Solid-Phase Synthesis of Dihydropyrans by Eu(fod)$_3$-Catalysed [4+2] Heterocycloaddition of Vinyl Ethers with Benzylidenepyruvic Acid Esters. Comparison with Conventional Homogeneous Liquid Phase Conditions

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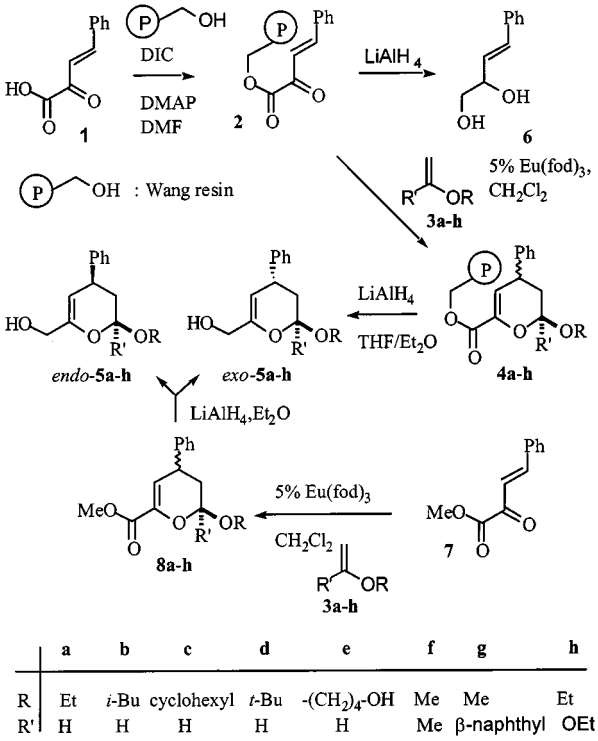
The OH groups of Wang resin were esterified with benzylidenepyruvic acid (**1**) to give the immobilized 1-oxabutadiene **2**. The latter reacted with vinyl ethers **3a–h** (dienophiles) in the presence of Eu(fod)$_3$, and the resulting adducts **4a–h** underwent reductive cleavage with $LiAlH_4$ to afford the dihydropyrans **5a–h** in high (62 to 100%) overall yields. A similar sequence carried out under conventional homogeneous liquid phase conditions led to significantly lower yields. The *endo*/*exo* selectivity of the cycloaddition reaction was the same in both cases.

Introduction

In view of developing combinatorial chemistry, which is expected to become a powerful tool for accelerating the discovery of useful new drugs, in recent years a growing number of organic reactions have been carried out with reactants linked to insoluble polymeric carriers. Accordingly, a few examples of Diels–Alder and hetero Diels–Alder reactions performed under such heterogeneous conditions have been reported.[1]

We describe herein the Eu(fod)$_3$-catalyzed [4+2] heterocycloadditions of various soluble electron-rich dienophiles with an insoluble carrier-bound 1-oxabutadiene (**2**) obtained by esterification of the free OH groups of Wang resin with benzylidenepyruvic acid **1** in the presence of diisopropylcarbodiimide (DIC)/DMAP (Scheme 1). Completion of this anchoring reaction was ascertained by subsequent $LiAlH_4$ reduction which afforded the diol **6** in quantitative yield. The supported heterodiene **2** was treated with the dienophilic vinyl ethers **3a–h** in the presence of a catalytic amount (5 mol-%) of Eu(fod)$_3$ in refluxing dichloromethane. Reductive cleavage of the expected supported heterocycloadducts **4a–h** was then smoothly achieved by means of $LiAlH_4$ in ether/THF at 20 °C followed by mild hydrolysis with aqueous Na_2SO_4, and gave high overall yields[2] of epimeric mixtures of the primary allylic alcohols *endo*-**5a–h** (major epimer) and *exo*-**5a–h** (Table). The products were found to be practically free of impurities, as evidenced from the ^{1}H- and ^{13}C-NMR spectra. When this three-step solid-phase sequence was conducted without any Eu(fod)$_3$ catalyst in the second step, diol **6** was obtained as the sole product, which shows the failure of such uncatalyzed heterocycloaddition under solid-phase conditions. Another striking feature, readily demonstrated by the results in Table 1, is that the solid-phase cycloaddition is very *endo*-selective, particularly so in the case of the adducts **5a–c**,**e** (obtained from vinyl ethers of primary and secondary alcohols), with *endo*/*exo* ratios ranging from 94:6 to >97:3.



	a	b	c	d	e	f	g	h
R	Et	*i*-Bu	cyclohexyl	*t*-Bu	-(CH$_2$)$_4$-OH	Me	Me	Et
R'	H	H	H	H	H	Me	β-naphthyl	OEt

Scheme 1

The syntheses of the adducts **5a–h** were then carried out under conventional liquid phase conditions, as previously described. [3] Thus, the Eu(fod)$_3$-catalyzed heterocycloaddition of methyl benzylidenepyruvate **7** with the vinyl ethers **3a–h** in dichloromethane gave the epimeric adducts **8a–h**, which were in turn reduced to the allylic alcohols **5a–h** by means of $LiAlH_4$ in ether at room temperature. The results are displayed in Table 1. It appears that the *endo*/*exo* selectivity is almost the same both under solid-phase and under homogeneous liquid-phase conditions. With the exception

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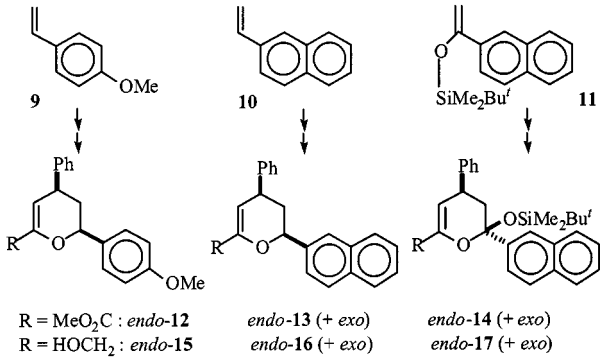
of the β-naphthyl adduct **5g**, it can be seen *that the overall yields are substantially higher under solid-phase syntheses than under conventional homogeneous conditions.* Yield increase is particularly striking in the case of the adduct **5h** (yield is 22% in liquid phase and 86% in solid phase conditions).

Table 1. Syntheses of dihydropyrans **5a**–**h**

	Solid phase synthesis		Liquid phase synthesis	
	overall yield (%)	*endo*/*exo* ratio	overall yield (%)	endo/*exo* ratio
5a	100	> 97:3	87	> 97:3
5b	92	96:4	61	96:4
5c	100	>97:3	47	>97:3
5d	92	74:26	70	75:25
5e	82	94:6	57	96:4
5f	100	80:20	79	80:20
5g	62	74:26	77	80:20
5h	86	–	22	–

We next considered applying the above reaction schemes to other types of dienophiles of somewhat lower reactivity, such as the styrenes **9**, **10**, and the *O*-silyl vinyl ether **11**. Starting from methyl benzylidenepyruvate **7**, the epimeric *endo*/*exo* adducts **15–17** were obtained by $LiAlH_4$ reduction of the intermediate ester adducts **12–14** (Scheme 2). Solid phase synthesis of **15–17** was then carried out as described above for the adducts **5a–h**.



Scheme 2

The results displayed in Table 2 show that in these cases, and contrary to our observations when the vinyl ethers **3a**–**h** were used as dienophiles, the yields of the adducts **15–17** are much lower under solid phase conditions compared with those obtained by homogeneous liquid phase syntheses. The lack of reactivity of styrenic dienophiles **9**, **10** under solid-phase conditions might be due to unfavorable interactions in the *endo*-transition state between the aromatic nucleus and the matrix of the insoluble conjugate **2**. In the case of the silyl enol ether **11**, steric hindrance might restrict the formation of adducts **17** under solid phase conditions, owing to the bulkiness of both possible *endo*-directing groups. Some support for this phenomenon was already given above in the case of the β-naphthyl vinyl ether **3g** (Table 2).

Conclusion

The present study shows that the solid phase $Eu(fod)_3$-catalysed [4+2] heterocycloaddition of simple vinyl ethers may have advantages over the conventional homogeneous liquid-phase syntheses in terms of overall yields. However, the rather low "capacity" of the Wang resin is a drawback which cannot be neglected. For this reason, we are currently investigating other types of insoluble carriers which bear larger amounts of reactive OH groups than the Wang resin. From a more general point of view, our present results exemplify the efficiency of $LiAlH_4$ as reductive cleavage reagent of ester linkages. Indeed, the overall sequence is fully compatible with clean preparations of sensitive products.[4]

Experimental Section

General: IR: Nicolet 5DX and Genesis (Mattson). – NMR: Bruker AC 400 (400 MHz for ^1H; 100 MHz for ^{13}C). $CDCl_3$ was used as solvent and TMS as internal standard. – High resolution mass spectra were performed on a Varian MAT311 at the C.R.M.P.O. (Rennes).

General Experimental Procedure for Solid-Phase Syntheses: A solution of DIC (3 equiv.) in DMF (10 mL) was added at 0 °C to a suspension of commercial Wang resin (1 g; 0.8–1.1 mmol of OH groups; 1 equiv.) in a solution of benzylidenepyruvic acid **1** (3 equiv.) and DMAP (0.3 equiv.) in DMF (10 mL). After shaking for 1 h at 0 °C and 17 h at 20 °C, the mixture was filtered. The recovered resin was washed successively with CH_2Cl_2 (twice), petroleum ether, ether, acetone, CH_2Cl_2 (twice), and was dried at 20 °C. The resin was next suspended in a solution of the requisite vinyl ether (**3a**–**h**), $Eu(fod)_3$ ($5.5\ 10^{-2}$ mmol) in CH_2Cl_2 (10 mL) and the resulting mixture refluxed for 2 days with shaking. The resin was washed with CH_2Cl_2 (twice) and ether (twice). The dried resin was then added to a solution of $LiAlH_4$ (1 molar equiv.) in ether at 0 °C. After 1 h at 0 °C and 17 h at 20 °C, the reaction medium was hydrolyzed with saturated aqueous Na_2SO_4 (160 μL) and filtered through Celite. The solid was washed with CH_2Cl_2 and the combined filtrates evaporated under reduced pressure to afford the unstable dihydropyrans **5a**–**h**, which were then analyzed by ^1H- and ^{13}C-NMR spectroscopy.

Methyl 2-Ethoxy-4-phenyl-3,4-dihydro-2*H*-pyran-6-carboxylate (8a):[5] – A Typical Procedure for the Homogeneous Syntheses of the Adducts 8a–g: Ethyl vinyl ether **3a** (530 μL; 5 mmol) and the cata-

Table 2. Syntheses of dihydropyrans **15–17**

Compounds	Solid phase synthesis		Liquid phase synthesis	
	overall yield (%)	*endo*/*exo* ratio	overall yield (%)	*endo*/*exo* ratio
15	12	> 97:3	97	> 97:3
16	4	–	63	> 97:3
17	24	68:32	76	75:25

lyst Eu(fod)$_3$ (0.055 g, 5% molar) were added to a solution of methyl benzylidenepyruvate **7**[3a] (0.190 g, 1.0 mmol) in CH_2Cl_2 (5 mL) contained in a 10 mL flask equipped with a reflux condenser and a silica gel drying tube. The mixture was refluxed for 48 h, the solvent evaporated and the residue chromatographed on silica gel (ratio 40:1, eluent cyclohexane/AcOEt 90:10) to afford the adduct **8a**[5] (0.255 g, 0.97 mmol; 97%), *endo*/*exo* ratio >99:1.

Methyl 2-Isobutoxy-3,4-dihydro-4-phenyl-2*H*-pyran-6-carboxylate (8b): From **3b** and **7**, oil (99%). *endo*/*exo* ratio 98:2. – IR (film): $\tilde{\nu}$ = 1737 cm^{-1}, 1643. – ^{1}H NMR ($CDCl_3$): δ = 0.89 (broad d, *J* = 6.6 Hz, 3 H), 0.90 (d, *J* = 6.5 Hz, 3 H), 1.90 (m, 1 H), 2.07 (ddd, *J* = 7.5, 8.3, 13.7 Hz, 1 H), 2.37 (ddd, *J* = 1.5, 7.2, 13.7 Hz, 1 H), 3.34 (dd, *J* = 6.8, 9.1 Hz, 1 H), 3.76 (dt, *J* = 3.1, 8.3 Hz, 1 H), 3.84 (s, 3 H), 3.88 (dd, *J* = 6.5, 9.1 Hz, 1 H), 5.35 (d, *J* = 6.4 Hz, 1 H), 6.29 (d, *J* = 2.9 Hz, 1 H), 7.21–7.33 (m, 5 H). – ^{13}C NMR ($CDCl_3$): δ = 19.2, 19.3, 28.5, 35.9, 37.5, 52 .2, 76.2, 100.6, 114.5, 126.7, 127.6, 128.6, 142.6, 143.0, 163.6. – MSHR: calcd. for M$^+$ 290.1518 ($C_{17}H_{22}O_4$), found 290.1506.

Methyl 2-cyclohexyloxy-3,4-dihydro-4-phenyl-2*H*-pyran-6-carboxylate (8c): From **3c** and **7**, oil (99%). *endo*/*exo* ratio > 97:3. – IR (film): $\tilde{\nu}$ = 1733 cm^{-1}, 1643. – ^{1}H NMR ($CDCl_3$): δ = 1.20–2.10 (m, 11 H); 2.28 (dd, *J* = 7.4, 13.7 Hz, 1 H), 3.74 (ddd, *J* = 3.1, 7.1, 8.9 Hz, 1 H), 3.82 (s, 3 H); 3.86 (m, 1 H), 5.36 (d, *J* = 7.2 Hz, 1 H), 6.18 (d, *J* = 2.7 Hz, 1 H), 7.20–7.35 (m, 5 H). – ^{13}C NMR ($CDCl_3$): δ = 23.1, 23.2, 24.9, 31.0, 32.7, 35.8, 37.1, 51.5, 97.5, 113.7, 126.0, 126.8, 127.8, 141.9, 142.3, 162.8.

Methyl 2-*tert*-Butoxy-3,4-dihydro-4-phenyl-2*H*-pyran-6-carboxylate (8d): From **3d** and **7**, oil (97%). *endo*/*exo* ratio 77:23. – IR (film): $\tilde{\nu}$ = 1735 cm^{-1}, 1643. – ^{1}H NMR ($CDCl_3$): *endo*-**8d**, δ = 1.31 (s, 9 H), 1.97 (ddd, *J* = 8.4, 9.4, 13.4 Hz, 1 H), 2.19 (dddd, *J* = 1.1, 1.9, 7.0, 13.4 Hz, 1 H), 3.75 (ddd, *J* = 2.9, 7.0, 12.8 Hz, 1 H), 3.80 (s, 3 H), 5.38 (dd, *J* = 1.9, 8.3 Hz, 1 H), 6.13 (dd, *J* = 1.0, 2.9 Hz, 1 H), 7.19–7.34 (m, 5 H); *exo*-**8d,** δ = 1.33 (s, 9 H), 1.82 (dd, *J* = 2.5, 11.5 Hz, 1 H), 2.07 (m, 1 H), 3.80 (s, 3 H), 3.83 (m, 1 H), 5.65 (s, 1 H), 6.25 (dd, *J* = 1.5, 2.5 Hz, 1 H), 7.19–7.34 (m, 5 H). – ^{13}C NMR ($CDCl_3$): *endo*-**8d**, δ = 28.7, 37.4, 38.3, 52.1, 95.0, 113.9, 126.6, 127.4, 128.5, 142.8, 142.9, 163.3; *exo*-**8d**, δ =26.9, 34.1, 36.1, 52.1, 92.1, 115.2, 126.7, 127.6, 128.6, 140.9, 143.6, 163.7. – MSHR: calcd. for M$^+$: 290.1518 ($C_{17}H_{22}O_4$), found 290.1506.

Methyl 3,4-Dihydro-2-(4-hydroxybutoxy)-4-phenyl-2*H*-pyran-6-carboxylate (8e): From **3e** and **7**, oil (84%). *endo*/*exo* ratio 87:13. – IR (film): $\tilde{\nu}$ = 3339 cm^{-1}, 1729. – ^{1}H NMR ($CDCl_3$): *endo*-**8e**, δ = 1.64 (m, 4 H), 1.84 (s, 1 H), 1.99 (ddd, *J* = 7.8, 8.8, 13.6 Hz, 1 H), 2.30 (m, 1 H), 3.62 (m, 3 H), 3.72 (ddd, *J* = 3.1, 7.1, 8.9 Hz, 1 H), 3.81 (s, 3 H), 4.01 (dt, *J* = 5.8, 9.7 Hz, 1 H), 5.15 (dd, *J* = 2.1, 7.6 Hz, 1 H), 6.17 (dd, *J* = 1.0, 2.6 Hz, 1 H), 7.15–7.32 (m, 5 H). – ^{13}C NMR ($CDCl_3$): *endo*-**8e**, δ = 26.1, 29.4, 35.8, 37.4, 52.2, 62.5, 69.2, 100.1, 114.4, 126.8, 127.4, 128.5, 142.1, 142.7, 163.1; *exo*-**8e**, δ =25.1, 26.8, 35.7, 37.5, 52.2, 64.9, 68.5, 99.9, 114.2, 126.8, 127.5, 128.7, 142.1, 142.7, 162.9.

Methyl 3,4-Dihydro-2-methoxy-2-methyl-4-phenyl-2*H*-pyran-6-carboxylate (8f): From **3f** and **7**, oil (92%). *endo*/*exo* ratio 80:20. – IR (film): $\tilde{\nu}$ = 1724 cm^{-1}, 1650. – ^{1}H NMR ($CDCl_3$): *endo*-**8f**, δ = 1.51 (s, 3 H), 2.09 (d, *J* = 7.3 Hz, 2 H), 3.30 (s, 3 H), 3.63 (dt, *J* = 3.3, 7.3 Hz, 1 H), 3.83 (s, 3 H), 6.24 (d, *J* = 3.2 Hz, 1 H), 7.21–7.33 (m, 5 H); *exo*-**8f**, δ = 1.56 (s, 3 H), 2.20 (m, 2 H), 3.35 (s, 3 H), 3.77 (m, 1 H), 3.81 (s, 3 H), 6.24 (d, *J* = 3.2 Hz, 1 H), 7.21–7.33 (m, 5 H). ^{13}C NMR ($CDCl_3$): *endo*-**8f**, δ = 22.2, 37.2, 38.9, 49.1, 52.2, 101.2, 113.6, 126.6, 125.7, 128.4, 142.4, 143.2, 163.3; *exo*-**8f**, δ = 22.7, 35.7, 40.9, 49.3, 52.1, 99.6, 116.0, 126.8, 127.6, 128.7, 141.0, 143.1, 163.6.

Methyl 3,4-Dihydro-2-methoxy-2(2-naphthyl)-4-phenyl-2*H*-pyran-6-carboxylate (8g): From **3g** and **7**, oil (98%). *endo*/*exo* ratio 80:20. – IR (film): $\tilde{\nu}$ = 1731 cm^{-1}, 1681, 1650. –^{1}H NMR ($CDCl_3$): *endo*-**8g**, δ = 2.38 (dd, *J* = 8.0, 13.5 Hz, 1 H), 2.56 (dd, *J* = 7.0, 14.0 Hz, 1 H), 3.16 (s, 3 H), 3.31 (ddd, *J* = 3.3, 7.0, 8.0 Hz, 1 H), 3.91 (s, 3 H), 6.28 (d, *J* = 3.1 Hz, 1 H) 7.20–8.50 (m, 12 H); *exo*-**8g**, δ 1.80 (dd, *J* = 12.4, 13.5 Hz, 1 H), 2.53 (ddd; *J* = 1.5, 6.2, 13.6 Hz, 1 H), 3.19 (s, 3 H), 3.89 (s, 3 H), 4.01 (ddd, *J* = 2.6, 6.1, 12.2 Hz, 1 H), 6.39 (t, *J* = 1.8 Hz, 1 H), 7.20–8.15 (m, 12 H). – ^{13}C NMR ($CDCl_3$): *endo*-**8g**, δ = 36.8, 41.2, 50.3, 52.3, 103.0, 115.2, 123.6, 126.0, 126.3, 126.5, 126.7, 127.8, 128.0, 128.4, 128.5, 128.6, 129.5, 130.2, 132.9, 133.2, 136.5, 142.3, 142.9, 163.2; *exo*-**8g:** δ = 36.3, 42.8, 50.6, 52.2, 101.4, 116.4, 123.7, 125.9, 126.2, 126.4, 126.8, 127.5, 128.2, 128.4, 128.7, 133.1, 133.2, 137.3, 141.1, 142.7, 163.4. – MSHR: calcd. for M$^+$: 374.1518 ($C_{24}H_{22}O_4$), found 374.1515.

Methyl 2,2-Bis(ethoxy)-3,4-dihydro-4-phenyl-2*H*-pyran-6-carboxylate (8h): From **3h** and **7**, oil (64%). – IR (film): $\tilde{\nu}$ = 1731 cm^{-1}, 1648. – ^{1}H NMR ($CDCl_3$) δ = 1.20, 1.24 (2t, *J* = 7.1 Hz, 6 H), 1.86 (dd, *J* = 12.0, 13.1 Hz, 1 H), 2.38 (ddd, *J* = 1.3, 6.5, 13.2 Hz, 1 H), 3.67 (dq, *J* = 6.8, 7.0 Hz, 2 H), 3.69 (dq, *J* = 7.0, 9.8 Hz, 2 H), 3.78 (m, 1 H), 3.82 (s, 3 H), 6.22 (dd, *J* = 1.4, 2.2 Hz, 1 H), 7.22–7.91 (m, 5 H). – ^{13}C NMR ($CDCl_3$): δ = 15.0, 15.2, 36.4, 37.9, 52.2, 56.9, 58.8, 113.2, 115.5, 126.9, 127.5, 128.7, 129.0, 129.1, 141.6, 142.5, 162.8. – $C_{17}H_{22}O_5$ calcd. C 66.65, H 7.24 found C 66.35, H 7.09.

Methyl 3,4-Dihydro-2-(4-methoxyphenyl)-4-phenyl-2*H*-pyran-6-carboxylate (12): From **7** and **9**, solid (98%), m.p. 116 °C (Et_2O). *endo*/*exo* ratio 100:0. – IR (film): $\tilde{\nu}$ = 1716 cm^{-1}, 1653. – ^{1}H NMR ($CDCl_3$) δ = 1.98 (dt, *J* = 11.4, 13.8 Hz, 1 H), 2.34 (ddt, *J* = 1.2, 6.4, 13.8 Hz, 1 H), 3.79 (s, 3 H), 3.83 (s, 3 H), 3.86 (m, 1 H), 5.06 (dd, *J* = 1.2, 11.4 Hz, 1 H), 6.25 (t, *J* = 1.2 Hz, 1 H), 6.88 (d, *J* = 8.7 Hz, 2 H), 7.20–7.40 (m, 7 H). – ^{13}C NMR ($CDCl_3$): δ = 39.4, 39.7, 52.3, 55.3, 78.7, 113.9, 114.3, 126.9, 127.2, 127.6, 128.8, 132.4, 143.2, 145.2, 159.5, 163.4. – MSHR: calcd. for M$^+$: 324.1361 ($C_{20}H_{20}O_4$), found 324.1367. – $C_{20}H_{20}O_4$ calcd. C 74.05, H 6.20, found C 74.01, H 6.36.

Methyl 3,4-Dihydro-2-(2-naphthyl)-4-phenyl-2*H*-pyran-6-carboxylate (13): From **7** and **10**, oil (91%). *endo*/*exo* ratio >97:3. – IR (film): $\tilde{\nu}$ = 1729 cm^{-1}, 1643. – ^{1}H NMR ($CDCl_3$): *endo*-**13**, δ = 2.05 (dt, *J* = 11.5, 13.8 Hz, 1 H), 2.46 (tdd, *J* = 1.8, 6.4, 13.8 Hz, 1 H), 3.85 (s, 3 H), 3.91 (m, 1 H), 5.26 (dd, *J* = 1.8, 11.4 Hz, 1 H), 6.27 (t, *J* = 1.9 Hz, 1 H), 7.20–7.90 (m, 12 H); *exo*-**13**, δ = 2.19 (m, 1 H), 2.42 (m, 1 H), 3.80 (m, 1 H), 3.87 (s, 3 H), 5.16 (dd, *J* = 2.6, 9.3 Hz, 1 H), 6.30 (dd, *J* = 1.2, 5.1 Hz, 1 H), 7.24–7.89 (m, 12 H). – ^{13}C NMR ($CDCl_3$): *endo*-**13**, δ = 39.4, 39.6, 52.3, 79.0, 114.6, 124.0, 125.2, 126.0, 126.1, 126.9, 127.2, 127.6, 128.0, 128.3, 128.7, 129.0, 129.1, 133.1, 133.2, 137.6, 142.9, 145.1, 163.4; *exo*-**13**, δ = 36.2, 37.3, 52.3, 74.5, 112.4, 123.7–133.2, 137.7, 142.9, 143.9, 144.8, 163.3. – MSHR: calcd. for M$^+$: 344.1423 ($C_{23}H_{20}O_3$), found 344.1422.

Methyl 2-(*tert*-Butyldimethylsiloxy)-3,4-dihydro-2-(2-naphthyl)-4-phenyl-2*H*-pyran-6-carboxylate (14): From **7** and **11**, oil (96%). *endo*/*exo* ratio 75:25. – IR (film): $\tilde{\nu}$ = 1734 cm^{-1}, 1649. – ^{1}H NMR ($CDCl_3$): *endo*-**14**, δ = –0.32 (s, 3 H), –0.03 (s, 3 H), 0.92 (s, 9 H), 1.65 (dd, *J* = 12.8, 13.0 Hz, 1 H), 2.51 (ddd, *J* = 1.7, 5.6, 13.3 Hz, 1 H), 3.88 (s, 3 H), 3.95 (ddd, *J* = 2.2, 5.6, 12.3 Hz, 1 H), 6.37 (broad t, *J* = 1.8 Hz, 1 H), 7.13–8.47 (m, 12 H); *exo*-**14**, δ = –0.16 (s, 3 H), –0.15 (s, 3 H), 0.82 (s, 9 H), 2.21 (dd, *J* = 11.4, 13.5 Hz, 1 H), 2.65 (ddd, *J* = 1.4, 5.8, 11.4 Hz, 1 H), 3.09 (ddd, *J* = 2.4, 5.7, 11.4 Hz, 1 H), 3.91 (s, 3 H), 6.17 (dd, *J* = 1.3, 2.4 Hz, 1 H), 7.13–8.47 (m, 12 H). – ^{13}C NMR ($CDCl_3$): *endo*-**14**, δ = –4.5, –

4.8, 17.3, 25.0, 35.2, 43.7, 51.3, 98.5, 114.3, 123.1, 123.6, 125.3, 125.9, 126.5, 126.7, 126.8, 127.6, 127.8, 132.0, 132.1, 140.3, 140.9, 142.0, 162.5; *exo*-**14**, δ = –2.8, –3.4, 16.5, 26.0, 37.3, 43.9, 52.4, 102.0, 114.5, 123.7–128.7, 133.1, 133.2, 140.4, 142.7, 143.3, 163.1. – $C_{26}H_{34}O_4Si$ calcd. C 73.38, H 7.21, found C 73.33, H 7.29.

2-[(1-*tert*-Butyldimethylsiloxy)vinyl]naphthalene (**11**): A solution of sodium iodide (9.4 g, 62.5 mmol) in MeCN (65 mL) was added dropwise under nitrogen to a stirred mixture of 2-acetylnaphthalene (8.5 g, 50 mmol), Et_3N (8.7 mL; 62.5 mmol), and *t*$BuMe_2SiCl$ (9.4 g, 62.5 mmol). The mixture was stirred for 18 h at 20 °C, filtered, and the filtrate extracted with petroleum ether (3 × 50 mL). The petroleum extract was evaporated and the residue distilled under vacuum to give the unstable *O*-silyl enol ether **11** (10.3 g, 72%), b.p. (0.35 Torr) 135–140 °C. – IR (film): ṽ = 1594 cm^{-1}, 1133. – ^1H NMR ($CDCl_3$): δ = 0.23 (s, 6 H), 1.04 (s, 9 H), 4.53 (d, *J* = 1.6 Hz, 1 H), 5.02 (d, *J* = 1.6 Hz, 1 H), 7.41–8.08 (m, 7 H). – ^{13}C NMR ($CDCl_3$): δ = –4.60, 25.9, 91.8, 123.4, 124.3, 126.1, 126.7, 127.6, 128.5, 133.1, 133.2, 135.0, 155.8. – $C_{20}H_{20}O_4$ calcd. C 74.05, H 6.20, found C 74.01, H 6.36.

(2-Ethoxy-3,4-dihydro-4-phenyl-2*H*-pyran-6-yl)methanol (5a) from 8a: A Typical Procedure for the Homogeneous Syntheses of the Allylic Alcohols 5a–h from the Esters 8a–h: $LiAlH_4$ (0.071 g, 1.8 equiv.) was added portionwise to a solution of the ester **8a** (0.255 g, 0.97 mmol) in anhydrous ether (20 mL), contained in a two-necked 50 mL flask equipped with a septum, a stopper and an argon inlet with ice cooling. After complete transformation of the starting material (TLC), the reaction mixture was hydrolyzed with saturated aqueous Na_2SO_4 solution (160 μL) and stirred for a few minutes. The mixture was filtered through Celite, dried ($MgSO_4$) and evaporated. The residue (0.277 g) was chromatographed on silica gel (ratio 1:x40, eluent cyclohexane/AcOEt from 90:10 to 70:30), to give **5a** as a colourless oil (0.203 g, 0.89 mmol; 89%). *endo*/*exo* ratio >98:2. – IR (film): ṽ = 3400 cm^{-1}, 1652, 1602, 1128. – ^1H NMR ($CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3 H), 1.64 (s, 1 H), 1.86 (m, 1 H), 2.26 (ddt, *J* = 1.7, 6.4, 13.2 Hz, 1 H), 3.63 (m, 2 H), 3.98 (dq, *J* = 7.1, 9.5 Hz, 1 H), 4.05 (dd, *J* = 6.3, 13.0 Hz, 1 H), 4.12 (dd, *J* = 5.7, 13.0 Hz, 1 H), 4.87 (broad s, 1 H), 5.11 (dd, *J* = 1.9, 9.1 Hz, 1 H), 7.19–7.31 (m, 5 H). – ^{13}C NMR ($CDCl_3$): δ = 15.2, 37.2, 37.8, 63.0, 64.5, 100.2, 101.6, 126.5, 127.2, 128.5, 144.2, 151.4.

(3,4-Dihydro-2-isobutoxy-4-phenyl-2*H*-pyran-6-yl)methanol (5b): From **8b**, oil (61%). *endo*/*exo* ratio 96:4. – IR (film): ṽ = 3386 cm^{-1}, 2956, 1681. – ^1H NMR ($CDCl_3$): δ = 0.90 (d, *J* = 6.6 Hz, 6 H), 1.79 (m, 1 H), 1.89 (m, 2 H), 2.26 (ddt, *J* = 1.8, 6.7, 13.2 Hz, 1 H), 3.27 (dd, *J* = 6.9, 9.2 Hz, 1 H), 3.63 (m, 1 H), 3.71 (dd, *J* = 6.5, 9.2 Hz, 1 H), 4.05 (dd, *J* = 6.3, 13.1 Hz, 1 H), 4.12 (dd, *J* = 5.6, 13.1 Hz, 1 H), 4.88 (d, *J* = 0.9 Hz, 1 H), 5.08 (dd, *J* = 2.1, 8.6 Hz, 1 H), 7.19–7.31 (m, 5 H). – ^{13}C NMR ($CDCl_3$): δ = 19.2, 19.3, 28.5, 37.0, 37.5, 63.1, 75.9, 100.5, 101.5, 126.5, 127.2, 128.5, 144.3, 151.4. – MSHR: calcd for M^+: 262.1569 ($C_{16}H_{22}O_3$), found 262.1558.

(2-Cyclohexyloxy-3,4-dihydro-4-phenyl-2*H*-pyran-6-yl)methanol (5c): From **8c**, oil (47%). *endo*/*exo* ratio > 97:3. – IR (film): ṽ = 3430 cm^{-1}, 2931, 1681. – ^1H NMR ($CDCl_3$): δ = 0.85–2.00 (m, 11 H), 2.21 (ddt, *J* = 1.7, 6.4, 13.3 Hz, 1 H), 3.62–3.77 (m, 2 H), 4.04 (dd, *J* =5.6, 13.0 Hz, 1 H), 4.12 (dd, *J* = 4.6, 13.0 Hz, 1 H), 4.85 (br. s, 1 H), 5.23 (dd, *J* = 2.0, 9.1 Hz, 1 H), 7.20 (m, 5 H). – ^{13}C NMR ($CDCl_3$): δ = 23.9, 24.1, 25.6, 31.9, 33.6, 37.7, 37.9, 63.1, 76.6, 98.4, 101.4, 126.5, 127.2, 128.4, 144.4, 151.6.

(2-*tert*-Butoxy-3,4-dihydro-4-phenyl-2*H*-pyran-6-yl)methanol (5d): From **8d**, oil (71%). *endo*/*exo* ratio 75:25. – IR (film): ṽ = 3477 cm^{-1}, 2973, 1681. – ^1H NMR (CDCl3): *endo*-**5d**, δ = 1.30 (s, 9 H), 1.74 (dd, J = 5.9, 6.9 Hz, 1 H), 1.89 (ddd, J = 9.4, 11.2, 13.3 Hz, 1 H), 2.12 (ddt, J = 1.7, 6.6, 13.2 Hz, 1 H), 3.67 (m, 1 H), 4.04 (m, 2 H), 4.82 (broad s, 1 H), 5.31 (dd, J = 2.1, 9.4 Hz, 1 H), 7.20–7.30 (m, 5 H); *exo*-**5d**, δ = 1.68 (t, J = 6.2 Hz, 1 H), 1.78 (dd, J = 2.8, 10.3 Hz, 1 H), 2.01 (m, 1 H), 3.67 (m, 1 H), 4.04 (m, 2 H), 4.93 (m, 1 H), 5.38 (t, J = 3.0 Hz, 1 H), 7.20–7.30 (m, 5 H). – ^{13}C NMR ($CDCl_3$): *endo*-**5d** δ = 28.7, 38.4, 38.7, 63.1, 75.7, 95.1, 101.1, 126.5, 127.2, 128.5, 144.4, 151.9; *exo*-**5d**, δ = 28.8, 33.5, 37.0, 63.7, 74.9, 91.5, 101.4, 126.3, 127.5, 128.4, 145.3, 150.0. – MSHR: calcd. for M^+: 262.1569 ($C_{16}H_{22}O_3$), found 262.1584.

[3,4-Dihydro-2-(4-hydroxybutoxy)-4-phenyl-2*H*-pyran-6-yl]methanol (5e): From **8e**, oil (68%). *endo*/*exo* ratio 80:20. – IR (film): ṽ = 3360 cm^{-1}, 1679. – ^1H NMR ($CDCl_3$): *endo*-**5e**, δ = 1.65 (m, 4 H), 1.86 (ddd, *J* = 8.7, 10.2, 13.2 Hz, 1 H), 2.23 (ddt, *J* = 1.6, 6.4, 13.2 Hz, 1 H), 2.67 (s, 1 H), 3.02 (s, 1 H), 3.61 (m, 4 H), 3.94 (m, 1 H), 4.03 (d, *J* = 13.2 Hz, 1 H), 4.08 (d, *J* = 13.7 Hz, 1 H), 4.87 (broad s, 1 H), 5.08 (dd, *J* = 2.0, 8.8 Hz, 1 H), 7.17–7.30 (m, 5 H). – ^{13}C NMR ($CDCl_3$): *endo*-**5e**, δ = 26.3, 29.4, 37.0, 37.45, 62.4, 62.8, 69.0, 100.3, 101.5, 126.5, 127.5, 128.5, 144.3, 151.6; *exo*-**5e**, δ = 26.5, 29.7, 33.5, 35.7, 62.5, 63.2, 68.5, 97.0, 102.3, 127.2, 127.5, 128.5, 144.8, 150.0 – MSHR: calcd for [M^+ – $C_4H_{10}O_2$]: 188.0890 ($C_{12}H_{12}O_2$), found 188.0837.

(3,4-Dihydro-2-methoxy-2-methyl-4-phenyl-4*H*-pyran-6-yl)methanol (5f): From **8f**, oil (86%). *endo*/*exo* ratio 80:20. – IR (film): ṽ = 3421 cm^{-1}, 1679. – ^1H NMR ($CDCl_3$): *endo*-**5f**, δ = 1.48 (s, 3 H), 1.56 (s, 1 H), 2.00 (d, *J* = 8.0 Hz, 2 H), 3.32 (s, 3 H), 3.53 (dt, *J* = 2.4, 8.0 Hz, 1 H), 4.10 (AB, *J* = 7.2 Hz, 2 H), 4.91 (d, *J* = 2.4 Hz, 1 H), 7.20–7.32 (m, 5 H); *exo*-**5f**, δ = 1.48 (s, 3 H), 1.65 (t, *J* = 12.8 Hz, 1 H), 2.16 (ddd, *J* = 1.5, 6.2, 13.4 Hz, 1 H), 3.33 (s, 3 H), 3.66 (ddd, J = 1.6, 6.3, 12.2 Hz, 1 H), 4.06 (d, J = 6.6 Hz, 1 H), 4.*14* (d, J = 6.6 Hz, 1 H), 4.97 (broad s, 1 H), 7.20–7.32 (m, 5 H). – ^{13}C NMR ($CDCl_3$): *endo*-**5f**, δ = 22.8, 37.9, 40.0, 49.7, 63.8, 100.7, 101.7, 127.1, 128.2, 129.2, 145.3, 152.5; *exo*-**5f**, δ = 23.5, 35.6, 42.4, 49.6, 64.0, 99.5, 103.3, 127.3, 127.9, 129.1, 145.5, 150.7. – MSHR: calcd for M^+: 234.1256 ($C_{14}H_{18}O_3$), found 234. 1240.

[3,4-Dihydro-2-methoxy-2-(2-naphthyl)-4-phenyl-2*H*-pyran-6-yl]-methanol (5g): From **8g**, oil (79%). *endo*/*exo* ratio 80:20. – IR (film): ṽ = 3386 cm^{-1}, 1681. – ^1H NMR ($CDCl_3$): *endo*-**5g**, δ = 2.06 (t, *J* = 6.4 Hz, 1 H), 2.29 (dd, *J* = 9.2, 13.3 Hz, 1 H), 2.51 (ddd, *J* = 0.8, 6.3, 13.3 Hz, 1 H), 3.10 (m, 1 H), 3.15 (s, 3 H), 4.34 (t, *J* = 6.1 Hz, 2 H), 5.00 (d, *J* = 2.2 Hz, 1 H), 7.17–8.06 (m, 12 H); *exo*-**5g**, δ = 1.76 (dd, *J* = 12.3, 13.5 Hz, 1 H), 2.20 (t, *J* = 6.4 Hz, 1 H), 2.46 (ddd, *J* = 1.6, 6.0, 13.7 Hz, 1 H), 3.20 (s, 3 H), 3.90 (ddd, *J* = 1.5, 5.9, 12.2 Hz, 1 H), 4.31 (m, 2 H), 5.15 (broad s, 1 H), 7.17–8.06 (m, 12 H). – ^{13}C NMR ($CDCl_3$), *endo*-**5g**, δ = 36.2, 41.9, 50.2, 63.3, 102.2, 102.7, 123.7, 128.4, 132.9, 133.1, 137.0, 144.2, 151.4; *exo*-**5g**, δ = 35.6, 43.7, 50.3, 63.5, 100.8, 103.4, 123.7–128.4, 133.0, 133.1, 138.1, 144.2, 149.9. – MSHR: calcd. for M^+: 346.1563 ($C_{23}H_{22}O_3$), found 346.1557.

(2,2-Diethoxy-3,4-dihydro-4-phenyl-2*H*-pyran-6-yl)methanol (5h): From **8h**, oil (34%). – IR (film): ṽ = 3465 cm^{-1}, 1681. – ^1H NMR ($CDCl_3$): δ = 1.21 and 1.22 (2t, *J* = 7.0, 7.0 Hz, 6 H), 1.77 (dd, *J* = 12.0, 12.9 Hz, 1 H), 2.20 (s, 1 H), 2.34 (ddd, *J* = 1.3, 6.3, 12.9 Hz, 1 H), 3.62 (2q, *J* = 6.9, 6.9 Hz, 4 H), 3.69 (m, 1 H), 4.07 (d, *J* = 13.2 Hz, 1 H), 4.12 (d, *J* = 13.2 Hz, 1 H), 4.96 (broad s, 1 H), 7.19–7.33 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 15.1, 15.2, 37.1, 37.4, 56.3, 58.3, 62.7, 102.4, 112.7, 126.5, 127.3, 128.51, 144.0, 150.3. – MSHR: calcd. for M^+: 278.1518 ($C_{16}H_{22}O_4$), found 278.1536.

[3,4-Dihydro-2-(4-methoxyphenyl)-4-phenyl-2*H*-pyran-6-yl]methanol (15): From **12**, oil (99%). *endo*/*exo* ratio >98:2. – IR (film): ṽ =

3367 cm^{-1}, 1673. – ^{1}H NMR ($CDCl_3$): δ = 1.91 (dt, *J* = 11.5, 13.5 Hz, 1 H), 2.14 (m, 1 H), 2.25 (ddd, *J* = 1.7, 6.2, 13.6 Hz, 1 H), 3.74 (m, 1 H), 3.77 (s, 3 H), 4.04 (dd, *J* = 6.6, 13.0 Hz, 1 H), 4.14 (dd, *J* = 4.8, 13.0 Hz, 1 H), 4.93 (broad s, 1 H), 4.99 (dd, *J* = 1.5, 11.5 Hz, 1 H), 6.86–7.33 (m, 9 H). – ^{13}C NMR ($CDCl_3$): δ = 39.1, 40.1, 55.2, 63.3, 78.0, 101.4, 113.8, 125.3–128.5, 133.1, 144.8, 153.9, 159.4.

[3,4-Dihydro-2-(2-naphthyl)-4-phenyl-2*H*-pyran-6-yl]methanol (16): From **13**, oil (69%). *endo*/*exo* ratio >97:3. – IR (film): ṽ = 3401 cm^{-1}, 1673. – ^{1}H NMR ($CDCl_3$): *endo*-**16**, δ = 1.96 (t, *J* = 5.6 Hz, 1 H), 2.04 (m, 1 H), 2.40 (ddt, *J* = 1.7, 6.2, 13.6 Hz, 1 H), 3.82 (ddd, *J* = 1.2, 6.1, 11.3 Hz, 1 H), 4.13 (m, 1 H), 4.23 (dd, *J* = 4.5, 13.1 Hz, 1 H), 5.01 (broad s, 1 H), 5.23 (dd, *J* = 1.5, 11.5 Hz, 1 H), 7.19–7.86 (m, 12 H). – ^{13}C NMR ($CDCl_3$): *endo*-**16**, δ = 35.8, 38.3, 63.6, 73.8, 99.2, 124.0–128.6, 133.1, 133.3, 138.6, 145.5, 154.1; *exo*-**16**, δ = 39.1, 40.3, 63.4, 78.5, 101.8, 124.0–128.6, 133.0, 133.2, 138.4, 144.7, 153.9. – MSHR: calcd for M^+: 316.1463 ($C_{22}H_{20}O_3$), found 316.1457.

[2-(*tert*-Butyldimethylsiloxy)-3,4-dihydro-2-(2-naphthyl)-4-phenyl-2*H*-pyran-6-yl] methanol (17): From **14**, oil (79%). *endo*/*exo* ratio 75:25. – IR (film): ṽ = 3411 cm^{-1}, 1712. – ^{1}H NMR ($CDCl_3$): *endo*-**17**, δ = –0.27 (s, 3 H), 0.01 (s, 3 H), 0.96 (s, 9 H), 1.65 (t, *J* = 12.7 Hz, 1 H), 1.87 (t, *J* = 6.5 Hz, 1 H), 2.44 (ddd, *J* = 1.6, 5.2, 13.2 Hz, 1 H), 3.84 (m, 1 H), 4.27 (m, 2 H), 5.14 (broad s, 1 H), 7.18–8.05 (m, 12 H); *exo*-**17**, δ = –0.17 (s, 3 H), 0.11 (s, 3 H), 0.84 (s, 9 H), 1.97 (t, *J* = 6.6 Hz), 1 H), 2 .15 (dd, *J* = 11.8, 13.1 Hz, 1 H), 2.58 (ddd, *J* = 1.3, 5.2, 13.2 Hz, 1 H), 2.95 (m, 1 H), 4.10–4.30 (m, 2 H), 4.94 (broad s, 1 H), 7.18–8.05 (m, 12 H). – ^{13}C NMR ($CDCl_3$): *endo*-**17**, δ = –3.4, –3.4, 18.3, 26.0, 35.1, 45.9, 63.7, 99.0, 102.3, 123.7–128.6, 132.9, 133.0, 142.0, 144.5, 150.4; *exo*-**17**, δ = –3.1, –2.5, 17.9, 25.8, 36.6, 45.1, 63.3, 101.5, 101.8, 123.7–128.6, 141.0, 144.1, 152.0. – MSHR: calcd. for M^+: 446.2277 ($C_{25}H_{34}O_3Si$), found 446.2268.

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