Pyrylium Salts. III. Properties and Reactions of 2,6-Dicarbonyl Derivatives

KJELL UNDHEIM and CARL ERIK CARLBERG

Department of Chemistry, University of Oslo, Oslo 3, Norway

Some 2,6-dicarbonylpyrylium perchlorates have been prepared. These pyrylium ions are highly reactive and readily form 4H-adducts with enolisable carbonyl compounds and olefins. The adduct formation is reversible. Activated benzene derivatives are attacked. Alcohols can be dehydrogenated to the corresponding carbonyl derivatives. The equilibrium constant for pyrylium ion/4H-pyran pairs is related to the electron releasing properties of the substituents.

The pyrylium ion is less aromatic stabilized than the tropylium ion and without stabilising substituents the pyrylium ion is highly reactive. The initial products from reactions with nucleophiles or bases may readily be reacted further which makes pyrylium salts versatile synthetic intermediates.[2,3] We have recently reported a synthesis of the reactive 2,6-dimethoxycarbonylpyrylium perchlorate (6) and discussed some of its reactions.[1,4] The present work describes additional carbonyl derivatives (Scheme 1) which differ from the ester (6) in electronic activation. Self-condensation of the pyrylium ions is avoided by having carbonyl substituents without any activated hydrogen atom. Thus the amide (5) is formed from a secondary amine (4), and the α-carbon is part of an aromatic ring in (3).

1 a .X = OH
  b   X = Cl

2 a R = H
  b R = Me
  c R = OMe

3 a .R = H
  b   R = Me
  c   R = OMe

4

5

6
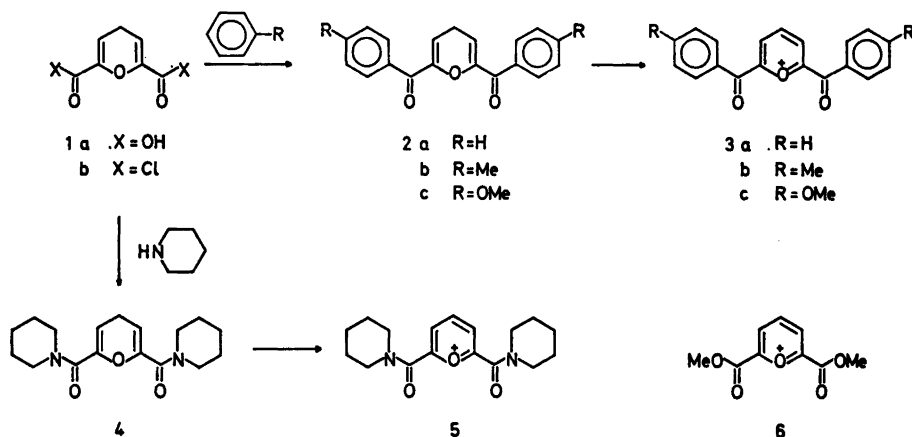
Scheme 1.

2,6-Dicarboxy-4H-pyran is readily available as synthetic starting material.[1,5] The amide (4) was prepared from its acid chloride. The latter reacted with benzene or benzene analogues under Friedel-Crafts conditions. Substituted benzenes gave exclusively (NMR) the *para*-acylated isomers (2b,c). The 4H-pyrans were then converted to the respective pyrylium salts

3

by reaction with triphenylmethyl perchlorate [6] in liquid SO_2. The NMR spectra in trifluoroacetic acid (TFA) have three low-field aromatic protons (AB_2) as expected for the pyrylium nucleus.[4] The shifts ($H\gamma$ 0.15 τ and $H\beta$ 0.75 τ) for the benzoyl derivative (*3a*) are as found for the ester (*6*). The shifts are slightly affected in the expected manner by the phenyl *para*-substituents (*3b,c*). The corresponding protons in the amide (*5*) are at higher fields (0.4 and 1.25 τ), but at lower fields (1.0 and 1.5 τ), than in 2,6-diphenylpyrylium perchlorate

which was prepared [2] for comparative reasons.

Variable anisotropy effects of the 2,6-substituents will affect the chemical shifts of the pyrylium protons. This may partly explain why these protons in the ester (*6*) and the benzoyl derivative (*3a*) have similar chemical shifts although the latter is the more reactive. Generally, however, the relative chemical shifts are indicative of the electron density in the pyrylium system and thereby informative about the relative reactivity as increased electron release will stabilize the pyrylium system.

3a,5   7 R=Ph, 8 R=N⟨⟩

a R¹ =H, R² =COMe

b R¹ =H, R²=COPh

c R¹⟩ = -COCH₂ Me / R² = -COCH₂ Me
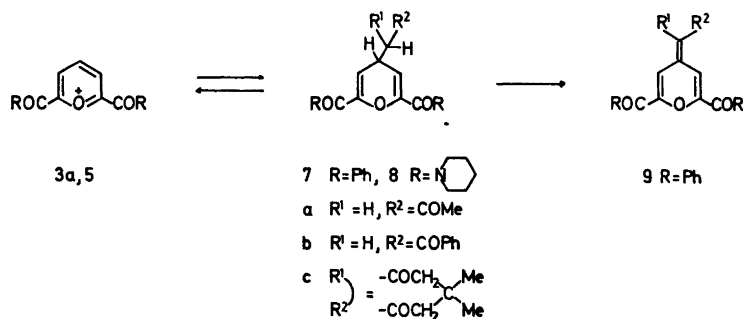
Scheme 2.

The 2,6-disubstituted pyrylium ions are attacked by a nucleophile at C-4 with formation of a 4*H*-pyran adduct. The NMR discussion above indicates that the 2,6-diphenylpyrylium ion should be the least reactive of the substances under consideration. For its reactions with activated methylene groups such as in acetonylacetone and benzoylacetone it requires the presence of a strong base.[7,8] The ester (*6*) however, attacks much less activated groups such as the methyl group in acetone or acetophenone in the cold without base addition.[1] A further comparison is available with the tropylium ion which reacts slowly with acetone on heating but readily attacks activated methylene groups in such compounds as malonic and acetoacetic ester.[9] The benzoyl derivatives (*3*) in preliminary experiments showed similar reactions and were no less reactive than the ester (*6*). Studies of the benzoyl series were therefore limited to the simplest derivative (*3a*). Both the pyrylium salts (*3a*) and (*5*) can be dissolved in acetone cooled below -10 °C without reaction. On allowing a solution of the benzoyl derivative (*3a*) in deuterioacetone (15 % con-

centration) to slowly warm up it was shown by NMR that a rapid reaction (1−2 min) ensued at about -10 °C. The amide (*5*) started to react at about -8 °C requiring about 10 min for completion of the reaction. The reaction appears autocatalytic through the perchloric acid liberated in the process. Acid catalysis was confirmed by an immediate reaction on dissolution of the pyrylium salt (*3a*) in deuterioacetone at -20 °C into which had been passed dry HCl. The function of the acid is presumably to promote enolisation of the ketonic reagent.[10]

Preparatively 4*H*-pyrans (*8a,b*) are available from the amide (*5*) by dissolution of the latter in excess acetone or acetophenone. Difficulties were experienced in preparative isolation of the benzoyl derivatives (*7a,b*) due to ease of oxidation to (*9*) and subsequent polymerisations. Such difficulties were not encountered in the reactions of the ester (*6*).[1] With equimolar quantities of the benzoyl derivative (*3a*) and the ketonic reagents in liquid SO_2 at -20 °C NMR showed only the presence of the 4-anhydro products (*9a,b*) and the parent 4*H*-pyran (*2a*). Similar hydride exchange processes have been

observed for the ester (6)[1] and in reactions of (3a) with anisole as discussed below. The carbamoyl group in (5), on the other hand, stabilizes the pyrylium nucleus sufficiently to prevent hydride transfer from the adducts (8a,b). With equimolar amounts of dimedone

in SO_2 both (3a) and (5) form the 4H-adducts (7c,8c). The reduced tendency for dehydrogenation in this case may be associated with the increase in steric hindrance to the transfer of the hydride ion from C-4.

Adduct formation between the pyrylium ion
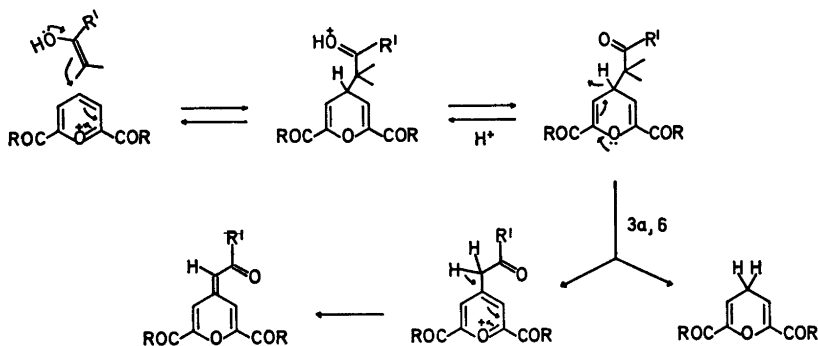
Scheme 3.

and the ketonic reagent is reversible (Scheme 3). Heating a solution of the phenacyl-4H-pyran (8b) in TFA at 70 °C produced some of the parent pyrylium ion (5). After perchloric acid addition only the pyrylium ion (5) was present.

In the discussion of the reaction between the pyrylium ion and the ketonic reagents, it was postulated that the reaction proceeds *via* enolised ketone. As a consequence the pyrylium ion would also be expected to react with other suitably substituted double bonds. Thus with styrene an almost explosive, exothermic polymerisation occurred on addition of the benzoyl pyrylium salt (3a). The less reactive amide (5) required about 15 min in the cold before being consumed, while 2,6-diphenylpyrylium perchlorate had not caused any significant polymerisation after heating at 70 °C for 1 h. Ethyl cinnamate was polymerised by (3a) on heating. A carbonium type intermediate for this process is indicated in Scheme 4. Depending on reaction conditions the ionic intermediate can polymerise the olefin by a cationic mechanism, expel a proton to form an olefin, add the anion or any other nucleophile present, or reverse the process back to the precursor pyrylium ion. The ionic intermediate corresponds to the carbonium ion intermediate in E_1-elimination and should preferentially give the thermodynamically more stabilized olefin. Rapid and reversible formation

of an ionic intermediate was strongly indicated by addition of (3a) or (5) to solutions of ethyl *cis*-cinnamate and its *p*-methoxy homologue in deuterioacetonitrile in the cold. The NMR spectra of the solutions showed only *trans*-cinnamic acid immediately after mixing the reagents.
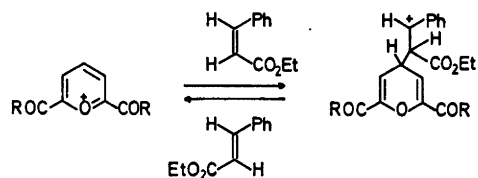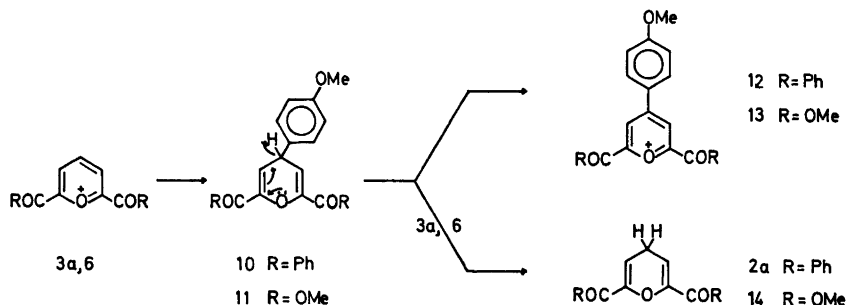

Scheme 4.

The behaviour towards aromatic nucleophiles was subsequently studied. 2,6-Diphenylpyrylium perchlorate is unreactive to simple phenyl derivatives but forms adducts at C-4 with the nucleophilic Grignard reagents.[7] Activated benzene such as phenol is attacked by the tropylium ion on heating.[11] Both the benzoyl derivative (3a) and the ester analogue (6), but not the amide (5), were found to react with anisole in liquid SO_2. None of the pyrylium salts would attack toluene. The 4H-adducts (10) and (11)[12] initially formed by *para*-substitution of anisole (NMR) reacted further to form the correspond-

ing 4-anisylpyrylium salts (12,13). The hydride abstraction by unsubstituted pyrylium ion from the 4H-adduct is a rapid process compared to anisole addition since the anisylpyrylium salts (12,13) and the respective 4H-pyrans are formed in almost equimolar amounts. Presumably the driving force for the redox process is the great increase in resonance stabilisation of the pyrylium nucleus brought about by the anisole radical.

Scheme 5.

A guide to relative redox potentials for the various cations investigated is available by equilibration studies. The triphenylmethyl cation is used both to generate the tropylium ion from cycloheptatriene and the pyrylium ions from the respective 4H-pyrans. Mixing equimolar amounts of cycloheptatriene and 2,6-dimethoxycarbonylpyrylium perchlorate in acetonitrile results in complete (NMR) hydride transfer from cycloheptatriene to the pyrylium nucleus.[1] Both the benzoyl derivative (3a) and the amide (5) were found to react with cycloheptatriene in the same manner. Within the pyrylium series equilibration studies between redox pairs were attempted in several solvents (15 % concentration) at 20 °C by the use of NMR. The hydride exchange reactions (Scheme 6) under these conditions required days (5 − 7) to reach equilibrium and reproducible quantitative measurements were difficult to achieve because of competing side reactions. The best results were obtainable in TFA.
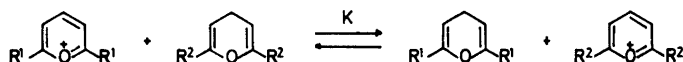
Scheme 6.

By these crude measurements the equilibrium constants were of the order: $K_{3a/6} = 0.9$; $K_{5/3a} = 1.3$ and $K_{5/6} = 1.2$. The values show that the pyrylium ion with the more electron releasing substituents is thermodynamically the more stable. It is also evident that increase in the electron releasing properties of the substituents stabilizes the pyrylium nucleus to a greater extent than it stabilizes the 4H-pyran. As a consequence pyrylium ions without electron releasing substituents are most effective for hydride abstractions and can be used for dehydrogenation of other kinds of molecules. Thus the pyrylium salts (3a,5,6) on heating with molar amounts of diphenylcarbinol in nitromethane for half an hour fully converted the carbinol (chromatography) to benzophenone.

EXPERIMENTAL

All NMR spectra were determined on a 60 MHz Varian A-60A spectrometer.
Synthesis of 2,6-dibenzoyl-4H-pyrans (2). Anhydrous aluminium chloride (0.048 mol) was added gradually (15 − 30 min) at 10 − 25 °C to 2,6-dichlorocarbonyl-4H-pyran (0.024 mol) in benzene or its analogues (0.144 mol). Reaction temperature and time were varied individually as follows: (2a)(50 °C, 4 h); (2b)(25 °C, 6 h); (2c)(10 °C, 4 h). The reaction mixture was next

poured onto ice (100 g) and conc. HCl (5 ml), and the precipitated ketone collected by filtration.

2,6-Dibenzoyl-4H-pyran (2a). Yield 82 %, m.p. 189 − 190 °C (benzene). (Found: C 78.42; H 4.90. Calc. for $C_{19}H_{14}O_3$: C 78.61; H 4.86), τ (TFA) 3.85 (2 H, t, $H^{3,5}$), 6.65 (2 H, t, H^4, $J_{3,4}$ 4 Hz), 2.0 − 2.7 (10 H, m, 2 × Ph), v_{max} (KBr) 1645 cm⁻¹ (CO).

2,6-Di-p-*methylbenzoyl-4H-pyran* (2b). Yield 69 %, m.p. 162 °C (EtOH). (Found: C 78.97; H 5.69. Calc. for $C_{21}H_{18}O_3$: C 79.19; H 5.70), τ (TFA) 3.85 (2 H, t, $H^{3,5}$), 6.65 (2 H, t, H^4 $J_{3,4}$ 4 Hz), 2.1 − 2.9 (8 H, A_2B_2, 2 × Ph), 7.5 (6 H, 2 × Me) v_{max} (KBr) 1645 cm⁻¹ (CO).

2,6-Di-p-*methoxybenzoyl-4H-pyran* (2c). Yield 60 %, m.p. 160 °C (EtOH). (Found: C 71.88; H 5.26. Calc. for $C_{21}H_{18}O_5$: C 71.99; H 5.18), τ (TFA) 3.85 (2 H, t, $H^{3,5}$), 6.65 (2 H, t, H^4, $J_{3,4}$ 4 Hz), 1.8 − 2.9 (8 H, A_2B_2, 2 × Ph), 5.95 (6 H, 2 × OMe), v_{max} (KBr) 1640, 1650 cm⁻¹ (CO).

Synthesis of 2,6-di-N-piperidylcarbonyl-4H-pyran (4). A solution of piperidine (13.30 g, 0.14 mol) in dioxane (40 ml) was added over 1 h to a solution of 2,6-dichlorocarbonyl-4H-pyran (4.94 g, 0.024 mol) in dioxane (150 ml) and benzene (20 ml) in the cold. The solution was poured into water (200 ml) after 3 h, the solution acidified with HCl and the amide isolated by ether extraction. The combined ether extracts were evaporated and the residual yellow material crystallised from ethanol; m.p. 146 − 148 °C, yield 3.80 g (52 %). (Found: C 67.30; H 8.14. Calc. for $C_{17}H_{24}N_2O_3$: C 67.08; H 7.95). τ (TFA) 4.25 (2 H, t, $H^{3,5}$), 6.85 (2 H, t, H^4, $J_{3,4}$ 4 Hz), 5.9 − 6.4, 8.0 − 8.4, (20 H, m, 2 × piperidine) v_{max} (KBr) 1630 cm⁻¹ (CO).

Synthesis of 2,6-dibenzoylpyrylium perchlorate (3). The 2,6-dibenzoyl-4H-pyran (0.015 mol) was added to liquid SO₂ (100 ml) at − 30 °C and the mixture stirred while triphenylmethyl perchlorate (0.015 mol) was added gradually under anhydrous conditions. The reaction mixture was left at room temperature after completion of the addition until all the SO₂ had evaporated. The residue was treated with anhydrous ether (150 ml) and stirred vigorously for 10 min. If the oily residue after SO₂ evaporation did not crystallise, it was solidified at about − 40 °C and the solid pulverised under ether. The treatment with anhydrous ether was generally repeated three times. The insoluble pyrylium salt thus obtained was pure enough for elemental analysis. It is highly hygroscopic and must be stored in dry atmosphere in an airtight flask.

2,6-Dibenzoylpyrylium perchlorate (3a). Yield 87 %, m.p. 164 − 166 °C (decomp). (Found: C 58.74; H 3.60. Calc. for $C_{19}H_{13}O_3.ClO_4$: C 58.70; H 3.37). τ (TFA) 0.75 (2 H, AB₂, $H^{3,5}$), 0.15 (H, H^4, $J_{3,4}$ 8 Hz), 1.8 − 2.8 (10 H, 2 × Ph).

2,6-Di-p-*methylbenzoylpyrylium perchlorate* (3b). Yield 82 %, m.p. 150 − 152 °C (decomp.). (Found: C 60.25; H 4.35. Calc. for

$C_{21}H_{17}O_3.ClO_4$: C 60.51; H 4.11). τ (TFA) 0.95 (2H, AB₂, $H^{3,5}$), 0.25 (H, H^4, $J_{3,4}$ 8 Hz), 1.8 − 2.8 (8 H, A_2B_2, 2 × Ph), 7.5 (6 H, 2 × Me).

2,6-Di-p-*methoxybenzoylpyrylium perchlorate* (3c). Yield 79 %, m.p. 156 − 158 °C (decomp.). (Found: C 55.98; H 4.01. Calc. for $C_{21}H_{17}O_5.ClO_4$: C 56.20; H 3.82). τ (TFA) 0.85 (2 H, AB₂, $H^{3,5}$), 0.20 (H, H^4, $J_{3,4}$ 8Hz), 1.6 − 3.0 (8 H, A_2B_2, 2 × Ph), 5.95 (6 H, 2 × OMe).

2,6-Di-N-piperidylcarbonylpyrylium perchlorate (5). The pyrylium salt was prepared from 2,6-di-N-piperidylcarbonyl-4H-pyran in the same way as the ketones above. The yield was 85 %, m.p. 150 − 152 °C (decomp.). (Found: C 50.43; H 5.74. Calc. for $C_{17}H_{23}N_2O_3.ClO_4$: C 50.69; H 5.76) τ (TFA) 1.25 (2 H, AB₂, $H^{3,5}$), 0.4 (H, H^4, $J_{3,4}$ 8 Hz), 5.6 − 6.5, 7.9 − 8.4 (20 H, 2 × piperidine).

4-Acetylmethyl-2,6-di-N-piperidylcarbonyl-4H-pyran (8a). 2,6-Di-N-piperidylcarbonylpyrylium perchlorate (2.01 g, 0.005 mol) was added to acetone (25 ml) with stirring and the solution left in the cold for 1 h. Evaporation left an oily material which on trituration with ether gave a crystalline solid, m.p. 100 − 102 °C; yield 1.30 g (72 %). (Found: C 66.49; H 7.80. Calc. for $C_{20}H_{28}N_2O_4$: C 66.64; H 7.83) τ (CDCl₃) 4.45 (2 H, d, $H^{3,5}$, $J_{3,4}$ 3.5 Hz), 7.1 (2 H, d, CH₂CO, $J_{CH_2,4}$ 6 Hz), 7.85 (3 H, CH₃CO), 6.0 − 6.6, 8.0 − 8.5 (20 H, 2 × piperidine); H^4 is superimposed on the piperidine protons in the 6.0 − 6.6 region; v_{max} (KBr) 1630 (CO − N), 1710 cm⁻¹ (− CO − C).

4-Benzoylmethyl-2,6-di-N-piperidylcarbonyl-4H-pyran (8b) was prepared as above from acetophenone in 78 % yield, m.p. 154 − 156 °C. (Found: C 70.80; H 7.02. Calc. for $C_{25}H_{30}N_2O_4$: C 71.07; H 7.16), τ (TFA) 4.5 (2 H, d, $H^{3,5}$, J 3.5 Hz), 6.85 (2 H, d, CH₂CO, $J_{CH_2,4}$ 6 Hz), 2.2 − 3.0 (5 H, Ph), 6.2 − 6.8, 8.3 − 8.6 (20 H, 2 × piperidine); H^4 is superimposed on the piperidine protons in the 6.2 − 6.8 region; v_{max} (KBr) 1630 (CO − N), 1680 cm⁻¹ (CO − C).

4-(5,5-Dimethyl-1,3-dione-2-cyclohexyl)-2,6-di-N-piperidylcarbonyl-4H-pyran (8c). 2,6-Di-N-piperidylcarbonylpyrylium perchlorate (2.01 g, 0.005 mol) was dissolved in liquid SO₂ (25 ml) at − 30 °C and dimedone (0.70 g, 0.005 mol) added with stirring. The SO₂ was then allowed to evaporate and the residual oily material crystallised by trituration with ether; yield 1.57 g (71 %), m.p. 140 − 142 °C. (Found: C 67.92; H 7.92. Calc. for $C_{25}H_{34}N_2O_5$: C 67.85; H 7.74), τ (CD₃CN) 4.75 (2 H, d, $H^{3,5}$, $J_{3,4}$ 4 Hz), 5.5 (H, t, H^4), 7.4 − 7.6 (4 H, CH₂CO), 8.9 − 9.0 (6 H, 2 × Me), 6.2 − 6.8, 8.2 − 8.6 (20 H, 2 × piperidine). These values are for the enolic tautomer (75 %); non-enolised molecules differ in that the H^4 proton and the COCHCO proton seem to be in the 6.2 − 6.6 region; v_{max} (KBr) 1630 (CO − N), 1600 cm⁻¹ (CO − C =).

2,6-Dibenzoyl-4-(5,5-dimethyl-1,3-dione-2-cyclohexyl)-4H-pyran (7c) was prepared as above from 2,6-dibenzoylpyrylium perchlorate and

dimedone in 78 % yield, m.p. 122−124 °C. (Found: C 75.51; H 5.42. Calc. for $C_{27}H_{24}O_5$: C 75.68; H 5.65), τ (CD_3CN) 4.2 (2 H, d, $H^{3,5}$, $J_{3,4}$ 4 Hz), 5.2 (H, t, H^4), 7.2−7.4 (4 H, 2 CH_2CO), 8.8−9.0 (6 H, 2 Me), 2.0−2.7 (10 H, 2×Ph); these values are for the enolic tautomer (85 %); ν_{max} (KBr) 1645 (CO-aryl), 1590 cm^{-1} (CO−C=).

*2,6-Dibenzoyl-4-*p*-methoxyphenylpyrylium perchlorate (12).* 2,6-Dibenzoylpyrylium perchlorate (1.94 g, 0.005 mol) was dissolved in liquid SO_2 (25 ml) at −30 °C and anisole (0.66 g, 0.006 mol) added gradually with stirring under anhydrous conditions. The solution was then left at room temperature until all the SO_2 had evaporated. The residual oily material was solidified on treatment with anhydrous ether and the ether decanted. The ether treatment was repeated three times before the residue was extracted twice with anhydrous dioxane to remove 2,6-dibenzoyl-4*H*-pyran. The remaining pyrylium salt (1.05 g) corresponds to 82 % of theoretical yield of the pyrylium salt; m.p. 155−156 °C (decomp.). (Found: C 62.93; H 4.01. Calc. for $C_{26}H_{19}O_4$·ClO_4: C 63.10; H 3.87), τ (TFA) 0.95 (2 H, $H^{3,5}$), 5.8 (3 H, OMe), 1.3−2.8 (4 H, A_2B_2, subst. Ph), 1.3−2.8 (10 H, 2×Ph).

REFERENCES

1. Østensen, E. T. and Undheim, K. *Acta Chem. Scand.* **27** (1973) 2184. Part II.
2. Dimroth, K. and Wolf, K. H. In Foerst, W. and Kirchner, F. K., Eds., *Newer Methods of Preparative Organic Chemistry*, Academic, New York 1964, Vol. III, p. 357.
3. Balaban, A. T., Schroth, W. and Fischer, G. *Advan. Heterocycl. Chem.* **10** (1969) 241.
4. Undheim, K. and Østensen, E. T. *Acta Chem. Scand.* **27** (1973) 1385.
5. Blaise, E. E. and Gault, H. *Bull. Soc. Chim. Fr.* (1907) 129.
6. Dauben, H. J., Honnen, L. R. and Harmon, K. M. *J. Org. Chem.* **25** (1960) 1442.
7. Dimroth, K. and Wolf, K. H. *Angew. Chem.* **72** (1960) 777.
8. Krøhnke, F. and Dickoré, K. *Chem. Ber.* **92** (1957) 46.
9. Vol'pin, M. E., Akhrem, I. S. and Kursanov, D. N. *Zh. Obshch. Khim.* **30** (1960) 1187.
10. Vol'pin, M. E., Akhrem, I. S., Teret'eva, E. A. and Kursanov, D. N. *Izv. Akad. Nauk. SSSR Otd. Khim. Nauk.* **5** (1963) 802.
11. Looker, J. J. *J. Org. Chem.* **32** (1967) 2941.
12. Undheim, K. and Andengaard, O. *Unpublished work.*

Received December 22, 1973.