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TRIFLUOROACETOXYSULPHENYLATION OF UNSATURATED NITRILES AS A ROUTE TO LACTONES

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Abstract Use of manganic acetate as oxidant permits efficient trifluoroacetoxysulphenylation of unsaturated nitriles with organic disulphides. The adducts in a cobaltous chloride promoted hydrolysis afford alkyl- or aryl-thio substituted lactones.

In the preceding paper[1] we describe two important extensions of the original Trost procedure[2] for hydroxysulphenylation of alkenes. We find that manganic acetate can advantageously replace lead tetraacetate as the oxidant of the disulphide. Secondly, functionalised alkenes in particular unsaturated esters may be used in procedures which permit efficient regiocontrol of the hydroxysulphenylation. In seeking to extend the hydroxysulphenylation procedures based on manganic acetate and lead tetraacetate we have examined additions to other functionalised alkenes. Here we report the trifluoroacetoxysulphenylation of unsaturated nitriles a process which is markedly more efficient when manganic acetate is used instead of lead tetraacetate. The adducts, vicinal trifluoroacetoxy sulphides readily afford lactones on cobalt chloride promoted hydrolysis and hence the procedure of trifluoroacetoxysulphenylation of unsaturated nitriles followed by hydrolysis provides a novel route to an important class of substituted lactones.

Trifluoroacetoxysulphenylation of allyl cyanide (1), 4-cyanobut-1-ene (2)[3] and 5-cyanopent-1-ene (3)[4] using diphenyl disulphide (4) di-p-tolyl disulphide (5) and di-n-propyl disulphide (6) was effected in dichloromethane/trifluoroacetic acid (4:1) with manganic acetate or lead tetraacetate as the added oxidant. Results are shown in Table 1. Mixtures of the trifluoroacetoxysulphides derived from Markovnikov and anti-Markovnikov addition could be isolated on work up, or following a hydrolysis under basic conditions mixtures of hydroxysulphides could be isolated. The hydroxysulphides were readily separated by chromatography and for all the hydroxysulphides (7-24) shown in Table 1 satisfactory analytical and spectroscopic data were obtained.

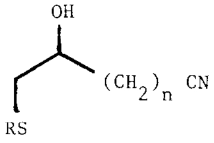
The results in Table 1 establish that whereas trifluoroacetoxysulphenylation of unsaturated nitriles can be effected in only low yield using lead tetraacetate the use of manganic acetate permits good yields (55-85%) of hydroxysulphides to be isolated after hydrolysis. Unlike the trifluoroacetoxysulphenylation of esters of allylic alcohols where high regioselectivity is observed the additions to these unsaturated nitriles are characterised by a lower regioselectivity. The observed regioselectivities might be controlled by the electron withdrawing inductive effect of the substituent nitrile group, an effect apparent in additions[1] to the allylic trifluoroacetates, or by a neighbouring group participation by the nitrile group, an effect apparent in additions[1] to allylic acetates. We tentatively

Table 1

Hydroxysulphides from Addition to Unsaturated Nitriles.

Alkene	Added Oxidant	Disulphide	Markovnikov Product (%)[a]	Anti-Markovnikov Product (%)[a]
1	$Mn(OAc)_3$	4	7 (20)	8 (66)
1	$Mn(OAc)_3$	5	9 (15)	10 (73)
1	$Mn(OAc)_3$	6	11 (11)	12 (46)
2	$Mn(OAc)_3$	4	13 (28)	14 (47)
2	$Mn(OAc)_3$	5	15 (36)	16 (47)
2	$Mn(OAc)_3$	6	17 (24)	18 (49)
3	$Mn(OAc)_3$	4	19 (42)	20 (14)
3	$Mn(OAc)_3$	5	21 (50)	22 (14)
3	$Mn(OAc)_3$	6	23 (72)	24 (5)
1	$Pb(OAc)_4$	4	7 (3)	8 (18)
2	$Pb(OAc)_4$	4	13 (9)	14 (12)
1	$Pb(OAc)_4$	6	11 (3)	12 (15)
2	$Pb(OAc)_4$	6	17 (7)	18 (24)

[a] Isolated yields after chromatographic separation



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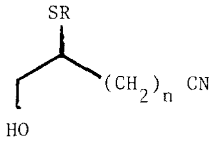
9 R=$pMeC_6H_4$; n=1
11 R=nPr; n=1
13 R=Ph; n=2
15 R=$pMeC_6H_4$; n=2
17 R=nPr; n=2
19 R=Ph; n=3
21 R=$pMeC_6H_4$; n=3
23 R=nPr; n=3



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10 R=$pMeC_6H_4$; n=1
12 R=nPr; n=1
14 R=Ph; n=2
16 R=$pMeC_6H_4$; n=2
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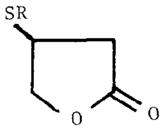

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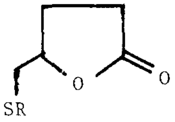
27 R=nPr



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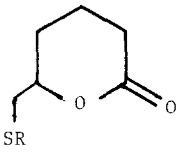

31 R=Ph
32 R=$pMeC_6H_4$
33 R=nPr

Table 2

Cobaltous Chloride Promoted Lactonisations

Starting Hydroxynitrile	Product	Yield (%)[a]
7	25	70
8	25	93
9	26	85
10	26	87
19	28	86
20	28	90

[a] Isolated yield of pure lactone after chromatographic purification

conclude that the inductive effect is the major factor controlling the observed selectivity Hence this inductive effect leads to the dominance of anti-Markovnikov addition to allyl cyanide but in 5-cyanopent-1-ene normal Markovnikov addition is observed as little effect is transmitted by the remote substituent. These results cannot be effectively compared with other trifluoroacetoxysulphenylations, because of the limited available data for this reaction but afford an interesting comparison with other additions leading to sulphenylation. In sulphenolactonisation[5] involving unsaturated esters[6] or acids,[6,7] processes noted to be characterised by a number of disadvantages, sulphenoetherification[8] and sulphenocycloamination[9] the observed regiochemistry is substantially determined by the demands of the participating neighbouring group.

Access to the hydroxynitriles (7-24) suggested a possible route to alkylthio- and arylthio-substituted lactones, compounds not well reported in the literature, yet the subject[10] of recent synthetic interest. The success of such a route clearly depends on whether the pairs of regioisomers e.g. (7) and (8), obtained by addition to an unsaturated nitrile both afford the same lactone under conditions chosen to hydrolyse the nitrile functionality. We report in Table 2 the consequence of reactions in aqueous cobaltous chloride, conditions which permit the efficient conversion of regioisomeric pairs to single alkylthio- or arylthio substituted lactones. Hence in Table 3 we report the successful formation of lactones obtained by the two step process of initial formation of trifluoroacetoxysulphides using manganic acetate and the subsequent conversion of the mixture of regioisomers to a single lactone.

There is good literature precedent for our observations. A number of metal ion promoted hydrolyses of nitriles have been reported[11] and cobalt salts are particularly efficient. Cobaltous chloride has been used to promote intramolecular nucleophilic attack at a co-ordinated nitrile group previously.[12] Secondly it is well established from the recent work of Warren's group[13] that under acidic conditions phenylthio migration permits a number of useful transformations including participation by a neighbouring ester functionality to afford lactones via episulphonium ion intermediates.

Of the three types of lactone described in this paper the 4-substituted-4,5-dihydrofuran-2-(3H) ones (4-substituted butyro lactones) (25-27) are the most well known because of their relationship to butenolides. Although other syntheses of 4-thio substituted butyrolactones have been reported[10,14] the present method seems advantageously simple and direct. The other lactones (28-33) have not been previously reported.

Additions using phenylsulphenyl chloride have not been used to give such lactones in contrast to the widely used phenylselenyl chloride. The disadvantages associated with the use of phenylsulphenyl chloride make this alternative mode of hydroxysulphenylation and cobalt chloride promoted lactonisation a valuable extension to the important area in synthesis of sulphenolactonisation.

Table 3

Two Step Conversion of Unsaturated Nitriles to Lactones

Alkene	Disulphide	Alcohols Affording Intermediate Trifluoroacetates	Lactone	Yield (%)[a]
1	4	7 and 8	25	65
1	5	9 and 10	26	65
1	6	11 and 12	27	61
2	4	13 and 14	28	75
2	5	15 and 16	29	75
2	6	17 and 18	30	69
3	4	19 and 20	31	85
3	5	21 and 22	32	73
3	6	23 and 24	33	80

[a] Isolated yield of pure lactone after chromatographic purification

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