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5-Arylidene Derivatives of *Meldrum*'s Acid as Synthons in Pyrano[4,3-*b*]pyran Synthesis

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Summary. The reactions of 5-arylidene derivatives of *Meldrum*'s acid with ethyl vinyl ether or *N*-vinyl-2-oxazolidinone yielded *trans-trans*-(2,4:4,7)-pyrano[4,3-*b*]pyrans, *cis-trans*-(2,4:4,7)-pyrano[4,3-*b*]pyrans, or diastereoisomeric mixtures of pyrano[4,3-*b*]pyrans and reactions with 3,4-dihydro-2*H*-pyran afforded *Michael* adducts. The reactions of 5-arylidene derivatives of *Meldrum*'s acid with cyanoacetic acid derivatives do not provide appropriate pyrans.

Keywords. Pyrans; α,β-Unsaturated ketone; Enol ethers; *Michael* addition.

Introduction

Polyfunctionalized pyran derivatives are common structural subunits in a variety of important natural products, including carbohydrates, alkaloids, polyether antibiotics, pheromones, and iridoids. The inverse-electron-demand hetero-*Diels-Alder* (H*DA*) reactions of α,β-unsaturated carbonyl compounds with electron-rich alkenes give excellent access to substituted 3,4-dihydro-2*H*-pyrans [1–5]. The reactivity of α,β-unsaturated carbonyl compounds can be enhanced by introducing electron-withdrawing substituents [6–10]. Recently, we have reported that H*DA* reactions of 3-cyano-1-oxa-1,3-butadienes with enol ethers [11, 12], styrenes [13], or *N*-vinyl-2-oxazolidinone [14] lead efficiently to 3,4-dihydro-2*H*-pyran-5-carbonitriles.

The same α,β-unsaturated carbonyl compounds can be used as substrates in pyran synthesis by conjugate addition-cyclization with CH-acids like malononitrile or cyanoacetate [15–20]. It has been found that cyano, alkoxycarbonyl, acyl, aryl, or phenylthio substituents in the enone system enabled sequential O-cyclization to the pyran ring. Therefore, the 5-arylidene derivatives of *Meldrum*'s acid seem to be excellent reagents in pyran synthesis both by H*DA* reaction and by conjugate addition-cyclization. There are very few examples in literature describing the H*DA* reactions of 5-ylidene substituted *Meldrum*'s acids with alkenes. *Polansky et al.* have described cycloadditions of two alkylidene (R = isopropyl, *t*-butyl) and one 5-arylidene (Ar=*Ph*) derivatives of *Meldrum*'s acid to ethyl vinyl ether or 1,1-dimethoxyethene [21]. They afford a mixture of *cis*/*trans* diastereoisomers of pyrano[2,3-*d*][1,3]dioxin-4(5*H*)-ones, but pure diastereoisomers have not been separated from byproducts. *Tietze et al.* have used 5-ylidene derivatives of *Meldrum*'s acid, possessing alkene substituents, in an intramolecular H*DA* reaction [22, 23].

Results and Discussion

The first aim of this work was to investigate reactions of 5-arylidene *Meldrum*'s acids with different alkenes possessing electron-donating groups: enol ethers, *N*-vinyl-2-oxazolidinone, and *p*-substituted styrene derivatives. We wanted to compare the reactivity of the above-mentioned compounds towards these former derivatives. The second aim was to

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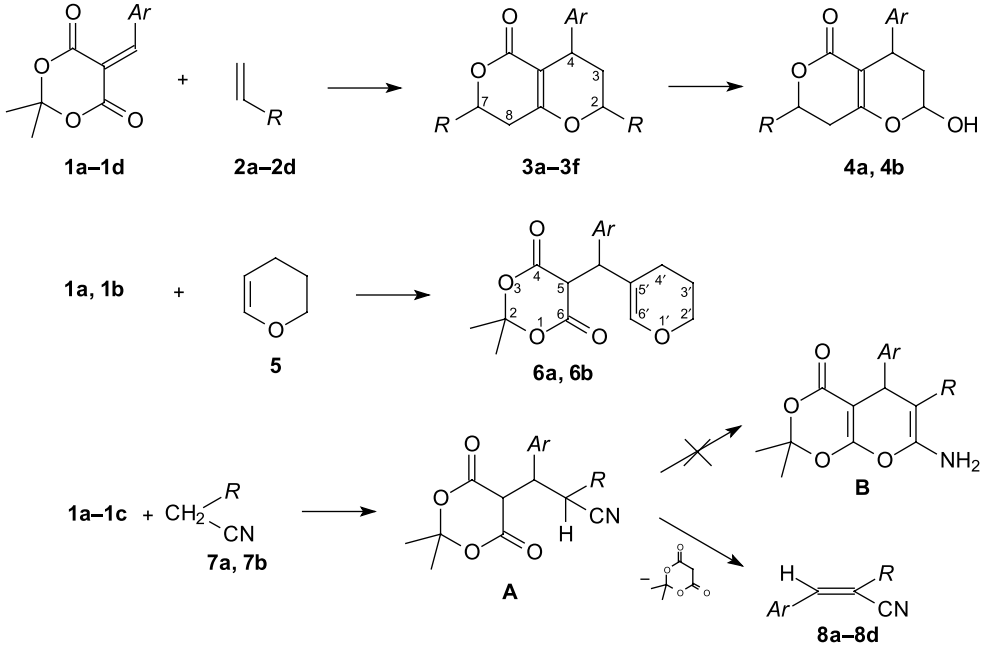
study the *Michael* addition of the quoted α,β-unsaturated carbonyl compounds with cyanoacetic acid derivatives as a potential method of pyran synthesis.

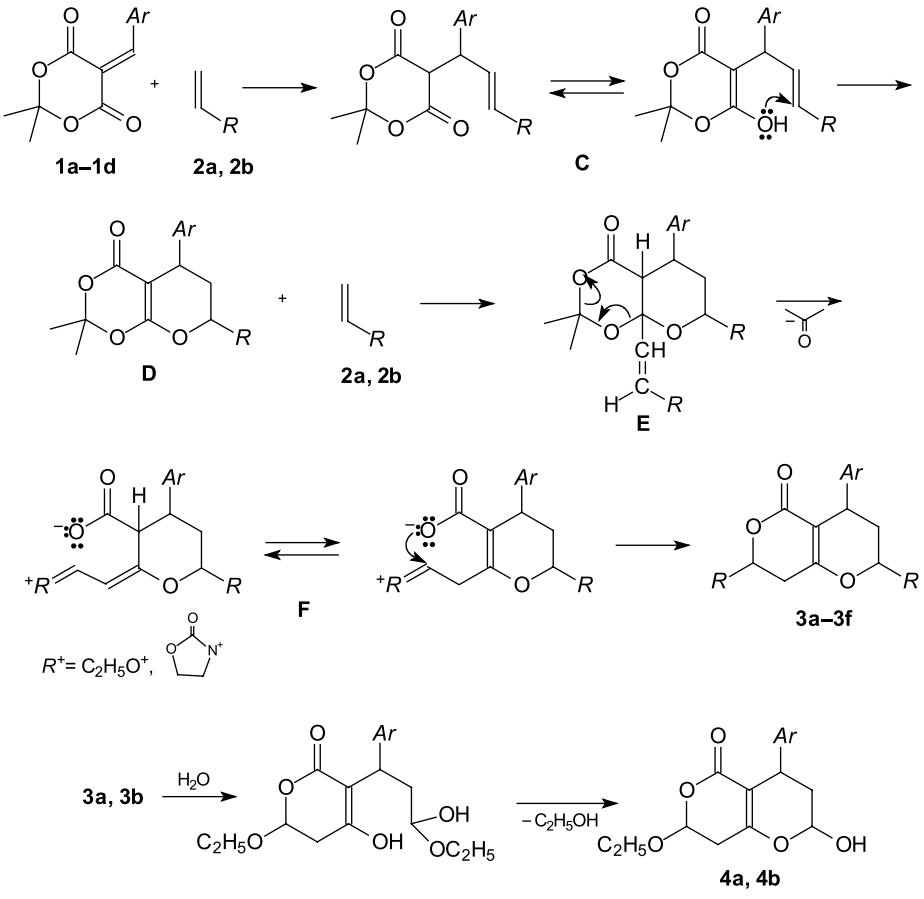
5-Arylidene derivatives of *Meldrum*'s acid **1a**–**1d** were obtained according to the methods described in literature [24]. It is worth to note that *Knoevenagel* condensations of *Meldrum*'s acid and aldehydes are not quite selective and often an undesirable bisadduct is obtained due to *Michael* addition with a second molecule of *Meldrum*'s acid. New methods of conducting these *Knoevenagel* condensations are still investigated [25–28].

The reactions of potential heterodienes **1a**–**1d** with dienophiles **2a**–**2d** were performed at ambient temperature for 1–2 days in methylene chloride (**2a** and **2b**) and in boiling acetonitrile, or else toluene (**2c** and **2d**). They afforded one diastereoisomer of pyrano[4,3-b]pyrans **4a**, **4b**, **3e**, and **3f** or diastereoisomeric mixture **3c** and **3d** in 33–46% yield (Scheme 1). The progress of the reactions was monitored by TLC. Compounds **4a**, **4b**, and **3c**–**3f** were separated by column chromatography and purified further by crystallization. Since the reactions of styrenes **2c**–**2d** with **1a** and **1b** in methylene chloride at room temperature failed, the reaction mixtures were heated in boiling acetonitrile or toluene. In all cases unchanged compounds **1a** and **1b** were isolated. According to Ref. [21], we expected to obtain



substrates		product	Ar	R
1a	**2a**	**4a**	*p*-CH_3O-C_6H_4	OC_2H_5
1b	**2a**	**4b**	*p*-NO_2-C_6H_4	OC_2H_5
1c	**2a**	**3c**		OC_2H_5
1d	**2a**	**3d**		OC_2H_5
1a	**2b**	**3e**	*p*-CH_3O-C_6H_4	
1b	**2b**	**3f**	*p*-NO_2-C_6H_4	
1b	**2c**	**-**	*p*-NO_2-C_6H_4	*p*-CH_3O-C_6H_4
1b	**2d**	**-**	*p*-NO_2-C_6H_4	*p*-CH_3-C_6H_4
1a	**5**	**6a**	*p*-CH_3O-C_6H_4	-
1b	**5**	**6b**	*p*-NO_2-C_6H_4	-
1a	**7a**	**8a**	*p*-CH_3O-C_6H_4	CN
1b	**7a**	**8b**	*p*-NO_2-C_6H_4	CN
1c	**7a**	**8c**		CN
1a	**7b**	**8d**	*p*-CH_3O-C_6H_4	$COOCH_3$

Scheme 1



Scheme 2

pyrano[2,3-*d*][1,3]dioxin-4(5*H*)-one derivatives by H*DA* cycloadditions, however, the described reactions provide pyrano[4,3-*b*]pyrans. The proposed mechanism of the formation of **3a**–**3f** is shown in Scheme 2.

In the first step, a *Michael* addition of reactant **2a**–**2b** to α,β-unsaturated ketone **1a**–**1d** afforded intermediates **C**, followed by ring closure leading to intermediates **D**. Next, a *Michael* addition of compounds **2a**–**2b** across the enone moiety of α,β-unsaturated lactone **D** furnished **E**. The elimination of acetone afforded intermediate **F** possessing a carboxylate anion and an oxonium or immonium functionality. In the final step, addition of the carboxylate anion to the onium functionalities resulted in the unexpected pyrano[4,3-*b*]pyrans **3a**–**3f**. The compounds **3a** and **3b** could not be recovered unchanged and after chromatography **4a** and **4b** were obtained. Probably, **3a** and **3b** hydrolyzed during column chromatography on silica gel and recrystallization to 2-hydroxy pyrano[4,3-*b*]pyrans **4a** and **4b** (Scheme 2).

Compounds **4a**, **4b**, and **3c**–**3f** were characterized by ^{1}H, ^{13}C NMR, IR, mass spectra, and elemental analysis. ^{1}H and ^{13}C signal assignments were confirmed by two-dimensional NMR COSY and HETCOR spectra. The relative *cis* and *trans* configuration of C-2, C-4, C-7 substituents were assigned on the basis of ^{1}H NMR spectra and crystallographic methods. In the ^{1}H NMR spectra of **4a** and **4b** the signal of 7-H appeared as a doublet of doublets at $\delta = 5.54$–5.58 ppm with the coupling con-

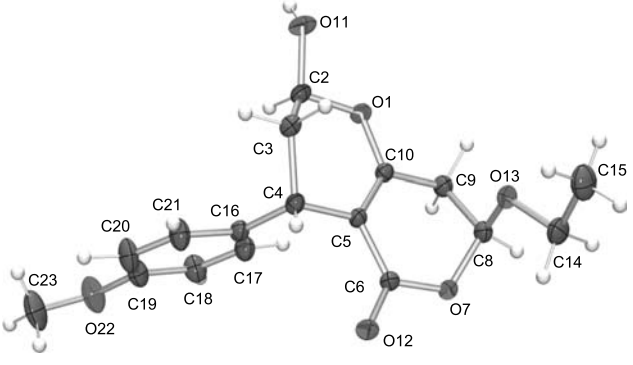


Fig. 1. A perspective view of **4a** with the atom numbering scheme

stants $^3J = 5.0–6.0$ and 3.9–4.5 Hz, due to coupling with two protons at C-8 (Table 1). Thus, 7-H occupies an *equatorial* position, and the ethoxy group adopts an *axial* orientation (Fig. 1). For compounds **4a** and **4b** signals of protons at C-2 ($\delta = 5.08–5.18$ ppm) and C-4 ($\delta = 3.75–3.97$ ppm) positions are broad and it is impossible to assign the complete stereochemistry. A ^{1}H NMR spectrum of **4b** was also recorded at temperature 373 K. It is worth to note that in the spectrum measured at higher temperature the signal one from the protons 8-H is a doublet of doublets at $\delta = 2.58$ ppm with the coupling constants $^2J = 17.4$ Hz, $^3J = 6.3$ Hz, and $^5J = 2.4$ Hz. The third coupling constant refers to the coupling of proton 8-H with the proton 4-H. In the COSY spectrum of **4b** there is a cross peak correlating 4-H with 8-H. The final stereochemistry of **4a** and **4b** was determined by X-ray analysis of the derivative **4a**. A perspective view of the molecule with the crystallographic numbering scheme is given in Fig. 1. The asymmetric unit contains two molecules of the compound (for clarity, only one was presented in Fig. 1) with slightly different conformations (the RMS deviation of superimposed molecules is equal to 0.4 Å). The crystal structure is stabilized by several intermolecular hydrogen bonds, of which the strongest are O11–H11 $\cdots$ O7 (2.957 Å, 120.6°) and O11–H11 $\cdots$ O12 (2.854 Å, 171.2°). The hydroxy group at C-2 occupies an *equatorial* position, the aryl group 4-Ar adopts a *pseudo-axial* orientation, and 7-ethoxy group is in the *axial* position (Fig. 1). The relative configurations of substituents at stereogenic positions are *trans-trans* (2,4:4,7).

Compounds **3c** and **3d** were obtained as a mixture of diastereoisomers and we were not able to separate the pure diastereoisomers by column and PTL chromatography. It proved likewise impossible to determine the ratio of particular diastereoisomers on the basis of ^{1}H NMR analysis. For compounds **3e** and **3f** the configurations were deduced from the chemical shift values and coupling constants of protons 2-H, 4-H, and 7-H of the pyrano[4,3-*b*]pyran (Table 1).

The ^{1}H NMR spectra of **3e** and **3f** reveal the signals of proton 2-H as a doublet of doublets at $\delta = 5.72$ ppm with large and small coupling constants ($^3J = 11.0–11.7$ and 1.5–1.6 Hz) due to coupling with the *axial* and *equatorial* protons 3-H. Thus, the hemiaminalic proton at C-2 obviously adopts the *axial* position, and the large oxazolidinyl moiety occupies the *equatorial* position (Fig. 2).

Table 1. Signals of proton 2-H, 4-H, and 7-H in ^{1}H NMR spectra of pyrano[4,3-*b*]pyrans **4a**, **4b**, **3e**, and **3f**

Compound	m 2-H δ/ppm $J_{3ax,2}\|J_{3eq,2}$ Hz	m 4-H δ/ppm $J_{3ax,4}\|J_{3eq,4}\|J_{8,4}$ Hz	dd 7-H δ/ppm $J_{8ax,7}\|J_{8eq,7}$ Hz
4a	5.08 br t 6.5	3.75 br	5.54 5.0|4.5
4b	5.18 br	3.97 br t 6.6	5.58 6.0|3.9
3e	5.72 dd 11.7|1.6	3.98 ddd 11.4|6.6|3.0	6.04 12.6|3.6
3f	5.72 dd 11.0|1.5	4.20 ddd 11.5|6.0|2.75	6.03 12.5|3.8

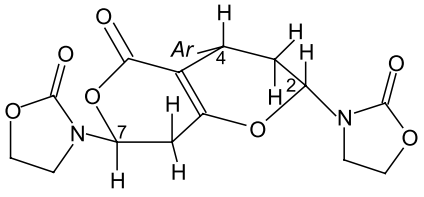


Fig. 2. *Cis-trans*(2,4:4,7) configurations of pyrano[4,3-b] pyrans **3e** and **3f** based on ^{1}H NMR analysis

In the ^{1}H NMR spectra of **3e** and **3f** the signal of 4-H appears as a doublet of doublets at $\delta = 3.98–4.20$ ppm with the coupling constants $^3J = 11.4–11.5$, 6.0–6.6 Hz and $^5J = 2.75–3.0$ Hz, due to coupling with two protons at C-3 (Table 1). The third value refers to the coupling of 4-H with *pseudo-axial* proton at position C-8 (8-H for **3e** $\delta = 2.96$ ppm, ddd, $J = 17.1$, 12.6, 3.1 Hz and for **3f** $\delta = 3.20$ ppm, ddd, $J = 17.5$, 12.8, 3.0 Hz). Thus, 4-H occupies a *pseudo-axial* position, and the aryl groups *Ar* adopt *pseudo-equatorial* orientation (Fig. 2). The signal of proton 7-H is a doublet of doublets at $\delta = 6.03–6.04$ ppm with the coupling constants $^3J = 12.5–12.6$ and 3.6–3.8 Hz (Table 1), hence 7-H must be *axial* and the oxazolidinyl moiety is in the *equatorial* position (Fig. 2). Thus we can assume that for compounds **3e** and **3f** the relative configurations of substituents at C-2, C-4, and C-7 positions are *cis-trans* (2,4:4,7).

Next, the reactions of 5-arylidene *Meldrum*'s acids **1a** and **1b** with cyclic enol ether **5** were studied. The reactions of compounds **1a** and **1b** with 3,4-dihydro-2*H*-pyrane **5** were performed in methylene chloride at room temperature for 1–2 days and *Michael* adducts **6a** and **6b** were obtained with 49–52% yields (Scheme 1). *Michael* adducts **6a** and **6b** structure was established on the basis of analytical

and spectroscopic data. ^{1}H and ^{13}C signal assignments were confirmed by two-dimensional NMR COSY and HETCOR spectra. The presence of two singlets at $\delta = 1.69$ ppm and $\delta = 1.78$ ppm in the ^{1}H NMR spectra indicates that in contrast to the reactions described above the elimination of acetone does not occur and the product contains 1,3-dioxin-4,6-dione ring. The ^{1}H NMR spectra revealed a doublet at $\delta = 4.01$–4.06 ppm with coupling constants $^3J = 3.0$–3.3 Hz for proton 5-H and a doublet at $\delta = 4.49$–4.57 ppm ($^3J = 3.0$ Hz) for aliphatic C*HAr* proton coupled with 5-H. The proton at C-6′ position resonates as a doublet at $\delta = 6.41$ ppm with $^4J = 0.6$ Hz.

In the next series of experiments we investigated the reactions of 5-arylidene derivatives of *Meldrum*'s acids **1a**–**1c** with cyanoacetic acid derivatives **7a** and **7b** as a potential method of pyran synthesis. These reactions were carried out in boiling acetonitrile, in the presence of piperidine and resulted in formation of the arylidenemalononitriles **8a**–**8c** and arylidene derivative methyl cyanoacetate **8d** in yields of 59–64% (Scheme 1). Compounds **8a**–**8d** have been extensively described in literature [29, 30].

In the first step of the reactions the *Michael* adducts **A** are furnished (Scheme 1). Intermediates **A** did not undergo cyclization with 4*H*-pyran **B** formation but the elimination of *Meldrum*'s acid led to undesired **8a**–**8d**. We tried to carry out the reaction of *p*-methoxybenzylidene *Meldrum*'s acid **1a** with malononitrile **7a** under mild conditions. The reagents mixture and piperdine in acetonitrile were kept at room temperature for 2 weeks. The result was the same as previously, but the time needed to complete the conversion was longer.

In conclusion, reactions of 5-arylidene derivatives of *Meldrum*'s acid with ethyl vinyl ether and *N*-vinyl-2-oxazolidinone lead to pyrano[4,3-*b*]pyrans, as the result of reactions: a *Michael* addition, a cyclization, a *Michael* addition, an elimination of acetone, and finally ring closure by addition. The configurations of isolated diastereoisomers of pyrano[4,3-*b*]-pyrans were assigned as *trans-trans* (2,4:4,7) and *cis-trans* (2,4:4,7). The present results indicate that 5-arylidene derivatives of *Meldrum*'s acid can act as valuable reagents in pyran synthesis. The reactions of 5-arylidene-2,2-dimethyl-4,6-dioxo-1,3-dioxanes with cyclic enol ether result in *Michael* adducts. Styrenes are not suitable reagents on account of their inertness towards 5-arylidene derivatives of *Meldrum*'s acid. The second potential method of pyran synthesis, *i.e.* reactions of 5-arylidene *Meldrum*'s acids with cyanoacetic acid derivatives lead to arylidenemalononitriles and cannot be used to obtain pyrans.

Experimental

Melting points were determined on a *Boetius* hot stage apparatus. IR spectra: Bruker IFS 48 in KBr pellets. ^{1}H NMR, ^{13}C NMR, COSY, and HETCOR spectra: Bruker AMX 500 (^{1}H: 500.14 MHz, ^{13}C: 125.76 MHz), Bruker Avance II 300 (^{1}H: 300.18 MHz, ^{13}C: 75.48 MHz), in $CDCl_3$, *DMSO*-d_6 with *TMS* as an internal standard. Mass spectra: Finningan Mat 95 (70 eV). Microanalyses were performed with Euro EA 3000 Elemental Analyzer, their results agreed satisfactorily with the calculated values. Crystallographic Data: KappaCCD (Nonius) diffractometer using MoKα radiation, X-ray data measured at room temperature. The structure was solved by direct methods and refined by the full-matrix least-squares method on F^2 using SHELX97 program system.

Meldrum's acid was obtained according to a procedure described in Ref. [31]. 5-Arylidene-2,2-dimethyl-4,6-dioxo-1,3-dioxanes **1a**–**1d** were prepared by a procedure reported in Ref. [24]. *N*-Vinyl-2-oxazolidinone **2b** was synthesized according to the procedure described in Ref. [32].

*General Procedure for the Preparation of **4a**, **4b**, **3c**–**3f**, **6a**, and **6b***

A solution of the 5-arylidene derivatives of *Meldrum*'s acid **1a**–**1d** (2 mmol) in 20 cm^3 anhydrous dichloromethane and 1.44 g ethyl vinyl ether (**2a**, 20 mmol, 10 equiv), 0.45 g *N*-vinyl-2-oxazolidinone (**2b**, 4 mmol, 2 equiv), 4 mmol styrenes **2c** and **2d** (2 equiv) or 1.68 g 3,4-dihydro-2*H*-pyran **5** (20 mmol, 10 equiv) was kept at room temp. for the time 1 day (**4b**, **3e**, **3f**, **6b**) and 2 days (**4a**, **3c**, **3d**, **6a**). 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 petrol ether:*t*-butyl methyl ether 1:2 (**4a**), *t*-butyl methyl ether (**3c**, **3d**, **4b**), $CHCl_3$: methanol 20:1 (**3e**, **3f**), or $CHCl_3$ (**6a**, **6b**) as an eluent. Recrystallization from *t*-butyl methyl ether (**4a**, **4b**, **6a**), methanol (**3e**), $CHCl_3$ (**3f**), *t*-butyl methyl ether:methanol 3:1 (**6b**) gave crystalline colorless products. Compounds **3a** and **3b** hydrolyzed during column chromatography and recrystallization yielded **4a** and **4b**. Since styrenes **2c** and **2d** did not react with 5-arylidene derivatives of *Meldrum*'s acid **1a** and **1b** under the reaction conditions described above, we changed the solvent to anhydrous acetonitrile or toluene and appropriate solutions were refluxed for 24 h. After this time substrate **1a** and **1b** was separated from the reaction mixture.

(2RS,4RS,7RS)-7-Ethoxy-2-hydroxy-4-(4-methoxyphenyl)-5-oxo-2,3,4,5,7,8-hexahydropyrano[4,3-b]pyran (**4a**, $C_{17}H_{20}O_6$)

Colorless crystals; mp 175°C; yield 33%; IR (KBr): $\bar{\nu} = 3305$ (OH), 2979, 2932, 2834 (CH), 1670 (C=O), 1635 (C=C), 1272,

1250, 1159, 1132, 1011 (C–O) cm^{-1}; ^1H NMR (500.14 MHz, *DMSO*-d_6): $\delta = 1.16$ (t, $J = 7.0$ Hz, 3 OCH_2CH_3), 1.89 (br d, $J = 13.5$ Hz, 1 3-H_{ax}), 1.98 (ddd, $J = 5.5$, 13.5, 6.0 Hz, 1 3-H_{eq}), 2.57 (dd, $J = 17.0$, 5.0 Hz, 1 8-H), 2.93 (dd, $J = 17.0$, 4.0 Hz, 1 8-H), 3.63 (dq, $J = 14.5$, 7.0 Hz, 1 OCH_2CH_3), 3.72 (s, 3 OCH_3), 3.75 (br, 1 4-H), 3.81 (dq, $J = 14.5$, 7.0 Hz, 1 OCH_2CH_3), 5.08 (t, $J = 6.5$ Hz, 1 2-H), 5.54 (dd, $J = 5.0$, 4.5 Hz, 1 7-H), 6.84 (d, $J = 8.5$ Hz, 2 ArH), 7.09 (d, $J = 8.5$ Hz, 2 ArH), 7.53 (br, 1 OH) ppm; ^{13}C NMR (125.76 MHz; DMSO-d_6): $\delta = 14.8$ (OCH_2CH_3), 32.7 (C-8), 33.7 (C-4), 37.2 (C-3), 54.9 (OCH_3), 64.0 (OCH_2CH_3), 93.1 (C-2), 97.9 (C-7), 100.5 (C-4a), 113.6, 128.2, 136.2, 157.6 (ArC), 163.3 (C-8a), 163.9 (C-5) ppm; MS (EI, 70 eV): m/z (%) = 320 (71)$[M]^{+\bullet}$, 302 (17), 276 (16), 275 (32), 274 (18), 231 (27), 230 (29), 205 (33), 134 (100), 99 (94), 71 (81).

Crystal structure analysis: Compound **4a** with formula $C_{17}H_{20}O_6$ crystallizes in the monoclinic system, space group $P2_1/a$, with unit cell parameters $a = 16.8953(2)$, $b = 9.5789(2)$, $c = 21.5910(3)$ Å, $\beta = 112.070(1)°$, $V = 3238.2(1)$ $Å^3$, $Z = 4$, $Z'8$. A total of 7412 independent reflections (R(int) = 0.0474) were collected on a sample (size $0.25 \times 0.20 \times 0.20\,mm^3$). Final R indices for $I > 2\sigma(I)$ were equal $R1 = 0.0487$, w$R2 = 0.1143$ and $R1 = 0.0850$, w$R2 = 0.1313$ for all data. The final difference *Fourier* map of electron density was featureless with the largest peak and hole of 0.154 and $-0.196\,e \cdot Å^{-3}$. The structural data were deposited at the Cambridge Crystallographic Data Centre. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk) under reference number CCDC 617449.

(2RS,4RS,7RS)-7-Ethoxy-2-hydroxy-4-(4-nitrophenyl)-5-oxo-2,3,4,5,7,8-hexahydropyrano[4,3-b]pyran (**4b**, $C_{16}H_{17}NO_7$)
Colorless crystals; mp 195°C; yield 41%; IR (KBr): $\bar{\nu} = 3334$ (OH), 3108, 3072, 3045, 2989, 2966 (CH), 1659 (C=O), 1635 (C=C), 1515, 1349 (NO_2), 1145, 1085 (C–O) cm^{-1}; ^1H NMR (500.14 MHz, *DMSO*-d_6, 293 K): $\delta = 1.16$ (t, $J = 7.1$ Hz, 3 OCH_2CH_3), 1.91 (br d, $J = 13.8$ Hz, 1 3-H_{ax}), 2.11 (ddd, $J = 6.6$, 6.6, 13.8 Hz, 1 3-H_{eq}), 2.58 (dd, $J = 17.4$, 6.0 Hz, 1 8-H), 2.97 (dd, $J = 17.4$, 3.9 Hz, 1 8-H), 3.64 (dq, $J = 9.6$, 7.1 Hz, 1 OCH_2CH_3), 3.82 (dq, $J = 9.6$, 7.1 Hz, 1 OCH_2CH_3), 3.97 (br t, $J = 6.6$ Hz, 1 4-H), 5.18 (br, 1 2-H), 5.58 (dd, $J = 6.0$, 3.9 Hz, 1 7-H), 7.51 (d, $J = 8.5$ Hz, 2 ArH), 7.69 (br, 1 OH), 8.14 (d, $J = 8.5$ Hz, 2 ArH) ppm; ^1H NMR (500.14 MHz, *DMSO*-d_6; 373 K) 1.17 (t, $J = 7.2$ Hz, 3 OCH_2CH_3), 1.97 (m, 1 3-H_{ax}), 2.19 (m, 1 3-H_{eq}), 2.58 (ddd, $J = 17.4$, 6.3, 2.4 Hz, 1 8-H), 2.90 (dd, $J = 17.4$, 3.9 Hz, 1 8-H), 3.66 (dq, $J = 9.9$, 6.9 Hz, 1 OCH_2CH_3), 3.82 (dq, $J = 9.9$, 6.9 Hz, 1 OCH_2CH_3), 3.98 (t, $J = 6.0$ Hz, 1 4-H), 5.20 (br, 1 2-H), 5.54 (dd, $J = 6.3$, 4.2 Hz, 1 7-H), 7.25 (br, 1 OH), 7.47 (d, $J = 8.7$ Hz, 2 ArH), 8.09 (d, $J = 9.0$ Hz, 2 ArH) ppm; ^{13}C NMR (125.76 MHz, DMSO-d_6): $\delta = 14.9$ (OCH_2CH_3), 32.9 (C-8), 34.3 (C-4), 36.6 (C-3), 64.2 (OCH_2CH_3), 92.8 (C-2), 98.1 (C-7), 99.9 (C-4a), 123.4, 128.4, 128.7, 129.1, 146.0, 152.6 (ArC), 163.9 (C-8a), 164.1 (C-5) ppm; MS (EI, 70 eV): m/z (%) = 335 (20) $[M]^{+\bullet}$, 317 (12), 290 (23), 289 (17), 244 (15), 220 (15), 218 (19), 158 (67), 99 (100), 72 (64), 71 (88).

2,7-Diethoxy-4-(2-furyl)-5-oxo-2,3,4,5,7,8-hexahydropyrano[4,3-b]pyran (**3c**, $C_{16}H_{20}O_6$)
Pale yellow oil; yield 40%; IR (film): $\bar{\nu} = 3110$, 3075, 2964, 2928 (CH), 1712 (C=O), 1641 (C=C), 1169, 1132, 1047 (C–O) cm^{-1}; ^1H NMR (300.18 MHz, $CDCl_3$): $\delta = 1.19$ (m, 6 OCH_2CH_3), 2.12 (m, 2 3-H), 2.61 (m, 2 8-H), 3.78 (m, 4 OCH_2CH_3), 4.15 (m, 1 4-H), 5.27 (m, 1 2-H), 5.49 (m, 1 7-H), 6.69 (m, 1 H-furyl), 7.62 (m, 1 H-furyl), 7.85 (m, 1 H-furyl) ppm; ^{13}C NMR (75.48 MHz, $CDCl_3$): $\delta = 14.1$, 15.9 (OCH_2CH_3), 30.5, 31.7, 33.8, 34.2, 36.7, 37.5, 37.9 (C-8, C-4, C-3), 63.8, 64.7, 64.9, 65.3, 65.4, 65.5, 65.6 (OCH_2CH_3), 96.8, 97.2, 98.3, 98.4, 99.2, 99.7, 99.8 (C-2, C-7, C-4a), 115.9, 116.6, 116.8, 124.2, 124.5, 124.7, 126.3, 126.7, 127.8, 146.9, 148.5, 149.6, 150.2 (C-2′, C-3′, C-4′, C-5′ furyl), 161.7, 161.9, 162.5, 162.7 (C-8a, C-5) ppm; MS (EI, 70 eV): m/z (%) = 308 (100) $[M]^{+\bullet}$, 263 (21), 236 (19), 218 (25), 189 (49), 163 (43), 99.1 (27), 94 (21), 71 (19).

2,7-Diethoxy-4-(2-thienyl)-5-oxo-2,3,4,5,7,8-hexahydropyrano[4,3-b]pyran (**3d**, $C_{16}H_{20}O_5S$)
Pale yellow oil; yield 38%; IR (film): $\bar{\nu} = 3103$, 3068, 2977, 2931 (CH), 1717 (C=O), 1652 (C=C), 1174, 1126, 1051 (C–O) cm^{-1}; ^{13}C NMR (300.18 MHz, $CDCl_3$) $\delta = 1.23$ (m, 6 OCH_2CH_3), 2.24 (m, 2 3-H), 2.69 (m, 2 8-H), 3.71 (m, 4 OCH_2CH_3), 4.23 (m, 1 4-H), 5.14 (m, 1 2-H), 5.43 (m, 1 7-H), 6.88 (m, 2H-thienyl), 7.15 (m, 1H-thienyl) ppm; ^{13}C NMR (75.48 MHz, $CDCl_3$): $\delta = 14.9$, 15.1 (OCH_2CH_3), 30.2, 30.3, 30.4, 33.2, 35.9, 36.1, 36.5, 37.4 (C-8, C-4, C-3), 64.4, 64.6, 64.9, 65.0, 65.1, 65.2, 65.5, 65.6 (OCH_2CH_3), 97.0, 97.3, 98.2, 98.3, 99.2, 99.4, 99.9 (C-2, C-7, C-4a), 122.9, 123.6, 123.9, 124.2, 124.5, 124.7, 126.3, 126.4, 126.8, 127.0, 146.9, 147.4, 147.6, 147.7 (C-2′, C-3′, C-4′, C-5′ thienyl), 161.0, 161.3, 162.0, 162.3 (C-8a, C-5) ppm; MS (EI, 70 eV): m/z (%) = 324 (100%) $[M]^{+\bullet}$, 279 (29), 252 (21), 234 (31), 205 (60), 179 (40), 167 (33), 137 (23), 110 (23), 99.1 (33), 71 (17).

(2RS,4SR,7SR)-4-(4-Methoxyphenyl)-5-oxo-2,7-di(2-oxo-3-oxazolidinyl)-2,3,4,5,7,8-hexahydropyrano[4,3-b]pyran (**3e**, $C_{21}H_{22}N_2O_8$)
Colorless crystals; mp 242°C; yield 42%; IR (KBr): $\bar{\nu} = 3134$, 2996, 2959, 2919 (CH), 1766, 1749, 1702 (C=O), 1647 (C=C), 1274, 1192, 1068, 1034 (C–O) cm^{-1}; ^1H NMR (500.14 MHz, $CDCl_3$): $\delta = 2.03$ (ddd, $J = 11.5$, 11.5, 13.8 Hz, 1 3-H_{ax}), 2.37 (ddd, $J = 1.8$, 6.6, 13.5 Hz, 1 3-H_{eq}), 2.53 (dd, $J = 3.7$, 17.5 Hz, 1 8-H_{eq}), 2.96 (ddd, $J = 17.1$, 12.6, 3.1 Hz, 1 8-H_{ax}), 3.60 (m, 2 4′-H), 3.78 (s, 3OCH_3), 3.74 (dd, $J = 17.1$, 8.0 Hz, 1 4″-H), 3.85 (dd, $J = 17.1$, 8.2 Hz, 1 4″-H), 3.98 (ddd, $J = 11.4$, 6.6, 3.0 Hz, 1 4-H_{ax}), 4.42 (m, 4 5′-H, 5″-H), 5.72 (dd, $J = 11.7$, 1.6 Hz, 1 2-H_{ax}), 6.04 (dd, $J = 12.6$, 3.6 Hz, 1 7-H), 6.85 (d, $J = 8.7$ Hz, 2ArH), 7.12 (d, $J = 8.7$ Hz, 2ArH) ppm; ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 31.3$ (C-8), 37.2 (C-4), 37.5 (C-3), 39.8 (C-4′, C-4″), 55.31 (OCH_3), 62.6 (C-5′, C-5″), 78.7 (C-2), 82.0 (C-7), 105.9 (C-4a), 114.4, 127.7, 133.8, 157.1 (ArC), 157.4, 158.6 (C-2′, C-2″), 163.5 (C-8a), 163.7 (C-5) ppm; MS (EI, 70 eV): m/z (%) = 430 (29%) $[M]^{+\bullet}$, 343 (29), 317 (45), 273 (17), 256 (16), 204 (36), 113 (100).

(2RS,4SR,7SR)-4-(4-Nitrophenyl)-5-oxo-2,7-di(2-oxo-3-oxazolidinyl)-2,3,4,5,7,8-hexahydropyrano[4,3-b]pyran (**3f**, $C_{20}H_{19}N_3O_9$)

Colorless crystals; mp 233°C; yield 46%; IR (KBr): $\bar{\nu}=$ 3118, 3073, 2964, 2921 (CH), 1765, 1755, 1691 (C=O), 1646 (C=C), 1515, 1347 (NO_2), 1275, 1194, 1109, 1070 (C–O) cm^{-1}; ^1H NMR (300.18 MHz, *DMSO*-d_6): $\delta=2.02$ (ddd, $J=11.0$, 11.75, 12 Hz, 1 3-H_{ax}), 2.37 (ddd, $J=1.5$, 6.3, 13.3 Hz, 1 3-H_{eq}), 2.67 (dd, $J=3.5$, 17.5 Hz, 1 8-H_{eq}), 3.20 (ddd, $J=17.5$, 12.8, 3.0 Hz, 1 8-H_{ax}), 3.68 (m, 4 4′-H, 4″-H), 4.20 (ddd, $J=11.5$, 6.0, 2.75 Hz, 1 4-H_{ax}), 4.38 (m, 4 5′-H, 5″-H), 5.72 (dd, $J=11.0$, 1.5 Hz, 1 2-H_{ax}), 6.03 (dd, $J=12.5$, 3.8 Hz, 1 7-H), 7.58 (d, $J=9.0$ Hz, 2ArH), 8.17 (d, $J=9.0$ Hz, 2ArH) ppm; ^{13}C NMR (75.48 MHz, DMSO-d_6): $\delta=30.3$ (C-8), 35.2 (C-4), 37.3 (C-3), 39.5 (C-4′, C-4″), 62.6 (C-5′, C-5″), 78.8 (C-2), 81.7 (C-7), 102.9 (C-4a), 123.5, 128.2, 146.1, 151.8 (ArC), 156.8, 156.9 (C-2′, C-2″), 163.6 (C-8a), 163.9 (C-5) ppm; MS (EI, 70 eV): m/z (%) = 445 (35) $[M]^{+\bullet}$, 399 (14), 358 (25), 332 (58), 312 (11), 289 (13), 287 (21), 271 (17), 219 (32), 113 (100).

5-[(3,4-Dihydro-2H-pyran-5-yl)(4-methoxyphenyl)methyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (**6a**, $C_{19}H_{22}O_6$)

Colorless crystals; mp 109°C; yield 49%; IR (KBr): $\bar{\nu}=3058$, 3030, 2956, 2941, 2919, 2865, 2823 (CH), 1789, 1754 (C=O), 1672 (C=C), 1275, 1015 (C–O) cm^{-1}; ^1H NMR (300.18 MHz, $CDCl_3$) $\delta=1.69$ (s, $3CH_3$), 1.79 (s, $3CH_3$), 1.87 (m, 4 3′-H, 4′-H), 3.83 (s, $3OCH_3$), 3.92 (m, 2 2′-H), 4.01 (d, $J=3.0$ Hz, 1 5-H), 4.49 (d, $J=3.0$ Hz, 1ArC*H*), 6.39 (d, $J=0.7$ Hz, 1 6′-H), 6.79 (d, $J=8.5$ Hz, 2ArH), 7.12 (d, $J=8.5$ Hz, 2ArH) ppm; ^{13}C NMR (75.48 MHz, $CDCl_3$): $\delta=21.8$, 22.9 (C-3′, C-4′), 27.4 (CH_3), 29.0 (CH_3), 48.6 (Ar-*C*H), 49.9 (C-5), 55.3 (OCH_3), 66.2 (C-2′), 106.0 (C-2), 110.9 (C-5′), 113.59, 128.35, 136.8, (ArC), 144.1 (C-6′), 157.3 (ArC), 164.2, 165.1 (C-4, C-6) ppm; MS (EI, 70 eV): m/z (%) = 346 (9) $[M]^{+\bullet}$, 288 (6), 262 (6), 260 (47), 203 (100.00), 143 (7), 84 (8).

5-[(3,4-Dihydro-2H-pyran-5-yl)(4-nitrophenyl)methyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (**6b**, $C_{18}H_{19}NO_7$)

Colorless crystals; mp 136°C; yield 52%; IR (KBr): $\bar{\nu}=3114$, 3100, 3048, 3000, 2986, 2963, 2941, 2923, 2878 (CH), 1787, 1746 (C=O), 1669 (C=C), 1512, 1342 (NO_2), 1209, 1148, 1017 (C–O) cm^{-1}; ^1H NMR (300.18 MHz, $CDCl_3$): $\delta=1.69$ (s, $3CH_3$), 1.78 (s, $3CH_3$), 1.91 (m, 4 3′-H, 4′-H), 3.96 (m, 2 2′-H), 4.06 (d, $J=3.3$ Hz, 1 5-H), 4.57 (d, $J=3.0$ Hz, 1ArC*H*), 6.41 (d, $J=0.6$ Hz, 1 6′-H), 7.54 (d, $J=8.4$ Hz, 2ArH), 8.16 (d, $J=8.7$ Hz, 2ArH) ppm; ^{13}C NMR (75.48 MHz, $CDCl_3$): $\delta=22.1$, 23.2 (C-3′, C-4′), 27.6 (CH_3), 28.2 (CH_3), 47.5 (Ar-*C*H), 49.6 (C-5), 65.3 (C-2′), 105.2 (C-2), 110.2 (C-5′), 123.49, 130.11 (ArC), 143.5 (C-6′), 146.3, 147.0 (ArC), 163.9, 164.6 (C-4, C-6) ppm; MS (EI, 70 eV): m/z (%) = 361 (4) $[M]^{+\bullet}$, 303 (7), 277 (4), 275 (51), 218 (100.00), 143 (6), 84 (5).

*Reactions of 5-Arylidene Derivatives of Meldrum's Acid **1a–1c** with Cyanoacetic Acid Derivatives **7a** and **7b***

To a solution of 5 mmol **1a–1c** and 6 mmol malononitrile (**7a**, 0.40 g) or methyl cyanoacetate (**7b**, 0.60 g) in 20 cm^3 anhydrous acetonitrile a few drops of piperidine were added. The reaction mixtures were refluxed for 3 h. The progress of the reactions was monitored by TLC. The solvent was evaporated and the oily residue was treated with methanol. The precipitate was filtered off and recrystallized from methanol. Reactions led to arylidenemalononitriles **8a–8c** or arylidene derivative of methyl cyanoacetate **8d** in yields of 59–64%. Compounds **8a–8d** are described in Refs. [29, 30]. Reaction of 1.31 g *p*-methoxybenzylidene *Meldrum acid* **1a** (5 mmol) and 0.40 g malononitrile (**7a**, 6 mmol) in 20 cm^3 acetonitrile solution with a few drops of piperidine was carried out at room temperature for 2 weeks. After further purification arylidenemalononitrile **8a** was isolated in 61% yield.

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