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Note

Ceric ammonium nitrate catalyzed efficient and chemoselective method for protection and deprotection of 4-oxo-4*H*-1-benzopyran-3-carbaldehydes

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A chemoselective, solvent-free, mild and efficient method for the synthesis of acylals and their deprotection to 4-oxo-4*H*-1-benzopyran-3-carbaldehydes catalyzed by ceric ammonium nitrate (CAN) are carried out in good yields and all compounds **2a-h** are characterized by IR, ^{1}H NMR and ^{13}C NMR spectral data.

Keywords: Ceric ammonium nitrate, 4-oxo-4*H*-1-benzopyran-3-carbaldehydes

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Acylals are useful protecting groups for aldehyde as they are stable in neutral and basic media[1,2]. Selective protection and deprotection of carbonyl groups frequently play an important role in the multistep organic synthesis. Acylals are important building blocks for the synthesis of dienes in Diels-Alder reactions[3], homoallylic acetates[4] and nitrile[5].

The preparation of acylals, generally, has been achieved by using strong protic acids such as H_2SO_4 (ref. 6), H_3PO_4 or CH_3SO_3H (ref. 7), and Naflon-H (ref. 8). Lewis acids such as $ZnCl_2$ (ref. 9), $FeCl_3$ (ref. 10), PCl_3 (ref. 11), I_2 (ref. 12), $Sc(OTf)_3$ (ref. 13), WCl_6(ref. 14) and solid acidic catalysts like zeolites[15,16], graphite[17], zirconium sulfophenyl phosphonate[18] and caly[19] have also been used as alternative catalysts for the formation of acylals. Recently $Zn(BF_4)_2$ (ref. 20), $InCl_3$ (ref. 21), Amberlyst-15 (ref. 22) have also been reported as catalysts for this conversion. These methods have not been entirely satisfactory, owing to drawbacks such as low yields, long reaction time, expensive and highly toxic catalysts.

Results and Discussion

In continuation of our work on chemoselective protection and deprotection of aldehyde and ketone[23] and on 4-oxo-4*H*-1-benzopyran-3-carbaldehyde[24-26], we have developed the chemoselective methodology for protection and deprotection of formyl group of 4-oxo-4*H*-1-benzopyran-3-carbaldehyde as acylals catalyzed by ceric ammonium nitrate. Acylals were prepared in the absence of any solvent. The 4-oxo-4*H*-1-benzopyran-3-carbaldehyde has three reactive centers, viz. carbon-carbon double bond, α, β-unsaturated carbonyl group i.e. pyrone ring and formyl group. Of these three reactive centers, the reaction chemoselctively occurs at formyl group. In this methodology the reactions are completed in shorter time period with good yields. In addition, the conditions applied for the synthesis and deprotection of acylals are very mild as compared to the reported methods. The acylals were prepared in solvent-free condition and isolated by simple quenching in water and neutralization with sodium bicarbonate while for deprotection of acylals only water quenching is sufficient.

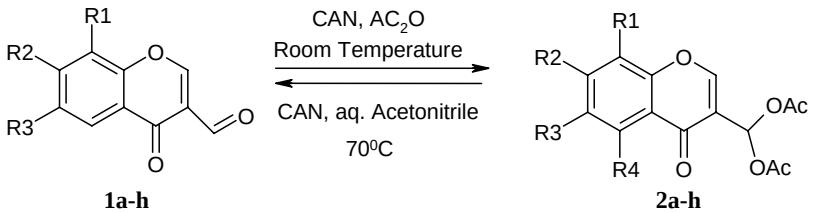
Experimental Section

The starting material 4-oxo-4*H*-1-benzopyran-3-carbaldehydes were prepared by reported method using Vilsmeir-Haack reaction on corresponding 2-hydroxyacetophenones. The acetic anhydride was double distilled before using. Melting point of all compounds were taken in open capillary in paraffin bath. The progress of the reaction was monitored on TLC. IR spectra were recorded in KBr disc on FTIR instrument; and ^{1}H NMR and ^{13}C NMR spectra on 300 MHz and 75 MHz spectrometers, respectively using $CDCl_3$ as a solvent and TMS as an internal standard.

General procedure for synthesis of acylals. To the stirred suspension of 4-oxo-4*H*-1-benzopyran-3-carbaldehydes **1a-h** (10 mmoles) in acetic anhydride (20 mmoles), 6 mol% of ceric ammonium nitrate was added at room temperature. The progress of the reaction was monitored by TLC. After completion of reaction (TLC) in time period as listed in **Table I**, the reaction mixture was quenched directly in 2 *M* sodium

Table I — Chemoselective synthesis of acylals **2a-h** and their deprotection to of 4-oxo-4*H*-1-benzopyran-3-carbaldehydes catalyzed by ceric ammonium nitrate and ^{1}H and ^{13}C NMR data of **2a-h**

Compd	R_1	R_2	R_3	m.p. ^{0}C	Preparation of acylals		Deprotection of acylals		^{1}H NMR	^{13}C NMR
					Time (hr)	Yeild (%)	Time (hr)	Yeild (%)		
2a	H	H	CH_3	150	4	88	2	88	2.14 (s, 6H), 2.45 (s, 3H), 7.35-7.38 (d, 1H, *J*=8.05), 7.48-7.49 (d, 1H, *J*=8.05), 7.8 (s, 1H), 7.51 (s, 1H), 8.08 (s, 1H)	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
2b	H	H	Cl	170	2	82	2	91	2.13 (s, 6H), 7.42-7.45 (d, 1H, *J*=8.78 Hz), 7.61- 7.63 (dd, 1H, *J*=2.20 & 8.78 Hz), 7.77 (s, 1H), 8.10 (s, 1H), 8.15 (d, 1H, *J*=2.20 Hz)	174.23, 168.68, 155.43, 154.90, 134.81, 132.16, 125.73, 125.49, 120.37, 120.17, 85.23, 20.09
2c	H	CH_3	H	147	2	81	2	92	2.10 (s, 6H), 2.4 (s, 3H), 7.35 (s, 1H), 7.45 (d, 1H, *J*=8.78 Hz), 7.78 (d, 1H, *J*=8.78 Hz), 7.94 (s, 1H), 8.06 (s, 1H)	175.40, 168.69, 155.12, 154.83, 136.15, 133.75, 125.55, 124.17, 119.77, 118.68, 85.49, 85.64, 21.37
2d	H	H	H	144	2	89	3	90	2.13 (s, 6H), 7.4 (s, 1H), 8.2 (s, 1H), 7.5-8.2 (m, 4H)	175.47, 168.77, 154.88, 153.77, 135.68, 126.88, 124.27, 119.79, 118.22, 85.64, 21.37
2e	Cl	H	Cl	189	3	90	2	90	2.13 (s, 6H), 7.72 (d, 1H, *J*=2.20Hz), 7.77 (s, 1H), 8.06 (d, 1H, *J*= 2.20Hz), 8.18 (s, 1H)	173.58, 168.59, 155.31, 150.95, 134.68, 131.90, 126.31, 124.94, 124.45, 120.60, 84.91, 21.08
2f	CH_3	H	Cl	162	2	85	2	90	2.14 (s, 6H), 2.50 (s, 3H), 7.36 (s, 1H), 7.77 (s, 1H), 8.06 (s, 1H), 8.16 (s, 1H)	175.35, 168.21, 155.20, 154.52, 135.35, 132.80, 125.40, 123.80, 119.25, 130.34, 85.40, 84.50, 22.20
2g	H	H	Br	171	2	85	2	90	2.14 (s, 6H), 7.4 (d, 1H, *J*=8.78Hz), 7.8 (dd, 2H, *J*=2.3 & 8.7 Hz), 8.19 (s, 1H), 8.4 (s, 1H)	173.56, 168.17, 154.93, 137.09, 128.53, 125.38, 120.07, 119.84, 84.81, 77.63, 76.36, 20.68
2h	H	H	F	156	2	87	2	92	2.13 (s, 6H), 7.3 (d, 1H, *J*=8.78 Hz), 7.79 (dd, 2H, *J*= 2.3 & 8.7 Hz), 8.2 (s, 1H), 8.5 (s, 1H)	173.58, 168.23, 154.85, 137.25, 128.65, 125.30, 120.15, 119.90, 84.88, 77.55, 76.32, 20.63



1a-h **2a-h**

Scheme I

bicarbonate solution and extracted with ethyl acetate. The organic layer was twice washed with water and dried over magnesium sulfate and concentrated on rotary evaporator till dryness. The residue was recrystallized from ethanol to afford pure acylals **2a-h** (**Scheme I**).

Deprotection of acylals to 3-formylchromone. To the suspension of acylals **2a-h** (10 mmoles) in aqueous acetonitrile (1:1), 6 mol % ceric ammonium nitrate was added and the resulting suspension was heated at 70°C for required time period as listed in

Table I. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature, quenched in water and extracted with ethyl acetate. The ethyl acetate layer was dried over magnesium sulfate and concentrated on rotary evaporator. The residue obtained was recrystallized from the proper solvent to afford the pure product.

Conclusion

We have synthesized the acylals of 4-oxo-4*H*-1-benzopyran-3-carbaldehydes chemoselectively catalyzed by ceric ammonium nitrate in absence of any solvent while deprotection of acylals is carried out by the same catalyst in aqueous acetonitrile (1:1) in good yields at room temperature and at 70°C, respectively. Such type of protection and deprotection for heterocyclic moiety has been carried out for the first time. In addition to this, the catalyst used is inexpensive, easily available, non-corrosive and solvent-free, which makes the reactions convenient, more economical and environmentally benign. The compounds are characterized by IR, ^{1}H NMR and ^{13}C NMR spectra **(Table I)**.

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