cm^{-1}, CCDC deposition number: 133090. Centrosymmetric molecules associate in the crystal structure *via* the common carboxylate dimer motif such that O(1'')-H...O(1')' is 1.67 Å, O(1'')...O(1')' is 2.645(4) Å and the O(1'')-H...O(1')' angle is 177 °.

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