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Synthesis of 3,4-dihydro-2*H*-pyrans by hetero-Diels–Alder reactions of functionalized α,β-unsaturated carbonyl compounds with *N*-vinyl-2-oxazolidinone

Aleksandra Pałasz*

Department of Organic Chemistry, Jagiellonian University, Ingardena 3, Pl-30060 Kraków, Poland. E-mail: palasz@chemia.uj.edu.pl

Received 24th March 2005, Accepted 13th July 2005
First published as an Advance Article on the web 29th July 2005

Cycloadditions of 3-aryl-2-benzoyl-2-propenenitriles **1a–d** and 3-phenylsulfonyl-3-buten-2-one **1e** to *N*-vinyl-2-oxazolidinone **2** proceed regio- and diastereoselectively yielding *cis* and *trans* diastereoisomers of 4-aryl-3,4-dihydro-2-(2-oxo-3-oxazolidinyl)-2*H*-pyrans **3a–e** in 37–65% yield. Cycloadducts *cis*-**3** were the major products. Reaction of 5-arylidene-1,3-dimethylbarbituric acids **4a–c** with dienophile **2** afforded mixtures of 2*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*)-diones *trans* **5a–c** and products **6a–c** resulted from an elimination of 2-oxazolidinone, in 50–52% yield. To confirm the experimental results, semiempirical AM1 and PM3 calculations of frontier orbital energies have been performed.

Introduction

Hetero-Diels–Alder reactions of α,β-unsaturated carbonyl compounds containing a 1-oxa-1,3-butadiene system with electron-rich olefins lead to 3,4-dihydro-2*H*-pyran derivatives which are valuable precursors for the synthesis of many natural products such as carbohydrates, alkaloids and antibiotics.[1–10] These reactions have been classified as cycloadditions with inverse electron demand.[11] The reactivity of α,β-unsaturated carbonyl compounds in hetero-Diels–Alder reactions is generally low and the reactions require high temperature[12–13] or high pressure.[14–15] The reactivity can be enhanced by introducing electron-withdrawing substituents into the 1-oxa-1,3-butadiene system.[16–19] Aza-substituted dienophiles have been used more rarely than their oxygenated counterparts so far. Electron-rich enamines were used in inverse electron demand [4 + 2] cycloaddition[20–24] but none reported the use of weaker dienophiles such as enamides or enecarbamates. The first example of using *N*-vinyl-2-oxazolidinone as the dienophile in inverse electron demand heterocycloaddition was recently described.[25] Also the first examples of such heterocycloadditions of allenamides and allenimides were examined.[26–27] Recently, we have reported that Diels–Alder reactions of some 3-cyano-1-oxa-1,3-butadienes with enol ethers[28] or styrenes[29] lead efficiently to 2-alkoxy-3,4-dihydro-2*H*-pyran-5-carbonitriles. Also, we have examined the influence of cyano, carbonyl, ethoxycarbonyl groups[30] or sulfur containing substituents[31] at C-3 in 1-oxa-1,3-butadienes on the intramolecular hetero-Diels–Alder reaction. The efficiency of these cycloadditions prompted me to extend these reactions to cycloadditions with enecarbamate.

Results and discussion

3-Aryl-2-benzoyl-2-propenenitriles **1a–d**, 3-sulfur substituted-3-buten-2-ones **1e–g** and 5-arylidene-1,3-dimethylbarbituric acids **4a–c** were used in experiments as heterodienes. The aim of the studies was to investigate the reactivity of *N*-vinyl-2-oxazolidinone **2** as a dienophile component in hetero-Diels–Alder reactions, and to determine the influence of a large 2-oxazolidinone group on the diastereoselectivity of cycloadditions. Also the influence of phenyl, 4-nitrophenyl or 4-methoxyphenyl groups present in enones on diastereoselectivity and yields of products was compared. Compounds **1a–d**[28,32] and **1e–g**[33–35] were obtained according to the methods described in literature. They exist mainly as *E* isomers with *s*-*Z* conformation, which is suitable for Diels–Alder cycloaddition.[28] The reactions of heterodienes **1a–g** with dienophile **2** were performed in boiling toluene and afforded mixtures of the *cis* **3a–e** and *trans* **3a–e** diastereoisomers (Scheme 1).

The diastereoisomers could be separated only partially by column chromatography. I managed to isolated all pure *cis* **3a–e** compounds but only two pure *trans* diastereoisomers **3d** and **3e**. In contrast to sulfone **1e**, sulfides **1f** and **1g** were inert.

According to the literature,[2] in hetero-Diels–Alder reactions, the *cis*-product can be formed either by an *endo-E-syn* or *exo-Z-syn* orientation, whereas the *trans*-product is obtained either by an *exo-E-anti* or an *endo-Z-anti* transition structure. For these reactions the high *endo*/*exo* selectivity was observed. The *cis* **3a–e** diastereoisomers resulted from interaction in the transition state of the *E*-isomer of heterodienes **1a–e** and *endo* orientation of the dienophile were the main products in all cases (Table 1). These results are in agreement with findings described by Dujardin *et al.*[25] They first used *N*-vinyl-2-oxazolidinone as the dienophile in inverse electron demand heterocycloaddition and for the *E* isomer of aryl-substituted benzylidene pyruvates, *cis* cycloadducts were obtained as the major products. This means that *N*-vinyl-2-oxazolidinone is *endo*-selective in these reactions.

Next, the reactions of 5-arylidene-1,3-dimethylbarbituric acids **4a–c** with dienophile **2** (Scheme 2) were investigated. Heterodienes **5a–c** were obtained according to the general reaction protocol described in the literature.[36]

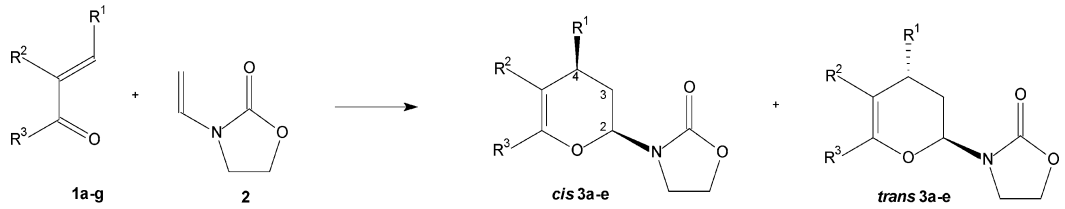
The cycloadditions were conducted in boiling toluene and were completed within 3–5 hours providing mixtures of the *trans* diastereoisomer of 2*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*)-diones **5a–c**, and compounds **6a–c** resulted from an elimination of 2-oxazolidinone. The ratios of compounds **5**/**6** were determined on the basis of ^{1}H NMR spectra of crude products.

Table 1 Synthesis of dihydropyrans **3a–e**

Diene	Products	Reaction time/h	Yield[a] (%)	Ratio of *cis*/*trans*[b]
1a	**3a**	14	59	20 : 1
1b	**3b**	10	61	>100 : 1
1c	**3c**	17	57	20 : 1
1d	**3d**	8	65	10 : 1
1e	**3e**	32	41	9 : 1

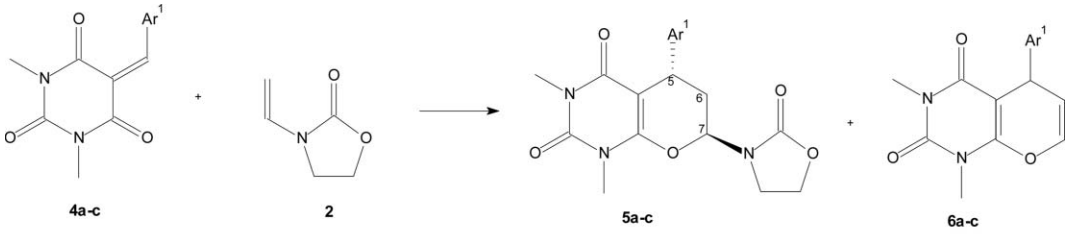
[a] Isolated yields after column chromatography. [b] Ratio based on ^{1}H NMR (500 MHz) spectra of crude products.

DOI: 10.1039/b504210k



1	3	R^1	R^2	R^3
1a	3a	C_6H_5	CN	C_6H_5
1b	3b	p-NO_2- C_6H_4	CN	C_6H_5
1c	3c	p-CH_3O- C_6H_4	CN	C_6H_5
1d	3d	p-NC- C_6H_4	CN	C_6H_5
1e	3e	p-NO_2- C_6H_4	$PhSO_2$	CH_3
1f	-	p-NO_2- C_6H_4	PhS	CH_3
1g	-	CH_3CONH	PhS	CH_3

Scheme 1



4	5/6	Ar^1
4a	5a/6a	C_6H_5
4b	5b/6b	p-NO_2-C_6H_4
4c	5c/6c	p-CH_3O-C_6H_4

Scheme 2

Compounds **5** and **6** were separated by column chromatography and purified further by crystallization (Table 2). All pure *trans* **5a–c** diastereoisomers and products **6a**, **6c** were isolated.

Interestingly **5/6** ratios are dependent on the nature of Ar^1 aryl substituents in the heterodiene. For the most reactive heterodiene **4b** (Ar^1 = p-NO_2–C_6H_4) the reaction regioselectivity was the highest and the cycloadduct **5b** was obtained as a major product. In contrast, reactions of less reactive heterodienes **4a** (Ar^1 = C_6H_5) and **4c** (Ar^1 = p–CH_3O–C_6H_4) afford equimolar mixtures of compounds **5/6** (Table 2).

Cycloadducts **3**, **5**, **6** were characterized by ^1H, ^{13}C NMR, IR, and mass spectra. The relative *cis* and *trans* configurations of 2*H*-dihydropyrans *cis* **3a–e**, *trans* **3d–e** and *trans* **5a–c** were assigned on the basis of ^1H NMR spectra. For compounds **3** the configurations were deducted from the chemical shift values and coupling constants of protons attached to C-2 and C-4 of the dihydropyran ring that exists in a half-chair conformation[37] (Table 3).

The ^1H NMR spectra of *cis* **3a–e** and *trans* **3d–e** reveal the signals of proton 2-H as a doublet of doublets at δ = 5.42–5.96 ppm with large and small coupling constants (^3J = 11.0–12.0 and 1.5–2.5 Hz) due to coupling with the axial and equatorial protons at 3-H. Thus, the hemiaminalic proton at C-2 obviously adopts the axial position, and the large oxazolidinyl moiety occupies the equatorial position (Fig. 1).

Table 2 Synthesis of dihydropyrans **5a–c** and **6a–c**

Diene	Products	Reaction time/h	Yield[a] (%)	Ratio of **5/6**[b]
4a	**5a/6a**	4	50	1 : 0.8
4b	**5b/6b**	3	52	7 : 1
4c	**5c/6c**	5	50	1 : 1.5

[a] Isolated yields after column chromatography. [b] Ratio based on ^1H NMR (500 MHz) spectra of crude products.

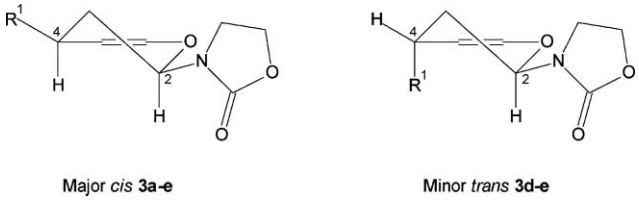


Fig. 1 Preferred *cis*/*trans* configurations of cycloadducts **3a–e** based on ^1H NMR analysis.

In the ^1H NMR spectra of *cis* **3a–e** the signal of 4-H appeared as a doublet of doublets at δ = 3.97–4.30 ppm with the coupling constants ^3J = 11.5–12.0 and 6.0–7.5 Hz, due to coupling with two protons at C-3 (Table 3). In the spectrum of *cis* **3e** the signal of 4-H is as a doublet of doublets of doublets due to the coupling

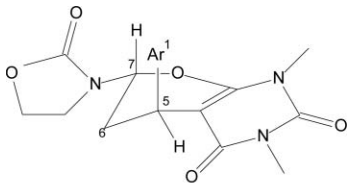
Table 3 Signals of proton 2-H and 4-H (or 7-H and 5-H) in ^{1}H NMR spectra of dihydropyrans **3a–e**, **5a–c**

Compound	dd 2-H δ(ppm) $J_{3ax,2}/J_{3eq,2}$ (Hz)	dd 4-H δ(ppm) $J_{3ax,4}/J_{3eq,4}$(Hz)
cis-**3a**	5.93 11.5/1.5	4.01 11.8/6.3
cis-**3b**	5.96 11.0/1.5	4.17 12.0/6.5
cis-**3c**	5.91 11.0/1.5	3.97 11.5/6.0
cis-**3d**	5.94 11.3/2.0	4.11 11.5/6.5
trans-**3d**	5.57 11.5/2.0	4.14 5.5/1.5
cis-**3e**	5.59 11.5/1.5	ddd 4.30 11.5/7.5, $J_{6\text{-}CH3,4}$ 1.5
trans-**3e**	5.42 12.0/2.5	4.45 5.5/2.0
	dd 7-H $J_{6ax,7}/J_{6eq,7}$	dd 5-H $J_{6ax,5}/J_{6eq,5}$
trans-**5a**	5.64 11.8/1.5	4.23 5.5/2.0
trans-**5b**	5.65 11.8/2.0	4.35 6.5/2.0
trans-**5c**	5.42 12.0/2.0	4.11 5.5/2.0

of 4-H with the protons of the methyl group at position C-6 (δ = 2.39 ppm, d, $J_{4,6\text{-}CH3}$ 1.5 Hz). Thus, 4-H occupies a *pseudo*-axial position, and the aryl groups Ar^1 adopt a *pseudo*-equatorial orientation (Fig. 1). Minor *trans* isomers **3d–e** exhibit a *pseudo*-axial position of the aryl group Ar^1 attested by the small ^3J value of proton 4-H with protons 3-H ($J_{3ax,4}$ = 5.5 Hz and $J_{3eq,4}$ = 1.5–2.0 Hz) (Fig. 1).

The assignment of the 5,7-*trans* configuration to adducts **5a–c** was based also on the common features displayed by the ^{1}H NMR spectra. The signal of proton 5-H is a doublet of doublets at δ = 4.11–4.35 ppm with the coupling constants ^3J = 5.5–6.5 and 2.0 Hz (Table 3), hence 5-H must be *pseudo*-equatorial, and the aryl group Ar^1 is in the *pseudo*-axial position (Fig. 2). Proton 7-H of *trans* cycloadducts **5a–c** resonates as a doublet of doublets at δ = 5.42–5.65 ppm with large and small coupling constants ^3J = 11.8–12.0 and 1.5–2.0 Hz. Thus, proton 7-H must be axial, and the oxazolidinyl moiety occupies the equatorial position (Fig. 2).

In order to confirm the experimental results, frontier orbital (HOMO and LUMO) energies of heterodienes **1a–g**, **4a–c** and dienophile **2** were calculated by semiempirical AM1 and PM3 methods using the Hyper Chem 7.51 suite of programs. The calculated frontier orbital energies are listed in Table 4.



trans **5a-c**

Fig. 2 Preferred *trans* configuration of cycloadducts **5a–c** based on ^{1}H NMR analysis.

The given values always represent the *E* configuration heterodiene. In hetero-Diels–Alder reactions with inverse electron demand, the HOMO orbital of the dienophile overlaps with the LUMO orbital of the heterodiene so energy differences E_{LUMO}(**H**) − E_{HOMO}(**2**) were discussed. The obtained results are in agreement with observations concerning the influences of electron withdrawing and electron releasing substituents on

Table 4 Energies of HOMO and LUMO orbitals of heterodienes **1a–g**, **4a–c** and *N*-vinyl-2-oxazolidinone **2**

Heterodiene **H**	Method	E_{HOMO}/eV	E_{LUMO}/eV	E_{LUMO}(**H**) − E_{HOMO}(**2**)
1a	AM1	−9.619	−1.050	8.249
	PM3	−9.740	−0.816	8.597
1b	AM1	−10.208	−1.813	7.487
	PM3	−10.254	−1.936	7.477
1c	AM1	−9.133	−1.007	8.293
	PM3	−9.236	−0.949	8.464
1d	AM1	−9.930	−1.462	7.838
	PM3	−10.051	−1.317	8.096
1e	AM1	−10.379	−1.843	7.464
	PM3	−10.429	−1.464	7.948
1f	AM1	−8.646	−0.648	8.649
	PM3	−9.215	−0.712	8.701
1g	AM1	−8.138	−0.569	8.730
	PM3	−8.635	−0.534	8.879
2	AM1	−9.299	0.872	—
	PM3	−9.413	0.631	—
4a	AM1	−9.767	−1.202	8.098
	PM3	−9.774	−1.324	8.089
4b	AM1	−10.582	−1.855	7.445
	PM3	−10.478	−1.543	7.870
4c	AM1	−9.208	−1.228	8.072
	PM3	−9.313	−1.065	8.348

LUMO energy in 1-oxa-1,3-dienes. As expected the nitro and cyano groups as strong electron withdrawing groups decrease the energy of the LUMO and the energy differences $E_{LUMO}(\mathbf{H}) - E_{HOMO}(\mathbf{2})$ are smaller for compounds **1b** and **1d** than for **1a** and **1c**. The same conclusions apply to heterodienes **4a–c**. The semiempirical calculations explained also the inertness of heterodienes **1f–g**. For these compounds, energy differences $E_{LUMO}(\mathbf{H}) - E_{HOMO}(\mathbf{2})$ are the highest, so they are unreactive.

In summary, the present results indicate that *N*-vinyl-2-oxazolidinone **2** can act as a valuable dienophile in inverse electron demand heterocycloaddition. This compound was found to be less reactive than enol ethers because similar reactions of dienes **1a–c** with enol ethers occurred at room temperature[28] whereas reactions with **2** required heating in boiling toluene. The presence of electron withdrawing groups (*p*-cyanophenyl, *p*-nitrophenyl) in the dienophile **1b**, **1d**, **1e**, **4b** increases the rate and the yield of these reactions. Interestingly, also, the diastereoselectivity of the cycloaddition was highest for these compounds.

Experimental

Melting points were determined on a Boetius hot stage apparatus. IR spectra: Bruker IFS 48 in KBr pellets. NMR spectra: Bruker AMX 500 (^{1}H: 500.14 MHz, ^{13}C: 125.76 MHz) in $CDCl_3$, DMSO with TMS as an internal standard. ^{13}C signal assignments were confirmed by XHCORR and DEPT methods. Mass spectra: Finningan Mat 95 (70 eV). Microanalyses were performed with a Euro EA 3000 Elemental Analyzer.

3-Aryl-2-benzoyl-2-propenenitriles **1a–d** were obtained according to a procedure reported in refs. 28 and 32. Sulfones and sulfides **1e–g** were prepared by a procedure described in refs. 33–35: 3-phenylsulfonyl-4-(4-nitrophenyl)-3-buten-2-one **1e**,[33] 3-phenylsulfenyl-4-(4-nitrophenyl)-3-buten-2-one **1f**,[34] 4-acetylamino-3-phenylsulfenyl-3-buten-2-one **1g**.[35] *N*-Vinyl-2-oxazolidinone **2** was synthesized according to a procedure described in the literature.[25] The general method of preparation of 5-arylidene-1,3-dimethylbarbituric acids **4a–c** is described in the literature.[36]

General preparation of hetero-adducts 3a–e, 5a–c, 6a–c

A solution of the α,β-unsaturated carbonyl compounds **1a–e**, **4a–c** (2 mmol) in anhydrous toluene (10 ml) and *N*-vinyl-2-oxazolidinone **2** (2 mmol) was refluxed for the time given in Tables 1–2. The progress of the reactions was monitored by TLC. The solvent was evaporated and the mixture was separated and purified by column chromatography on silica gel using chloroform or *tert*-butyl-methyl ether as an eluent. Recrystallization from the appropriate solvent gave **3a–e**, **5a–c**, **6a–c** with yields listed in Tables 1–2.

(2*RS*,4*SR*)-3,4-Dihydro-2-(2-oxo-3-oxazolidinyl)-4,6-diphenyl-2*H*-pyran-5-carbonitrile *cis*-3a. (408 mg, 59%) colourless crystals, mp 179 °C (ethanol); (Found: C, 72.9; H, 5.2; N, 8.2. $C_{21}H_{18}N_2O_3$ requires C, 72.8; H, 5.2; N, 8.1%); ν_{max}(KBr disk)/cm^{-1} 3027, 2923, 2962, 2883 (CH), 2200 (CN), 1767 (CO), 1611 (C=C); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.10 (1H, dt, *J* 11.8, 13.5, 3-H$_{ax}$), 2.41 (1H, ddd, *J* 1.5, 6.3, 13.5, 3-H$_{eq}$), 3.58 (1H, dt *J* 8.8, 5.3, 4′B-H), 3.74 (1H, q, *J* 8.5, 4′A-H), 4.01 (1H, dd, *J* 11.8, 6.3, 4-H), 4.39 (1H, q, *J* 8.5, 5′B-H), 4.42 (1H, ddd, *J* 8.8, 8.5, 5.5, 5′A-H), 5.93 (1H, dd, *J* 11.5, 1.5, 2-H) and 7.33–7.79 (10H, m, Ph); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 35.5 (C-3), 39.8 (C-4), 41.8 (C-4′), 62.5 (C-5′), 81.9 (C-5), 88.6 (C-2), 118.7 (CN), 127.5, 128.0, 128.4, 129.2, 131.3, 132.2, 140.3 (ArC), 157.4 (C-6) and 165.5 (C-2′); *m*/*z*(EI) 346 (M$^+$, 13%), 328 (11), 259 (20), 233 (21), 113 (100), 105 (59) and 77 (38).

(2*RS*,4*SR*)-3,4-Dihydro-4-(4-nitrophenyl)-2-(2-oxo-3-oxazolidinyl)-6-phenyl-2*H*-pyran-5-carbonitrile *cis*-3b. (477 mg, 61%) colourless crystals, mp 201 °C (ethanol); (Found: C, 64.5; H, 4.3; N, 10.7. $C_{21}H_{17}N_3O_5$ requires C, 64.5; H, 4.4; N, 10.7%); ν_{max}(KBr disk)/cm^{-1} 3056, 2923, 2854 (CH), 2203 (CN), 1760 (CO), 1611 (C=C), 1522, 1350 (NO_2); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.10 (1H, ddd, *J* 11.0, 12.0, 13.3, 3-H$_{ax}$), 2.44 (1H, ddd, *J* 1.5, 6.3, 13.3, 3-H$_{eq}$), 3.61 (1H, dt *J* 8.3, 5.5, 4′B-H), 3.76 (1H, q, *J* 8.5, 4′A-H), 4.17 (1H, dd, *J* 12.0, 6.5, 4-H), 4.40 (1H, q, *J* 8.5, 5′B-H), 4.44 (1H, dt, *J* 8.5, 5.5, 5′A-H), 5.96 (1H, dd, *J* 11.0, *J* 1.5, 2-H) and 7.43–8.28 (9H, m, ArH); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 34.8 (C-3), 39.8 (C-4), 41.5 (C-4′), 62.6 (C-5′), 81.8 (C-5), 86.8 (C-2), 118.3 (CN), 124.5, 128.4, 128.5, 128.6, 131.7, 131.75, 147.7 (ArC), 157.3 (C-6) and 166.5 (C-2′); *m*/*z*(EI) 391 (M$^+$, 21%), 304 (23), 278 (9), 261 (9), 113 (100), 105 (64) and 77 (35).

(2*RS*,4*SR*)-3,4-Dihydro-4-(4-methoxyphenyl)-2-(2-oxo-3-oxazolidinyl)-6-phenyl-2*H*-pyran-5-carbonitrile *cis*-3c. (440 mg, 57%) colourless crystals, mp 167 °C (ethanol); (Found: C, 70.2; H, 5.3; N, 7.5. $C_{22}H_{20}N_2O_4$ requires C, 70.2; H, 5.4; N, 7.4%); ν_{max}(KBr disk)/cm^{-1} 3066, 2999, 2925, 2843 (CH), 2202 (CN), 1770 (CO), 1603 (C=C), 1522, 1350 (NO_2); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.08 (1H, q, *J* 12.0, 3-H$_{ax}$), 2.37 (1H, ddd, *J* 1.5, 6.3, 13.3, 3-H$_{eq}$), 3.58 (1H, dt *J* 8.3, 5.5, 4′B-H), 3.74 (1H, q, *J* 8.5, 4′A-H), 3.97 (1H, dd, *J* 11.5, 6.0, 4-H), 4.38 (1H, q, *J* 8.5, 5′B-H), 4.42 (1H, dt, *J* 8.5, 5.5, 5′A-H), 5.91 (1H, dd, *J* 11.0, 1.5, 2-H) and 6.93–7.78 (9H, m, ArH); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 35.5 (C-3), 39.8 (C-4), 41.0 (C-4′), 55.3 (OCH_3), 62.5 (C-5′), 81.9 (C-5), 89.0 (C-2), 118.7 (CN), 128.4, 128.5, 131.2, 132.2, 132.3, 157.4 (ArC), 159.3 (C-6) and 165.2 (C-2′); *m*/*z*(EI) 376 (M$^+$, 5%), 358 (10), 289 (13), 263 (70), 113 (7), 105 (100) and 77 (42).

(2*RS*,4*SR*)-4-(4-Cyanophenyl)-3,4-dihydro-2-(2-oxo-3-oxazolidinyl)-6-phenyl-2*H*-pyran-5-carbonitrile *cis*-3d. (436 mg, 59%) colourless crystals, mp 186 °C (*tert*-butyl-methyl ether/ethanol 2 : 1); (Found: C, 71.2; H, 4.5; N, 11.4. $C_{22}H_{17}N_3O_3$ requires C, 71.2; H, 4.6; N, 11.3%); ν_{max}(KBr disk)/cm^{-1} 3056, 2981, 2930 (CH), 2201, 2229 (CN), 1765 (CO), 1609 (C=C); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.08 (1H, q, *J* 12.5, 3-H$_{ax}$), 2.42 (1H, ddd, *J* 2.0, 6.5, 13.5, 3-H$_{eq}$), 3.60 (1H, dt *J* 8.3, 5.5, 4′B-H), 3.74 (1H, q, *J* 8.0, 4′A-H), 4.11 (1H, dd, *J* 11.5, 6.5, 4-H), 4.39 (1H, q, *J* 8.5, 5′B-H), 4.45 (1H, ddd, *J* 8.8, 9.0, 5.0, 5′A-H), 5.94 (1H, dd, *J* 11.3, 2.0, 2-H) and 7.43–7.78 (9H, m, ArH); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 34.9 (C-3), 39.8 (C-4), 41.8 (C-4′), 62.5 (C-5′), 81.8 (C-5), 86.9 (C-2), 118.2 (CN), 118.3 (CN), 128.3, 128.4, 128.5, 131.6, 131.8, 133.0, 145.7 (ArC), 157.3 (C-6) and 166.4 (C-2′); *m*/*z*(EI) 371 (M$^+$, 4%), 284 (22), 258 (35), 113 (36), 105 (100) and 77 (52).

(2*RS*,4*RS*)-4-(4-Cyanophenyl)-3,4-dihydro-2-(2-oxo-3-oxazolidinyl)-6-phenyl-2*H*-pyran-5-carbonitrile *trans*-3d. (44 mg, 6%) colourless crystals, mp 223 °C (*tert*-butyl-methyl ether/ethanol 2 : 1); (Found: C, 71.2; H, 4.5; N, 11.4. $C_{22}H_{17}N_3O_3$ requires C, 71.2; H, 4.6; N, 11.3%); ν_{max}(KBr disk)/cm^{-1} 3054, 2962, 2911 (CH), 2197, 2231 (CN), 1759 (CO), 1609 (C=C); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.16 (1H, ddd, *J* 2.0, 1.5, 13.0, 3-H$_{eq}$), 2.49 (1H, ddd, *J* 11,8, 6.0, 13.5, 3-H$_{ax}$), 3.61 (1H, dt *J* 8.5, 5.0, 4′B-H), 3.72 (1H, q, *J* 8.5, 4′A-H), 4.14 (1H, dd, *J* 5.5, 1.5, 4-H), 4.36 (1H, q, *J* 8.5, 5′B-H), 4.43 (1H, dt, *J* 8.5, 5.0, 5′A-H), 5.57 (1H, dd, *J* 11.5, 2.0, 2-H) and 7.45–7.84 (9H, m, ArH); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 32.6 (C-3), 40.0 (C-4), 40.2 (C-4′), 62.5 (C-5′), 77.6 (C-5), 83.6 (C-2), 118.2 (CN), 118.9 (CN), 128.3, 128.6, 128.8, 131.6, 131.8, 133.1, 146.2 (ArC), 157.2 (C-6) and 166.4 (C-2′); *m*/*z*(EI) 371 (M$^+$, 2%), 326 (100), 286 (4), 113 (18), 105 (16) and 77 (12).

(2*RS*,4*SR*)-3,4-Dihydro-6-methyl-4-(4-nitrophenyl)-2-(2-oxo-3-oxazolidinyl)-5-phenylsulfonyl-2*H*-pyran *cis*-3e. (320 mg, 37%) colourless crystals, mp 225 °C (ethanol); (Found: C, 56.7; H, 4.4; N, 6.4. $C_{21}H_{20}N_2O_7S$ requires C, 56.8; H, 4.5; N, 6.3; S, 7.2%); ν_{max}(KBr disk)/cm^{-1} 3110, 2964, 2850 (CH), 1745 (CO), 1607 (C=C), 1520, 1348 (NO_2), 1299, 1149 (S=O); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.01 (1H, dt, *J* 11.5, 12.0, 3-H$_{ax}$), 2.38 (1H, ddd,

J 1.5, 7.3, 13.0, 3-H_{eq}), 2.39 (3H, d, *J* 1.5, 6-CH_3), 3.52 (1H, dt *J* 8.5, 5.5, 4′B-H), 3.71 (1H, q, *J* 8.5, 4′A-H), 4.30 (1H, ddd, *J* 11.5, 7.5, 1.5, 4-H), 4.36 (1H, q, *J* 8.5, 5′B-H), 4.45 (1H, dt, *J* 8.5, 5.5, 5′A-H), 5.59 (1H, dd, *J* 11.5, 1.5, 2-H) and 7.25–7.97 (9H, m, ArH); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 20.0 (CH_3-6), 37.5 (C-3), 39.6 (C-4), 41.5 (C-4′), 62.2 (C-5′), 80.1 (C-2), 116.1 (C-5), 123.3, 126.3, 128.5, 128.6, 132.4, 142.4, 146.7, 148.9 (ArC), 157.0 (C-6) and 165.4 (C-2′); *m*/*z*(EI) 359 (19%), 326 (100), 304 (23), 278 (9), 261 (9), 113 (100), 105 (64) and 77 (35).

(2*RS*,4*RS*)-3,4-Dihydro-6-methyl-4-(4-nitrophenyl)-2-(2-oxo-3-oxazolidinyl)-5-phenylsulfonyl-2*H*-pyran *trans*-3e. (40 mg, 4.5%) colourless crystals, mp 223 °C (ethanol); (Found: C, 56.7; H, 4.5; N, 6.4. $C_{21}H_{20}N_2O_7S$ requires C, 56.8; H, 4.5; N, 6.3; S, 7.2%); ν_{max}(KBr disk)/cm^{-1} 3073, 2985, 2852 (CH), 1751 (CO), 1617 (C=C), 1522, 1350 (NO_2), 1303, 1150 (S=O); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.00 (1H, dt, *J* 2.0, 13.0, 3-H_{eq}), 2.29 (1H, ddd, *J* 12.0, 5.5, 13.0, 3-H_{ax}), 2.47 (3H, s, 6-CH_3), 3.53 (1H, dt *J* 8.5, 5.5, 4′B-H), 3.65 (1H, q, *J* 8.5, 4′A-H), 4.32 (1H, q, *J* 8.5, 5′B-H), 4.42 (1H, dt, *J* 8.5, 5.5, 5′A-H), 4.45 (1H, dd, *J* 5.5, 2.0, 4-H), 5.42 (1H, dd, *J* 12.0, 2.5, 2-H) and 7.21–8.07 (9H, m, ArH); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 19.1 (CH_3-6), 32.5 (C-3), 38.6 (C-4), 39.5 (C-4′), 62.1 (C-5′), 78.0 (C-2), 112.0 (C-5), 123.6, 126.8, 128.2, 128.5, 128.7, 128.9, 129.4, 132.8, 142.0, 146.8, 148.9 (ArC), 157.0 (C-6) and 164.4 (C-2′); *m*/*z*(EI) 391 (M^+, 21%), 304 (23), 278 (9), 261 (9), 113 (100), 105 (64) and 77 (35).

(5*RS*,7*RS*)-1,5,6,7-Tetrahydro-1,3-dimethyl-7-(2-oxo-3-oxazolidinyl)-5-phenyl-2*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*)-dione *trans*-5a. (180 mg, 25%) colourless crystals, mp 184 °C (*tert*-butyl-methyl ether/ethanol 4 : 1); (Found: C, 60.4; H, 5.3; N, 11.7. $C_{18}H_{19}N_3O_5$ requires C, 60.5; H, 5.4; N, 11.8%); ν_{max}(KBr disk)/cm^{-1} 3059, 2955, 2919 (CH), 1770, 1701, 1642 (CO), 1600 (C=C); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.09 (1H, dt, *J* 2.0, 13.5, 6-H_{eq}), 2.25 (1H, ddd, *J* 12.0, 5.5, 13.5, 6-H_{ax}), 3.23 (3H, s, CH_3), 3.32 (3H, s, CH_3), 3.56 (1H, dt, *J* 8.5, 5.0, 4′B-H), 3.63 (1H, q, *J* 8.5, 4′A-H), 4.23 (1H, dd, *J* 5.5, 2.0, 5-H), 4.28 (1H, q, *J* 8.5, 5′B-H), 4.38 (1H, dt, *J* 8.5, 5.0, 5′A-H), 5.64 (1H, dd, *J* 11.8, 1.5, 7-H) and 7.05–7.34 (5H, m, Ph); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 28.0 (CH_3), 28.8 (CH_3), 33.4 (C-6), 34.6 (C-5), 39.9 (C-4′), 62.4 (C-5′), 80.7 (C-4a), 87.6 (C-7), 127.2, 127.3, 128.9, 142.6 (Ph), 151.1 (C-8a), 155.9 (C-4), 157.0 (C-2) and 162.0 (C-2′); *m*/*z*(EI) 357 (M^+, 49%), 270 (99), 243 (100), 202 (61), 169 (37), 156 (34), 115 (61), 87 (38) and 77 (22).

(5*RS*,7*RS*)-1,5,6,7-Tetrahydro-1,3-dimethyl-5-(4-nitrophenyl)-7-(2-oxo-3-oxazolidinyl)-2*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*)-dione *trans*-5b. (0.42 g, 52%) colourless crystals, mp 225 °C (ethanol); (Found: C, 53.8; H, 4.5; N, 14.0. $C_{18}H_{18}N_4O_7$ requires C, 53.7; H, 4.5; N, 13.9%); ν_{max}(KBr disk)/cm^{-1} 2990, 2951, 2926, 2850 (CH), 1763, 1703, 1636 (CO), 1596 (C=C), 1518, 1346 (NO_2); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.18 (1H, dt, *J* 2.0, 13.5, 6-H_{eq}), 2.44 (1H, ddd, *J* 12.0, 6.5, 14.0, 6-H_{ax}), 3.31 (3H, s, CH_3), 3.41 (3H, s, CH_3), 3.67 (1H, dt *J* 8.5, 5.0, 4′B-H), 3.73 (1H, q, *J* 8.5, 4′A-H), 4.35 (1H, dd, *J* 6.5, 2.0, 5-H), 4.40 (1H, q, *J* 8.5, 5′B-H), 4.50 (1H, dt, *J* 8.8, 5.0, 5′A-H), 5.65 (1H, dd, *J* 11.8, 2.0, 7-H), 7.40 (2H, d, *J* 9.0, ArH) and 8.20 (2H, d, *J* 9.0, ArH); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 27.8 (CH_3), 28.7 (CH_3), 32.7 (C-6), 34.6 (C-5), 39.7 (C-4′), 62.3 (C-5′), 80.3 (C-4a), 86.4 (C-7), 124.0, 128.1, 129.0, 147.0, 149.7 (ArC), 150.6 (C-8a), 156.1 (C-4), 156.3 (C-2) and 161.7 (C-2′); *m*/*z*(EI) 402 (M^+, 5%), 315 (100), 289 (8), 156 (12) and 127 (15).

(5*RS*,7*RS*)-1,5,6,7-Tetrahydro-5-(4-methoxyphenyl)-1,3-dimethyl-7-(2-oxo-3-oxazolidinyl)-2*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*)-dione *trans*-5c. (186 mg, 24%) colourless crystals, mp 179 °C (methanol); (Found: C, 58.9; H, 5.4; N, 10.9. $C_{19}H_{21}N_3O_6$ requires C, 58.9; H, 5.5; N, 10.9%); ν_{max}(KBr disk)/cm^{-1} 3056, 2921, 2852 (CH), 1770, 1698, 1642 (CO), 1583 (C=C); δ_H(500 MHz; $CDCl_3$; Me_4Si) 2.09 (1H, dt, *J* 2.0, 13.5, 6-H_{eq}), 2.36 (1H, ddd, *J* 12.0, 5.5, 13.5, 6-H_{ax}), 3.14 (3H, s, CH_3), 3.26 (3H, s, CH_3), 3.64–3.72 (2H, m, 4′-H), 3.73 (3H, s, OCH_3), 4.11 (1H, dd, *J* 5.5, 2.0, 5-H), 4.33 (1H, q, *J* 8.5, 5′B-H), 4.42 (1H, dt, *J* 8.8, 6.0, 5′A-H), 5.42 (1H, dd, *J* 12.0, 2.0, 7-H), 6.88 (2H, d, *J* 8.5, ArH) and 7.17 (2H, d, *J* 8.5, ArH); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 27.4 (CH_3), 28.3 (CH_3), 32.5 (C-6), 33.0 (C-5), 39.0 (C-4′), 54.9 (OCH_3), 62.7 (C-5′), 80.4 (C-4a), 86.8 (C-7), 113.7, 128.5, 135.3, 150.5 (ArC), 155.8 (C-8a), 156.8 (C-4), 157.8 (C-2) and 161.2 (C-2′); *m*/*z*(EI) 387 (M^+, 3%), 300 (100), 185 (37), 169 (26) and 115 (15).

1,5-Dihydro-1,3-dimethyl-5-phenyl-2*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*)-dione 6a. (135 mg, 25%) yellow crystals, mp 203 °C (ethanol); (Found: C, 66.6; H, 5.2; N, 10.4. $C_{15}H_{14}N_2O_3$ requires C, 66.7; H, 5.2; N, 10.4%); ν_{max}(KBr disk)/cm^{-1} 3082, 2961, 2853 (CH), 1726, 1661 (CO), 1601, 1576 (C=C); δ_H(500 MHz; $CDCl_3$; Me_4Si) 3.38 (6H, s, 1-CH_3, 3-CH_3), 7.41–7.42 (4H, m, ArH), 7.66–7.67 (2H, m, 5-H, ArH), 8.20 (1H, d, *J* 12.0, 7-H) and 8.59 (1H, dd, *J* 14.8, 12.5, 6-H); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 28.0 (CH_3), 28.6 (CH_3), 114.5 (C-5), 125.1, 129.1, 131.5, 135.3, 151.4, 154.2, 157.3 (C-4a, C-6, C-7, C-8a, Ph), 161.6 (C-4) and 162.2 (C-2); *m*/*z*(EI) 270 (M^+, 100%), 184 (15), 156 (19), 115 (11), and 77 (8).

1,5-Dihydro-1,3-dimethyl-5-(4-methoxyphenyl)-2*H*-pyrano[2,3-*d*]pyrimidine-2,4(3*H*)-dione 6c. (156 mg, 26%) yellow crystals, mp 189 °C (ethanol); (Found: C, 63.7; H, 5.4; N, 9.2. $C_{16}H_{16}N_2O_4$ requires C, 64.0; H, 5.4; N, 9.3%); ν_{max}(KBr disk)/cm^{-1} 3077, 2952, 2837 (CH), 1719, 1658 (CO), 1598, 1565 (C=C); δ_H(500 MHz; $CDCl_3$; Me_4Si) 3.365 (3H, s, 1-CH_3), 3.37 (3H, s, 3-CH_3), 3.86 (3H, s, OCH_3), 6.93 (2H, d, *J* 8.5, ArH), 7.38 (1H, d, *J* 15.0, 5-H), 7.62 (2H, d, *J* 8.5, ArH), 8.18 (1H, d, *J* 12.5, 7-H) and 8.47 (1H, dd, *J* 15.3, 12.5, 6-H); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 27.9 (CH_3), 28.6 (CH_3), 55.5 (OCH_3), 113.5 (C-5), 114.7, 123.1, 128.3, 131.3, 151.5, 154.7, 157.9, 161.9 (C-4a, C-6, C-7, C-8a, ArC), 162.5 (C-4) and 162.7 (C-2); *m*/*z*(EI) 300 (M^+, 100%), 228 (11), 185 (27) and 115 (18).

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