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Ceric Ammonium Nitrate as a Convenient Catalyst for Chemoselective Thioacetalisation

Pijus Kumar Mandal and Subhas Chandra Roy*

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta - 700 032, India.

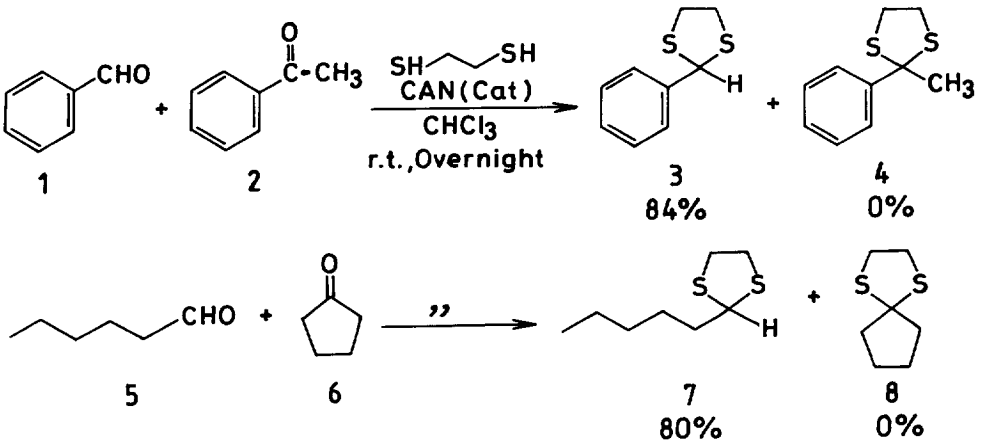
Abstract : A new, mild and chemoselective protection of aldehydes as 1,3-dithiolanes using ceric ammonium nitrate as a catalyst is described. High yields are obtained at room temperature even in the presence of ketones. While alicyclic ketones may also be protected at elevated temperature, aromatic and acyclic ketones remained uneffected.

The conversion of carbonyl moieties into thioacetals and thioketals constitutes an important part of many organic synthetic transformations,[1] since these sulfur functionalities are unattractive towards a wide variety of reagents. Dithioacetals are also useful in organic synthesis as acyl carbanion equivalents.[2] Numerous methods that are reported for this conversion include the use of protic acids, Lewis acids and some silicon reagents.[1,3] Recently Nafion-H catalyst,[4] silica gel treated with thionyl chloride,[5] anhydrous lanthanum trichloride[6] and stoichiometric amount of boron trifluoride etherate,[7] Amberlyst-15 catalyst[8] have also been employed for chemoselective thioacetalisation.

However, many of these methods suffer from harsh conditions, expensive reagents and sometimes cumbersome extraction procedures. Although, there are chemoselective methods for thioacetalisation of aldehydes in presence of ketones, very little is known about the selectivity amongst different types of ketone functionalities.

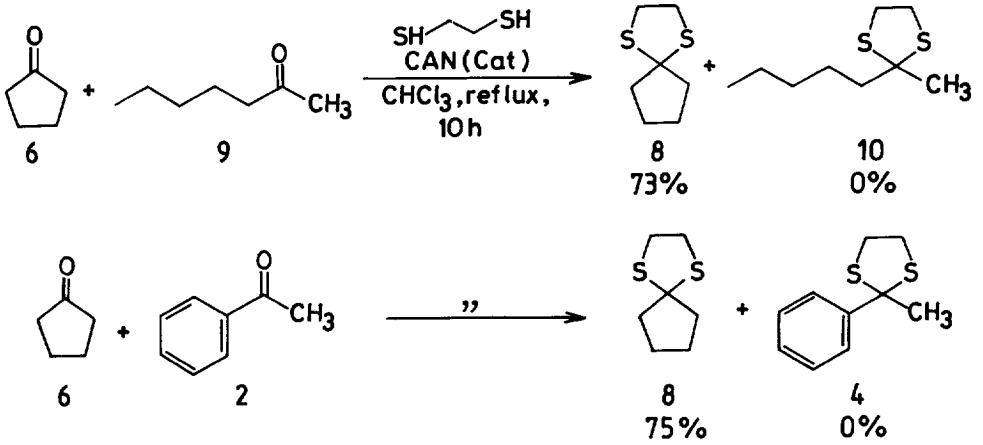
Recently we have reported[9] ceric ammonium nitrate (CAN) catalysed tetrahydropyranylation of various types of alcohols. Now we report that a catalytic amount of CAN is a remarkably effective reagent for highly chemoselective thioacetalisation of carbonyl moieties. Both reaction conditions and work-up procedures are very simple and convenient. We have found that CAN effectively catalyses the thioacetalisation of aldehydes with 1,2-ethandithiol at room temperature in presence of ketones. For example, when a mixture of benzaldehyde 1 and acetophenone 2 was allowed to react with one equivalent of ethanedithiol and a catalytic amount of

CAN in chloroform for overnight at ambient temperature, a high yield of 3 was obtained and the ketone was recovered unchanged (Scheme-1). Similar results were obtained when the experiment was performed on a mixture of 5 and 6.



Scheme-1

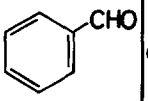
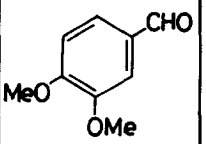
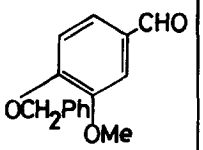
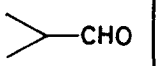
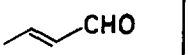
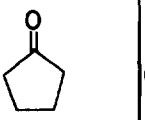
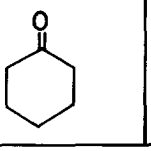
This method may be extended to protect alicyclic ketones simply by refluxing the reaction mixture for 10 h. Interestingly, aromatic ketones, γ-lactones and acyclic ketones did not react at all even at elevated temperature for longer period. When a mixture of 6 and 9 was refluxed for



Scheme-2

10 h with CAN and 1,2-ethanedithiol in chloroform a good yield of 8 was obtained and the acyclic ketone 9 recovered unchanged (Scheme-2). Similar results were obtained when the experiment was performed on a mixture of 6 and 2. It is noteworthy that to our knowledge there is no method reported so far where alicyclic ketones can be protected as thioketal in presence of acyclic ketones. Results with various aldehydes and ketones are summarised in the Table.

Table: Conversion of carbonyl compounds to thioacetals and thioketals with CAN

Entry	Substrate	Reaction condition	Product	Yield (%)[a]
1		$CHCl_3$, r.t., overnight	Thioacetal	85
2		"	Thioacetal	96
3		"	Thioacetal	96
4		"	Thioacetal	80
5		"	Thioacetal	64[b]
6		"	Thioacetal	70
7		$CHCl_3$, reflux, 10h	Thioketal	82
8		"	Thioketal	87

[a] All are isolated yields and are not optimised [b] Yield is low due to volatility of the product.

No isomerisation or 1,4-addition was observed in case of α,β-unsaturated aldehyde (entry 6). Various aromatic ketones e.g., acetophenone, benzophenone, 4-chromanone and acyclic ketones e.g., 2-pentanone, 2-heptanone did not react at all even under prolonged refluxing.

In conclusion, the mild reaction conditions and simple work-up procedures make this an ideal protocol for the protection of aldehydes or alicyclic ketones as dithiolanes. Furthermore, high chemoselectivities of the reaction make this an important tool in synthetic organic chemistry.

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Experimental

All starting materials were commercially available and products were isolated and identified by IR and ^{1}H NMR or by comparison with known samples which were prepared according to the literature procedures.[5,10] Melting points were determined in capillary tubes and are uncorrected. IR spectra were determined with a Perkin-Elmer 298 spectrometer. ^{1}H NMR spectra were recorded in Varian EM 360L instrument in $CDCl_3$ (unless otherwise stated) with TMS as internal reference. Chemical shifts were expressed in ppm, coupling constants in Hz. Solvents and reagents were purified by standard procedures as necessary. Petroleum ether of boiling range from 60 °C to 80 °C was used for column chromatography.

General Procedure : A mixture of the aldehyde (2.0 mmol), 1,2-ethanedithiol (2.1 mmol) and CAN (0.2 mmol) in anhydrous $CHCl_3$ (10 ml) was stirred overnight at room temperature (25 °C). The reaction mixture was diluted with $CHCl_3$ (50 ml) washed with 5% aqueous NaOH solution (3 x 20 ml) and dried (Na_2SO_4). Solvent was removed under reduced pressure and the brown residue was chromatographed over silica gel (60-120 mesh) (5% ethylacetate in petroleum ether) to afford the thioacetal. For acyclic ketones the procedure was identical except the reaction mixture was refluxed for 10 h.

3,4-Dimethoxy benzaldehyde thioacetal : m.p. 66-67 °C. IR (KBr) ν_{max} 2960, 2860, 1610, 1600, 1530, 1480, 1470, 1430, 1350, 1280, 1270, 1240, 1160, 1050 cm^{-1}; ^{1}H NMR δ 3.10-3.63 (m, 4H), 3.86 (s, 3H), 3.90 (s, 3H), 5.63 (s, 1H), 6.70-7.26 (m, 3H).

3-Methoxy-4-benzyloxy benzaldehyde thioacetal : m.p. 76-77 °C. IR (KBr) ν_{max} 2960, 2900, 1610, 1600, 1525, 1480, 1430, 1400, 1280, 1230, 1150, 1050, 1020, 880 cm^{-1}; ^{1}H NMR δ 3.0-3.60 (m, 4H), 3.86 (s, 3H), 5.10 (s, 2H), 5.60 (s, 1H), 6.66-7.20 (m, 3H), 7.21-7.50 (m, 5H).

1-Hexanal thioacetal : Viscous oil. IR (Neat) ν_{max} 3000, 2960, 2900, 1480, 1400, 1300 cm^{-1}; ^1H NMR δ 0.73-2.10 (m, 11H), 3.23 (s, 4H), 4.50 (t, J=8 Hz, 1H).

Crotonaldehyde thioacetal : Viscous oil. IR (Neat) ν_{max} 3000, 2960, 1520, 1470, 1430, 1390, 1300, 1170, 980 cm^{-1}; ^1H NMR δ 1.70 (d, J=7 Hz, 3H), 3.26 (s, 4H), 4.93-5.10 (m, 1H), 5.43-5.98 (m, 2H).

Thioacetalisation of 1 in presence of 2 : A mixture of benzaldehyde **1** (212 mg, 2.0 mmol) and acetophenone **2** (240 mg, 2.0 mmol) with ethanedithiol (206 mg, 2.2 mmol) and CAN (110 mg, 0.2 mmol) in $CHCl_3$ (10 ml) was stirred at room temperature overnight. The raction mixture was diluted with $CHCl_3$ (50 ml), washed with 5% aquous NaOH solution (3 x 20 ml) and dried (Na_2SO_4). The organic solution was concentrated under reduced pressure and the residue was chromatographed over silica gel (60-120 mesh) (5% ethyl acetate in petroleum ether) to afford the thioacetal **3** (305 mg, 84%) and the starting ketone **2** (215 mg, 90%). Thioketalisation of **6** in presence of **9** was performed following the same procedure except the reaction mixture was refluxed for 10 h to furnish the thioketal **8** (73%) and the unreacted ketone **9** (92%).

References :

1. (a) Green, T.W.; "Protective Groups in Organic Synthesis", John Wiley, New York, **1981.**
(b) Loewanthal, H.J.E.; "Protective Groups in Organic Chemistry", McOmie, J.F.W. Ed., Plenum, New York and London, **1973.**
2. (a) Haptmann, H.; Campos, M.M.; J. Am. Chem. Soc., **1950**, 72, 1405-1406.
(b) Patai, S.; "The Chemistry of the thiol group", John Wiley, New York, **1974.**
3. For some recent methods of thioacetalisation see :
(a) Sato, T.; Yoshida, E.; Kobayashi, T.; Otero, J.; Noazaki, H.; Tetrahedron Lett., **1988**, 29, 3971-3974.
(b) Corey, E.J.; Shimoji, K.; Tetrahedron Lett., **1983**, 24, 169-172.
(c) Satoh, T.; Uwaya, S.; Yamakawa, K.; Chem. Lett., **1983**, 667-670.
(d) Patney, H.K.; Tetrahedron Lett., **1991**, 32, 2259-2260.
4. Olah, G.A.; Narang, S.C.; Meidar, D.; Salem, G.F.; Synthesis, **1981**, 282-283.
5. Kamitori, T.; Hojo, K.; Masuda, R.; Kimura, T.; Yoshida, T.; J. Org. Chem., **1986**, 51, 1427-1431.

6. Garlaschelli, L.; Vidari, G.; Tetrahedron Lett., **1990**, 31, 5815-5816.
7. soderquist, J.A.; Miranda, E.I.; Tetrahedron Lett., **1986**, 27, 6305-6306.
8. Perni, R.B.; Synth. Commun., **1989**, 19, 2383-2387.
9. Maity, G.; Roy, S.C.; Synth. Commun., **1993**, 23, 1667-1671.
10. (a) Reid, E.E.; Jelinek, A.; J. Org. Chem., **1950**, 15, 448-449.
(b) Platen, M.; Stekhan, E.; Chem. ber., **1984**, 117, 1679-1694.
(c) Robbe, Y.; Fernandez, J.P.; Dubief, R.; Chapat, J.P.; Sentenac-Roumanou, H.; Fatome, M.; Laval, J.D.; Eur. J. Med. Chem., **1982**, 17, 235-240.

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