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CLEAVAGE OF THIOACETALS BY CLAY-SUPPORTED METAL NITRATES

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Abstract : Thioacetals are cleaved into aldehydes and ketones, under very mild conditions, by K-10 clay-supported ferric or cupric nitrate.

WIDESPREAD use is made of thioacetals in organic synthesis, mostly for protection or *umpolung* of the reactivity of a carbonyl group[1]. Regeneration of the carbonyl function from its latent form in these compounds is a crucial step[2-4].

We report here two new procedures for obtaining back a ketone or aldehyde from the corresponding bis-thioacetals, using either clay-supported ferric nitrate ("clayfen")[5] or clay supported cupric nitrate ("claycop"). Both reagents are highly efficient (Table 1) and stand comparison with alternate methods, whereas the ease of set-up and work-up, together with the mild experimental conditions, show advantages over existing methods.

"Clayfen" is prepared as previously described[6] from a mixture of 45 g of iron(III) nitrate nonahydrate, 60 g of K-10 bentonite clay and 750 ml of acetone. It may be kept a few days under *n*-pentane, in an uncapped flask, and can be reactivated by mere evaporation of pentane, in a rotary vacuum evaporator, on a water bath below 50°C. We prefer however, to use freshly-prepared reagent. "Claycop" is prepared in like manner, adding 60 g of K-10 clay to a solution of 40 g of copper(II) nitrate trihydrate in 750 ml of acetone. The resulting suspension is placed in a rotary vacuum evaporator and the solvent is eliminated under reduced pressure (water jet aspirator) on a water bath at 50°C. After 30 minutes, the dry solid crust adhering to the walls of the flask is flaked off with a spatula, and solvent evaporation is resumed for another 30 minutes, yielding about 100 g of "claycop", as a light blue free flowing powder which, unlike "clayfen", shows no loss of reactivity after standing in an open powder box for one month.

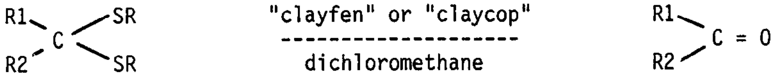
Stirring 0.01 mole of thioacetal (or thioketal) for a few hours, at room temperature, with 10.4 g of "clayfen" (11 mM of ferric nitrate) (method A) or with 12.1 g of "claycop" (20 mM of copper nitrate) (method B) in 120 ml of toluene, of n-pentane or, preferably, of dichloromethane rapidly results in evolution of nitrogen oxides. Stirring is maintained until disappearance of those oxides. The clay is then filtered off, and washed twice with 50 ml portions of the solvent. The resulting pale yellow or slightly green solution is filtered through a small quantity of neutral aluminium oxide, and the solvent is evaporated under vacuum. In the case of dithiane and dithiolane derivatives, this affords the pure carbonyl compounds, identified by comparison (melting point, mixed melting point, T.L.C. on silicagel, ir and pmr spectra, capillary gas chromatography) with authentic samples. In the case of dithioethyl derivatives, a further purification step is necessary to get rid of by-products resulting from the oxydation of the thio-moiety (see below).

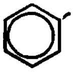
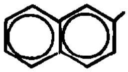
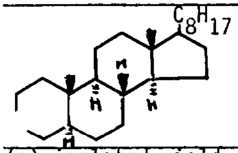
The rationale for the choice of those reagents and conditions comes from consideration of the following observations :

1. it has been recently demonstrated that NO^+-releasing reagents are efficient in transforming S,S-acetals into the corresponding carbonyl compounds[4,7].
2. "clayfen", in its reactions with alcohols and thiols, is equivalent to a source of NO^+ nitrosonium ions[5,8]. Exploratory experiments with "claycop" show similar reactivity patterns.
3. oxydation of dithiols by either "clayfen" or "claycop" leads to products (presumably polymeric) which are insoluble in hydrocarbons or in dichloromethane, and are easily removed, together with the clay residues, by a simple filtration.
4. despite its oxidizing properties, "clayfen" is totally inoccuous towards the carbonyl group, even in benzaldehydes[5,6,9].

The results shown in Table 1 for a wide variety of substrates, indicate an essentially quantitative conversion into carbonyl compounds. From the double point of view of the ease of work-up and the isolated yield, the nitrato reagents are particularly efficient when the thiocaetal moiety is part of a cyclic sub-unit, such as dithiane or dithiolane : in these

Table 1 : Dethioacetalisation of some representative substrates :



Thioaketal				Reaction conditions		Carbonyl compounds	
R1	R2	R	Lit. Ref.	Time (Hours)	Method	Yield (%)(a)	M.P. (Lit. [21])
	H	$-(CH_2)_3-$	12	5	A	100	--
				5	B	100	--
		$-C_2H_5$	13	2.5	A(b)	99.4	48
				4	B(b)	99.5	47-48
							(49)
		$-(CH_2)_2-$	14	3	A	100	47-48
				6	B	100	48
		$-(CH_2)_3-$	15	2.5	A	98.3	46-48
				5	B	97.3	46-47
	H	$-(CH_2)_2-$	14	2	A	98.7	59-60
				6	B	99.6	59
							(59)
$n-C_9H_{19}$	H	$-C_2H_5$	16	3	A(c)	86.7	--
				3	B(c)	87.5	--
		$-(CH_2)_3-$	17	4	A	99.1	--
				4	B	91.2	--
$n-C_9H_{19}$	$-CH_3$	$-(CH_2)_3-$	18	4	A	98.5	--
				4	B	98.1	--
$n-C_4H_9$	$n-C_4H_9$	$-(CH_2)_3-$	18	6	A	98.0	--
				6	B	98.4	--
		$-C_2H_5$	19	5	A(d)	61.7	125-8
				5	B(d)	60.6	125-7
							(128.9)
		$-(CH_2)_2$	20	4	A(d)	71.8	126-8
				4	B	96.8	125-7

(a) isolated yield
(b) washed with n-pentane after solvent evaporation
(c) purified by column chromatography (silica-gel) using toluene as mobile phase
(d) washed with acetone after solvent evaporation.

cases, by-products are virtually absent from the organic solution, and one can take full advantage of the ease of work-up characteristic of supported reagents[9,11]. In the case of open-chain thioacetals, such as the dithioethyl acetals tested here, presence in the organic phase of important quantities of by-products resulting from the degradation of the thio-residue necessitates complementary purification procedures; a mere wasing suffices with solid carbonyl compounds, but can nevertheless lead to some losses in the isolated quantities; in the case of liquid carbonyl compounds however, it is advisable to use colum chromatography to obtain pure carbonyl products.

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