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PAPER

Phase-transfer-catalyzed cyclization reaction of nucleophilic addition to electron-deficient 1,3-conjugated enynes for the synthesis of functionalized 4*H*-pyrans†

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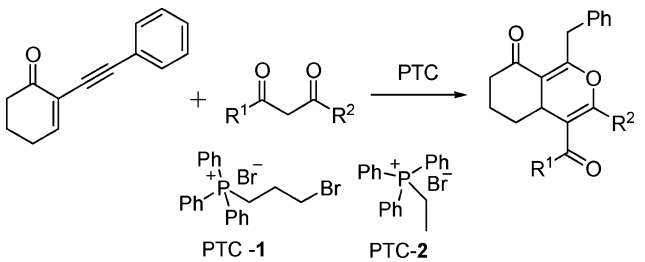
A variety of substituted 4*H*-pyrans are readily prepared in moderate to good yields under the mild reaction conditions by nucleophilic addition to electron-deficient 1,3-conjugated enynes with phase-transfer catalysis (PTC).

Introduction

4*H*-Pyrans are important and common structural units in natural compounds,[1,2] and have been identified as potential and specific IK_{Ca} channel blockers[3] that are proposed as potential therapeutic agents for diseases such as sickle cell anaemia, secretory diarrhoea, cystic fibrosis, autoimmune diseases and restenosis.[4] As a result, a number of routes leading to differently-substituted 4*H*-pyrans have been described in the literature.[5] Recently, Zhang and co-workers have demonstrated a DBU-catalyzed reaction of 1-(1-alkynyl)-2-alken-1-ones with 1,3-dicarbonyl compounds to produce 4*H*-pyrans; however, an amount of 20 mol% catalyst[6] was used, the reaction temperature was as high as 100 °C and the reaction time was long.[6,7]

Results and discussion

Phase-transfer catalysis (PTC) has long been recognized as a versatile methodology for organic synthesis in both industrial and academic laboratories, featuring a simple reaction procedure, safe, inexpensive, environmentally friendly reagents, the absence of anhydrous solvents, an ease of scale-up and metal-free conditions.[8] In our ongoing efforts to explore mild and efficient cyclization reactions for the synthesis of heterocyclic compounds initiated by PTC,[9] we report herein a versatile method to construct highly functionalized and multi-substituted 4*H*-pyrans by PTC domino reactions consisting of Michael additions of electron-deficient enynes to nucleophiles. To the best of our knowledge, this report is the first example of the synthesis of substituted 4*H*-pyrans by PTC (Scheme 1).



Scheme 1

In an initial study, we choose 1,3-conjugated enyne **1a** and nucleophile methyl acetoacetate (**2a**) as model substrates to begin our investigation. When we used 5 mol% PTC-1 and 2.0 equiv. K_2CO_3 as the base in CH_3CN at 60 °C (Table 1, entry 1), to our delight, the desired product, 4*H*-pyran **2aa**, was formed in 37% yield after 12 h. Encouraged by this result, we further optimized the reaction conditions. Other solvents, such as 1,4-dioxane, DMSO, DMF, CH_3OH, CH_2Cl_2 and 1,2-dichloroethane, were also tested; CH_2Cl_2 gave the best yield of 60% (Table 1, entries 2–7). Following on from this, a screen of bases revealed that Cs_2CO_3 was superior to the other examples tested (Table 1, entries 8–12). Reducing the reaction temperature lowered the yield (Table 1, entry 13). When PTC-2 was examined, the desired product, **2aa**, was only obtained in a 45% yield (Table 1, entry 14). Other PTCs, such as Bu_4NI, Et_4NBr, Bu_4NCl and $Bu_4NF{\cdot}3H_2O$, were also evaluated; the results indicate that the use of $Bu_4NF{\cdot}3H_2O$ improved the reaction yield of **2aa** to 80% (Table 1, entries 15–18). It is noteworthy that in the absence of base, the reaction didn't work very well (Table 1, entry 19). Thus, we chose the following reaction conditions as optimum for all subsequent cyclizations: 0.20 mmol of **1a**, 0.40 mmol of nucleophile, 5 mol% of $Bu_4NF{\cdot}3H_2O$ and 0.40 mmol of Cs_2CO_3 in CH_2Cl_2 at 60 °C.

Having established the optimal conditions of the present reaction, we next initiated an intermolecular study of the addition reaction using 1,3-conjugated enyne **1a** and various nucleophiles. As depicted in Table 1, the corresponding substituted 4*H*-pyrans were produced in moderate to good yields and with a high selectivity. Not only β-keto esters, but also simple β-diketones (such as 1,3-diketones) and cyclic β-diketones (such as

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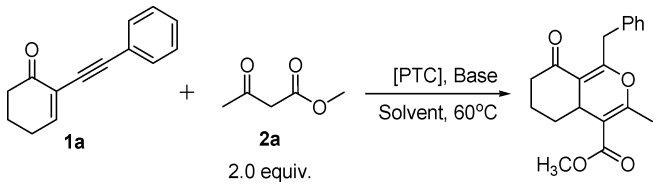
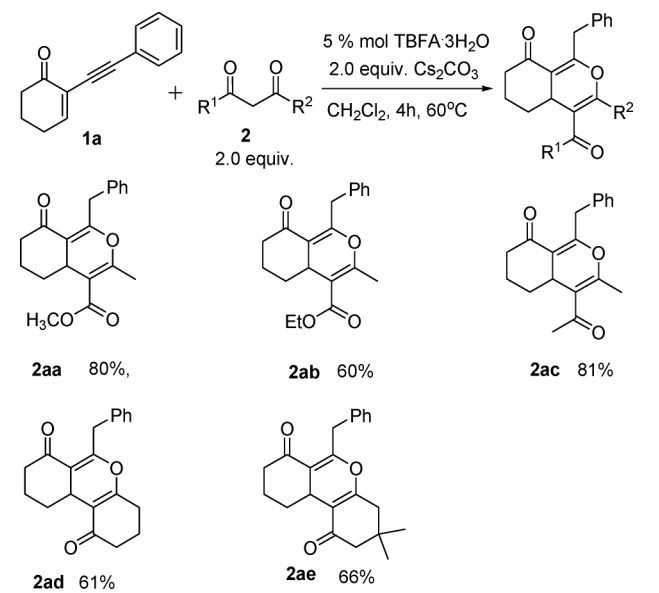
Table 1 Optimization of the PTC intramolecular cyclization of 1,3-conjugated enyne **1a** and **2a**[a]



Entry	[PTC]	Base	Solvent	Time/h	Yield (%)[b]
1	PTC-1	K_2CO_3	CH_3CN	12	37
2	PTC-1	K_2CO_3	1,4-Dioxane	16	20
3	PTC-1	K_2CO_3	DMSO	5	28
4	PTC-1	K_2CO_3	DMF	12	11
5	PTC-1	K_2CO_3	CH_3OH	12	(Mixture)
6	PTC-1	K_2CO_3	CH_2Cl_2	12	60
7	PTC-1	K_2CO_3	1,2-Dichloroethane	12	50
8	PTC-1	Na_2CO_3	CH_2Cl_2	18	20
9	PTC-1	KO^{t}Bu	CH_2Cl_2	14	25
10	PTC-1	NaOAc	CH_2Cl_2	18	29
11	PTC-1	KOAc	CH_2Cl_2	18	19
12	PTC-1	Cs_2CO_3	CH_2Cl_2	5	70
13	PTC-1	Cs_2CO_3	CH_2Cl_2	5	53[c]
14	PTC-2	Cs_2CO_3	CH_2Cl_2	5	45
15	TBAI	Cs_2CO_3	CH_2Cl_2	5	64
16	TEAB	Cs_2CO_3	CH_2Cl_2	5	56
17	TBAC	Cs_2CO_3	CH_2Cl_2	4	64
18	TBAF·$3H_2O$	Cs_2CO_3	CH_2Cl_2	4	80
19		Cs_2CO_3	CH_2Cl_2	12	15

[a] Reactions were carried out on 0.2 mmol **1a**, 2.0 equiv. **2a**, 2.0 equiv. base and 5 mol% equiv. PTC in 2.0 mL solvent in air at 60 °C. [b] Isolated yield. [c] The reaction was run at 40 °C.

Table 2 PTC cyclization of 1,3-conjugated enyne **1a** with nucleophiles



1,3-cyclohexanedione and 5,5-dimethylcyclohexane-1,3-dione), were effective nucleophiles in this transformation (Table 2, **2aa**–**2ae**). In conclusion, the reaction is mild, easily conducted and 100% atom-economic.

We then turned our attention to the cyclization reaction using chained 1,3-conjugated enynes; the results are summarized in

Table 3 PTC cyclization of chained 1,3-conjugated enynes with nucleophiles

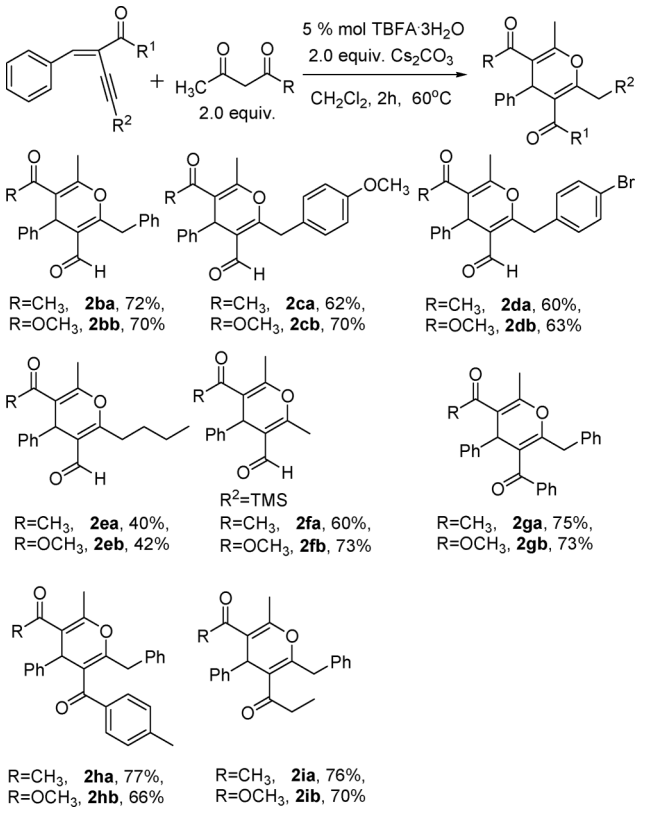


Table 3. It should be highlighted that: (1) The reaction was also 100% atom-economic. (2) No matter whether the alkyne is bearing aryl or aliphatic groups, the reaction proceeded smoothly to give the corresponding highly functionalized 4*H*-pyran, and the TMS group underwent cyclization and desilylation at the same time (Table 3, **2b**–**2f**). (3) Even by making R^1 phenyl, aryl or ethyl, the reaction still worked very well and gave good results (**2g**–**2i**). (4) Overall, this procedure displayed tolerance of the presence of aryl and alkyl substituents at both the carbonylic carbon (R^1) and the triple bond position (R^2) (**2b**–**2i**).

Although the NMR spectroscopic data support the formation of functionalized 4*H*-pyrans, the structure of **2fb** was unambiguously confirmed by an X-ray crystal structure analysis (Fig. 1).†

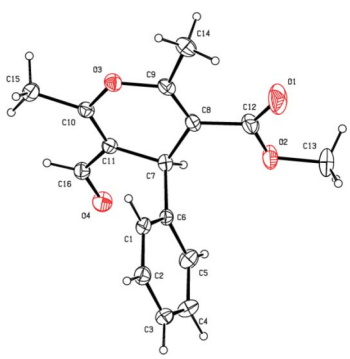


Fig. 1 The X-ray crystal structure of **2fb**.

Conclusions

In summary, we have developed a protocol for the preparation of functionalized 4*H*-pyrans by PTC Michael additions of electron-deficient enynes to nucleophiles. Notably, this process exhibits the following very attractive features: the best atom-economy, good functional group tolerance, an environmentally-friendly catalyst, a short reaction time, a low reaction temperature and good scale-up possibilities.

Experimental

General methods

All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on gel GF254 plates. Silica gel (200–300 meshes) was used for column chromatography and the distillation range of the petroleum used was 60–90 °C. ^{1}H and ^{13}C NMR spectra were recorded on Varian Mercury 300 or 400 MHz instruments using $CDCl_3$ as the solvent. IR spectra were obtained using a Nicolet NEXUS 670 FT-IR instrument. Elemental analyses were performed on a Germanic VARLIOLE instrument.

Typical procedure for the preparation of 2

To a solution of **1** (0.20 mmol) in 2.0 mL of CH_2Cl_2 was added Cs_2CO_3 (130.3 mg, 0.40 mmol) in the reaction vessel. The mixture was allowed to stir at room temperature for 1 min before TBAF·3H_2O (3.15 mg, 5 mol%) was added. The vessel was then sealed and the resulting mixture heated at 60 °C. When the reaction was considered complete, as determined by TLC analysis, the reaction was allowed to cool to room temperature before quenching with a saturated aqueous solution of ammonium chloride. The mixture was then extracted with EtOAc. The combined organic extracts were washed with water and saturated brine. The organic layers were dried over Na_2SO_4 and filtered. Solvents were evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford **2**.

Ethyl 1-benzyl-5,6,7,8-tetrahydro-3-methyl-8-oxo-4*aH*-isochromene-4-carboxylate (2ab)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.21 (m, 5H), 4.25–4.16 (m, 2H), 3.86–3.83 (d, J = 14.0 Hz, 1H), 3.72–3.69 (d, J = 14.0 Hz, 1H), 3.50–3.47 (m, 1H), 2.56–2.49 (m, 2H), 2.44–1.90 (m, 4H), 1.88–1.85 (m, 2H), 1.62–1.55 (m, 1H), 1.30–1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.4, 167.1, 156.8, 153.5, 137.3, 129.0, 128.3, 126.5, 113.7, 106.8, 60.2, 41.0, 36.0, 33.3, 31.7, 21.3, 18.5, 14.2. IR (neat, cm^{-1}): 3394, 2938, 1740, 1681, 1163, 736, 702. Anal. calc. for $C_{20}H_{22}O_4$: C 73.60; H 6.79; found: C 73.69; H 6.69%.

4-Acetyl-1-benzyl-4*a*,5,6,7-tetrahydro-3-methylisochromen-8-one (2ac)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.21 (m, 5H), 3.88–3.84 (d, J = 14.0 Hz, 1H), 3.70–3.67 (d, J = 14.0 Hz, 1H), 3.56–3.53 (m, 1H), 2.58–2.37 (m, 2H), 2.24 (s, 3H), 1.99 (s, 3H), 1.95–1.86 (m, 3H), 1.64–1.58 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.9, 199.9, 153.8, 153.3, 137.1, 128.9, 128.3, 126.5, 115.7, 113.4, 41.0, 36.0, 33.8, 32.1, 29.2, 21.5, 18.3. IR (neat, cm^{-1}): 3384, 2931, 1717, 1678, 1176, 1083, 701. Anal. calc. for $C_{19}H_{20}O_3$: C 77.00; H 6.80; found: C 77.09; H 6.77%.

6-Benzyl-3,4,8,9,10,10*a*-hexahydro-2*H*-benzo[*c*]chromene-1,7-dione (2ad)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.26 (m, 5H), 3.86–3.82 (d, J = 14.0 Hz, 1H), 3.74–3.70 (d, J = 14.0 Hz, 1H), 3.42–3.38 (m, 1H), 2.59–2.30 (m, 7H), 1.97–1.90 (m, 4H), 1.48–1.42 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.8, 197.6, 165.2, 152.8, 137.0, 129.0, 128.4, 126.6, 115.7, 114.1, 41.3, 37.1, 35.9, 31.0, 30.7, 27.1, 21.7, 20.1. IR (neat, cm^{-1}): 3306, 2947, 1699, 1657, 1170, 1133, 724. Anal. calc. for $C_{20}H_{20}O_3$: C 77.90; H 6.54; found: C 77.79; H 6.46%.

6-Benzyl-3,4,8,9,10,10*a*-hexahydro-3,3-dimethyl-2*H*-benzo[*c*]chromene-1,7-dione (2ae)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.20 (m, 5H), 3.86–3.82 (d, J = 14.0 Hz, 1H), 3.74–3.70 (d, J = 14.0 Hz, 1H), 3.43–3.39 (m, 1H), 2.59–2.52 (m, 2H), 2.43–2.37 (m, 1H), 2.36–2.18 (m, 4H), 1.96–1.88 (m, 2H), 1.48–1.43 (m, 1H), 1.01 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.8, 197.5, 163.4, 152.4, 137.1, 128.9, 128.3, 126.6, 115.6, 112.8, 51.0, 41.2, 40.7, 35.9, 31.7, 30.9, 30.5, 28.5, 27.9, 21.6. IR (neat, cm^{-1}): 3305, 2958, 1700, 1387, 1162, 913, 728. Anal. calc. for $C_{22}H_{24}O_3$: C 78.54; H 7.19; found: C 78.61; H 7.25%.

5-Acety-2-benzyl-6-methyl-4-phenyl-4*H*-pyran-3-carbaldehyde (2ba)

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.0, 7.34–7.22 (m, 10H), 4.86 (s, 1H), 4.05–4.02 (d, J = 15.2 Hz, 1H), 3.93–3.90 (d, J = 15.2 Hz, 1H), 2.34 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 187.8, 164.4, 157.3, 143.3, 135.4, 128.8, 128.6, 128.4, 128.3, 127.3, 127.1, 118.8, 115.8, 35.9, 34.8, 29.6, 18.7. IR (neat, cm^{-1}): 3313, 3029, 1663, 1160, 949, 702. Anal. calc. for $C_{22}H_{20}O_3$: C 79.50; H 6.06; found: C 79.60; H 6.15%.

Methyl 6-benzyl-5-formyl-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (2bb)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98, 7.34–7.13 (m, 10H), 4.85 (s, 1H), 4.03–3.99 (d, J = 14.8 Hz, 1H), 3.95–3.91 (d, J = 14.8 Hz, 1H), 3.59 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.8, 166.5, 164.3, 144.1, 135.5, 128.7, 128.4, 128.1, 128.1, 127.2, 126.7, 118.4, 108.8, 51.4, 35.2, 34.7, 18.3. IR (neat, cm^{-1}): 3427, 1714, 1699, 1161, 1087, 700. Anal. calc. for $C_{22}H_{20}O_4$: C 75.84; H 5.79; found: C 75.80; H 5.71%.

2-(4-Methoxybenzyl)-5-acetyl-6-methyl-4-phenyl-4*H*-pyran-3-carbaldehyde (2ca)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.99 (s, 1H), 7.26–7.19 (m, 4H), 7.18–7.15 (dd, J = 4.0, 8.4 Hz, 1H), 7.13–7.11 (d, J = 8.8 Hz, 2H), 6.86–6.84 (d, J = 8.8 Hz, 2H), 4.84 (s, 1H), 3.97–3.93 (d, J = 14.8 Hz, 1H), 3.85–3.81 (d, J = 14.8 Hz, 1H), 3.79 (s, 3H), 2.32 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 187.8, 164.8, 158.8, 157.2, 143.4, 129.4, 128.6, 128.3, 127.3, 127.0, 118.6, 115.8, 114.3, 55.2, 35.9, 34.0, 29.6, 18.7. IR (neat, cm^{-1}): 3420,

2928, 1660, 1249, 1158, 700. Anal. calc. for $C_{23}H_{22}O_4$: C 76.22; H 6.12; found: C 76.28; H 6.18%.

Methyl 6-(4-methoxybenzyl)-5-formyl-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (2cb)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 7.24–7.22 (d, J = 6.0 Hz, 4H), 7.15–7.14 (d, J = 8.4 Hz, 3H), 6.86–6.84 (d, J = 8.4 Hz, 2H), 4.83 (s, 1H), 3.97–3.93 (m, 2H), 3.78 (s, 3H), 3.61 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.8, 166.6, 164.8, 158.8, 158.6, 144.2, 129.4, 128.2, 128.1, 127.4, 126.6, 118.2, 114.2, 108.8, 55.2, 51.4, 35.2, 33.9, 18.4. IR (neat, cm^{-1}): 3410, 2951, 1714, 1669, 1246, 1158, 1036, 732. Anal. calc. for $C_{23}H_{22}O_5$: C 73.00; H 5.86; found: C 73.07; H 5.79%.

2-(4-Bromobenzyl)-5-acetyl-6-methyl-4-phenyl-4*H*-pyran-3-carbaldehyde (2da)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.96 (s, 1H), 7.46–7.43 (d, J = 8.4 Hz, 2H), 7.27–7.24 (m, 5H), 7.09–7.07 (d, J = 8.0 Hz, 2H), 4.84 (s, 1H), 3.97–3.94 (d, J = 15.2 Hz, 1H), 3.88–3.84 (d, J = 15.2 Hz, 1H), 2.31 (s, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.7, 187.6, 163.6, 157.1, 143.2, 134.4, 131.9, 130.1, 128.6, 128.2, 127.2, 121.3, 118.9, 115.8, 35.9, 34.2, 29.6, 18.7. IR (neat, cm^{-1}): 3407, 2925, 1661, 1160, 1020, 800. Anal. calc. for $C_{22}H_{19}BrO_3$: C 64.25; H 4.66; found: C 64.28; H 4.58%.

Methyl 6-(4-bromobenzyl)-5-formyl-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (2db)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.95 (s, 1H), 7.47–7.44 (d, J = 8.4 Hz, 2H), 7.25–7.21 (m, 5H), 7.12–7.10 (d, J = 8.4 Hz, 2H), 4.84 (s, 1H), 3.99–3.89 (m, 2H), 3.62 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.7, 166.5, 163.5, 158.5, 144.0, 134.5, 131.9, 130.2, 128.2, 128.1, 126.8, 121.3, 118.7, 108.9, 51.5, 35.4, 34.2, 18.4. IR (neat, cm^{-1}): 3430, 2949, 1714, 1670, 1161, 1080, 733. Anal. calc. for $C_{22}H_{19}BrO_4$: C 61.84; H 4.48; found: C 64.75; H 4.41%.

5-Acetyl-2-butyl-6-methyl-4-phenyl-4*H*-pyran-3-carbaldehyde (2ea)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.83 (s, 1H), 7.26–7.17 (m, 5H), 4.80 (s, 1H), 2.69–2.58 (m, 2H), 2.39 (s, 3H), 2.14 (s, 3H), 1.66–1.60 (m, 2H), 1.39–1.34 (m, 2H), 0.94–0.91 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.0, 187.8, 167.1, 157.2, 143.6, 128.6, 128.2, 126.9, 118.3, 115.8, 35.8, 29.9, 29.6, 28.6, 22.1, 18.8, 13.7. IR (neat, cm^{-1}): 3407, 2929, 1661, 1176, 1030, 747. Anal. calc. for $C_{19}H_{22}O_3$: C 76.48; H 7.43; found: C 76.59; H 7.49%.

Methyl 6-butyl-5-formyl-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (2eb)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.83 (s, 1H), 7.26–7.13 (m, 5H), 4.79 (s, 1H), 3.63 (s, 3H), 2.70–2.65 (m, 2H), 2.42 (s, 3H), 1.70–1.63 (m, 2H), 1.43–1.36 (m, 2H), 0.96–0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.8, 167.1, 166.8, 158.5, 144.4, 128.1, 128.1, 126.6, 118.9, 51.5, 35.1, 29.9, 28.5, 22.1, 18.4, 13.7. IR (neat, cm^{-1}): 3399, 2956, 1715, 1669, 1175, 1039, 698. Anal. calc. for $C_{19}H_{22}O_3$: C 76.48; H 7.43; found: C 76.58; H 7.36%.

5-Acetyl-2,6-dimethyl-4-phenyl-4*H*-pyran-3-carbaldehyde (2fa)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.83 (s, 1H), 7.27–7.16 (m, 5H), 4.79 (s, 1H), 2.39 (s, 3H), 2.29 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.1, 188.1, 163.3, 157.1, 143.5, 128.6, 128.3, 127.0, 118.3, 115.8, 35.8, 29.6, 18.9, 15.4. IR (neat, cm^{-1}): 3433, 2925, 1660, 1194, 1022, 700. Anal. calc. for $C_{16}H_{16}O_3$: C 74.98; H 6.29; found: C 74.88; H 6.37%.

Methyl 5-formyl-2,6-dimethyl-4-phenyl-4*H*-pyran-3-carboxylate (2fb)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.82 (s, 1H), 7.26–7.12 (m, 5H), 4.79 (s, 1H), 3.62 (s, 3H), 2.42 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.1, 166.7, 163.3, 158.3, 144.3, 128.1, 126.6, 117.9, 108.9, 51.4, 35.1, 18.5, 15.3. IR (neat, cm^{-1}): 3416, 2925, 1714, 1670, 1192, 1021, 699. Anal. calc. for $C_{16}H_{16}O_4$: C 70.57; H 5.92; found: C 70.68; H 5.84%.

5-Acety-2-benzyl-6-methyl-4-phenyl-4*H*-pyran-3-benzaldehyde (2ga)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.46 (m, 3H), 7.34–7.30 (t, J = 7.6 Hz, 2H), 7.24–7.05 (m, 10 H), 4.92 (s, 1H), 3.42–3.29 (m, 2H), 2.30 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 197.2, 158.2, 150.6, 143.3, 138.4, 136.4, 132.9, 128.9, 128.7, 128.6, 128.4, 127.7, 127.2, 126.7, 117.2, 113.8, 41.9, 37.1, 29.6, 19.1. IR (neat, cm^{-1}): 3397. 2961, 1693, 1598, 1209, 1026, 699. Anal. calc. for $C_{28}H_{24}O_3$: C 82.33; H 5.92; found: C 82.27; H 5.88%.

Methyl 6-benzyl-5-benzoyl-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (2gb)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.58 (d, J = 8.4 Hz, 2H), 7.48–7.46 (d, J = 7.6 Hz, 1H), 7.36–7.32 (m, 2H), 7.25–7.07 (m, 10H), 4.86 (s, 1H), 3.55 (s, 3H), 3.49–3.38 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 167.1, 159.7, 151.1, 143.9, 138.1, 136.6, 132.8, 128.8, 128.6, 128.5, 128.4, 128.3, 127.7, 126.8, 126.6, 117.1, 106.5, 51.3, 41.1, 37.0, 18.7. IR (neat, cm^{-1}): 3400, 3028, 1714, 1164, 1088, 698. Anal. calc. for $C_{23}H_{24}O_4$: C 79.22; H 5.70; found: C 79.16; H 5.66%.

5-Acetyl-2-benzyl-6-methyl-4-phenyl-4*H*-pyran-3-(4-methybenzaldehyde) (2ha)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.45 (d, J = 8.0 Hz, 2H), 7.25–7.18 (m, 6H), 7.15–7.05 (m, 6H), 4.91 (s, 1H), 3.43–3.28 (m, 2H), 2.35 (s, 3H), 2.29 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 196.8, 158.3, 149.9, 143.9, 143.3, 136.5, 135.7, 129.3, 129.0, 128.8, 128.6, 128.3, 127.7, 127.1, 126.6, 117.2, 113.7, 41.9, 37.1, 29.6, 21.6, 19.1. IR (neat, cm^{-1}): 3434, 2924, 1602, 1209, 1171, 1133, 737. Anal. calc. for $C_{29}H_{26}O_3$: C 82.44; H 6.20; found: C 82.38; H 6.14%.

Methyl 6-benzyl-5-(4-methybenzoyl)-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (2hb)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.51 (d, J = 8.0 Hz, 2H), 7.24–7.08 (m, 12H), 4.85 (s, 1H), 3.55 (s, 3H), 3.49–3.36 (m, 2H), 2.35 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 167.2, 159.8, 150.4, 143.9, 143.8, 136.7, 135.5, 129.2, 129.1, 128.7, 128.4, 128.3, 127.7, 126.9, 126.6, 117.2, 106.4, 51.2, 41.2, 37.0, 21.6, 18.7.

IR (neat, cm^{-1}): 3409, 2981, 1685, 1179, 1044, 758. Anal. calc. for $C_{29}H_{26}O_4$: C 79.43; H 5.98; found: C 79.49; H 5.91%.

5-Acetyl-2-benzyl-6-methyl-4-phenyl-4*H*-pyran-3-propionaldehyde (2ia)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.18 (m, 10H), 4.85 (s, 1H), 4.03–3.92 (m, 2H), 2.60–2.53 (m, 2H), 2.45–2.39 (m, 3H), 2.22–2.21 (d, J = 7.2 Hz, 3H), 0.98–0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.1, 198.0, 157.1, 156.0, 144.1, 137.0, 128.9, 128.8, 128.7, 128.5, 128.0, 127.1, 126.7, 117.2, 39.2, 37.1, 34.8, 30.6, 19.4, 7.9. IR (neat, cm^{-1}): 3432, 2927, 1689, 1597, 1183, 1027, 701. Anal. calc. for $C_{24}H_{24}O_3$: C 79.97; H 6.71; found: C 79.90; H 6.80%.

Methyl 6-benzyl-5-propionyl-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (2ib)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.17 (m, 10H), 4.81 (s, 1H), 4.07–3.98 (m, 2H), 3.67 (s, 3H), 2.65–2.55 (m, 1H), 2.42–2.32 (m, 1H), 2.25 (s, 3H), 0.97–0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.9, 167.1, 158.7, 156.9, 144.4, 137.3, 128.9, 128.6, 128.4, 128.1, 127.0, 126.6, 116.2, 108.3, 51.4, 38.9, 37.0, 34.4, 18.8, 7.85. IR (neat, cm^{-1}): 3406, 2942, 1697, 1603, 1186, 1076, 701. Anal. calc. for $C_{24}H_{24}O_4$: C 76.57; H 6.43; found: C 76.66; H 6.50%.

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References

1 S. Hatakeyama, N. Ochi, H. Numata and S. Takano, *J. Chem. Soc., Chem. Commun.*, 1988, 1202.
2 R. González, N. Martín, C. Seoane, J. L. Marco, A. Albert and F. H. Cano, *Tetrahedron Lett.*, 1992, **33**, 3809.
3 K. Urbahns, E. Horváth, J.-P. Stasch and F. Mauler, *Bioorg. Med. Chem. Lett.*, 2003, **13**, 2637.
4 (*a*) B. S. Jensen, D. Strobaek, S. P. Olesen and P. Christophersen, *Curr. Drug Targets*, 2001, **2**, 401; (*b*) R. Kohler, H. Wulff, I. Eichler, M. Kneifel, D. Neumann, A. Knorr, I. Grgic, D. Kampfe, H. Si, J. Wibawa, R. Real, K. Borner, S. Brakemeier, H. D. Orzechowski, H. P. Reusch, M. Paul, K. G. Chandy and J. Hoyer, *Circulation*, 2003, **108**, 1119.
5 (*a*) A. John, P. J. P. Yadav and S. Palaniappan, *J. Mol. Catal. A: Chem.*, 2006, **248**, 121; (*b*) G. I. Shakibaei, P. Mirzaei and A. Bazgir, *Appl. Catal., A*, 2007, **325**, 188; (*c*) Z. Ye, R. Xu, X. Shao, X. Xu and Z. Li, *Tetrahedron Lett.*, 2010, **51**, 4991; (*d*) M. Bayat, N. Z. Shiraz and S. S. Asayesh, *J. Heterocycl. Chem.*, 2010, **47**, 857.
6 X. Yu, H. Ren, Y. Xiao and J. Zhang, *Chem.–Eur. J.*, 2008, **14**, 8481.
7 Y. Xiao and J. Zhang, *Chem. Commun.*, 2009, 3594.
8 (*a*) E. V. Dehmlow, S. S. Dehmlow, *Phase Transfer Catalysis*, VCH, Weinheim, Germany, 3rd edn, 1993; (*b*) C. M. Starks, C. L. Liotta, M. Halpern, *Phase-Transfer Catalysis*, Chapman & Hall, New York, 1994; (*c*) *Handbook of Phase-Transfer Catalysis*, ed. Y. Sasson and R. Neumann, Blackie Academic & Professional, London, 1997; (*d*) Phase-Transfer Catalysis, ed. M. E. Halpern, *ACS Symp. Ser. 659*, American Chemical Society, Washington, DC, 1997; (*e*) T. Hashimoto and K. Maruoka, *Chem. Rev.*, 2007, **107**, 5656.
9 J. Hu, L.-Y. Wu, X.-C. Wang, Y.-Y. Hu, Y.-N. Niu, X.-Y. Liu, S. Yang and Y.-M. Liang, *Adv. Synth. Catal.*, 2010, **352**, 351.