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THE FACILE REMOVAL OF THE ETHYLENE HEMITHIOACETAL AND -KETAL PROTECTING GROUP.

THE REACTION OF CHLORAMINE-T WITH 1,3-OXATHIOLANES.

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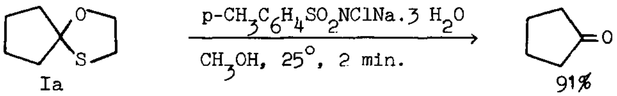
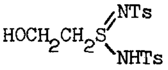
The importance of the ethylene hemithioacetal or -ketal protecting group in steroid chemistry is well documented.[1] The oxathiolanes derived from steroids and other aldehydes and ketones are generally stable. Regeneration of the carbonyl compounds previously required acid catalyzed hydrolysis or Raney nickel desulphurization.[1a,2]

We now wish to report that when 1,3-oxathiolanes are treated with a solution of sodium N-chloro-p-toluenesulphonamide (Chloramine-T) in water, ethanol or methanol under mild conditions, good to excellent yields of the corresponding aldehydes or ketones are obtained (Table). For example, 1,4-oxathiaspiro[4,4]nonane, Ia, affords cyclopentanone in 91% yield when treated for two minutes with Chloramine-T in 85% methanol-water at 25°C (equation 1). Cyclopentanone was identified by its semicarbazone derivative and determined quantitatively by GLC. It is clear from the present results that a wide variety of 1,3-oxathiolanes will undergo the reaction and that other functional groups can be tolerated using Chloramine-T under the reaction conditions. For example, ethyl acetoacetate is obtained in 96% yield from ethyl 2-methyl-1,3-oxathiolane-2-acetate, Ie.

(1)


The other products vary with the amount of Chloramine-T used. In all cases there can be isolated p-toluenesulphonamide and a compound mp 159° (dec.) identified as 2-hydroxyethyl p-toluenesulphonimidosulphine-p-toluenesulphonylimine, II, by elemental analysis ($C_{16}H_{20}N_2O_5S_3$), IR spectrum (OH at 3465 cm^{-1}, NH at 2660 cm^{-1}, Nujol), and NMR spectrum (two methylene triplets,



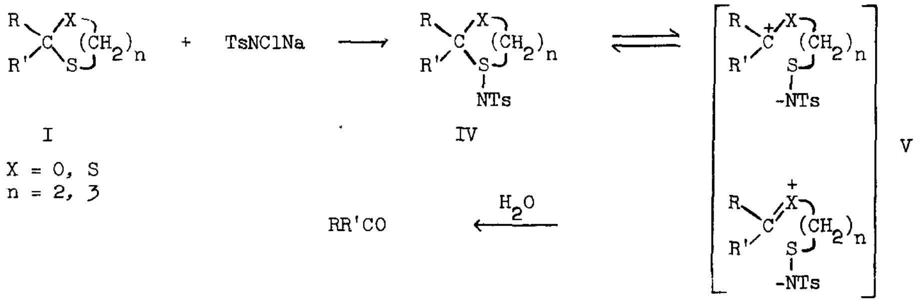
$$HOCH_2CH_2S(=NTs)NHTs$$

(Ts = $p\text{-}CH_3C_6H_4SO_2\text{-}$)

II

3.48 δ (SCH_2) and 4.18 δ (OCH_2) J_{AB} = 4.9 cps, pyridine-d_5). Compounds closely related to II are formed in the reactions of Chloramine-T or -B with a variety of organosulphur compounds.[3] A third product, bis [2-hydroxyethyl]disulphide, III, is formed when less than two moles of Chloramine-T per mole of oxathiolane is used. III can be eliminated from the reaction mixture by reaction with more Chloramine-T to form II as might be expected by analogy with the behaviour of other disulphides.[3b,c,d]

On the basis of these results and the observation that 1,3-dithiolanes and 1,3-dithianes behave similarly[7], the reaction may be viewed as proceeding via the formation of an unstable sulphilimine[8], IV, and a zwitterion, V (reaction2). We defer a full discussion of mechanism until later.



The present results indicate that a new method is now available for the removal, under mild conditions, of the ethylene hemithioacetal or -ketal protecting group. The existence of this method in addition to older methods of greater severity adds a new dimension to the practice of carbonyl group protection during synthesis.

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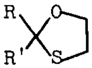
Table

Preparation of Oxathiolanes and their Reaction with Chloramine-T

Oxathiolanes  Preparation and Properties							Reaction with Chloramine-T		
Compound	R	R'	Synthetic Method, Ref.	bp (Torr) or [mp] °C	Yield,%	Ref.	Moles Chloramine-T Mole Oxathiolane	Reaction medium	Yield of RR'CO
Ia	$(CH_2)_4$		4	73 (10)	66	4	1.03	85% MeOH-H_2O	91[a]
b	$(CH_2)_5$		1b	90 (10)	58	1a	0.88	96% EtOH-H_2O	88[a]
c	$(CH_2)_6$		4	84 (2)	62	4	1.03	85% MeOH-H_2O	98[a]
d	$(CH_3)_3C$	CH_3	4	[39.1-40]	60	5	1.79	MeOH	85[a]
e	CH_3	$CH_2CO_2C_2H_5$	4	79-81 (1)	66	1a	1.00	96% EtOH-H_2O	96[a]
f	C_6H_5	CH_3	1a	85-88 (1)	44	1a	0.89	96% EtOH-H_2O	88[a]
g	C_6H_5	C_6H_5	4	[52.3-52.5]	33	6	2.18	96% MeOH-H_2O	100[b]
h	$(CH_3)_2CH$	H	1a	66 (24)	67	2d	2.0	H_2O	62[a]
i	C_6H_5	H	1a	92 (1)	54	2d	0.88	96% EtOH-H_2O	90[a]

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a) Yield and identification by GLC analysis basis oxathiolane. Estimated error ± 4%; b) Isolated as a solid

In many cases the carbonyl compounds were isolated and identified completely.