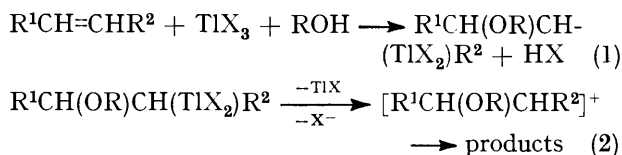


Oxymetallation. Part 15.¹ Oxidation of Hex-1-ene by Thallium(III) Trifluoroacetate in Methanol

By A. J. Bloodworth* and David J. Lapham, Christopher Ingold Laboratories, Chemistry Department, University College London, 20 Gordon Street, London WC1H 0AJ

Hex-1-ene reacts with thallium(III) acetate in methanol to afford 2-methoxyhexylthallium diacetate which undergoes no appreciable decomposition when kept in methanol at room temperature for one week, but which, upon treatment with solid potassium bromide and a catalytic amount of 2,6-dimethyl-18-crown-6, cleanly affords a high yield of 1-bromo-2-methoxyhexane (1). By contrast, the methoxythallation adduct obtained with thallium(III) trifluoroacetate undergoes oxidative dethallation fairly rapidly (*ca.* 85% dethallation after 2 h) to give 1,2-dimethoxyhexane (2) and 2-methoxyhexanol (3) as major products. It is suggested that compounds (2) and (3) arise by facile ligand exchange followed by transfer of methoxy- or hydroxy-groups from thallium to C-1 in an S_Ni process. If the methoxythallation is carried out with thallium(III) trifluoroacetate in dichloromethane with methanol (2 equiv.) the oxidative dethallation is complete after only 1 h, but 1-methoxyhexan-2-ol (4) and 2-methoxy-1-trifluoroacetoxyhexane (5) are obtained as additional products. It is suggested that ligand exchange is not effective under these conditions and that dethallation *via* an oxonium ion, which leads to compounds (2)–(4), competes with the S_Ni process which affords compound (5). Only small amounts (<10%) of hexan-2-one are obtained in the oxidations.

OXIDATION of alkenes by thallium(III) salts has proved a valuable procedure in organic synthesis.² Mechanistically, the method is believed to involve oxythallation of the alkene [equation (1)] followed by oxidative dethallation of the resultant adduct, possibly, but not necessarily, *via* a metal-free cationic intermediate [equation (2)].



The ease of dethallation and the nature of the final products depend not only on the type of alkene and solvent used, but also on the identity of the anion (X) associated with thallium. Variation of the thallium(III) salt represents a potentially valuable way to control product distribution, yet it has received surprisingly little attention. Most oxidations have been carried out with thallium(III) nitrate or with the markedly different thallium(III) acetate. The nitrate has been the preferred reagent in organic synthesis because it generally gives fast reactions and good product specificity. By contrast, the acetate tends to give complex mixtures of products and elevated temperatures are often required to bring about the dethallation at an acceptable rate. However, the greater stability of the organothallium diacetates has facilitated mechanistic studies in this area.

We felt that thallium(III) trifluoroacetate could provide an oxidant of intermediate reactivity which might reasonably be expected to afford a narrower range of products than the acetate and a different distribution than the nitrate. It might also prove possible to obtain mechanistic information about any synthetically useful transformations that occur. The reaction of thallium(III) trifluoroacetate with alkenes has been little investigated³⁻⁶ and, as far as we are aware, no reactions in

alcohol solvents have been carried out. We were particularly interested in alkoxythallation since we envisaged that eventually this might be incorporated into a synthesis of crown ethers in a modification of the alkoxymercuriation-based procedure we have recently reported.⁷ Thus, we have studied the reaction of thallium(III) trifluoroacetate and methanol with hex-1-ene, which was chosen, on the basis of experimental convenience, as a representative terminal alkene for which a substantial amount of vicinal dimethoxylation, the model for a crown ether synthesis, might reasonably be expected. For the purposes of comparison we have also carried out some similar reactions with thallium(III) acetate.

RESULTS

Thallium(III) salt was added in one portion to a stirred solution of hex-1-ene in dry solvent under nitrogen. After an appropriate time the mixture was treated with potassium bromide, either as the solid together with a drop of 2,6-dimethyl-18-crown-6⁷ to aid phase-transfer, or as an aqueous solution. The resultant thallium(I) bromide was filtered off and the organic products were isolated by extraction into dichloromethane followed by distillation. Product analysis was carried out by g.l.c. and by ¹³C n.m.r. spectroscopy using the intensities of signals arising from carbon atoms linked to hydroxy- or methoxy-groups. The results are shown in the Table.

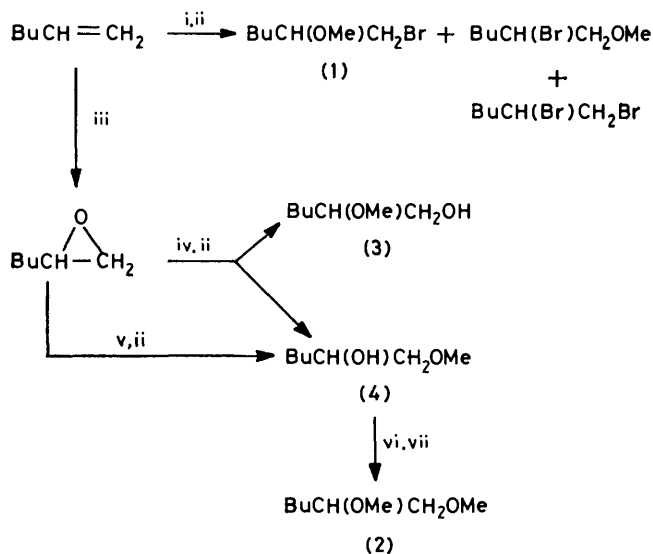
In every experiment a negative test for Tl^{III} ions (no brown precipitate upon addition of a few drops of the solution to water) was observed prior to treatment with potassium bromide and the isolated product mixture accounted for *ca.* 70–90% of the starting hex-1-ene. Products (1)–(4) were identified from their spectroscopic data and by independent synthesis (Scheme 1). Product (5) was identified from its mass spectrum which showed a fragmentation pattern very similar to those for compounds (1)–(3), but markedly different to that for the independently synthesized isomer, 1-methoxy-2-trifluoroacetoxyhexane (9). Product (6) was identified by comparison with a commercial sample of hexan-2-one. The isolation of a mixture of compound (1) and 2-bromo-1-methoxyhexane has been

Products from the reaction of hex-1-ene (10 mmol) with TlX_3 (10 mmol) followed by treatment with KBr (30 mmol)

Expt.	X	Solvent	Reaction time ^a / h	Work up ^b	Products (mol %)						Hex-1-ene uptake ^c (%)	
					(1)	(2)	(3)	(4)	(5)	(6)		
1	OAc	MeOH	5 min	P	98						2	90
2	OAc	MeOH	168	P	99						1	68
3	O_2CCF_3	MeOH	5 min	P	97						3	89
4	O_2CCF_3	MeOH	168	P		41	56				3	91
5	O_2CCF_3	MeOH ^d	72	A		44	46				10	78
6	O_2CCF_3	MeOH	2	P	18	48	26				8	80
7	O_2CCF_3	MeOH	2	P	14	47	29				10	82
8	O_2CCF_3	MeOH	2	A	32	36	21				9	79
9	O_2CCF_3	CH_2Cl_2 ^e	1	P		14	34	27	21		3	77
10	O_2CCF_3	CH_2Cl_2 ^e	1	A	5	16	26	24	19	10		87

^a Time between addition of TlX_3 and treatment with KBr. ^b P = phase-transferred KBr; A = aqueous KBr. ^c Percentage of starting alkene accounted for by observed products. ^d H_2O (10 mmol) added after uptake of TlX_3 was complete (<1 min). ^e Contained MeOH (20 mmol).

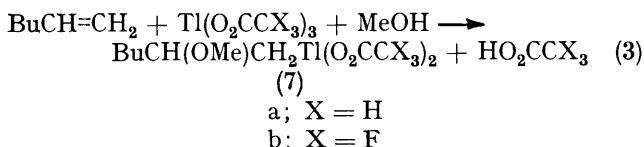
described before, but the isomers were not separated; ⁸ compounds (2)—(5) are previously unreported.



SCHEME 1. Independent synthesis of compounds (1)—(4). Reagents: i, Br_2 ; ii, MeOH; iii, $3-ClC_6H_4CO_3H$; iv, H^+ ; v, NaOMe; vi, Na; vii, MeI.

DISCUSSION

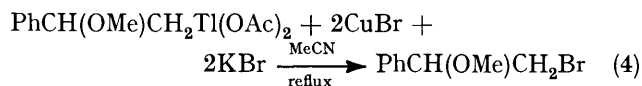
Methoxythallation [equation (3)] is fast and complete, as evidenced by the rapid uptake of thallium(III) salt and the negative test obtained for Tl^{III} ions, within a few minutes of mixing the reagents. The product from



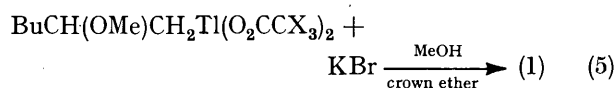
reaction with thallium(III) acetate was isolated as a viscous, moisture-sensitive oil by rapidly removing the solvent under reduced pressure, and was identified by 1H n.m.r. spectroscopy as 2-methoxyhexylthallium diacetate (7a). The $TlCH_2$ and $Tl-CH_2CH$ protons provided the most diagnostic features of the spectrum, each giving rise to a pair of widely separated multiplets due to coupling with thallium. The chemical shift and coupling constant (average for ^{203}Tl and ^{205}Tl) for the

$TlCH_2$ group were very similar to those reported ⁹ for the corresponding protons in $PhCH(OMe)CH_2Tl(OAc)_2$.

As with the closely related 2-methoxyoctylthallium diacetate,¹⁰ the isolated adduct (7a) was too labile to permit more thorough characterization and thus we looked for a clean high-yielding reaction that would provide a stable and readily characterized derivative. We chose bromodethallation which, for the corresponding styrene adduct, has been carried out in 87% yield by treatment with a mixture of copper(I) bromide and potassium bromide in refluxing acetonitrile [equation (4)].⁹ As shown by the results of Expt. 1 (Table), we



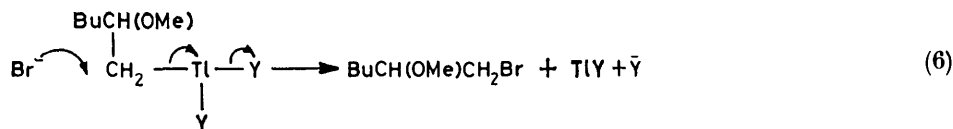
achieved a comparable conversion of compound (7a) into 1-bromo-2-methoxyhexane (1) by phase-transfer of solid potassium bromide into a methanolic solution of the adduct [equation (5); X = H]. This is a significant



result in that other workers have reported only very low yields for the bromodethallation of the styrene adduct using potassium bromide in refluxing methanol *in the absence of a crown ether*.⁹ It has also been shown that $PhCH(OMe)CH_2Tl(OAc)_2$ gives mainly 2-phenylethanal upon treatment with aqueous potassium bromide,⁹ but we were able to effect bromodethallation of compound (7b) in methanol with this reagent (Expt. 8). Indeed, a higher yield of compound (1) was obtained than when phase-transferred bromide was used (Expts. 6 and 7), which suggests a slightly faster rate of bromodethallation for the aqueous reagent.

It has been shown that the copper(I)-mediated bromodethallation proceeds mainly by a radical pathway,¹¹ but it seems probable that a polar mechanism operates under our conditions. It has been suggested that similar substitutions with potassium thiocyanate¹² and potassium selenocyanate,¹³ which do not require a phase-transfer catalyst, involve anion exchange followed by dethallation, but the detailed mechanism of the final step has not been discussed. It seems to us that the high

yield and regioselectivity of our bromodethallation is incompatible with an S_N1 -type of process and, bearing in mind the high nucleophilicity of alkali-metal halides when complexed with crown ethers, we suggest that an S_N2 displacement after and/or before anion exchange is the most likely pathway [equation (6); $Y = Br$ or OAc]. However, an S_Ni mechanism which involves transfer of bromine from thallium to the methylene group cannot be



ruled out. We feel that an alternative mechanism which involves deoxythallation, thallium(III) oxidation of bromide to bromine, and methoxybromination of the liberated alkene is less likely and, in an independent experiment, we showed that 32% of 1,2-dibromohexane and 15% of 2-bromo-1-methoxyhexane, which are *not* products of the reaction of compound (7a) with potassium bromide, are formed when hex-1-ene is treated with bromine in methanol (Scheme 1).

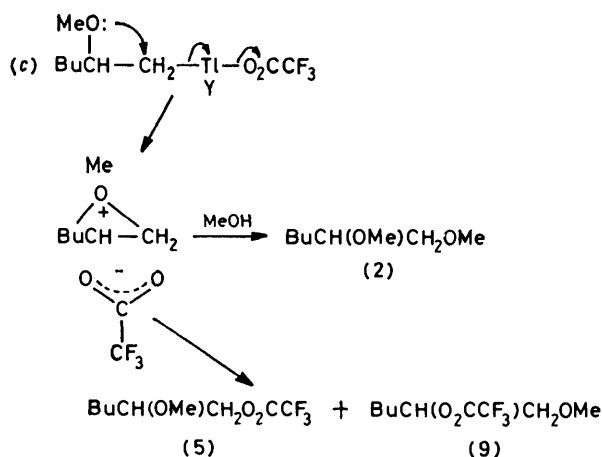
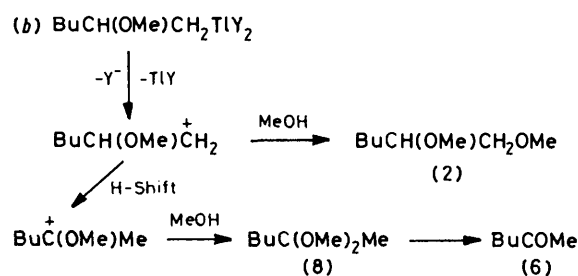
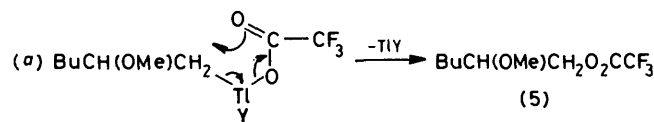
Thus, to interpret the other results in the Table we have taken the yield of 1-bromo-2-methoxyhexane (1) to represent a lower limit for the amount of methoxythallation adduct (7) which remains at the commencement of work-up. Hence, the results of Expt. 2 indicate that the methoxythallation adduct (7a), obtained with thallium(III) acetate, does not undergo any substantial dethallation when kept in methanol at room temperature over a period of one week. The influence of the thallium(III) salt used upon the reactivity of the resultant methoxythallation adduct is illustrated dramatically by the results of Expts. 3 and 4 which were carried out under exactly the same conditions as for Expts. 1 and 2 except that thallium(III) trifluoroacetate was used in place of the acetate. Bromodethallation after 5 min (Expt. 3) produced a high yield of 1-bromo-2-methoxyhexane (1) which confirms the formation of the methoxythallation adduct (7b) [equations (3) and (5); $X = F$]. However, attempted bromodethallation after one week (Expt. 4) gave *none* of compound (1), which indicates that, in contrast with the acetate-derived adduct (7a), the trifluoroacetate-derived product (7b) undergoes complete dethallation during this time.

The major products obtained from Expt. 4 were 1,2-dimethoxyhexane (2) (38%) and 2-methoxyhexanol (3) (51%) which represents a much improved yield of *vic*-dimethoxyalkane compared with the 10% of 1,2-dimethoxyoctane obtained in the decomposition of 2-methoxyoctylthallium diacetate in methanol at 65 °C.¹⁰ The products obtained from the latter decomposition have been accounted for in terms of three competing modes of unimolecular dethallation.¹⁰ The corresponding reactions for 2-methoxyhexylthallium bistrifluoroacetate (7b) are shown in Scheme 2, but it is immediately apparent that none of them give rise to the

principal product actually obtained, namely 2-methoxyhexanol (3).

In view of the fact that the S_Ni reaction [mode (a)] was the major decomposition pathway for 2-methoxyoctylthallium diacetate¹⁰ and that our work-up procedure involves aqueous washing after the treatment with potassium bromide, it is tempting to suggest that compound (3) arises *via* hydrolysis of 2-methoxy-1-

trifluoroacetoxyhexane (5). However, compound (5) was obtained from reactions in dichloromethane (Expts. 9 and 10) and shown to survive the conditions of work-up.



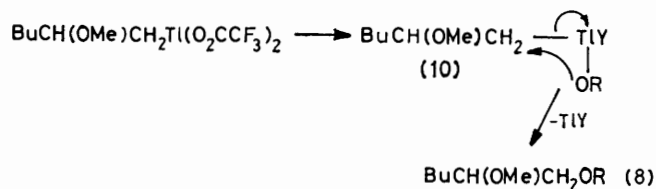
SCHEME 2 Possible modes of unimolecular decomposition of compound (7b).

Other workers have also shown that 1,2-bis(trifluoroacetoxy)octane is not hydrolysed under similar conditions.³ An alternative explanation for the formation of compound (3), in which water participates *before* work-up, must therefore be sought.

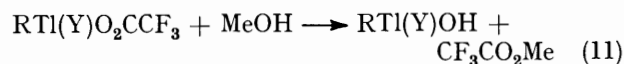
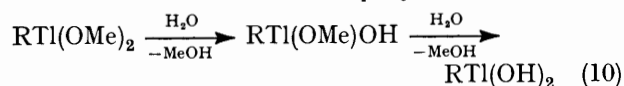
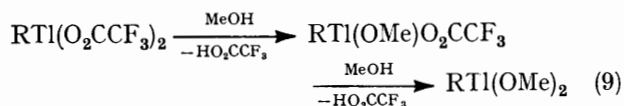
A source of the water needed to hydrolyse the organothallium compound is readily identified, for it is easily demonstrated by a simple n.m.r. experiment that trifluoroacetic acid, which is liberated during the oxythallation [equation (3)], is rapidly esterified by methanol [equation (7)]. A satisfactory mechanism for hydrolysis



must explain the high yield and regiospecificity of the alcohol formation. An S_N2 process, analogous to that proposed for bromodethallation [equation (6)], can be discounted since the stronger nucleophile, methanol, is present in some 80-fold higher concentration than the nucleophile water. We believe that 2-methoxyhexanol (3) is formed by an S_Ni process *after ligand exchange* [equation (8); R = H] and that this is probably also the main pathway for formation of 1,2-dimethoxyhexane (2) [equation (8); R = Me].



Ligand exchange does not occur readily in 2-methoxyalkylthallium diacetates, as evidenced by the isolation of such compounds from methanolic solution and the fact that one of their major decomposition routes involves the S_Ni transfer of acetate to the carbon originally bearing thallium.¹⁰ However, trifluoroacetate is a better leaving group than acetate and a progressive methanolysis can be envisaged [equation (9); R = BuCH(OMe)CH₂]. Each molecule of trifluoroacetic acid thus liberated will give rise to a molecule of water upon esterification [equation (7)]. The organothallium methoxides can be expected to undergo hydrolysis readily to provide species with the requisite hydroxy-group on thallium [equation (10)]. Direct hydrolysis of organothallium trifluoroacetates seems unlikely in view of the relatively low concentration of water, but a methanolysis which involves acyl-oxygen fission can be envisaged, and leads directly to an organothallium hydroxide [equation (11)]. Several possibilities thus exist for species (10) which actually undergoes dethallation [equation (8)].



In support of the above suggestion, we obtained evidence that thallium(III) trifluoroacetate itself undergoes methanolysis. Thus, a mixture of the thallium(III)

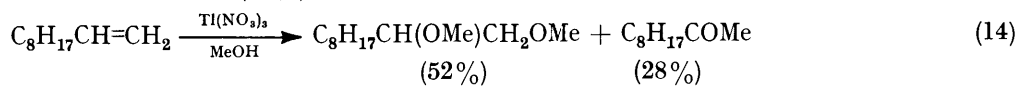
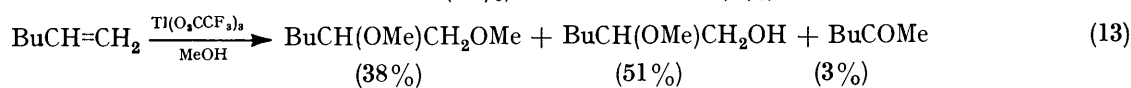
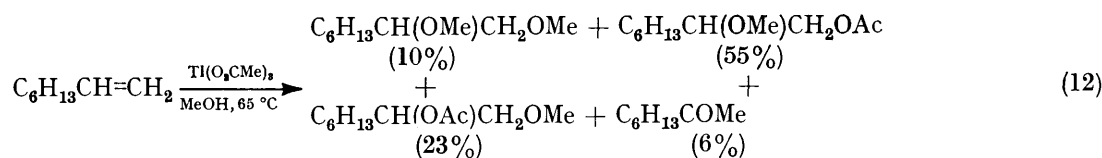
salt and methanol (2 equiv.) in dichloromethane gave a quantitative yield of methyl trifluoroacetate as shown by ¹H n.m.r. spectroscopy. Under these conditions the reaction was slow, taking 24 h to complete, but a higher rate can be expected when methanol is the solvent. A moderately fast ligand exchange for the adduct (7b) in methanol is required by the observation (Table, Expts. 6–8) that 68–86% of dethallation had taken place after 2 h. Another observation consistent with the ideas expressed above concerning the origin of compound (3) was the fact that the addition of water (1 equiv.) at the completion of methoxythallation had little effect upon product distribution (compare Expts. 4 and 5).

Apart from compounds (1)–(3), the only other product observed in the oxythallation-dethallation reactions in methanol (Expts. 1–8) was a small amount (1–10%) of hexan-2-one (6). This may be formed during work-up by hydrolysis of the corresponding dimethylacetal (8) (*cf.* ref. 10) and, if so, the result indicates that dethallation *via* a free carbocation [Scheme 2, mode (b)] contributes in a minor way to the decomposition of the adduct (7). However, it should be noted that 1–3% of the ketone is observed even when most of the methoxythallation adduct is still intact at the time of bromodethallation (Expts. 1–3), and possibly this derives from the decomposition of small amounts of the hydroxythallation adduct. Whatever the source of the ketone, the yield of it is markedly lower than that of the decan-2-one (28%) observed in the oxidation of dec-1-ene by thallium(III) nitrate trihydrate in methanol.⁴

A comparison of our data for the oxidation of hex-1-ene by thallium(III) trifluoroacetate [equation (13)] with other workers' results for the oxidation of oct-1-ene by thallium(III) acetate [equation (12)]¹⁰ and the oxidation of dec-1-ene by thallium(III) nitrate [equation (14)]⁴ illustrate the kind of control over product distribution that can be accomplished by variation of the thallium(III) salt employed.

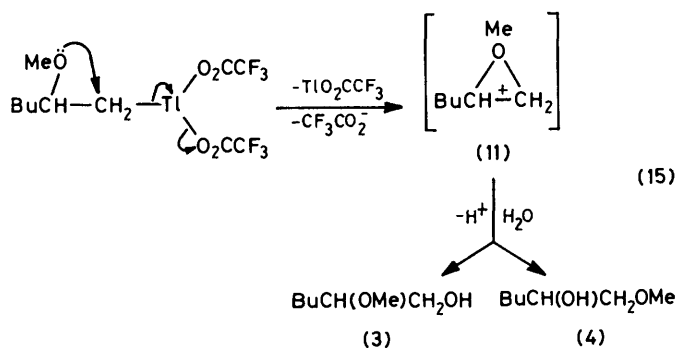
As a model for the conditions envisaged for an oxythallation-based crown ether synthesis, we treated hex-1-ene with thallium(III) trifluoroacetate in dichloromethane which contained methanol (2 equiv.) (Table, Expts. 9 and 10). Decomposition of the methoxythallation adduct was markedly faster than in neat methanol as shown by the fact that after only 1 h a nearly quantitative yield of thallium(I) trifluoroacetate was precipitated when the reaction mixture was cooled in ice. The extent of decomposition was confirmed by the fact that subsequent bromodethallation afforded 0–5% of 1-bromo-2-methoxyhexane (1). The yields of 1,2-dimethoxyhexane (2) and 2-methoxyhexanol (3) were considerably lower than those for reaction in methanol (*cf.* Expts. 4 and 5), and the product additionally contained 1-methoxyhexan-2-ol (4) and 2-methoxy-1-trifluoroacetoxyhexane (5) as principal components.

It is clear that the mechanism of dethallation is drastically altered when the adduct is generated in dichloromethane rather than in methanol and we believe that this arises primarily because ligand-exchange



processes [equations (9)—(11)] are no longer effective. In this case, only methanol 1 equiv. is available to displace trifluoroacetate from thallium and furthermore ligand exchange must compete with esterification [equation (7)] of the trifluoroacetic acid liberated during oxythallation [equation (3)].

Formation of the new products (4) and (5) can be accounted for by the continued presence of trifluoroacetate ligands in the methoxythallation adduct. Thus, compound (5) probably arises by an S_Ni process [Scheme 2, mode (a)] and the absence of the isomer (9) appears to rule out an ion-pair mechanism [Scheme 2, mode (c)]. However, the presence of the fluorine atoms will attenuate the nucleophilicity of the carbonyl group and enhance the ability of the carboxylate moiety to behave as a leaving group. Thus, ionisation to give a metal-free cationic intermediate will compete with the S_Ni process (Scheme 2). It appears that the oxonium ion (11) is formed in preference to the primary carbocation $\text{BuCH}(\text{OMe})\overset{+}{\text{C}}\text{H}_2$, and capture of the ion (11) by water (generated as described above) then accounts for the formation of compound (4) [equation (15)]. The



fact that the yield of hexan-2-one (6) was similar to that obtained in methanol also speaks against any substantially increased participation by the carbocation [Scheme 2; mode (b)].

EXPERIMENTAL

Thallium(III) acetate¹⁴ and thallium(III) trifluoroacetate¹⁵ were prepared from thallium(III) oxide according to published procedures. Methanol and dichloromethane were dried by distillation from calcium oxide and phosphorus pentoxide, respectively. 2,6-Dimethyl-18-crown-6 was prepared as described previously.⁷ All other reagents were

commercial samples and, except for hex-1-ene which was redistilled, were used without further purification. All reactions, except the independent syntheses of compounds (1), (3), and (9), were carried out under dry nitrogen. ¹H N.m.r. spectra (60 MHz) were recorded with a Perkin-Elmer R12 instrument and ¹³C n.m.r. spectra (20 MHz) with a Varian CFT 20 spectrometer and multiplicities were determined by off-resonance decoupling. Mass spectra were obtained on g.l.c. fractions by using a VG 7070 instrument with a Finigan INCOS 2 400 data system coupled to a Pye 204 gas chromatograph fitted with an OV 17 column; temperature programming over the range 70—160 °C and helium carrier gas were used.

Oxidations.—Thallium(III) salt (10 mmol) was added in one portion to a well stirred solution of hex-1-ene (10 mmol) in methanol (30 cm³) (Expts. 1—8) or in dichloromethane (30 cm³) which contained methanol (20 mmol) (Expts. 9 and 10). After an appropriate time (see the Table), solid potassium bromide (30 mmol) was added to the mixture followed by one drop of 2,6-dimethyl-18-crown-6. The mixture was stirred for a further 8 h and then allowed to stand overnight. Water (30 cm³) was added, the mixture was filtered through Celite, and the filtrate was extracted with dichloromethane (3 × 75 cm³). The combined dichloromethane extract was washed with saturated sodium hydrogencarbonate (20 cm³), dried (MgSO₄), and the solvent removed on a rotary evaporator at 0 °C/≥15 mmHg. The residue was distilled at 60—80 °C/12 mmHg to afford the oil which was analysed by g.l.c. and n.m.r. spectroscopy. Alternatively, the reaction mixture was treated with aqueous potassium bromide (30 mmol in 25 cm³), stirred for 8 h, left overnight, and then filtered through Celite and treated as above.

G.l.c. analyses were carried out using a Pye 204 instrument fitted with a flame ionization detector and a Perkin-Elmer 50 m SCOT column which contained liquid support phase SP 2100. The oven temperature was 70 °C and the carrier gas was nitrogen (14 lb in⁻²). Under these conditions the products eluted with retention times in the following order: (6) < (2) = (4) < (5) < (3) < (1). The composition of each mixture was determined (i) from the relative peak areas of the chromatogram and (ii) from the relative intensities of signals for similar carbon atoms in the ¹³C n.m.r. spectrum. In general, the two methods agreed within 2% and averaged mol fractions are given in the Table. *N.B.* The relative amounts of compounds (2) and (4) could only be determined by ¹³C n.m.r. spectroscopy since their g.l.c. retention times were identical.

For one reaction with thallium(III) acetate in methanol (*cf.* Expt. 1), the solvent was removed rapidly under reduced pressure and the resultant viscous oil, believed to be 2-methoxyhexylthallium diacetate (7a), was dissolved in

CDCl₃ to record its ¹H n.m.r. spectrum; δ_{H} 3.65(dm, ³J_{TI} 1 460 Hz, CHOMe), 3.45 (s, OMe), 3.15 (dm, ²J_{TI} 895 Hz, CH₂TI), 2.15 (s, OCOMe), and 1.6—0.8 m (9 H, Bu).

The chemical shift for CH₂TI is appreciably lower than that (δ_{H} 2.03) reported¹⁰ for the corresponding protons in 2-methoxyoctylthallium diacetate. Accordingly we prepared the oct-1-ene adduct, but our sample exhibited virtually identical chemical shifts and TI—H coupling constants with those of the hex-1-ene derivative (above).

Independent Syntheses.—(a) 1-Bromo-2-methoxyhexane (1). Bromine (10 mmol) in methanol (20 cm³) was added to a stirred solution of hex-1-ene (10 mmol) in methanol (30 cm³) at 0 °C over a period of 20 min. The solvent was removed at ≥ 15 mmHg to yield an oil which was dissolved in diethyl ether (50 cm³), and then water (50 cm³) and saturated sodium hydrogencarbonate (10 cm³) were added, and the mixture was shaken vigorously. The layers were separated and the aqueous layer was extracted with diethyl ether (2 \times 50 cm³). The diethyl ether layers were combined, dried (MgSO₄), and the solvent was removed at ≥ 15 mmHg to yield an oil (1.56 g) which was shown by g.l.c. and ¹³C n.m.r. spectroscopy to contain compound (1) (53%), 2-bromo-1-methoxyhexane (15%), δ_{C} 77.16 (C-1), 53.45 (C-2), 36.34, 29.44, 21.99, 13.97, and 58.91 (OMe), and 1,2-dibromohexane (32%); δ_{C} 52.76 (d, C-2), 36.07, 35.64, 28.82, 21.93, and 13.87; recovery of hex-1-ene-derived products was 79%. This result is in excellent agreement with that of a previous study.⁸

(b) 1-Methoxyhexan-2-ol (4). Crude 1,2-epoxyhexane (0.5 g; prepared from hex-1-ene and *m*-chloroperbenzoic acid¹⁶) was added to methanolic sodium methoxide [prepared from sodium (0.17 g) and methanol (50 cm³)] and the mixture was refluxed for 4 h. The solvent was removed under reduced pressure and the residue was dissolved in diethyl ether (30 cm³), washed with water (30 cm³), and the aqueous layer extracted with more diethyl ether (2 \times 30 cm³). The ethereal layers were combined, dried (MgSO₄), and the solvent was removed under reduced pressure to afford a quantitative yield of the crude compound (4).

(c) 1,2-Dimethoxyhexane (2). Sodium (0.17 g) was added to the crude compound (4) (4.0 g) and the mixture was warmed and stirred for 30 min to aid dissolution of the metal. Methyl iodide (0.5 cm³) was added and the gently warmed mixture was stirred for 30 min, water (30 cm³) was then added, and the solution extracted with diethyl ether (3 \times 30 cm³). The combined ethereal extract was dried (MgSO₄) and the diethyl ether was removed under reduced pressure to yield an oil (3.4 g), shown by ¹³C n.m.r. spectroscopy to be a mixture of compound (2) (18%) and the starting material (4).

(d) 2-Methoxyhexanol (3). Aqueous perchloric acid (60%; 4 drops) was added to a solution of 1,2-epoxyhexane (2.0 g) in methanol (4.0 cm³) and the mixture was stirred for 30 min. Removal of the solvent under reduced pressure afforded a quantitative yield of a mixture of compounds (3) (40%) and (4) (g.l.c.; ¹³C n.m.r.).

(e) 1-Methoxy-2-trifluoroacetoxyhexane (9). Trifluoroacetic acid (0.38 cm³) and trifluoroacetic anhydride (3 drops) were added to the crude compound (4) (0.5 g) and the mixture was stirred for 1.5 h. Removal of the volatile material at 20 °C/ ≥ 15 mmHg gave a mixture of compound (9) (45%) and the starting material (4) (g.l.c.). Compound (9) had the same g.l.c. retention time as compound (5), but a profoundly different mass spectrum (see below).

Product Characterization.—(a) 1-Bromo-2-methoxyhexane (1). An analytical sample of compound (1) was obtained by preparative g.l.c. of the product obtained from Expt. 1 using a Pye 204 instrument fitted with a column (1 m \times $\frac{1}{4}$ in o.d.) packed with 15% di-isodecyl phthalate on Chromosorb W AWDMCS 80—100 at 130 °C and nitrogen carrier gas (17 lb in⁻²); δ_{H} 3.38 [6 H, s and overlapping m, CH(OMe)CH₂Br] and 1.6—0.8 m (9 H, Bu); δ_{C} 80.42 (d, C-2), 57.35 (q, OMe), 34.45 (t, C-1), 32.63, 27.42, 22.74, and 14.01; M^+ < 0.01% of base peak, peaks at m/z 137 (35%) and 139 (36%) ($M - \text{Bu}$)⁺, 101 (100%) ($M - \text{CH}_2\text{Br}$)⁺, 69 (67%) ($M - \text{CH}_2\text{Br} - \text{MeOH}$)⁺, and 45 (65%) (Found: C, 43.8; H, 8.05; Br, 40.7. C₇H₁₅BrO requires C, 43.09; H, 7.75; Br, 40.96%).

(b) 1,2-Dimethoxyhexane (2). Lead tetra-acetate (10 mmol) was added to a solution of hex-1-ene (10 mmol) in methanol (30 cm³) and the mixture was stirred for 24 h. Most of the methanol was removed under reduced pressure and the residue was added to water. The mixture was filtered through Celite and the filtrate was extracted with diethyl ether, washed with aqueous sodium hydrogencarbonate, dried (MgSO₄), and the diethyl ether removed to leave an oil (0.86 g) shown (¹³C n.m.r.) to be mainly compound (2). An analytical sample was obtained by preparative g.l.c. using the same conditions as for compound (1); δ_{H} 3.40 (s), 3.38 [9 H, s and overlapping m, CH(OMe)CH₂OMe] and 1.6—0.8 (9 H, m, Bu); δ_{C} 80.27 (d, C-2), 75.02 (t, C-1), 59.09 (q, OMe), 57.41 (q, OMe), 31.13, 27.72, 22.98, and 14.07; M^+ < 0.01% of base peak, peaks at m/z 101 (92%) ($M - \text{CH}_2\text{OMe}$)⁺, 89 (15%) ($M - \text{Bu}$)⁺, 69 (95%) ($M - \text{CH}_2\text{OMe} - \text{MeOH}$)⁺, and 45 (100%) (Found: C, 65.7; H, 11.9. C₈H₁₈O₂ requires C, 65.71; H, 12.41%).

(c) 2-Methoxyhexanol (3). Compound (3) was not separately isolated and the following data are derived from a mixture of compounds (3) (40%) and (4); δ_{H} 3.7 (br s, OH), 3.45 [6 H, s and overlapping m, CH(OMe)CH₂OH] and 1.6—0.8 m (9 H, Bu); δ_{C} 82.21 (d, C-2), 63.85 (t, C-1), 57.13 (q, OMe), 30.34, 27.72, 23.00, and 14.05; M^+ < 0.01% of base peak, peaks at m/z 101 (92%) ($M - \text{CH}_2\text{OH}$)⁺, 75 (18%) ($M - \text{Bu}$)⁺, 69 (95%) ($M - \text{CH}_2\text{OH} - \text{MeOH}$)⁺, and 45 (100%).

(d) 1-Methoxyhexan-2-ol (4). An analytical sample was obtained by preparative g.l.c. [conditions as for compound (1)] of the product obtained from reaction of 1,2-epoxyhexane with sodium methoxide; δ_{H} 3.7 (br s, OH), 3.40 [6 H, s and overlapping m, CH(OMe)CH₂OH] and 1.6—0.8 m (9 H, Bu); δ_{C} 77.52 (t, C-1) 70.24 (d, C-2), 58.95 (q, OMe), 33.10, 27.88, 22.86, and 14.03; M^+ < 0.01% of base peak, peaks at m/z 87 (63%) ($M - \text{CH}_2\text{OMe}$)⁺, 75 (21%) ($M - \text{Bu}$)⁺, 69 (100%) ($M - \text{CH}_2\text{OMe} - \text{H}_2\text{O}$)⁺, 45 (57%), and 41 (68%) (Found: C, 62.7; H, 11.65. C₇H₁₆O₂ requires C, 63.60; H, 12.20%).

(e) 2-Methoxy-1-trifluoroacetoxyhexane (5). Compound (5) was not separately isolated; M^+ < 0.01% of base peak, peaks at m/z 171 (52%) ($M - \text{Bu}$)⁺, 101 (96%) ($M - \text{CH}_2\text{O}_2\text{CCF}_3$)⁺, 69 (100%) ($M - \text{CH}_2\text{O}_2\text{CCF}_3 - \text{MeOH}$)⁺, and 45 (60%). *N.B.* As expected, the isomer 1-methoxy-2-trifluoroacetoxyhexane (9) showed no strong peak at m/z 101 [due to BuCH(OMe)⁺].

We thank the S.R.C. for financial support.

[1/955 Received, 15th June, 1981]

REFERENCES

- Part 14, A. J. Bloodworth and J. L. Courtneidge, *J. Chem. Soc., Perkin Trans. 1*, preceding paper.

- ² Recent reviews include (a) A. McKillop and E. C. Taylor, *Chem. Brit.*, 1973, **9**, 4; (b) A. McKillop and E. C. Taylor in 'Advances in Organometallic Chemistry,' vol. 11, eds F. G. A. Stone and R. West, Academic Press, N.Y., 1973, p. 147; (c) A. McKillop, *Pure Appl. Chem.*, 1975, **43**, 463; and (d) A. McKillop and E. C. Taylor, *Endeavour*, 1976, **35**, 88.
- ³ A. Lethbridge, R. O. C. Norman, and C. B. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1973, 2763.
- ⁴ A. McKillop, J. D. Hunt, F. Kienzle, E. Bigham, and E. C. Taylor, *J. Am. Chem. Soc.*, 1973, **95**, 3635.
- ⁵ G. Emmer and E. Zbiral, *Tetrahedron*, 1977, **33**, 1415.
- ⁶ Y. Yamada, A. Shibata, K. Iguchi, and H. Sanjoh, *Tetrahedron Lett.*, 1977, 2407.
- ⁷ A. J. Bloodworth, D. J. Lapham, and R. A. Savva, *J. Chem. Soc., Chem. Commun.*, 1980, 925.
- ⁸ W. H. Puterbaugh and M. S. Newman, *J. Am. Chem. Soc.*, 1957, **79**, 3469.
- ⁹ S. Uemura, K. Zushi, A. Tabata, A. Toshimitsu, and M. Okano, *Bull. Chem. Soc. Jpn.*, 1974, **47**, 920.
- ¹⁰ A. Lethbridge, R. O. C. Norman, and C. B. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1929.
- ¹¹ S. Uemura, A. Toshimitsu, M. Okano, T. Kawamura, T. Yonezawa, and K. Ichikawa, *J. Chem. Soc., Chem. Commun.*, 1978, 65.
- ¹² H. Mitano, T. Ando, and Y. Yukawa, *Chem. Lett.*, 1972, 455.
- ¹³ S. Uemura, A. Toshimitsu, M. Okano, and K. Ichikawa, *Bull. Chem. Soc. Jpn.*, 1975, **48**, 1925.
- ¹⁴ S. Uemura, H. Miyoshi, M. Okano, and K. Ichikawa, *J. Chem. Soc., Perkin Trans. 1*, 1981, 993.
- ¹⁵ A. McKillop, J. D. Hunt, M. J. Zelesko, J. S. Fowler, E. C. Taylor, G. McGillivray, and F. Kienzle, *J. Am. Chem. Soc.*, 1971, **93**, 4841.
- ¹⁶ A. J. Bloodworth and G. S. Bylina, *J. Chem. Soc., Perkin Trans. 1*, 1972, 2433.