

## Pyrylium Salts

### II. <sup>1</sup> Reactions of the 2,6-Dimethoxycarbonylpyrylium Cation with Carbon Nucleophiles

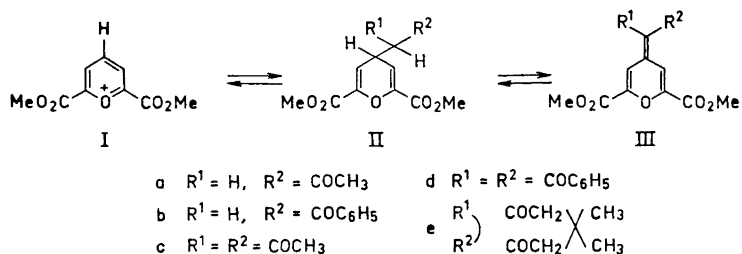
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The 2,6-dimethoxycarbonylpyrylium cation reacts with carbonyl activated methyl or methylene carbon in the cold to 4H-pyrans. A concurrent redox process may occur whereby the more stabilised pyrylium ion is formed. Of the 1,3-dicarbonyl-4H-pyrans prepared, only a cyclohexane-1,3-dione was largely enolised in chloroform. The NMR spectra in chloroform of the 4-acetonylidene- and the 4-phenacylidene-4H-pyrans are interpreted to mean preference for *s-cis*-conformation, this tendency decreasing with further substitution.

Recently we reported on the synthesis of the 2,6-dimethoxycarbonylpyrylium cation and some of its reactions with hydroxy and amino nucleophiles and bases.<sup>1</sup> The work reported in this paper deals with studies of its reactivity towards carbon nucleophiles. Dissolution of the perchlorate of the pyrylium cation I in acetone resulted in immediate formation of an acetone adduct. The NMR spectrum (CDCl<sub>3</sub>) shows the  $\beta$ -pyranyl protons as a doublet at 4.0  $\tau$  ( $J = 3.5$  cps) and the  $\gamma$ -proton at about 6.3  $\tau$  coupled (7.0 cps) to methylene protons at 7.3  $\tau$ . The methoxy protons and the additional methyl protons appear as singlets at 6.2 and 7.8  $\tau$ , respectively. These data are only consistent with the 4H-pyran IIa (Scheme 1). The acetophenone (IIb) and the acetyl-acetone (IIc) derivatives were also prepared using the ketone both as solvent and reagent. The dibenzoylmethane (IIId) and the cyclic dimedone (IIe) derivatives were synthesised in liquid SO<sub>2</sub>. Using equivalent amounts of reagents in liquid SO<sub>2</sub>, the monoketones IIa and IIb reacted further, as discussed below, to the methylene analogues (IIIa and IIIb).

To relate the reactivity of the 2,6-dimethoxycarbonylpyrylium ion to that of other previously studied pyrylium ions, 2,6-diphenylpyrylium perchlorate was synthesised.<sup>2</sup> The latter was found not to react with acetone. With stronger nucleophiles such as carbanions and Grignard reagents, however, the 2,6-



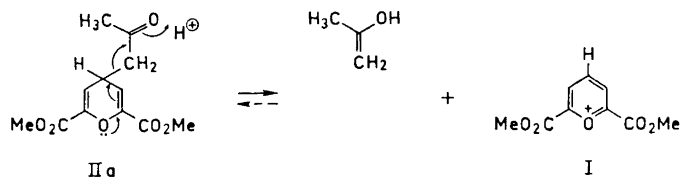
Scheme 1.

diphenylpyrylium cation undergoes addition to the 4-position.<sup>3,4</sup> A further comparison is available with the tropylium ion. The latter has been reported to react slowly with acetone on heating but is readily attacked by more activated compounds such as malonic acid and acetoacetic acid.<sup>5</sup> The lower reactivity of the tropylium ion is in good agreement with the relative redox potential as discussed below.

The reaction between I and acetone at room temperature is very fast. By lowering the temperature it was found that below about  $-10^\circ\text{C}$  no significant reaction rate was observed. At this temperature region, however, the reaction is rapid once initiated which suggests autocatalysis through the perchloric acid liberated in the reaction. Kinetic studies of the reaction between the tropylium ion and aldehydes have shown that the rate constant was independent of the tropylium ion concentration but proportional to the hydrogen ion concentration. From these observations it was concluded that the tropylium ion reacts with the enolised carbonyl compound and that enol formation is the rate determining step.<sup>6</sup> We have not carried out quantitative studies but have qualitatively demonstrated acid catalysis in agreement with enolisation of the carbonyl reagent as the rate determining step. Thus passage of dry HCl gas into an acetone solution of the dimethoxycarbonylpyrylium salt at  $-40^\circ\text{C}$  resulted in very rapid conversion to the 4H-pyran.

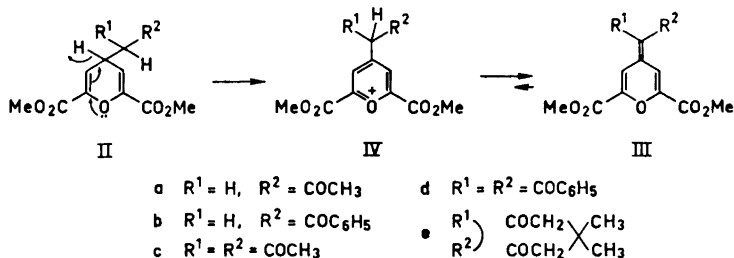
Reversibility in the formation of 4H-pyrans in acid solution, especially in the case of 2,6-diphenyl-4H-pyrans, has been reported.<sup>2</sup> This was also demonstrated for the acetyl derivative IIa by heating in trifluoroacetic acid (TFA) with added perchloric acid at  $60-70^\circ\text{C}$ , presumably because the liberated acetone is distilled off. In cold solution the equilibrium was too far in favour of the 4H-pyran for detection of the pyrylium ion I by NMR. For corresponding 2,6-diphenyl-4H-pyrans the equilibrium is in favour of the pyrylium salt. This difference in behaviour is caused by the different electronic effects of the 2,6-substituents on the stabilisation of the pyrylium cation. The breakage of the exocyclic carbon-carbon bond with regeneration of aromaticity bears some resemblance to acid catalysed enolisation where in this case the pyran oxygen acts as an intramolecular base (Scheme 2).

Treatment of the 4H-pyrans II with triphenylmethyl perchlorate in liquid  $\text{SO}_2$ , the reagent used for hydride abstraction in the preparation of I and the 4-methyl analogue VII (Scheme 5) from the respective 4H-pyrans, resulted in the isolation of the anhydro-bases III. The acid strength of IV is such that it



Scheme 2.

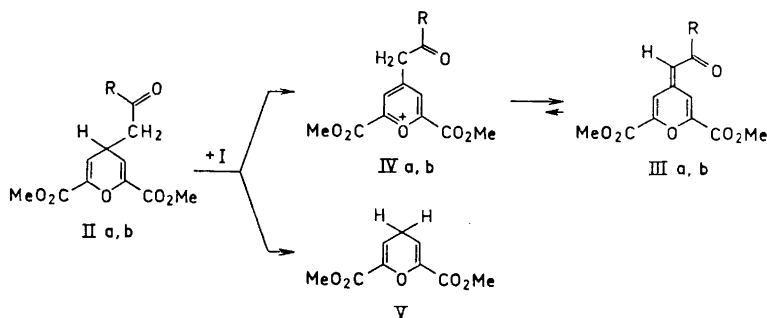
is largely dissociated. In the 4-methyl analogue VII, however, the lack of carbonyl activation required treatment with a base such as an amine for anhydro-base formation (III,  $R^1 = R^2 = H$ ).<sup>1</sup> The acetylacetylidene IIIc is an exception to the above reaction in that it was best prepared from IIc through dehydrogenation by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in benzene solution.



Scheme 3.

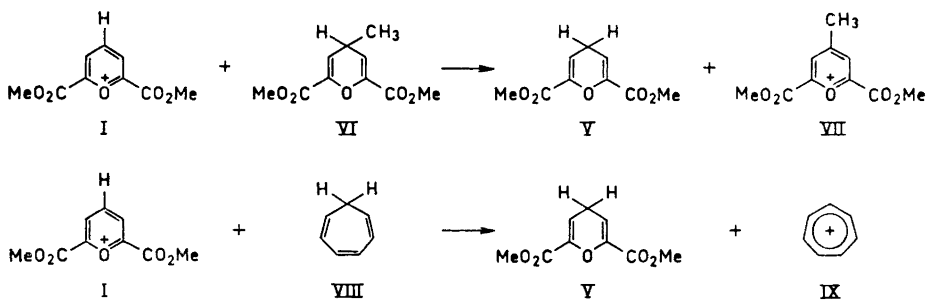
The acetylidene IIIa in TFA contains an exocyclic proton but no apparent methylene protons from protonation of the exocyclic  $\alpha$ -carbon. The  $\beta$ -pyranyl protons are non-equivalent occurring at 1.2 and 2.5  $\tau$  in TFA and at 1.4 and 3.1  $\tau$  in  $CDCl_3$ , respectively. The 4-methylpyrylium analogue VII has its  $\beta$ -protons at 1.0  $\tau$  (TFA).<sup>1</sup> In TFA-*d*, however, the exocyclic vinyl proton was exchanged in the course of 1–2 min. The relative chemical shifts and nonequivalence of the pyranyl protons together with the rapid deuteration must mean that IIIa is protonated only to a small extent in TFA. This low basicity is in accordance with low pyrylium resonance contribution to the ground state of IIIa as discussed below.

As mentioned above, in the reaction between equivalent amounts of the dimethoxycarbonylpyrylium ion and acetone or acetophenone in liquid  $SO_2$ , the anhydro-base III was obtained directly. The product composition in this reaction shows that the initial 4H-pyran II suffers hydride abstraction to the pyrylium salt IV, the hydride abstractor being the pyrylium ion I. The presence in the product of nearly equivalent amounts of the ketone reagent, 2,6-dimethoxycarbonyl-4H-pyran and the anhydro-base III shows that hydride abstraction from IIa and IIb is a much faster reaction than adduct formation. For the 1,3-dicarbonyl derivatives, however, the order is reversed presumably for sterical reasons.



Scheme 4.

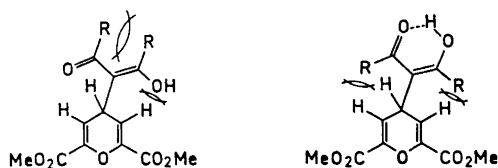
The driving force in the hydride exchange between the 4H-pyran II and I lies in the relative stabilities of the pyrylium ions I and IV. A 4-substituent will stabilise the pyrylium cation. This was readily seen in an NMR experiment with equivalent amounts of the cation I and the 4-methyl-4H-pyran VI in TFA. Thus after 2 days all the pyrylium cation I had been reduced to its 4H-pyran (V) with concurrent oxidation of VI to the 4-methylpyrylium ion VII. Similarly the greater stability of the tropylium ion was demonstrated by dissolving the cation I and cycloheptatriene in acetonitrile. The NMR spectrum, recorded after 20 min, contained only proton signals from the tropylium ion and the 4H-pyran.



Scheme 5.

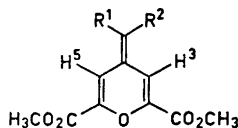
Integration of the NMR spectra (Table 1) of the pyranyl ketones (II) showed that both the mono-carbonyl and the acyclic 1,3-dicarbonyl derivatives exist almost entirely in the ketone form. The keto-enol equilibria of 1,3-dicarbonyl compounds are solvent sensitive, the enol tautomer being the more important in non-polar solvents.<sup>7,8</sup> In the present case the *cis*-enol, however, will be destabilised relative to the ketone because of steric repulsion between the pyranyl group and the substituents on the carbonyl groups (Scheme 6). In the *trans*-enol, the main interaction is between the R-groups. On the other hand the NMR spectrum of the cyclic 1,3-dicarbonyl derivative IIe shows this

to be about 80 % enolised. In this case the steric interaction between the dimedone and the pyran ring is little affected by the degree of enolisation, and IIe is therefore enolised very much as dimedone itself.<sup>9,10</sup>



Scheme 6.

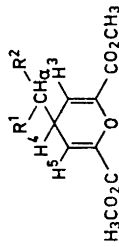
The chemical shifts for the  $\beta$ -pyranyl protons in the pyranyl ketones II have been shifted slightly upfield (up to 0.2  $\tau$ ) relative to the corresponding shift in the 4-methyl derivative (VI). The shifts are probably caused by anisotropy effects from the carbonyl group, the shift being largest in the acyclic dicarbonyl compounds. In the anhydro-bases III, however, the chemical shifts for the  $\beta$ -pyranyl protons have been moved considerably downfield. These shifts are also at lower field than in the parent methylene derivative III ( $R^1 = R^2 = H$ ).<sup>1</sup>

Table 2. NMR spectra of 4H-dehydropyrans recorded in  $CDCl_3$ .

Comp.	Substituents		Chemical shift in $\tau$ values				Coupling in cps	
	$R^1$	$R^2$	$H^3$	$H^5$	$R^1$	$R^2$		
IIIa	H	$CH_3CO$	1.40	3.07	4.10	7.75	6.08	$J_{3,5} = 2.0$
b	H	$C_6H_5CO$	1.25	2.92	3.38	2.0–2.6	6.07	$J_{3,5} = 2.0$
c	$CH_3CO$	$CH_3CO$	2.33	2.33	7.67	7.67	6.08	—
d	$C_6H_5CO$	$C_6H_5CO$	2.17	2.17	2.2–2.9		6.10	—
e	$(CH_3)_2C(CH_2CO)_2$		0.87	0.87	$CH_3:8.92; CH_2:7.45$		6.02	—

Table 2 shows that the  $\beta$ -protons appear at different fields in the monocarbonyl derivatives, the signal at about 3  $\tau$  being comparable with 3.2  $\tau$  in the methylene analogue (III,  $R^1 = R^2 = H$ ). In the cyclic diketone IIIe both  $\beta$ -pyranyl protons resonate at 0.9  $\tau$ . The carbonyl groups in the cyclohexylidene system (IIIe) are prevented from moving far away from the coplanarity of the pyran ring. The  $\beta$ -pyranyl protons are therefore in the deshielding zone of the carbonyl group resulting in a downfield chemical shift. Application of this to the monoketone IIIa leads to the assignment of the lower chemical shift signal to the

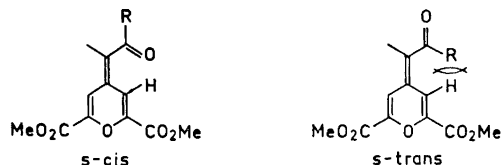
Table 1. NMR spectra of 4H-pyrans recorded in CDCl<sub>3</sub>.



Comp.	Substituents		Chemical shifts in $\tau$ values					OCH <sub>3</sub>	Couplings in cps	
	R <sup>1</sup>	R <sup>2</sup>	H <sup>3</sup>	H <sup>5</sup>	H <sup>4</sup>	H <sub>2</sub>	R <sup>1</sup>			R <sup>2</sup>
IIa	H	CH <sub>3</sub> CO	4.00 <sup>b</sup>	4.00 <sup>b</sup>	6.2-6.5 <sup>d</sup>	7.28 <sup>b</sup>	7.28 <sup>b</sup>	7.83 <sup>a</sup>	6.18 <sup>a</sup>	$J_{3,4}=3.5$ $J_{4,\alpha}=7.0$
b	H	C <sub>6</sub> H <sub>5</sub> CO	3.88 <sup>b</sup>	3.88 <sup>b</sup>	5.6-6.3 <sup>d</sup>	6.78 <sup>b</sup>	6.78 <sup>b</sup>	1.9-2.7 <sup>d</sup>	6.18 <sup>a</sup>	$J_{3,4}=3.5$ $J_{4,\alpha}=7.0$
c	CH <sub>3</sub> CO	CH <sub>3</sub> CO	4.05 <sup>b</sup>	4.05 <sup>b</sup>	6.0-6.2 <sup>d,e</sup>	7.77 <sup>a</sup>	7.77 <sup>a</sup>	7.77 <sup>a</sup>	6.17 <sup>a</sup>	$J_{3,4}=4.0$ $J_{4,\alpha}=7.0$
d	C <sub>6</sub> H <sub>5</sub> CO	C <sub>6</sub> H <sub>5</sub> CO	3.97 <sup>b</sup>	3.97 <sup>b</sup>	5.5-5.8 <sup>d</sup>	4.43 <sup>b</sup>	1.9-2.8 <sup>d</sup>	1.9-2.8 <sup>d</sup>	6.27 <sup>a</sup>	$J_{3,4}=4.0$ $J_{4,\alpha}=8.0$
e	CH <sub>3</sub> CH <sub>3</sub>	CH <sub>2</sub> CO CH <sub>2</sub> CO	3.90 <sup>b</sup>	3.90 <sup>b</sup>	6.1-6.3 <sup>d,e</sup>	CH <sub>3</sub> :8.90;	CH <sub>2</sub> :7.62 <sup>a</sup>	CH <sub>3</sub> :8.90;	6.18 <sup>a</sup>	$J_{3,4}=3.5$
f	CH <sub>3</sub> CH <sub>3</sub>	CH <sub>2</sub> CO CH=C(OH)	4.05 <sup>b</sup>	4.05 <sup>b</sup>	5.33 <sup>c</sup>	2.5-2.9 <sup>f</sup>	CH <sub>3</sub> :8.90;	CH <sub>2</sub> :7.62 <sup>a</sup>	6.18 <sup>a</sup>	$J_{3,4}=3.5$

<sup>a</sup> Singlet, <sup>b</sup> doublet, <sup>c</sup> triplet, <sup>d</sup> multiplet, <sup>e</sup> superimposed, <sup>f</sup> enolic OH.

$\beta$ -pyranyl proton which is in front of the carbonyl group in the *s-cis* conformation (Scheme 7).

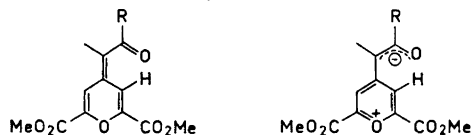


Scheme 7.

The *s-trans* conformation is thought destabilised by steric repulsion between the carbonyl methyl group and the  $\beta$ -pyranyl hydrogen atom. The preferential assignment of a *s-cis* conformation also agrees well with conclusions reached in conformational studies of related simple open-chain  $\alpha,\beta$ -unsaturated ketones by means of infrared and Raman spectroscopy.<sup>11</sup> The higher field (0.5  $\tau$ ) signal for the deshielded pyranyl proton in IIIa than in the cyclohexylidene derivative IIIe, however, suggests a greater deviation from coplanarity of the exocyclic  $\alpha,\beta$ -unsaturated carbonyl system for the former.

Steric repulsion between the substituents on the carbonyl carbons in the acyclic 1,3-dicarbonyl compound IIIc will force the carbonyl groups considerably out of plane in both *s-cis* and *s-trans* conformations resulting in an upfield shift (0.5  $\tau$ ) of the now equivalent  $\beta$ -pyranyl protons. The NMR data in Table 2 show that the aromatic analogues IIIb and III d behave similarly to the discussed aliphatic derivatives IIIa and IIIc.

The chemical shifts for the pyranyl protons in IIIa were not affected by increase in temperature. The energy barrier for rotation around the exocyclic double bond in IIIa was not reached by heating in dimethyl sulphoxide- $d_6$  to 150°C. In the literature a somewhat related 2,6-dimethylpyran has been reported to behave similarly while the superior electron releasing properties of the nitrogen in the pyridine analogue results in low energy barrier for rotation.<sup>12</sup> This indicates a relatively low ground state contribution to resonance from the pyrylium form (Scheme 8) which is not unexpected because of the destabilising effect from the methoxycarbonyl groups on the pyrylium cation.



Scheme 8.

## EXPERIMENTAL

The NMR spectra were recorded on a 60 Mc/s instrument.

*4-Acetylmethyl-2,6-dimethoxycarbonyl-4H-pyran* (IIa). 2,6-Dimethoxycarbonylpyrylium perchlorate (2.96 g, 0.01 mol) was added to acetone (50 ml) with stirring and the

solution was left in the cold overnight. The solvent was then evaporated and the residual oil dissolved by warming in ethanol; a colourless, crystalline material was separated on cooling. The yield was 75 % (1.92 g), m.p. 125°C. (Found: C 56.46; H 5.84. Calc. for  $C_{12}H_{14}O_6$ : C 56.69; H 5.55.) Molecular weight by MS: Found 254.0796. Calc. for  $C_{12}H_{14}O_6$ : 254.0790.

4-Benzoylmethyl-2,6-dimethoxycarbonyl-4H-pyran (IIb) was prepared as IIa using acetophenone. The yield was 75 %, m.p. 167–169°C (EtOH). Molecular weight by MS: Found 316.0948. Calc. for  $C_{17}H_{16}O_6$ : 316.0946.

4-Diacetylmethyl-2,6-dimethoxycarbonyl-4H-pyran (IIc) was prepared as IIa using acetylacetone. The yield was 91 %, m.p. 175°C (MeOH). Molecular weight by MS: Found 296.0897. Calc. for  $C_{14}H_{16}O_7$ : 296.0896.

4-Dibenzoylmethyl-2,6-dimethoxycarbonyl-4H-pyran (IIId). 2,6-Dimethoxycarbonyl-pyrylium perchlorate (1.48 g, 0.005 mol) was dissolved in liquid sulphur dioxide (25 ml) at  $-30^\circ\text{C}$  and dibenzoylmethane (1.12 g, 0.005 mol) added with stirring. The  $\text{SO}_2$  was then allowed to evaporate off, and the residual material was dissolved by heating in ethanol. The title compound crystallised out on cooling. The yield was 57 % (1.20 g), m.p. 163–165°C (EtOH). (Found: C 68.74; H 5.07. Calc. for  $C_{24}H_{20}O_7$ : C 68.56; H 4.80.) Molecular weight by MS: Found 420.1201. Calc. for  $C_{24}H_{20}O_7$ : 420.1209.

4-(5,5-Dimethyl-1,3-dione-2-cyclohexyl)-2,6-dimethoxycarbonyl-4H-pyran (IIe) was prepared from dimedone in  $\text{SO}_2$  as described for IIId. The yield was 81 %, m.p. 220°C (dilute EtOH). Molecular weight by MS: Found 336.1213. Calc. for  $C_{17}H_{20}O_7$ : 336.1209.

4-Benzoylmethylene-2,6-dimethoxycarbonylpyran (IIIb). 2,6-Dimethoxypyrylium perchlorate (1.48 g, 0.005 mol) was dissolved in liquid  $\text{SO}_2$  at  $-30^\circ\text{C}$  and acetophenone (0.3 g, 0.0025 mol) added with stirring. The  $\text{SO}_2$  was then allowed to evaporate in the cold and the residual material dissolved in ethanol by heating. The yellow crystalline title compound was precipitated on cooling; yield 62 % (0.48 g), m.p. 155°C (EtOH). (Found: C 64.88; H 4.79. Calc. for  $C_{17}H_{14}O_6$ : C 64.94; H 4.49.) Molecular weight by MS: Found 314.0793. Calc. for  $C_{17}H_{14}O_6$ : 314.0790.

4-Acetylmethylene-2,6-dimethoxycarbonylpyran (IIIa) was prepared from acetone in 82 % yield, m.p. 185–187°C (EtOH). Molecular weight by MS: Found 252.0628. Calc. for  $C_{12}H_{12}O_6$ : 252.0633.

4-Dibenzoylmethylene-2,6-dimethoxycarbonylpyran (IIIId). A solution of 4-dibenzoylmethyl-2,6-dimethoxycarbonyl-4H-pyran (0.57 g, 0.0014 mol) and triphenylmethyl perchlorate (0.46 g, 0.0014 mol) in anhydrous acetonitrile (10 ml) was refluxed for 30 min before evaporation of the solvent. The residual material was redissolved by heating with ethanol. Yellow needles crystallised out from the ethanol solution on cooling; yield 0.59 g (49 %), m.p. 187–190°C. (Found: C 68.87; H 4.37. Calc. for  $C_{24}H_{18}O_7$ : C 68.89; H 4.34.) Molecular weight by MS: Found 418.1052. Calc. for  $C_{24}H_{18}O_7$ : 418.1053.

4-(5,5-Dimethyl-1,3-dione-2-cyclohexylidene)-2,6-dimethoxycarbonylpyran (IIIe) was prepared from IIe and triphenylmethyl perchlorate as described for IIIId in 71 % yield, m.p. 210°C (EtOH). Molecular weight by MS: Found 334.1061. Calc. for  $C_{17}H_{18}O_7$ : 334.1052.

4-Diacetylmethylene-2,6-dimethoxycarbonylpyran (IIIc). A solution of 4-diacetylmethyl-2,6-dimethoxycarbonyl-4H-pyran (0.89 g, 0.003 mol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (0.68 g, 0.003 mol) in benzene (25 ml) was heated at 60°C for 20 min. The precipitated material was filtered off from the cold solution and the filtrate evaporated. The residue was redissolved by heating with ethanol. Yellow needles were precipitated from the cold ethanol solution; yield 0.70 g (70 %), m.p. 130°C (EtOH). Molecular weight by MS: Found 294.0731. Calc. for  $C_{14}H_{14}O_7$ : 294.0740.

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