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Microwave-induced protection and deprotection of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes catalysed by Envirocat EPZ10^{R}

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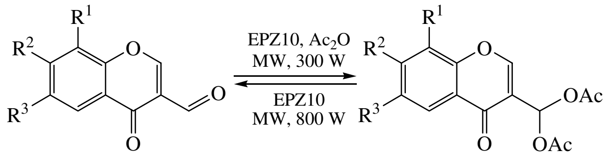
An efficient, solvent-free and chemoselective procedure for the synthesis of acylals and their deprotection to 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes catalysed by reusable Envirocat EPZ10^{R} under microwave irradiation has been carried out in good yield.

Acylals are useful protecting groups for aldehydes as they are stable in neutral and basic media.[1,2] Acylals are important building blocks for the synthesis of dienes in Diels–Alder reactions,[3] homoallylic acetates[4] and nitriles.[5] In addition, they are useful as cross-linking reagents[6] for cellulose in cotton and serve as activators.[7] Acylals are synthesised using protic acids such as $H_2SO_4^8$ or Lewis acids such as PCl_3^9 and $Sc(OTf)_3$.[10] Montmorillonite K-10 clay under microwave irradiation has been reported for the synthesis of acylals.[11] Recently, $Zn(BF_4)_2$[12] and $InCl_3$[13] have also been reported for this conversion.



1a–f **2a–f**

a $R^1 = R^2 = H, R^3 = Me$
b $R^1 = R^2 = H, R^3 = Cl$
c $R^1 = R^3 = H, R^2 = Me$
d $R^1 = R^2 = R^3 = H$
e $R^1 = R^3 = Cl, R^2 = H$
f $R^1 = Me, R^2 = H, R^3 = Cl$

Microwave-assisted organic reactions have attracted attention of chemists due to high reaction rates with the formation of cleaner products and the operational simplicity.[15–18] The catalysis of organic reactions by inorganic reagents supported on high-surface-area inorganic materials was described.[19] Envirocat^{R}, a new family of supported reagents, is a breakthrough in environmentally friendly chemistry.[20] These supported reagents are non-toxic powders. Envirocat EPZ10^{R} (clayzic) is such a supported catalyst that exhibits both Brönsted and Lewis acid characteristics.[20] The catalytic activity of EPZ10^{R} was reported for various reactions such as selective transdithioacetalization of acetals, ketals, oxathioacetals and oxathioketals,[21] Biginelli reaction[22] and Friedel–Crafts acylation.[23] Other applications of EPZ10^{R} include the olefination of benzaldehyde[24] and the formation of β-iodo ethers and iodohydrin.[25] Here, we report a microwave-induced, efficient and chemoselective procedure for the protection and deprotection of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes catalysed by reusable Envirocat EPZ10^{R}. The reactions are completed in a very short time as compared to conventional methods (Table 1). In each conversion, the catalyst was successfully recovered by filtration and recycled without significant loss in conversion.

In continuation of our work on chemoselective protection and deprotection of aldehydes and ketones,[26] study of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes[27–29] and utility of Envirocat EPZ10^{R} catalyst[20] as a protecting reagent, we have developed a microwave-induced procedure for the protection[†] and deprotection[‡] of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes catalysed by Envirocat EPZ10^{R}. 4-Oxo-(4*H*)-1-benzopyran-3-carbaldehydes

Table 1 Preparation of acylals catalysed by Envirocat EPZ10^{R}.

Compound	Conventional heating		Microwave irradiation		mp/°C
	t/h	Yield (%)	*t*/min	Yield (%)	
2a	2	67	1	84	150
2b	2	70	2	80	170
2c	1	65	1	75	147
2d	6	60	5	75	144
2e	1	80	1	90	189
2f	2	65	2	80	162

[†] Starting 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes were prepared by the Vilsmeir–Haack reaction of 2-hydroxyacetophenones. Acetic anhydride was double distilled before using. The uncorrected melting points of all compounds were taken in an open capillary in a paraffin bath. The progress of the reaction was monitored by TLC. Envirocat EPZ10^{R} from Contract Chemicals, Merseyside, England, was used. All experiments under microwave irradiation were carried out in a Model 800T domestic microwave oven (BPL, Appliances and Utilities Ltd., India) having a maximum power output of 800 W and a 2450 MHz frequency. IR spectra were recorded in KBr discs on a FTIR instrument. ^{1}H and ^{13}C NMR spectra were recorded on 300 MHz and 75 MHz spectrometers, respectively, using $CDCl_3$ as a solvent and TMS as an internal standard.

General procedure for the preparation of acylals.

A. Conventional heating. In a round-bottom flask, a mixture of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde (10 mmol), acetic anhydride (20 mmol) and Envirocat EPZ10^{R} (50 mg) was refluxed for a prescribed time (Table 1). After completion of reaction monitored by TLC, 10 ml of ethyl acetate was added to the reaction mixture. The catalyst was filtered off and washed with ethyl acetate (2×15 ml) for further uses. The filtrate was neutralised by a 2 M sodium bicarbonate (2×15 ml) solution. The organic layer was separated, dried over anhydrous $MgSO_4$ and concentrated on a rotary evaporator to dryness. The residue was recrystallised in ethanol to afford pure acylals.

B. Microwave irradiation. A mixture of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde (10 mmol) and acetic anhydride (20 mmol) was placed in a 25 ml conical flask containing Envirocat EPZ10^{R} (50 mg) and exposed to microwave irradiation at an output of 350 W for 45 s intervals to avoid quantitative loss of acetic anhydride (Table 1). After completion of reaction monitored by TLC, 10 ml of ethyl acetate was added to the reaction mixture. The catalyst was filtered off and washed with ethyl acetate (2×15 ml). The filtrate was neutralised by a 2 M sodium bicarbonate (2×15 ml) solution. The organic layer was separated, dried over anhydrous $MgSO_4$ and concentrated on a rotary evaporator. The residue was recrystallised from ethanol to afford pure acylals.

Table 2 Deprotection of acylals catalysed by Envirocat EPZ10^R.

Compound	With acidic Al_2O_3		Without acidic Al_2O_3	
	t/min	Yield (%)	*t*/min	Yield (%)
2a	4	90	7	85
2b	6	80	10	75
2c	6	75	9	70
2d	8	85	10	80
2e	3	90	6	85
2f	5	90	8	85

have three reactive centres: a carbon–carbon double bond, an α,β-unsaturated carbonyl group (pyrone ring) and a formyl group. The reaction chemoselectively occurs at the formyl group (Table 1). The acylals were isolated by quenching in water and neutralization with sodium bicarbonate, while solvent extraction is sufficient for deprotection.[§]

In view of green chemistry, the efficient recovery and reuse of the catalyst is highly preferable. In our process, Envirocat EPZ10^R was recovered conveniently from the reaction mixture through filtration and subsequent washing with ethyl acetate. In the synthesis of acylals, the catalytic activity of recovered Envirocat EPZ10^R was slightly lower than that of the fresh catalyst, and it remained unchanged in two further attempts without a loss of yield.

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[‡] *General procedure for the deprotection of acylals to 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde.*

A. With acidic alumina. In a 25 ml conical flask, 10 mmol of acylals and 1 g of acidic alumina were added to 50 mg of Envirocat EPZ10^R and mixed thoroughly. The reaction mixture was exposed to microwave irradiation (800 W) for a prescribed time (Table 2). After completion of reaction monitored by TLC, 10 ml of ethyl acetate was added to the reaction mixture. The catalyst and acidic alumina were filtered off and washed with ethyl acetate (2×15 ml) for further uses. The organic layer was dried over anhydrous $MgSO_4$ and concentrated on a rotary evaporator. The residue was recrystallised from a proper solvent to afford the pure product.

B. Without acidic alumina. In a 25 ml conical flask, 10 mmol of acylals was added to 50 mg of Envirocat EPZ10^R and mixed thoroughly. The reaction mixture was exposed to microwave irradiation (800 W) for a prescribed time (Table 2). After completion of reaction monitored by TLC, 10 ml of ethyl acetate was added to the reaction mixture. The catalyst was filtered off and washed with ethyl acetate (2×15 ml). The organic layer was dried over anhydrous $MgSO_4$ and concentrated on a rotary evaporator. The residue was recrystallised from a proper solvent to afford the pure product.

[§] *Acetoxy(6-methyl-4-oxo-4*H*-chromen-3-yl)methyl acetate* **2a**. IR (ν/cm^{-1}): 3050 (C–H_{Ar}), 1656 (C=$O_{Chromone}$), 1755 (OCOMe). ^{1}H NMR ($CDCl_3$) δ: 2.14 (s, 6H), 2.45 (s, 3H), 7.35–7.38 (d, 1H, *J* 8 Hz), 7.48–7.49 (d, 1H, *J* 8 Hz), 7.80 (s, 1H), 7.51–7.52 (s, 1H), 8.08 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 175.46, 168.76, 155.14, 154.88, 136.21, 135.78, 125.67, 124.27, 119.79, 118.31, 85.63, 21.34, 21.17. Calc. for $C_{15}H_{14}O_6$ (%): C, 62.07; H, 4.86. Found (%): C, 62.11; H, 4.82.

*Acetoxy(6-chloro-4-oxo-4*H*-chromen-3-yl)methyl acetate* **2b**. IR (ν/cm^{-1}): 3050 (C–H_{Ar}), 1643 (C=$O_{Chromone}$), 1750 (OCOMe), 1013 (C–Cl). ^{1}H NMR ($CDCl_3$) δ: 2.13 (s, 6H), 7.42–7.45 (d, 1H, *J* 8.7 Hz), 7.61–7.63 (dd, 1H, *J* 2.2 and 8.7 Hz), 7.77 (s, 1H), 8.10 (s, 1H), 8.15 (d, 1H, *J* 2.2 Hz). ^{13}C NMR ($CDCl_3$) δ: 174.23, 168.68, 155.43, 154.90, 134.81, 132.16, 125.73, 125.49, 120.37, 120.17, 85.23, 20.09. Calc. for $C_{14}H_{11}ClO_6$ (%): C, 54.12; H, 3.57. Found (%): C, 54.10; H, 3.55.

*Acetoxy(7-methyl-4-oxo-4*H*-chromen-3-yl)methyl acetate* **2c**. IR (ν/cm^{-1}): 3050 (C–H_{Ar}), 1656 (C=$O_{Chromone}$), 1758 (OCOMe). ^{1}H NMR ($CDCl_3$) δ: 2.10 (s, 6H), 2.40 (s, 3H), 7.35 (s, 1H), 7.45 (d, 1H, *J* 8.7 Hz), 7.78 (d, 1H, *J* 8.7 Hz), 7.94 (s, 1H), 8.06 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 175.40, 168.69, 155.12, 154.83, 136.15, 135.75, 125.55, 124.17, 119.77, 118.68, 85.49, 21.31, 21.11. Calc. for $C_{15}H_{14}O_6$ (%): C, 62.07; H, 4.86. Found (%): C, 62.08; H, 4.84.