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Radical Cation Reactions Associated with the Thiocarbonyl Group

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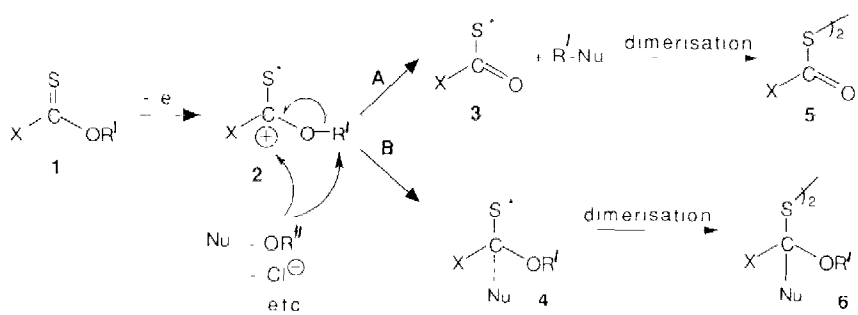
The radical cation reactions of different thiocarbonyl compounds were examined. Compounds ***7, 8, 11, 14*** *and* ***18*** *underwent a radical cation fragmentation in a photoinduced electron transfer (PET) reaction, in the presence of tris(4-bromophenyl)aminium hexachloroantimonate*

The preparative chemistry of radical cations has been restricted to few isolated reports with electron rich Π systems, and nitrogen containing organic molecules[1,2,3], this despite the implication of radical cation pathways in many biological processes[4]

Following our earlier efforts on the investigation of the reactivity of thiocarbonyl compounds we developed a novel reaction based on the ease of polarizability at this group. We observed that in the presence of commercially available *tris*(4-bromophenyl)aminium hexachloroantimonate as sensitizer and light, compounds containing the C=S function underwent photoinduced electron transfer (PET) reactions. Here we wish to present some of our results which illustrate the surprising outcome of these reactions.

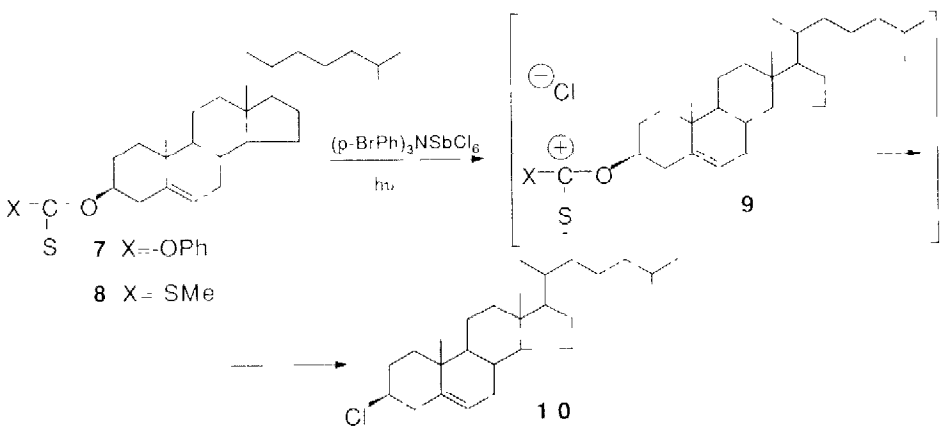


Scheme 1

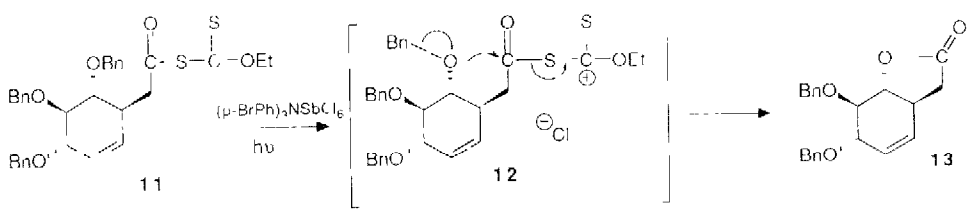
In our working hypothesis we anticipated, as depicted in the Scheme 1, that one electron oxidation of thiocarbonyl compounds could lead to a reactive radical cation species. One of the resonance structures can be represented by the distonic species **2**. In this structure the charge is on carbon, with the unpaired electron on sulphur. This newly created >C-S· functionality is very susceptible to intra or intermolecular nucleophilic attack. The positively charged carbon can interact with nucleophilic centers triggering complex rearrangements, according to path A or B. The electrophilic substitution proceeds particularly well when the leaving group, R^{II} is benzyl[3a] or silyl[4b]. In the most simple case, the radical cation species **2**, reacts with the chloride anion, generated from the sensitizer. We believe, that the thio-radical intermediates **3** and **4**, dimerize in the reaction to form bisulfide bridged compounds **5** and **6**. So the electron output of the reaction is necessarily stoichiometric.

The reactions were performed in a half-mmolar scale but some studies showed that quantities can be augmented without significant loss of selectivity and yield.

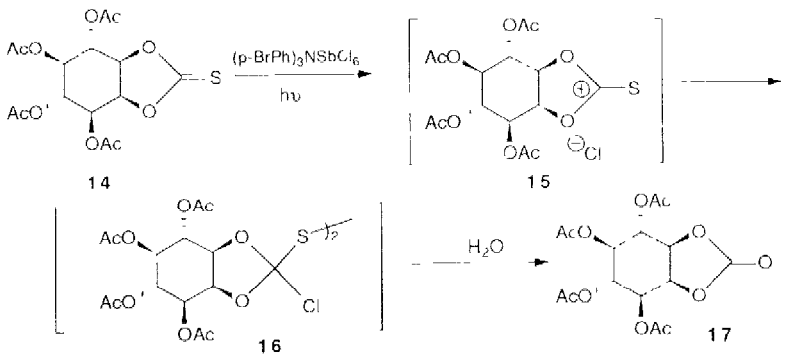
Compounds **7** and **8** were prepared from cholesterol, in the presence of NaH, using phenoxy thiochloroformate and carbon disulfide and methyl iodide following the published procedures[5] On irradiation with a 250W tungsten or halogen lamp, in the presence of 1 equivalent of *tris*(4-bromophenyl)aminium hexachloroantimonate, in toluene, under argon, compounds **7** and **8** underwent a radical cation fragmentation reaction It was found that the phenoxythiocarbonyl cholesterol derivative, **7**, reacted at room temperature in 10 minutes, to give the corresponding chloride in 92% yield (mp=96°C)[6] The only product observed was the compound with retention of configuration at C 3 (**10**) In this example the reaction follows the pathway A the single electron transfer (SET) process provides radical cation **9**, which react with the counterion Cl^-, to form the halogenated product **10** The same reaction, using the xanthate **8** as starting material gave the identical product however the reaction proceeded more slowly (30 minutes at 110°C)



In the next example, we illustrated that the reaction can be applied for lactonisation of a protected alcohol, **11**, under mild, essentially neutral conditions. **11** was prepared from the corresponding acid on activation with oxalyl chloride followed by reaction with potassium O ethyl xanthate[7] in methylene chloride The mixed anhydride, **11**, in the presence of 1 equivalent aminium salt and toluene on irradiation by a 250W halogen lamp underwent cyclisation The reaction was rapid at 110°C (10 minutes) and, in spite of the cyclic strain, only the trans lactone (**13**) was isolated (95%, mp=80°C)[8] The intramolecular electrophilic substitution took place on the β-carbon, the reaction follows the A mechanistic pathway A benzyl group was chosen as a leaving group for its capacity to stabilise the incipient carbocation

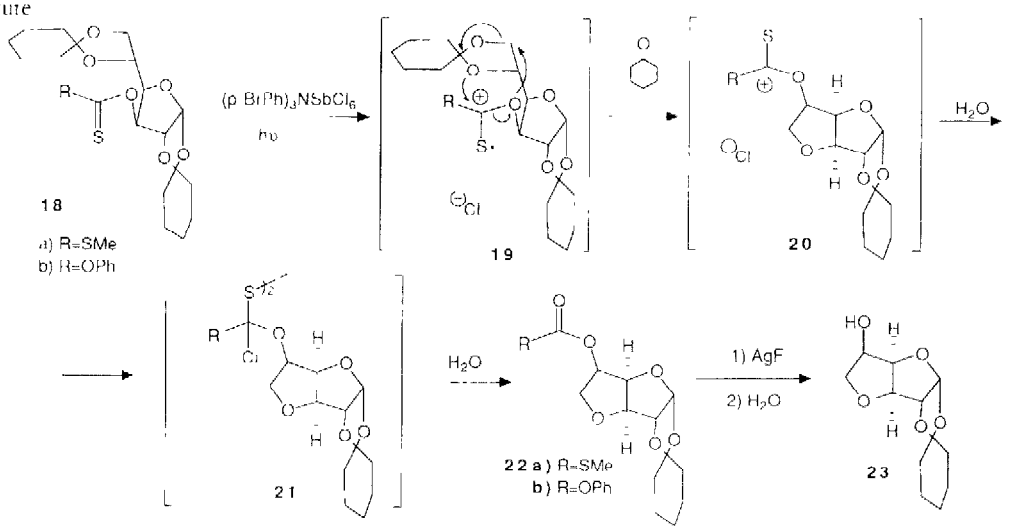


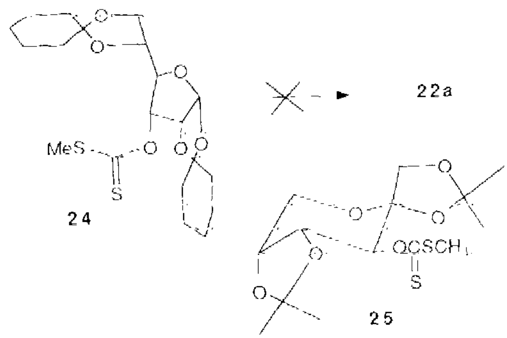
In the following experiment, the cyclic thionocarbonate, **14**[9], was irradiated, in presence of 1 equivalent of aminium salt at room temperature, and yielded the corresponding carbonate **17** (93%, mp=118°C)[8] The product obtained was characterised by X-Ray analysis This result, in fact, was very surprising and suggested the formation of a halogenated intermediate **16** which was hydrolysed in the work-up procedure, and hence the reaction follows the B mechanistic pathway



The xanthate derivative of the glucofuranose diketal **18a** was prepared from the corresponding 3 hydroxy derivative as described earlier[5] **18a** underwent an interesting rearrangement in presence of 1 eq of aminium salt and irradiation in toluene for 10 minutes at room temperature The bicyclic derivative **22a** was isolated in 89% yield as a pale yellow oil[8] The loss of the cyclohexanone in the reaction was evident by capillary GC using cyclohexanone as reference Formally, the reaction is an electrophilic substitution of the cyclohexylidene group triggering a complex rearrangement-cyclisation process In fact, the formation of tetrahydrofuran derivatives by electrophilic substitution of the ketal function is well documented in the literature[10] The driving force of the reaction is probably the steric congestion due to the very close proximity of the participating groups A halogenated intermediate can again be supposed as in the reaction **14->17** This sensitive intermediate may explain the formation of the methylthiocarbonate function at C-5 An interesting aspect of the reaction is that in contrast to the transformation of **7->10** the rearrangement is much slower when using the phenylthionocarbonate derivative as starting material The reaction needs prolonged irradiation (30 minutes) at 110°C and gives only poor yield (42%) of **22b** The structure of **22a** was confirmed also by transforming it into the corresponding free hydroxy compound **23**, using 1 eq of AgF The spectroscopic data of compound **23** was compared with the earlier reported isopropylidene protected derivative[11]

To prove the existence of a bissulfide bridged intermediate in the mixture, triphenylphosphine was added after irradiation and we isolated the corresponding oxidized product, $Ph_3P=S$ In a parallel experiment in the dark (without irradiation) we did not observe formation of $Ph_3P=S$ under similar conditions In fact the triphenylphosphine reacted rapidly with the radical cation sensitizer which resulted in the decoloration of the mixture





24 ✗→ 22a

25

The corresponding allose xanthate **24** gave, under the conditions described above, a number of products none of which corresponded to compound **22a**.

There was no formation of desired product in parallel experiments without aminium salt and/or in the dark. If less than 1 equivalent of sensitiser was used, the reaction was stopped after consumption of all the aminium salt.

Molecules with a crowded thiocarbonyl function like the fructose derived compound **25**, are poor substrates in the *tris*(4-bromophenyl)aminium hexachloroantimonate salt mediated PET reaction - even after prolonged irradiation of **25** only the starting material was recovered.

A typical procedure is as follows.

Under an argon atmosphere, 0.4 mMol of thiocarbonyl compound was dissolved in 5 ml of degassed, dry toluene and 326.6 mg (0.4 mMol) of *tris*(4-bromophenyl)aminium hexachloroantimonate was added to the solution. The mixture was irradiated, with vigorous stirring, by a 250W halogen lamp until the disappearance of the dark color of the aminium salt. The mixture was diluted with 10 ml of ether and filtered through a pad of celite. The clear solution was evaporated and chromatographed on a short column of silica gel.

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