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THE FACILE REMOVAL OF THE ETHYLENETHIOACETAL AND -KETAL PROTECTING GROUP.

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

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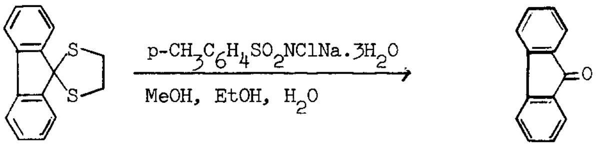
The discovery of a facile reaction between sodium N-chloro-p-toluenesulphonamide (Chloramine-T) and 1,3-oxathiolanes which affords the corresponding aldehydes and ketones in good to excellent yields[1] prompted us to explore the reaction of Chloramine-T with 1,3-dithiolanes (ethylenethioketals). The importance of the ethylenethioketal carbonlyl protecting group is well established[2,3] and the dithiolanes can be prepared from carbonyl compounds in excellent yields.[3] Reomval of cyclic thioketal protecting groups to regenerate aldehydes and ketons is usually performed by one of two types of methods: in one, related to a method used for open chain analogues, a heavy metal salt (Hg^{II} or Ag^{I}) is used in a hydrolytic medium[4]; in the other, oxidation of the sulfur is followed by basic cleavage of the resulting disulfone.[5] Other methods for removing the ethylene thioketal protecting group are therefore of interest.

We have found that a variety of 1,3-dithiolanes react smoothly with Chloramine-T in a aqueous methanol and/or ethanol to give the corresponding carbonyl compounds in good to excellent yields (Table). For example, Chloramine-T in 80% methanol was added to a stirred suspension of spiro[1,3-dithiole-2,9'-fluorene] in 2:1 vol methanol/ethanol, water was added, the reaction mixture was extracted with ether, the ether extract was extracted with 2N sodium hydroxide after which the ether solution was dried and the ether was evaporated.

Chromatography of the residue was effected with alumina (acid, activity I) and benzene and the eluate was recrystallized from benzene/ligroin to yield fluorenone, mp 82-83°, in 86% yield (Equation 1).

(1)



86%

Under similar conditions, cholestane-3-one was obtained from spiro[1,3-dithiole-2,3'-cholestane] in 75% yield.

The composition of the residue from this reaction is complex. Optimum yields of the carbonyl compounds are obtained by using as little as two moles of Chloramine-T per mole of dithiolane but the workup is less troublesome when 4 moles of Chloramine-T are used. By analogy with known reactions of Chloramine-T with organosulfur compounds it would be expected that the residue contains a mixture of polysulfides[6] and p-toluenesulfonimidosulfine-p-toluenesulfonylimines.[7] A working mechanistic hypothesis for the steps leading to the formation of the carbonyl compound has already been advanced.[1] Work is continuing on this potentially useful reaction.

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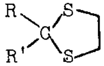
Table Preparation of dithiolanes and their reaction with Chloramine-T

Dithiolanes  preparation and properties					Reaction with Chloramine-T		
Aldehyde or ketone	Synthetic method, Ref.	bp (Torr) [mp], °C	yield, %	ref	$\frac{\text{Moles Chloramine-T}}{\text{Moles Dithiolane}}$	Reaction medium	Yield RR'C=O
Ethyl methyl	3e	38 (1)	90,5	3d	2	90% MeOH	98%[a]
Cyclopentanone	3e	65 (0.8)	87,5	3d	3	90% MeOH	81%[b]
Cyclohexanone	3e	76 (1)	94,5	3d	2	90% MeOH	95%[a]
Cyclohexanone				3d	1	90% EtOH	46%[a]
Benzaldehyde	3e	124 (1)	88	3a	2	90% MeOH	100%[a]
Acetophenone	3e	98 (0.3)	89	3d	2	90% MeOH	85.5%[a]
Acetophenone					2.5	90% MeOH	77.5%[b]
Fluorenone	3e	[122-123]	80	3d	4	90% MeOH/EtOH	86%[c]
Cholestane-3-one[d]	3a	[144-144,5]	96	8, 3e	4	90% MeOH	75%[c]

a) Yield and identification by GLC analysis basis dithiolane

b) Yield and identification based on the isolated semicarbazones

c) Yield and identification based on the isolated pure ketones

d) Kindly prepared by H. de Vries.