The Use of Alkoxotellurium(VI) Fluorides as Alkylating Agents

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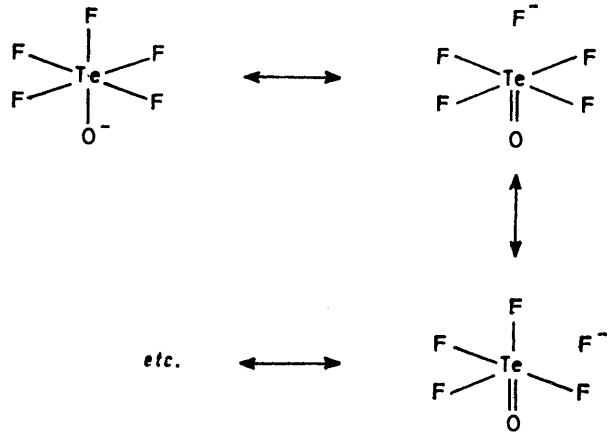
Methoxotellurium(VI) pentafluoride, TeF_5OMe, has been shown to be a more powerful methylating agent than $SO_2(OMe)_2$ but weaker than $FSO_2(OMe)$. Alkylation reactions involving the alkoxotellurium(VI) fluorides $TeF_{6-x}(OR)_x$, x = 1, 2, with pyridine, *NN*-dimethylformamide, and potassium phthalimide to yield $(C_5H_5NR)^+(TeOF_5)^-$, $[HC(OR)NMe_2]^+(TeOF_5)^-$, and *N*-alkylphthalimides, respectively, are described.

A NUMBER of alkoxotellurium(VI) fluorides $TeF_{6-x}(OR)_x$, x = 1—6, have been described [1-5] and since these compounds are the esters of the corresponding fluorohydroxy acids $TeF_{6-x}(OH)_x$, x = 1—6, [6] well established prejudice would suggest that the esters of these strong acids, especially TeF_5OR and $TeF_4(OR)_2$, should prove to be strong alkylating agents. This has been supported by the report that TeF_5OMe reacts with pyridine to form $(C_5H_5NMe)^+(TeOF_5)^-$.[2] This paper details a number of reactions in which the alkoxotellurium(VI) fluorides act as alkylating agents and examines some of the relative advantages and disadvantages of using these compounds in place of conventional reagents such as dimethyl sulphate.

RESULTS AND DISCUSSION

The methoxotellurium(VI) fluorides $TeF_{6-x}(OMe)_x$ are similar in form to the well known methoxosulphuryl fluorides $F_{2-x}SO_2(OMe)_x$. It has been shown [7] that methyl fluorosulphonate $FSO_2(OMe)$ is stronger in methylating power than dimethyl sulphate $SO_2(OMe)_2$ and by analogy it would be expected that TeF_5OMe would be a more powerful methylating agent than $TeF_4(OMe)_2$ which in turn would be more powerful than $TeF_3(OMe)_3$.

Some preliminary experiments showed that the reactions of these compounds with *NN*-dimethylformamide (DMF) conveniently identified the relative methylating strengths. By monitoring the progress reaction (1) [where X = $-OTeF_5$, $-OTeF_4(OMe)$, $-OTeF_3(OMe)_2$, and $-OSO_2(OMe)$] under identical experimental conditions using ^1H n.m.r. spectroscopy, it was found that the reaction involving TeF_5OMe was complete within 20 min, and that with $SO_2(OMe)_2$ was complete after 4 h, whereas *cis*-$TeF_4(OMe)_2$ required 10 h and a mixture of *mer*- and *fac*-$TeF_3(OMe)_3$ showed no reaction in 48 h. Methyl fluorosulphonate has been reported to react ' instantly ' at 25 °C.[7] Thus the relative order of methylating strengths is $FSO_2(OMe) > TeF_5OMe > SO_2(OMe)_2 > TeF_4(OMe)_2 > TeF_3(OMe)_3$. TeF_5OMe is a strong alkylating agent since on ionisation the pentafluoro-orthotellurate anion $(TeOF_5)^-$ is formed. A number of salts containing this anion have been prepared, most of which have been shown to be very stable.[8] A probable feature of this ion is resonance stabilisation by means of the structures shown below.[9] Molecular orbital calculations [10] have confirmed this delocalisation of charge. The formation of the $OTeF_4(OMe)^-$ ion by the ionisation of *cis*-$TeF_4(OMe)_2$ is, by



comparison, less favourable since one of the strongly electronegative fluorine atoms has been replaced by a mildly electronegative methoxo-group resulting in the ion being less well stabilised. An analogous effect is observed by comparing $FSO_2(OMe)$ with $SO_2(OMe)_2$. Consequently further substitution of methoxo-groups into the TeF_6 molecule will produce compounds of much reduced alkylating ability.

Although it is evident that the methyl esters of the fluorohydroxy-acids $TeF_{6-x}(OH)_x$ are weaker alkylating agents than the corresponding methyl esters of $F_{2-x}SO_2(OH)_x$, use of the esters of the former offers a number of advantages. These include (*a*) they are generally easily prepared from the corresponding (primary or secondary) alcohol and TeF_6; [2] (*b*) a wide range of organic groups can be incorporated into these molecules; [3,4] (*c*) they are sufficiently stable to undergo a number of reactions and to be stored for long periods of time; (*d*) the tellurium–fluorine moiety gives rise to distinctive ^{19}F n.m.r. and infra-red spectra thus enabling reactions to be easily monitored by these techniques.

Thus it is relatively simple to convert primary or secondary alcohols into powerful alkylating agents by treating them with TeF_6. The reaction has been extended to more complex molecules, *e.g.* polyols,[4] and sugars and steroids,[11] examples of which are derivatives

$$HC(O)NMe_2 + MeX \xrightarrow{33\ ^\circ C} [HC(OMe)NMe_2]^+X^- \quad (1)$$

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of glycerol, 1,2,3,4-di-*O*-isopropylidenegalactopyranose, and cholesterol. Initial studies show that the alkylation reactions can be extended to these more complex molecules.

All powerful alkylating agents are potentially hazardous materials [the dangers of working with $FSO_2(OMe)$ have been the subject of some recent correspondence[12-15]] and therefore they have to be handled with great care. The powerful odour of the simple volatile alkoxotellurium(VI) fluorides (the more complex derivatives of sugars, polyols, and steroids have no smell) means that the compounds must be handled under proper safety conditions and this reduces the possible dangers. Another advantage is that solutions of the compounds in *NN*-dimethylformamide can be used to undergo alkylation reactions *via* the intermediates $[HC(OR)NMe_2]^+(TeOF_5)^-$ which are both odourless and non-volatile, and can be stored for long periods.

It should be noted that the reaction between alkoxotellurium(VI) fluorides and nucleophiles does not always lead to alkylated products; there are two electrophilic sites within these molecules, the alkyl group and the tellurium atom. The tellurium is shielded from nucleophilic attack by oxygen and fluorine atoms bearing large negative charges,[16] but in some cases attack does take place at the tellurium atom rather than the alkyl group. An example of this type of reaction has been reported; [5] no dimethyl ether could be detected from the reaction of TeF_5OMe or *cis*-$TeF_4(OMe)_2$ with sodium methoxide and further substitution to produce $TeF_{6-x}(OMe)_x$, $x = 3$, 4, or 5, occurred. In some cases when strong bases such as potassium pyrrole were treated with mono- or di-alkoxotellurium(VI) fluorides, a black deposit was immediately formed which could not be identified. It is likely that the initial reaction was to form tellurium–nitrogen compounds, *e.g.* $C_4H_4NTeF_4(OR)$ or $C_4H_4NTeF_3(OR)_2$, which immediately decomposed.[17] No *N*-alkylpyrrole could be detected.

A number of simple alkylation reactions involving compounds of the type TeF_5OR and *cis*-$TeF_4(OR)_2$ have been studied using a variety of alkoxo-groups; detailed experimental information is presented in this paper for methylation and a selection from the other alkylation reactions observed [equations (2)—(9)].

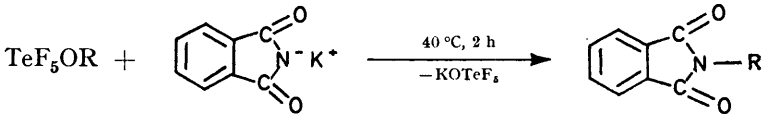
$$TeF_5OR + C_5H_5N \xrightarrow[\text{exothermic}]{-40\ ^\circ C} (C_5H_5NR)^+(TeOF_5)^- \quad (2)$$

(The conditions quoted are for TeF_5OMe; higher alkyl groups react more slowly, *e.g.* TeF_5OBu^s requires 15 h at 20 °C).

$$TeF_5OR + HC(O)NMe_2 \xrightarrow[0.5-24h]{25\ ^\circ C} [HC(OR)NMe_2]^+(TeOF_5)^- \quad (3)$$

$$TeF_5OR + C_6H_5CH{=}NMe \xrightarrow[1-24h]{25\ ^\circ C} (C_6H_5CH{=}NMeR)^+(TeOF_5)^- \quad (4)$$

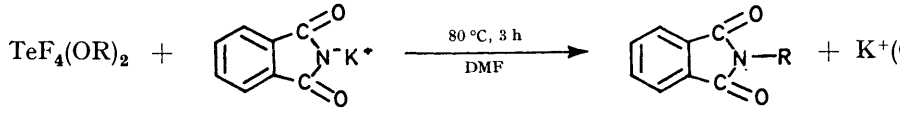
$$TeF_5OR + MeCN \xrightarrow[14\ days]{25\ ^\circ C} \text{no reaction} \quad (5)$$



(6)

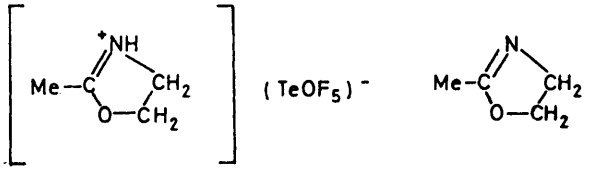
$$TeF_4(OR)_2 + C_5H_5N \xrightarrow[1\ h\ (for\ R = Me)]{25\ ^\circ C} (C_5H_5NR)^+(OTeF_4OR)^- \quad (7)$$

$$TeF_4(OR)_2 + HC(O)NMe_2 \xrightarrow[2\ h\ (for\ R = Me)]{60\ ^\circ C} [HC(OR)NMe_2]^+(OTeF_4OR)^- \quad (8)$$



(9)

The reactions of *NN*-dimethylformamide and *NN*-dimethylacetamide with TeF_5OR and *cis*-$TeF_4(OR)_2$ produced only the *O*-alkylated product similar to the reaction reported for $SO_2(OMe)_2$; [18] no *N*-alkylated material was observed with any of the compounds used. The reaction of $CH_3CONHCH_2CH_2OH$ with TeF_6 was of interest since the $CH_3CONHCH_2CH_2OTeF_5$ formed immediately the salt (1) by means of an intramolecular alkylation reaction. On reaction with KOH–MeOH, the salt (1) yielded 2-methyl-2-oxazoline (2).



(1) (2)

The reaction of alkylating agents with potassium phthalimide is a simple way of synthesising primary amines. The mild experimental conditions needed when alkoxotellurium(VI) fluorides are used (TeF_5OMe reacts exothermically on warming from −40 °C), and the range of alkoxo-derivatives available suggests that this may be a useful synthetic route to some less common primary amines. This is expecially valuable when more complex molecules containing 'alcoholic' OH groups such as steroids and sugars are used to form the TeF_5-

OR derivative since both the formation of the alkoxotellurium(VI) pentafluoride and the subsequent formation of the alkyl phthalimide are essentially quantitative.

The reaction with imines was less studied; although alkylation took place under very mild experimental conditions, decomposition of the salt formed with KOH solution failed to yield the expected secondary amine, and only a yellow precipitate, which could not be identified, was formed.

It has already been mentioned that ^1H and ^{19}F n.m.r. spectroscopy are excellent 'fingerprinting' techniques for studying these alkylation reactions; both TeF_5OR and $(TeOF_5)^-$ exhibit characteristic ^{19}F n.m.r. spectra which have been reported in detail elsewhere.[2,19] Both of these species exhibit AB_4 spectra, but the resonances of the $(TeOF_5)^-$ anion occur approximately 20 p.p.m. downfield from those due to TeF_5OR which greatly facilitates their respective identification. Dialkoxotellurium(VI) tetrafluorides give rise to symmetrical A_2B_2 ^{19}F n.m.r. spectra, consistent with the *cis* isomer; the *cis*-$[TeOF_4(OR)]^-$ ion gives rise to a more complex asymmetric A_2BC spectrum, again at low field. Analysis of such spectra has only recently been reported.[20]

^1H N.m.r. spectroscopy was also useful for studying these alkylation reactions, *e.g.* in the reaction of TeF_5OMe with DMF it was shown that the *O*-alkylated product was produced rather than the *N*-alkylated product. Infra-red spectroscopy was also useful since the $(TeOF_5)^-$ anion exhibits characteristic absorption at approximately 860 and 640 cm^{-1}.[9] The products of most of the alkylation reactions could be compared with literature data.

A number of solvents were suitable for these reactions including MeCN, CH_2Cl_2, Et_2O, $MeCO_2H$, and $MeOCH_2CH_2OMe$. It has already been mentioned that *NN*-dimethylformamide proved to be a useful solvent as the alkoxotellurium(VI) fluorides could be treated directly in solution, or could be stored in the alkylated form $[HC(OR)NMe_2]^+(TeOF_5)^-$ in solution.

EXPERIMENTAL

The preparations of the alkoxotellurium(VI) fluorides have been reported in detail elsewhere.[1-5] Most were purified by distillation under reduced pressure and stored in glass vessels with PTFE seals. All other reagents and solvents were purified and dried before use. ^1H and ^{19}F n.m.r. spectra were recorded at 60 MHz and 56.4 MHz respectively on a Perkin-Elmer R10 spectrometer. Proton chemical shifts are reported in p.p.m. relative to Me_4Si, and fluorine chemical shifts are reported in p.p.m. relative to $CFCl_3$ in all cases.

Determination of the Relative Alkylating Strengths of the Alkoxotellurium(VI) Fluorides.—The reactions of TeF_5OMe, *cis*-$TeF_4(OMe)_2$, *mer*- and *fac*-$TeF_3(OMe)_3$, and $SO_2(OMe)_2$ with DMF were carried out under identical experimental conditions in n.m.r. sample tubes. The molar ratio of alkylating agent to DMF was 1 : 4 in all cases, *i.e.* the amide also acted as solvent. The decrease with time of the ^1H n.m.r. signal due to, for example, TeF_5OMe at δ 4.25 was observed, whilst a new signal at δ 4.41 due to $[HC(OMe)NMe_2]^+$ gained in intensity. Full details of the n.m.r. spectra observed are given later.

Reaction of Alkoxotellurium(VI) Fluorides with Pyridine.—(*a*) TeF_5OMe (5.6 g, 22.1 mmol) was condensed under vacuum into a reaction flask containing pyridine (1.6 g, 20.2 mmol) at −196 °C. On allowing the mixture to warm slowly a vigorous reaction occurred at *ca.* −40 °C, giving a crystalline, white solid. After drying under vacuum, the product had melting point 204—205 °C, and yield 98.7%. It was identified by micro-analysis, ^1H and ^{19}F n.m.r., and infra-red spectroscopy as $(C_5H_5NMe)^+(TeOF_5)^-$.

(*b*) The reactions of TeF_5OR (R = Et, Pr, and Bu) with pyridine were carried out in a similar manner to that described above, but the reactions took place at 20 °C over periods up to 4 days, the products being pale yellow solids or oils. The *N*-alkyl pyridinium salts were identified by means of the methods described above.

(*c*) Cholesteroxotellurium(VI) pentafluoride [m.p. 153 °C; prepared from cholesterol (2.1 g, 5.4 mmol), anhydrous sodium fluoride (5 g, 119 mmol) and TeF_6 (2 g, 8.3 mmol) using $MeOCH_2CH_2OMe$ (20 ml) as solvent, and purified by column chromatography with benzene as eluant [11]] and pyridine in equimolar quantities were dissolved in benzene. Within 24 h the pyridinium salt had precipitated from solution as a gel. Removal of the benzene and drying of the gel under vacuum produced a white powder insoluble in most common solvents. Micro-analysis confirmed the formula $(C_5H_5N{\cdot}C_{27}H_{45})^+(OTeF_5)^-$.

(*d*) $TeF_4(OMe)_2$ (4.7 g, 17.7 mmol) was mixed with pyridine (1.4 g, 17.7 mmol) at 20 °C. White flakes of product formed slowly and the reaction was complete within 4 h. The product, a hygroscopic white solid, was identified by micro-analysis, ^1H and ^{19}F n.m.r., and infra-red spectroscopy as $(C_5H_5NMe)^+(OTeF_4OMe)^-$.

(*e*) Dialkoxotellurium(VI) fluorides of the type $TeF_4(OMe)(OR)$, where R = Et, Pr^i, and Bu^i, reacted with pyridine to give pale yellow oils. In all cases these products were identified as $(C_5H_5NMe)^+(OTeF_4OR)^-$.

Reactions with Amides.—(*a*) When TeF_5OMe (2.5 g, 9.89 mmol) was mixed with $MeC(O)NMe_2$ (0.85 g, 9.75 mmol) and allowed to stand at room temperature, a mass of crystals formed within two days. On evaporating the excess of alkylating agent *in vacuo*, the yield was found to be almost quantitative. The crystals melted at 136—138 °C. ^1H n.m.r. spectroscopy confirmed that the product was the *O*-methylated salt $[MeC(OMe)NMe_2]^+(TeOF_5)^-$.

(*b*) TeF_5OEt and TeF_5OBu^s reacted with an excess of DMF to give solutions of the salts $[HC(OR)NMe_2]^+(TeOF_5)^-$. Complete reaction occurred when the mixture was maintained at 20 °C for 24 h. Since amides are very weak bases, the solutions of these salts were further used to alkylate stronger nucleophiles.

(*c*) TeF_6 (26 g, 107.6 mmol) was condensed into a reaction vessel containing NaF (40 g; 0.95M) and $AcNHCH_2CH_2OH$ (10 g, 97 mmol) dissolved in MeCN (*ca.* 60 ml). The sodium fluoride acted as the hydrogen fluoride scavenger in the reaction. After the sealed reaction vessel had stood for 7 days at room temperature, a large excess of $CHCl_3$ was added to the reaction mixture and the $NaF–NaHF_2$ filtered off. The solvents were evaporated leaving a pale yellow solid identified as an oxazoline salt by ^1H and ^{19}F n.m.r. spectroscopy. This solid was refluxed with KOH in MeOH until a clear solution was obtained. After evaporat-

ing most of the methanol, a large excess of ether was added and the solution filtered and distilled. The fraction boiling at 108—110 °C was collected and identified by micro-analysis, and ^{1}H n.m.r. and infra-red spectroscopy, as 2-methyl-2-oxazoline (lit., b.p.[21] 111 °C).

Reactions with Potassium Phthalimide.—(*a*) TeF_5OMe was condensed at −196 °C onto a 1.1 molar excess of potassium phthalimide in DMF. The reaction vessel was allowed to warm slowly and at *ca.* −40 °C reaction started. After a further 10 min the reaction was complete and the methyl phthalimide was extracted.[22] The product was purified by sublimation under vacuum and the yield was found to be 94%. Micro-analysis and ^{1}H n.m.r. spectroscopy confirmed its identity.

(*b*) Other alkoxotellurium(VI) pentafluorides TeF_5OR (R = Et, Bu^s, Bu^i, and $[CH_2]_nOTeF_5$, n = 3, 5, 10) were treated with potassium phthalimide similarly. The alkyl phthalimides prepared were purified by sublimation, or in the case of the Bu^s derivative, distilled. In all cases yields were in excess of 80%, and the melting points of the solid derivatives corresponded to literature values.

(*c*) $TeF_4(OMe)_2$ (6.3 g, 23.7 mmol) was added to a solution of potassium phthalimide (9.3 g, 49.7 mmol) in DMF and the reaction mixture heated to 80 °C for 3 h. The methyl phthalimide was extracted, purified, and identified as in (*a*). The ^{1}H and ^{19}F n.m.r. spectra of the crude product indicated the presence of the $(OTeF_4OMe)^-$ anion.

Reaction of TeF_5OMe *with Potassium Succinimide.*—TeF_5OMe (5.0 g, 19.7 mmol) was condensed at −196 °C onto a solution of potassium succinimide (3.0 g, 21.9 mmol) in DMF (25 ml) and the reaction mixture allowed to warm to room temperature, whereupon it was stirred for 20 min. All volatile matter was removed from the reaction vessel under vacuum; the residue was extracted with CCl_4 which yielded methyl succinimide. The product was purified by sublimation and was identified by micro-analysis and melting point. The yield was 84%.

Reaction of TeF_5OMe *with* PhCH:NMe.—The imine PhCH:NMe [23] was dissolved in dry toluene and TeF_5OMe (0.96 mol. equiv.) added. The reaction reached completion after stirring for 2 h at 25—30 °C., during which time white flakes of product precipitated from solution. The reaction vessel was transferred to a dry-box and the product filtered off before being dried under vacuum. Infra-red, ^{1}H and ^{19}F n.m.r. spectroscopy identified the compound as $(PhCH{:}NMe_2)^+(TeOF_5)^-$. The compound decomposed rapidly in moist air liberating benzaldehyde.

Spectra.—The following examples illustrate the important features of the spectra observed.

(*a*) ^{1}H *N.m.r. spectra* (*in* CD_3CN *solution*).

$[HC(OMe)NMe_2]^+(TeOF_5)^-$, δ_a 8.89, δ_b 4.41, $\delta_{c/d}$ 3.43, 3.24
a b c/d

$[MeC(OMe)NMe_2]^+(OTeF_4OMe)^-$, δ_a 2.54, δ_b 4.23,
a b c/d e $\delta_{c/d}$ 3.38, 3.23, δ_e 3.80

$(C_5H_5NMe)^+(OTeF_4OMe)^-$, δ_a 8.40 (m), δ_b 4.33, δ_c 3.81
a b c

(*b*) ^{19}F *N.m.r. spectra* (*in* CD_3CN *solution*).

$(C_5H_5NMe)^+(TeOF_5)^-$, AB_4 spin system, δ_A 23.2, δ_B 38.8
J_{AB} 175 Hz

$[HC(OMe)NMe_2]^+(TeOF_5)^-$, AB_4 spin system,
δ_A 24.5, δ_B 40.1
J_{AB} 175 Hz

$(C_5H_5NMe)^+(TeOF_5)^-$, A_2BC spin system, not analysed.

(*c*) *Infra-red spectra.* All *N*-methyl pyridinium salts showed a characteristic absorption at 1 191 cm^{-1}.[24]

The pentafluoro-orthotellurate anion $(TeOF_5)^-$ exhibited strong absorptions near 860 cm^{-1} (s, Te–O) and at 625—640 cm^{-1} (vs, Te–F). The spectrum of the $(OTeF_4OMe)^-$ anion was similar except for an additional strong absorption near 1 005 cm^{-1} which is probably due to a Me–O vibration.

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