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S_N2 and E2 Branching of Main-Group-Metal Alkyl Intermediates in Alkane CH Oxidation: Mechanistic Investigation Using Isotopically Labeled Main-Group-Metal Alkyls

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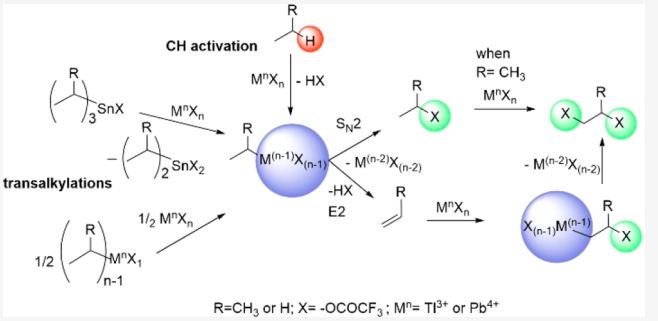
ABSTRACT: The main-group-metal alkyl compounds trialkyltin and dialkylthallium have been utilized to investigate the mechanism of functionalization of monoalkyl thallium and lead species, proposed to be putative intermediates in alkane (RH) functionalization, formed via CH activation of alkanes (methane, ethane, and propane) using electrophilic Tl(III) and Pb(IV) in trifluoroacetic acid (HTFA). Two different organometallic transalkylation methods were used to generate the putative intermediates *in situ*. The results herein strongly support a mechanism of CH activation to generate a main-group-metal alkyl intermediate which undergoes reductive functionalization to generate the products, R-TFA, and the reduced metal salt. In the case of ethane there are two products, ethyl trifluoroacetate (EtTFA) and 1,2-bis(trifluoroacetoxy)ethylene glycol ($EG(TFA)_2$), observed in the reaction mixture that are proposed to form in parallel from a common intermediate, $EtTl(TFA)_2$. The alkyl transfer studies herein strongly support the simultaneous formation of both species from this intermediate. Furthermore, studies conducted using regiospecifically isotopically labeled diethylthallium salts strongly support an S_N2 functionalization from $EtTl(TFA)_2$ to give EtTFA (and reduced Tl(TFA)) and an E2 elimination (also from $EtTl(TFA)_2$) to generate ethylene, which instantly reacts with an additional 1 equiv of $Tl(TFA)_3$ to generate $EG(TFA)_2$.



INTRODUCTION

Selective conversion of light alkanes (methane, ethane, propane) to functionalized products remains one of the longstanding, unsolved challenges in chemistry. This is an important problem because of the vast, underutilized reserves of natural gas (mostly methane with some ethane and propane) present within the US and worldwide.[1] Technology for the selective conversion of natural gas could lead to the augmentation or replacement of oil as the primary feedstock for chemicals, materials, and fuels. The selective conversion of alkanes (particularly methane) has proven to be particularly challenging, given the lack of functional groups on alkanes and the intrinsically lower reactivity of the CH bonds relative to the bonds in the products. Indeed, by almost every quantitative measure of reactivity, alkanes (i.e., methane) are *less reactive* than their desired products (i.e., methanol), making the prevention of product overoxidation (i.e., to CO_2) challenging.[2] This is why current, commercially available technologies for the conversion of natural gas to chemicals and fuels utilize multistep, indirect, high-temperature (>800 °C) processes.[3] A process that could convert natural gas at lower temperatures (~200 °C), selectively and directly, to chemicals and fuels would be simpler and more economical (*vide infra*).

One approach to this challenge is electrophilic CH activation (CHA) (Scheme 1), whereby soft, highly polarizable, electrophilic metal centers (M^nX_2) are utilized that can favorably interact with the very low energy electrons in the HOMO of alkanes, leading to heterolytic cleavage of the C−H bond and formation of a metal alkyl intermediate ($R-M^n-X$). Subsequent reductive functionalization (MRF) from this intermediate results in the desired product (R−X) and a reduced form of the metal electrophile (M^{n-2}). Using this strategy, systems have been developed based on Hg,[4,5] Pt,[6−8] Pd,[9,10] Ir,[11,12] Sb,[13] Ag, and Au[14] as well as other electrophilic metal centers.[2]

We recently reported,[15] to our knowledge, the first main-group systems, $Tl(TFA)_3$ and $Pb(TFA)_4$, that selectively and rapidly functionalize all of the alkanes in natural gas (methane,

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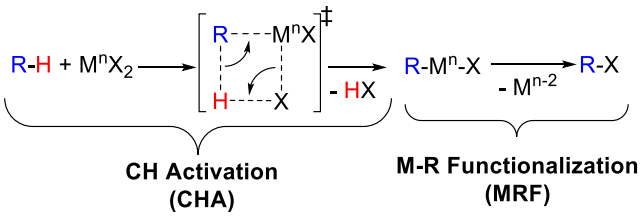
Scheme 1. Two-Step Mechanism for the Functionalization of Unactivated Alkanes (R−H) to Functionalized Products (R−X)[a]



[a]Step one involves CHA of R−H by an electrophilic metal species, M^nX_2, resulting in cleavage of the C−H bond and formation of a metal alkyl, R−M^n−X. Step two involves reductive functionalization of R−M^n−X (MRF) to give the oxidized product, R−X, and the reduced metal species, M^{n-2}.

ethane, and propane) to the corresponding mono- and diol esters in a non-superacid medium, HTFA ($F_3CC(O)OH$) at 180 °C (Figures 1 and 2). On the basis of initial studies with

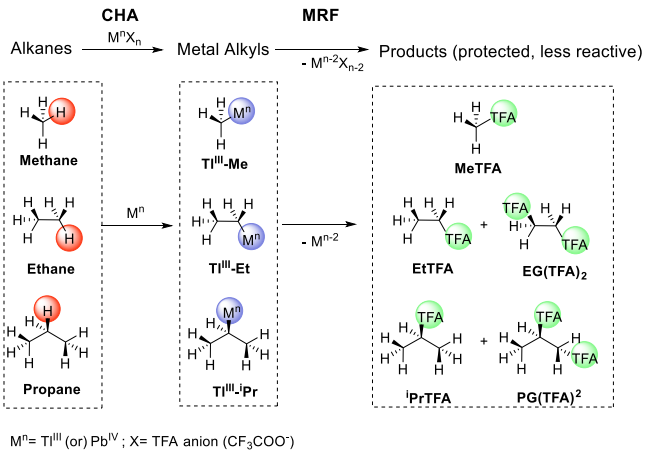


Figure 1. Main-group-metal complex mediated, stoichiometric CH activation to generate metal alkyl intermediates that functionalize to give oxidized products. With higher alkanes (ethane and propane), four-electron-oxidation products are also observed in addition to the expected two-electron-oxidation products. Because the corresponding alcohol products are esterified with HTFA and the CH activation mechanism is electrophilic, the products are effectively protected from undergoing subsequent oxidations with the main-group oxidants. A mixture of alkanes (as in natural gas) can also be functionalized selectively (see Figure 2).

methane, the reaction was proposed to proceed by stoichiometric C−H activation and M−R functionalization pathways (Figure 1). We were particularly intrigued by parallel and selective formation of both the mono- and diol esters from ethane and propane (Figures 1 and 2). Previous work with higher alkanes would predict[16] poorer selectivity for the higher alkanes relative to methane due to the increased number of C−H bonds in the substrates and products and the relatively harsh reaction conditions. The surprisingly high efficiency, selectivity, and parallel formation of multiple products in reactions of Tl (or Pb) with ethane (or propane) provided an excellent rationale for mechanistic study to understand the basis for this high selectivity. The work herein describes the detailed experimental studies of the independently generated putative M−Et intermediate predicted from the electrophilic CH activation of ethane with M^{n+} electrophile. The data further

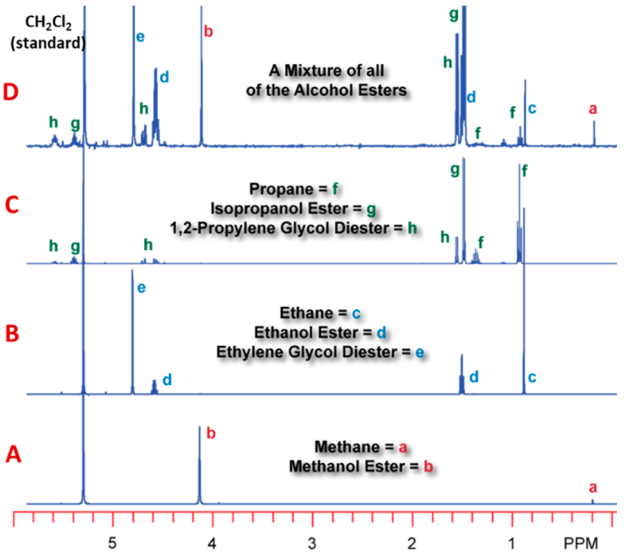


Figure 2. Overlay of ^{1}H NMR spectra of crude reaction mixtures of $Tl(TFA)_3$ with (A) methane, (B) ethane, (C) propane, and (D) a 100/8/1 methane/ethane/propane mixture.[15]

support a CH activation, M−R functionalization mechanism and offer a fundamental understanding of the basis for the parallel formation of the mono- and diol esters from the higher alkanes (i.e., ethane and propane) with these main-group oxidants.

The reaction of ethane with $Tl(TFA)_3$ in HTFA generated only the mono- and difunctionalized oxygenated products, ethanol trifluoroacetate ester (EtTFA) and ethylene glycol trifluoroacetate diester ($EG(TFA)_2$), respectively.[15] No other organic products such as ethylene or transient alkyl−Tl intermediates are observed. Consistent with rate-determining C−H cleavage reactions, studies with CD_3CH_3 showed a normal H/D kinetic isotope effect of 3.4/1 for the formation of EtTFA. The reactions of ethane in DTFA solvent showed no D incorporation in ethane (*d*-ethane), suggesting irreversible CH activation. Our expectation was that the products of this reaction would be generated from the sequential reactions ethane → EtTFA → $EG(TFA)_2$. Surprisingly, however, time course studies showed that EtTFA and $EG(TFA)_2$ were generated in parallel at a constant ∼2:1 ratio throughout the course of the reaction: i.e., the selectivity was independent of the concentrations of both ethane and $Tl(TFA)_3$ (which was the limiting reagent and was consumed as the reaction procdeded). Control studies with $^{13}CH_3CH_2TFA$ further confirmed that EtTFA is stable and not converted to ethane, ethylene, or $EG(TFA)_2$ under the reaction conditions. $EG(TFA)_2$ is similarly stable. Consistent with the lack of observation of ethylene, control experiments showed that addition of ethylene to solutions of $Tl(TFA)_3$ at 180 °C generated $EG(TFA)_2$, essentially on mixing, without observation of any Tl−R intermediates. Thus, considering the separate reaction in DTFA, the selectivity of the reaction of ethane with $Tl(TFA)_3$ in DFTA to the three expected products *d*-ethane, EtTFA, and $EG(TFA)_2$ is ∼0:2:1 within experimental error.[15]

The observations discussed above for the reaction between ethane and $Tl(TFA)_3$ led us to propose the overall mechanism for the reaction shown in Scheme 2. As can be seen, the three products are proposed to result from three fundamentally different branching reactions from the putative intermediate, $EtTl(TFA)_2$, generated from CH activation of ethane. Thus,

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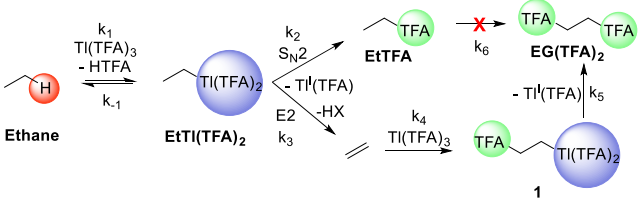
Scheme 2. Proposed Mechanism for the Functionalization of Ethane with $Tl(TFA)_3$[a]



[a]CH activation generates a metal alkyl, $EtTl(TFA)_2$ (k_1). Functionalization occurs either via S_N2-type attack by a TFA anion to give EtTFA (k_2) or E2-type elimination with a TFA anion to generate ethylene (k_3), which further reacts with $Tl(TFA)_3$ to give $EG(TFA)_2$ (k_4 and k_5). Controls demonstrate that EtTFA, once formed, does not convert to $EG(TFA)_2$ in the presence or absence of $Tl(TFA)_3$ under the reaction conditions (k_6). Formation of the metal alkyl intermediate via k_1 is irreversible, meaning that protonolysis (the microscopic reverse of CH activation) of $EtTl(TFA)_2$ to generate ethane does not occur (k_{-1}).

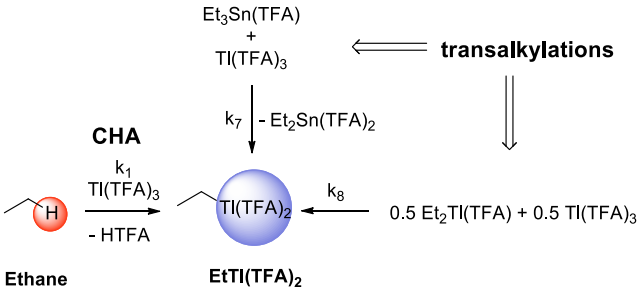
when the reaction is run in DTFA, *d*-ethane would generally be expected to form from k_{-1} (the microscopic reverse of C−H activation). However, as no *d*-ethane was observed, if the reaction proceeds by the proposed mechanism, then formation of the intermediate, $EtTl(TFA)_2$, via k_1 must be irreversible (i.e., k_2 and $k_3 \gg k_{-1}$). EtTFA is formed via an irreversible S_N2-type functionalization (step k_2) and $EG(TFA)_2$ is formed via an irreversible E2-type functionalization (k_3, k_4, and k_5). The lack of observation of ethylene or any Tl−R intermediates (such as **1** in Scheme 2) along with the observed rapid reaction of ethylene to selectively generate $EG(TFA)_2$ would suggest that k_4 and $k_5 > k_3$. Controls show that the subsequent formation of $EG(TFA)_2$ from EtTFA does not occur at an appreciable rate under the reaction conditions (k_6).[15]

On the basis of the mechanism proposed in Scheme 2, the above observations suggest that the selectivity of the reaction for *d*-ethane (when reaction is run in DTFA), EtTFA, and $EG(TFA)_2$ should be independent of the concentration of the putative intermediate, $EtTl(TFA)_2$, and should be set by the ratio of the branching rates $k_{-1}/k_2/k_3$ for the formation of ethane, EtTFA, and $EG(TFA)_2$, respectively. This correspondence between the observed ratio of products and the predicted ratio of rates for the three branching steps provided a good rationale for the study of this reaction mechanism. The key hypothesis is that, if the reaction of ethane with $Tl(TFA)_3$ proceeds as shown in Scheme 2, then the stoichiometric reaction of independently synthesized $EtTl(TFA)_2$ should, under similar reaction conditions, give the same ratio of products (ethane/ EtTFA/$EG(TFA)_2$ ≈ 0:2:1) as observed in the stoichiometric reaction between ethane and $Tl(TFA)_3$ in DTFA (*d*-ethane/EtTFA/$EG(TFA)_2$ = 0:2:1).

RESULTS AND DISCUSSION

The mechanistic studies were carried out in HTFA to ensure relevance to the reported conditions for reactions with ethane and to facilitate studies based on ^1H NMR spectroscopy. Initial efforts focused on detection of the putative intermediate, $EtTl(TFA)_2$, shown in Scheme 2. However, various attempts, such as carrying out reactions of ethane and $Tl(TFA)_3$ in HTFA at lower temperatures, in other solvents, and with more reactive alkanes such as isobutane failed to show any $R-TlX_2$ intermediates. This is consistent with the rarity of monoalkylthallium(III) compounds in the literature and the high reactivity attributed to these types of species.[17,18] In order to examine the chemistry of this intermediate in more detail, we focused on *in situ* generation by independent syntheses. The literature shows that alkyl transfers between the same, as well as different, main-group elements are facile, selective, predictable, and well-defined. Thus, dialkyl HgR_2 complexes have been shown to readily react with HgX_2 salts to selectively and reproducibly generate the expected monoalkyl species, RHgX, with well-defined kinetics.[19−22] Similar observations have been made with alkyltin species[23−25] R_nSnX_{4-n}, trialkyllead species[20,21] R_3PbX, and dialkylthallium species[17] R_2TlX. We hypothesized that we could independently generate $EtTl(TFA)_2$ *in situ* by similar alkyl transfer reactions. Scheme 3 shows the CH activation route for generating the putative $EtTl(TFA)_2$ intermediate from ethane as well as two alternative routes for generating the same intermediate *in situ* in the absence of ethane.

Scheme 3. Routes to Access $EtTl(TFA)_2$[a]



[a]Ethane can react with $Tl(TFA)_3$ via k_1 to give the putative intermediate, or the species can be accessed via organometallic transalkylation with $Et_3Sn(TFA)$ via k_7 or with $Et_2Tl(TFA)$ via k_8. In any case, functionalization of the formed intermediate should occur as described above in Scheme 2 regardless of the alkyl source used.

Alkyl and aryl transfer from organotin (R_nSnX_{4-n}) reagents are well-known, facile, well-defined, selective reactions that have been extensively utilized in organic and organometallic synthesis.[23] As shown in Scheme 3, we utilized this methodology to independently generate $EtTl(TFA)_2$ by *in situ* alkylation of $Tl(TFA)_3$ with $Et_3Sn(TFA)$ (k_7). $Et_3Sn(TFA)$ was generated *in situ* by addition of Et_4Sn to HTFA.[26] The resulting solution of $Et_3Sn(TFA)$ was stable for a few hours and only underwent slow protonolysis to generate $Et_2Sn(TFA)_2$). An important advantage of this approach, in addition to generating $EtTl(TFA)_2$, is the ease of synthesis of a wide range of organotin (R_nSnX_{4-n}) reagents that give ready access to a wide range of $RTl(TFA)_2$ intermediates for future study. However, an important disadvantage of this method is introduction of tin reagents that are not present in the ethane CH functionalization reaction, which could influence the course of these studies.

Due to concerns of handling alkyltin and alkyl thallium compounds at elevated temperatures, the majority of the studies were carried out at room temperature in sealed, glass NMR tubes. Controls indicate that the presence or exclusion of O_2 has no effect on these reactions. The addition of $Et_3Sn(TFA)$ to excess $Tl(TFA)_3$ (3.3 equiv relative to the ethyl groups on Sn) in HTFA at room temperature resulted in the generation of EtTFA and $EG(TFA)_2$ in an ∼2:1 ratio, which is the same as that observed in the reaction between

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Organometallics XXXX, XXX, XXX−XXX

$Tl(TFA)_3$ and ethane. Furthermore, ethane was not observed by ^1H NMR, consistent with k_2 and k_3 (shown in Scheme 2) being greater than k_{-1}.

Interestingly, the alkyl transfer between $Et_3Sn(TFA)$ and $Tl(TFA)_3$ to generate $Et_2Sn(TFA)_2$ and $EtTl(TFA)_2$ (eq 1) seems to occur upon mixing at room temperature, but the transfer between $Et_2Sn(TFA)_2$ and $Tl(TFA)_3$ seems to be much slower (eq 2). Thus, despite the presence of excess $Tl(TFA)_3$, only one of the ethyl groups on $Et_3Sn(TFA)$ was transferred and $Et_2Sn(TFA)_2$ remained in the reaction mixture and was only slowly converted to products, but most of the organotin was consumed if the reaction mixtures were left to sit for extended periods of time. The ^1H NMR spectrum for the functionalization reaction between $Et_3Sn(TFA)$ and $Tl(TFA)_3$ at room temperature, after 18 h, is compared to that for the reaction between $Tl(TFA)_3$ and ethane in Figure 3 (spectra A and B, respectively).

$$Et_3Sn(TFA) + TI(TFA)_3 \xrightarrow[RT]{fast} Et_2Sn(TFA)_2 + EtTI(TFA)_2 \quad (1)$$

$$Et_2Sn(TFA)_2 + TI(TFA)_3 \xrightarrow[RT]{fast} EtSn(TFA)_3 + EtTI(TFA)_2 \quad (2)$$

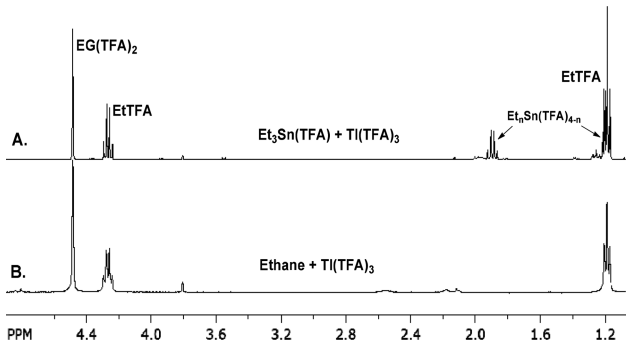

Figure 3. ^1H NMR spectra of (A) the reaction between $Et_3Sn(TFA)$ and $Tl(TFA)_3$ at RT 18 h after mixing and (B) the reaction between $Tl(TFA)_3$ and ethane at 180 °C. In both cases the ratio of EtTFA to $EG(TFA)_2$ is ~2:1.

Given that the $EtTl(TFA)_2$ generated via alkyl transfer was only transiently generated and not physically observed, we wanted to access it via a separate route. Interestingly, dialkylthallium species, R_2TlX, are well-known and stable unlike the monoalkyl species, $RTlX_2$.[27,28] We postulated that $Et_2Tl(TFA)$ could be used analogously to $Et_3Sn(TFA)$ as a second route to generate $EtTl(TFA)_2$ *in situ* (Scheme 3, k_8). This route was particularly appealing, as the alkyl transfer from $Et_2Tl(TFA)$ to $Tl(TFA)_3$ would be expected to generate 2 equiv of $EtTl(TFA)_2$ without the generation of any other non-Tl species that could interfere with the selectivity of the reaction. Control studies demonstrated that solutions of $Et_2Tl(TFA)$ in HTFA were stable up to 100 °C in the absence of $Tl(TFA)_3$ and did not generate any products such as ethane and butane. Interestingly, the temperature was observed to have little effect on the selectivity for EtTFA and $EG(TFA)_2$ (from RT to 125 °C; see the Supporting Information) and so most of the reactions between $Tl(TFA)_3$ and $Et_2Tl(TFA)$ were carried out at room temperature and ambient pressure in glass NMR tubes to minimize the handling of $Et_2Tl(TFA)$ at elevated temperatures and pressures (the compound is likely highly toxic). Control experiments indicate that there is no difference in reactivity in the presence or absence of O_2 and that the selectivity is unaffected by the order of addition of reagents.

The reactions were carried out by addition of 0.5 mL of a homogeneous, 250 mM solution of $Tl(TFA)_3$ to 0.5 mL of a 25 mM solution of $Et_2Tl(TFA)$ in HTFA in a J. Young NMR tube. The reaction was monitored by ^1H NMR. On the time scale of the NMR experiment, all of the $Et_2Tl(TFA)$ was consumed and three products were observed by ^1H NMR: EtTFA, $EG(TFA)_2$ and HO-CH_2CH_2-TFA (Figure 4,

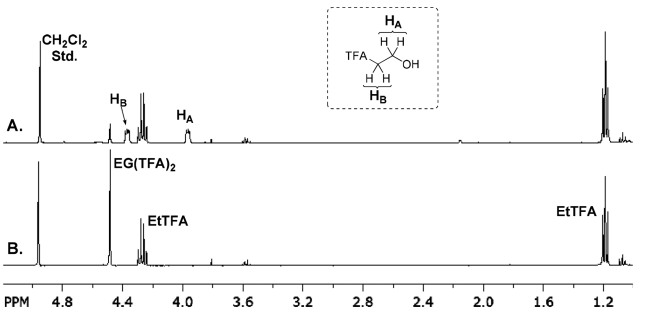

Figure 4. ^1H NMR spectra of the reaction between $Et_2Tl(TFA)$ and $Tl(TFA)_3$ (A) 30 min after mixing showing the formation of EtTFA, some $EG(TFA)_2$, and HO-CH_2CH_2TFA and (B) the same reaction after the mixture sat overnight, showing that the intermediate species quantitatively converts to $EG(TFA)_2$. The final ratio of EtTFA to $EG(TFA)_2$ is 2:1.

spectrum A). This third species, HO-CH_2CH_2-TFA, was slowly esterified at room temperature and, after 18 h, was quantitatively converted to $EG(TFA)_2$ with a final ratio of EtTFA:$EG(TFA)_2$ of ~2.1 (Figure 4, spectrum B). In addition to TFA-CH_2CH_2-TFA, HO-CH_2CH_2-TFA is also observed to form in the reaction of $Tl(TFA)_3$ with ethylene in HTFA. This is because our analyses suggest that the $Tl(TFA)_3$[35] is a hydrated species, consistent with Tl(III) having one of the highest known hydration energies. The synthesis of $Tl(TFA)_3$ requires heating Tl_2O_3 in the presence of HTFA with up to 20% water by volume, and despite our repeated efforts, we have no evidence that our attempts to prepare anhydrous $Tl(TFA)_3$ (such as by recrystallization from trifluoracetic anhydride) were ever successful. As such, in the reaction between $Tl(TFA)_3$ and ethylene (or ethane), water is just as likely (or perhaps more likely) to be the attacking nucleophile and generates an alcohol (or protonated alcohol) product which is then esterified (quickly in the case of EtOH and HO-CH_2CH_2-OH and more slowly for the second OH in TFA-CH_2CH_2-OH). This monoesterified glycol product then slowly converts to TFA-CH_2CH_2-TFA in HTFA at room temperature. Alternatively, heating the solution to 100 °C resulted in very rapid conversion of HO-CH_2CH_2-TFA to $EG(TFA)_2$. No ethane was detected in the reaction mixture, and the mass balance for EtTFA and $EG(TFA)_2$ was >95% on the basis of the amount of added $Et_2Tl(TFA)$. The intermediate species, HO-CH_2CH_2TFA, is also observed in the reaction between ethylene and $Tl(TFA)_3$ in HTFA when the reaction is carried out at room temperature and slowly converts to $EG(TFA)_2$. The intermediate is also observed upon addition of ethylene glycol, $HOCH_2CH_2OH$, to trifluoroacetic acid.[29]

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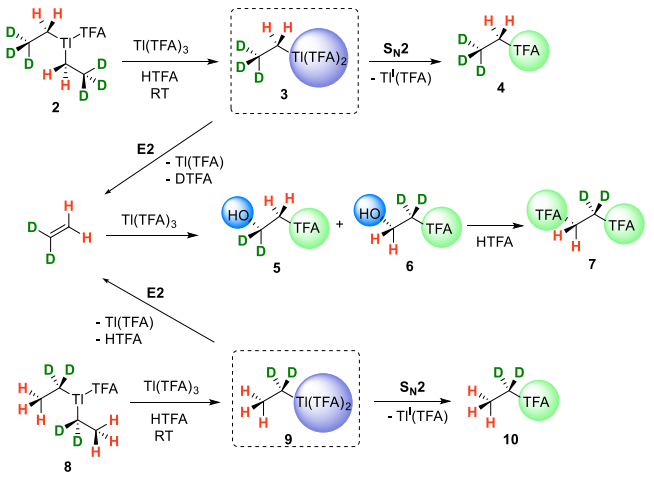
The observation of an identical intermediate in the reaction between ethylene and $Tl(TFA)_3$ as well as in the reaction of $Et_2Tl(TFA)$ and $Tl(TFA)_3$ compellingly suggests that free ethylene is formed in the functionalization reaction of $Et_2Tl(TFA)$, but we wanted to provide further, direct support for its formation as well as evidence that the functionalization of $Et_2Tl(TFA)$ was proceeding by alkyl transfer to generate 2 equiv of $EtTl(TFA)_2$ and not by a different mechanism such as outer-sphere electron transfer etc. In order to investigate this, we decided to make regiospecifically labeled diethylthallium compounds **2** and **8** (Scheme 4) and investigate their reactivity

Scheme 4. Functionalization of Deuterium-Labeled Diethyl Thallium Compounds 2 and 8[a]



[a]Alkyl transfer is expected to generate monoethyl thallium compounds **3** and **9**, respectively. As shown, the deuterium label is expected to be preserved in the S_N2 products, **4** and **10**. Evidence for free ethylene, resulting from an E2 mechanism, would be predicted to result in observation of both 2-hydroxyethyltrifluoroacetate intermediates, **5** and **6**, from both **2** and **8**.

with $Tl(TFA)_3$. As shown in Scheme 4, transalkylation with **2** or **8** would be expected to generate monoalkylthallium compound **3** or **9**, respectively. S_N2 functionalization from **3** would be expected to result in the formation of **4** with the deuterium label preserved in the product. Likewise, S_N2 functionalization from intermediate **9** should result in the formation of **10**. Elimination from either intermediate should lead to the observation of both **5** and **6** due to rapid reaction of the generated CD_2CH_2, and these species would be expected to slowly convert to **7**.

Fully consistent with the expected reactions shown in Scheme 4 (by extension from Schemes 2 and 3) addition of **2** to excess $Tl(TFA)_3$ was found to generate, after 10 h, only **4** and **7** in an ~3:1 ratio (Figure 5, spectrum A). In contrast, reactions with **8** lead only to **10** and **7**, now in a closer to ~2:1 ratio (Figure 5, spectrum C) observed in the ethane reactions.

This higher 3:1 ratio with **2** in comparison to the unlabeled $Et_2Tl(TFA)$ and **8** is expected. The E2-type reaction would be expected to show a primary KIE from **2** where a C−D bond is cleaved. In contrast, from **8**, the E2-type reaction involves cleavage of a C−H bond and the ratio of **4** to **7** would be expected to be more similar to that from the putative intermediate, $EtTl(TFA)_2$. No attempts at highly accurate quantitative analyses of the difference among **4**, **10**, and **7** from **2** or **8** were made, as secondary kinetic isotope effects (SKIEs)

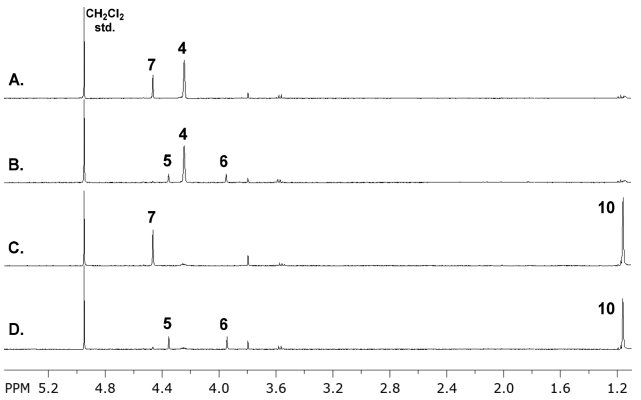


Figure 5. ^1H NMR stack plot for the functionalization of regiospecifically deuterated $Et_2Tl(TFA)$ species **2** and **8**. (A) Functionalization of **2** taken after 10 h at room temperature. Species **4** is present while **10** is not, showing retention of the deuterium label in the S_N2 functionalization. (B) Functionalization of **2** taken immediately upon mixing, showing the presence of **5** and **6** in a 1:1 ratio and suggesting the formation of free ethylene. Both **5** and **6** were seen to quantitatively convert to **7**. (C) Functionalization of **8** taken after 10 h at room temperature. Species **10** is present while **4** is not, showing retention of the deuterium label in the S_N2 functionalization. (D) Functionalization of **8** taken immediately upon mixing, showing the presence of **5** and **6** in a 1:1 ratio and suggesting formation of free ethylene. Both **5** and **6** were observed to quantitatively convert to **7**.

could be possible on both the S_N2 and E2-type pathways.[30,31] The SKIEs observed with **2** and **8** are consistent with literature reports for S_N2 and E2 reactions from alkyl halides.[31−33] When these functionalizations are carried out at room temperature, the intermediate species **5** and **6** are observed immediately after mixing, in both cases, in an ~1:1 ratio (Figure 5, spectrum B for **2** and spectrum D for **8**). This is evidence for the formation of free ethylene, as CH_2CD_2 generated from either **2** or **8** should add to $Tl(TFA)_3$ in a 1:1 ratio as the SKIE for addition would be expected to be small. Esterification from both **5** and **6** would generate **7**, as observed.

Similarly to ethane, propane was also found to generate two products, isopropyl trifluoroacetate (^{i}PrTFA) and 1,2-propylene glycol bis(trifluoroacetate) ($PG(TFA)_2$) (Table 1, entry 7). No *n*-propyltrifluoroacetate was ever observed. As such, the

Table 1. Products Obtained from Various Alkyl Sources with Tl(III) and Pb(IV)[a]

entry	oxidant	alkyl source	product (ratio)
1[b,c]	$Tl(TFA)_3$	methane	MeTFA
2[b]	$Tl(TFA)_3$	$Me_2Tl(TFA)$	MeTFA
3[b,c]	$Tl(TFA)_3$	ethane	EtTFA and $EG(TFA)_2$ (2:1)
4	$Tl(TFA)_3$	$Et_2Tl(TFA)$	EtTFA and $EG(TFA)_2$ (2:1)
5	$Tl(TFA)_3$	$Et_3Sn(TFA)$	EtTFA and $EG(TFA)_2$ (2:1)
6[c]	$Tl(TFA)_3$	$Et_3Sn(TFA)$	EtTFA and $EG(TFA)_2$ (3:1)
7[b,c]	$Tl(TFA)_3$	propane	^{i}PrTFA and $PG(TFA)_2$ (3:1)
8	$Tl(TFA)_3$	$^iPr_2Tl(TFA)$	^{i}PrTFA and $PG(TFA)_2$ (6:1)
9	$Tl(TFA)_3$	$^iPr_3Sn(TFA)$	^{i}PrTFA and $PG(TFA)_2$ (6:1)
10[b,c]	$Pb(TFA)_4$	methane	MeTFA
11[b,c]	$Pb(TFA)_4$	ethane	EtTFA and $EG(TFA)_2$ (2:1)
12	$Pb(TFA)_4$	Me_4Sn	MeTFA
13	$Pb(TFA)_4$	$Et_3Sn(TFA)$	EtTFA and $EG(TFA)_2$ (2.6:1)

[a]See the Experimental Section for details. [b]See ref 15 for experimental details. [c]Reaction at 180 °C.

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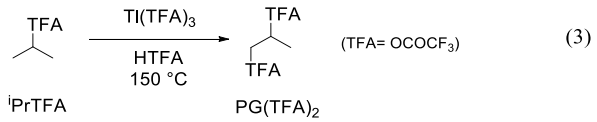
Organometallics XXXX, XXX, XXX−XXX

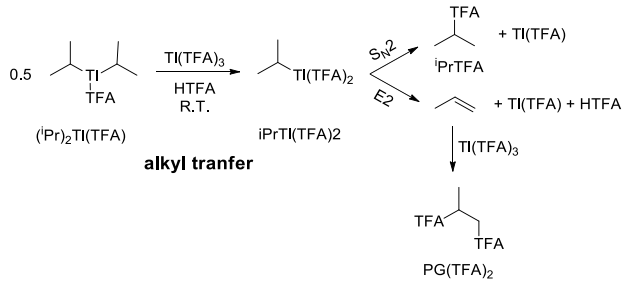
proposed mechanism involved C−H activation of a secondary C−H bond of propane by $Tl(TFA)_3$ to generate the $^{i}PrTl(TFA)_2$ intermediate. Functionalization of this intermediate by an S_N2 attack would generate $^{i}PrTFA$. An E2 elimination from this intermediate would generate propylene, which would be expected to generate the glycol species, analogously to the reaction with ethylene. Interestingly, unlike EtTFA, $^{i}PrTFA$ was found to be unstable under the reaction conditions used in the reaction between $Tl(TFA)_3$ and propane. It was observed to slowly convert to $PG(TFA)_2$, as shown in eq 3.



(3)

The observed ratio of the two products $^{i}PrTFA$ to $PG(TFA)_2$ under the actual reaction conditions was found to be ~3:1 (Table 1, entry 7). Although there was found to be some conversion of $^{i}PrTFA$ to $PG(TFA)_2$, we still wanted to study the functionalization from the putative intermediate, $^{i}PrTl(TFA)_2$. While the ratio of products would be predicted to be slightly higher than 3:1 (*vide infra*), we would not expect to see other products (i.e., *n*-propyltrifluoroacetate or 1,3-propylene glycol bis(trifluoroacetate)) and observation of these types of products would suggest an alternative reaction mechanism. As such, we thought that this would be a good system to apply our alkyl transfer methodology to study the functionalization behavior of the proposed intermediate (Scheme 5).

Scheme 5. Functionalization of $(^{i}Pr)_2Tl(TFA)$ with $Tl(TFA)_3$[a]



[a]Alkyl transfer generates $^{i}PrTl(TFA)_2$, which functionalizes via S_N2 to generate $^{i}PrTFA$ or via E2 to generate propylene. Propylene subsequently reacts with excess $Tl(TFA)_3$ to generate $PG(TFA)_2$. No other products, such as *n*-propyltrifluoroacetate or 1,3-propylene glycol bis(trifluoroacetate), would be expected.

As expected, addition of 10 equiv of $Tl(TFA)_3$ to $^{i}Pr_2Tl(TFA)$ gave only ^{i}Pr-TFA and $PG(TFA)_2$ in a ratio of ~6:1. No other products were observed. This provides very strong evidence for the reaction with propane also proceeding via a Tl−alkyl intermediate and, more specifically, a Tl−^{i}Pr intermediate resulting from C−H activation of a secondary C−H bond in propane. In addition to these systems, we have also used transalkylation techniques to generate the putative intermediates for the reactions between alkanes and $Pb(TFA)_4$ following an experimental procedure similar to that used in the case of Tl(III) systems. We found these reactions to be very similar to reactions involving Tl(III). The results of these studies are summarized in Table 1 along with the results of Tl(III). Similar to the case for Tl(III), Pb(IV) also reacts with ethylene in HTFA at RT to give $EG(TFA)_2$ (see the Supporting Information). These similarities in the reactivities of Pb(IV) and Tl(III) suggest that both systems proceed through an analogous CH activation and M−R functionalization mechanism in alkane oxidation reactions as discussed above. These observations persuaded us not to carry out any further regiospecific isotopic labeling studies with the Pb(IV) system.

CONCLUSIONS

The main-group electrophilic metal cations Tl(III) and Pb(IV) selectively oxidize mixtures of methane, ethane, and propane to alcohol esters.[15] Experimental and theoretical studies[15] taken together strongly support the proposed mechanism for alkane functionalization involving slow, irreversible electrophilic CH activation of alkanes, R−H, with the metal complex M^nX_2 to generate an XM^n−R intermediate, followed by fast M−R reductive functionalization to generate RX and M^{n-2}. Interestingly, in the reaction with ethane and propane two products have been observed to form simultaneously. In this report we have presented the mechanistic investigations of isotopically labeled compounds to support the proposed mechanism using alkylthallium compounds to demonstrate the product distribution. Facile alkyl transfer studies were used to generate the M^n−R intermediate (proposed to be forming in the reaction of alkane with Tl(III)) *in situ* using two independent routes. Most importantly, regiospecific labeling of the R group provided strong evidence for S_N2 and E2 pathways to generate EtTFA and ethylene products, respectively, from the XM^n−R intermediate. Ethylene further undergoes fast reaction with another 1 equiv of M^nX_2 to give the final product $EG(TFA)_2$. These mechanistic studies can also be extended to the reactions involving Pb(IV), as similar product selectivity/distribution was seen in reactions with methane, ethane, and propane.

More recently we have also shown that Sb(V)[13] and hypervalent I(III)[34] functionalize methane and ethane to alcohol esters in HTFA medium. These were also shown to proceed via a CH activation/MR functionalization mechanism. However, in the case of Sb(V), the $EG(TFA)_2$ product was shown to form not via a parallel E2 pathway from the Et−Sb^V intermediate but from the reaction of EtTFA with Sb(V) to generate ethylene. In the case of oxidation reaction of alkanes involving I(III), although S_N2 and E2 branching was observed, the S_N2 pathway was predominant.

In general, CH oxidation reactions of higher alkanes with electrophilic main-group-metal oxidants seem to be adopting a similar mechanism (Scheme 1) involving CH activation to generate the XM^n−R intermediate, which then undergoes functionalization to generate the RX product. However, the relative rates of the parallel S_N2 and E2 reactions of the XM^n−R intermediate that lead to difunctionalized products can vary substantially with the M^{n+} electrophiles.

EXPERIMENTAL SECTION

All air- and water-sensitive procedures were carried out either in a MBraun inert-atmosphere glovebox or using standard Schlenk techniques under argon. All deuterated solvents (Cambridge Isotopes) were used as received. $^{13}CH_4$ and $^{13}C_2H_6$ were purchased from Isotech and used as received. Methane, ethane, and propane gases were purchased from Praxair and used as received. $Tl(TFA)_3$,[35] $Pb(TFA)_4$,[36] and Me_2TlCl[28] were synthesized according to previously

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Organometallics XXXX, XXX, XXX−XXX

published procedures. Methyl 2,2,2-trifluoroacetate (MeTFA), ethyl 2,2,2-trifluoroacetate (EtTFA), isopropyl trifluoroacetate (^{i}PrTFA), 1-^{13}C-ethanol, ethylene glycol, and 1,2-propylene glycol were purchased (Aldrich or Oakwood Chemicals) and used as received. $CH_3{}^{13}CH_2TFA$, ethylene glycol bis(trifluoroactate) ($EG(TFA)_2$), and 1,2-propanediol bis(trifluoroacetate) ($PG(TFA)_2$) were synthesized via addition of the corresponding alcohol to neat trifuoroacetic anhydride (TFA_2O) followed by evaporation of the solvent. Et_2TlCl was synthesized according to the procedure reported by Gilman and Jones.[37] Triethyltin trifluoroacetate, $Et_3Sn(TFA)$, was prepared by addition of a known amount of tetraethyltin to trifluoroacetic acid, as has been previously described, and used *in situ*.[26] Ethyl iodide-1,1-d_2 ($H_3C\text{-}CD_2I$) and isopropyl iodide were purchased from Sigma-Aldrich and used as received. Ethyl iodide-2,2,2-d_3 ($D_3C\text{-}CH_2I$) was purchased from Cambridge Isotopes and used as received. Tetraethylstannane (Et_4Sn), tetraisopropylstannane ($i\text{-}Pr_4Sn$), and tetrapropylstannane ($n\text{-}Pr_4Sn$) were purchased from Sigma-Aldrich and used as received. Lithium reagents were purchased from Sigma-Aldrich and were all titrated by reported methods, prior to use.[38] NMR spectra were obtained on a Bruker Digital Avance III 400 (400.132 MHz for ^{1}H, 100.623 MHz for ^{13}C, and 230.908 for ^{205}Tl) spectrometer equipped with a BBOF probe. All ^{1}H NMR chemical shifts are reported in units of ppm and referenced to residual proton signals in deuterated solvent (for compound characterization) or an internal reference (dichloromethane or dimethyl sulfone) in the solvent. ^{13}C NMR spectra were referenced to ^{13}C signals for the solvent and ^{205}Tl NMR spectra were recorded using thallous nitrate in D_2O as a calibration standard (referenced at 0 ppm).[39] Gas measurements were analyzed with a Shimadzu GC-MS QP2010S instrument equipped with an Agilent HP-Plot Q column. All high-resolution mass spectra were obtained by the University of Illinois, Department of Chemistry, Mass Spectrometer Services on an ESI mass spectrometer. Elemental analysis was performed by Atlantic Microlab, Inc. of Norcross, GA. See the Supporting Information for the NMR spectra of the new compounds and reaction mixtures mentioned herein.

Synthesis of $Et_2Tl(TFA)$. An amberized vial with a Teflon cap and a magnetic stir bar was charged with 1 g (3.36 mmol) of Et_2TlCl and 560 mg (3.36 mmol, 1 equiv) of silver trifluoroacetate. Approximately 20 mL of methanol was added, and the suspension was stirred overnight. The reaction mixture was passed through a plug of Celite to get rid of precipitated silver chloride, and the solvent was removed in vacuo. The crude reaction mixture was then taken into dichloromethane containing 10% methanol, and it was passed through a small plug of alumina with dichloromethane containing 10% methanol as eluent. The solvent was removed *in vacuo* to give the title compound in approximately 95% yield. ^{1}H NMR (400 MHz, CD_3OD, δ/ppm): 1.84 (bd, 4H, J_{Tl-H} = 376.9 Hz), 1.53 (bd, 6H, J_{Tl-H} = 623.4 Hz). $^{13}C\{^{1}H\}$ NMR (400 MHz, CD_3OD, δ/ppm): 163.1 (q, J_{C-F} = 34.5 Hz), 118.4 (q, J_{C-F} = 293.3 Hz), 40.7 (bd, J_{Tl-C} = 2232.1 Hz), 11.1 (bd, J_{Tl-C} = 144.2 Hz). ^{205}Tl NMR (400 MHz, CD_3OD, δ/ppm): 3290.52 (m). HRMS (ESI): calcd for $C_4H_{10}Tl^+$ 261.0506, found 261.0518. Anal. Calcd for $C_6H_{10}F_3O_2Tl$: C, 19.19; H, 2.68; N, 0.00. Found: C, 19.56; H, 2.66; N, 0.00.

Synthesis of $(D_3C\text{-}CH_2)_2TlCl$. An oven-dried Schlenk flask, containing a magnetic stir bar, that had been evacuated and backfilled with argon was charged with 1.2 mL (2.38 g, 14.9 mmol) of $D_3C\text{-}CH_2I$ and 30 mL of dry diethyl ether. With stirring, this solution was cooled to −78 °C in a dry ice/acetone bath and 17 mL (28.31 mmol, 1.9 equiv) of a 1.66 M stock solution of *t*-BuLi in pentane was added dropwise via syringe. Upon complete addition, the solution was stirred for 5 min at −78 °C, and then it was removed from the bath and stirred at room temperature for an additional 1 h to ensure complete conversion to $D_3C\text{-}CH_2\text{-}Li$. A separate oven-dried Schlenk flask was charged with 2 g (6 mmol) of thallous iodide. To this was added 25 mL of dry diethyl ether and 1.2 mL of $D_3C\text{-}CH_2I$ (14.9 mmol, 2.5 equiv). The solution of the alkyllithium reagent was transferred into a dropping funnel and added slowly over about 45 min to the rapidly stirred suspension of thallous iodide at −20 °C. Upon addition, the reaction mixture was warmed to room temperature and stirred overnight. After it was stirred overnight, the solution was cooled to 0 °C in an ice bath and 1 M HCl was added slowly until the pH of the reaction mixture was ∼1−2. The precipitated $(D_3C\text{-}CH_2)_2TlCl$ was collected in a frit, the filter cake was washed first with three portions of 1 M HCl (25 mL each) and then three portions of deionized water (25 mL each). Air was pulled over the filter cake until it was sufficiently dry, and the product was collected and further dried in vacuo. The yield was 1.16 g (65%). ^{1}H NMR (400 MHz, DMSO-d_6, δ/ppm): 1.54 (bd, 4H J_{Tl-H} = 360.8 Hz). $^{13}C\{^{1}H\}$ NMR (400 MHz, DMSO-d_6, δ/ppm): 41.7 (bd, J_{Tl-C} = 2483.6 Hz), 12.2 (bs). HRMS (ESI): calcd for $C_4H_4D_6Tl^+$ 269.0903, found 269.0906. ^{205}Tl NMR (400 MHz, DMSO-d_6, δ/ppm): 3506.99 (bs).

Synthesis of $(H_3C\text{-}CD_2)_2TlCl$. An oven-dried Schlenk flask, containing a magnetic stir bar, that had been evacuated and backfilled with argon, was charged with 1.3 mL (2.5 g, 15.8 mmol) of $H_3C\text{-}CD_2I$ and 30 mL of dry diethyl ether. With stirring, this solution was cooled to −78 °C in a dry ice/acetone bath and 14.9 mL (30.9 mmol, 1.95 equiv) of a 2.07 M stock solution of *t*-BuLi in heptane was added dropwise via syringe. Upon complete addition, the solution was stirred for 5 min at −78 °C and then it was removed from the bath and stirred at room temperature for an additional 1 h to ensure complete conversion to $H_3C\text{-}CD_2\text{-}Li$. A separate oven-dried Schlenk flask was charged with 2 g (6 mmol) of thallous iodide. To this was added 25 mL of dry diethyl ether and 1.3 mL of $H_3C\text{-}CD_2I$ (15.8 mmol, 2.6 equiv). The solution of alkyllithium reagent was transferred into a dropping funnel and added slowly over about 45 min to the rapidly stirred suspension of thallous iodide at −20 °C. Upon addition, the reaction mixture was warmed to room temperature and stirred overnight. After the mixture was stirred overnight, the solution was cooled to 0 °C in an ice bath and 1 M HCl was added slowly until the pH of the reaction mixture was ∼1−2. The precipitated $(H_3C\text{-}CD_2)_2TlCl$ was collected in a frit, and the filter cake was washed first with three portions of 1 M HCl (25 mL each) and then three portions of deionized water (25 mL each). Air was pulled over the filter cake until it was sufficiently dry, and the product was collected and further dried *in vacuo*. The yield was 1.16 g (64%). ^{1}H NMR (400 MHz, DMSO-d_6, δ/ppm): 1.49 (bd, 6H, J_{Tl-H} = 619.8 Hz). $^{13}C\{^{1}H\}$ NMR (400 MHz, DMSO-d_6, δ/ppm): 41.5 (bd, J_{Tl-C} = 2460.0 Hz), 13.0 (bd, J_{Tl-C} = 114.6 Hz). HRMS (ESI): calcd for $C_4H_6D_4Tl^+$ 267.0778, found 267.0778. ^{205}Tl NMR (400 MHz, DMSO-d_6, δ/ppm) 3531.22 (bm).

Synthesis of $^{i}Pr_2TlCl$. The procedure was analogous to the preparation of Et_2TlCl, except that isopropyl iodide and isopropyllithium were used in place of ethyl iodide and ethyllithium, respectively. The yield was 685 mg (35%). ^{1}H NMR (400 MHz, CD_3OD, δ/ppm): 2.32 (bd, 2H, J_{Tl-H} = 261.2 Hz), 1.65 (bd, 12H, J_{Tl-H} = 581.7 Hz). $^{13}C\{^{1}H\}$ NMR (400 MHz, CD_3OD, δ/ppm): 60.1 (bd, J_{Tl-C} = 1868.0 Hz), 22.84 (bs). ^{205}Tl NMR (400 MHz, CD_3OD, δ/ppm): 3307.45 (bs).

Synthesis of $(D_3C\text{-}CH_2)_2Tl(TFA)$ (2). A procedure analogous to the synthesis of $Et_2Tl(TFA)$ was used, except that $(D_3C\text{-}CH_2)_2TlCl$ was used in place of Et_2TlCl. ^{1}H NMR (400 MHz, CD_3OD, δ/ppm): 1.78 (bd, 4H, J_{Tl-H} = 364.1 Hz). $^{13}C\{^{1}H\}$ NMR (400 MHz, CD_3OD, δ/ppm): 163.2 (q, J_{C-F} = 34.6 Hz), 118.4 (q, J_{C-F} = 293.3 Hz), 40.7 (bd, J_{Tl-C} = 2232.1 Hz), 11.1 (bd, J_{Tl-C} = 144.2 Hz). $^{19}F\{^{1}H\}$ NMR (400 MHz, CD_3OD, δ/ppm): −76.91. ^{205}Tl NMR (400 MHz, CD_3OD, δ/ppm): 3291.37 (bs). HRMS (ESI): calcd for $C_4H_4D_6Tl^+$ 269.0898, found 269.0929.

Synthesis of $(H_3C\text{-}CD_2)_2Tl(TFA)$ (8). A procedure analogous to the synthesis of $Et_2Tl(TFA)$ was used, except that $(H_3C\text{-}CD_2)_2TlCl$ was used in place of Et_2TlCl. ^{1}H NMR (400 MHz, CD_3OD, δ/ppm): 1.52 (bd, 6H, J_{Tl-H} = 628.6 Hz). $^{13}C\{^{1}H\}$ NMR (400 MHz, CD_3OD, δ/ppm): 163.2 (q, J_{C-F} = 34.6 Hz), 118.4 (q, J_{C-F} = 292.7 Hz), 40.3 (bd, J_{Tl-C} = 2233.9 Hz), 11.9 (bd, J_{Tl-C} = 148.9 Hz). $^{19}F\{^{1}H\}$ NMR (400 MHz, CD_3OD, δ/ppm): −76.90. ^{205}Tl NMR (400 MHz, CD_3OD, δ/ppm): 3294.85 (m). HRMS (ESI): calcd for $C_4H_6D_4Tl^+$ 267.0772, found 267.0777.

Synthesis of $^{i}Pr_2Tl(TFA)$. A procedure analogous to the synthesis of $Et_2Tl(TFA)$ was used, except that *i*-Pr_2TlCl was used in place of

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Organometallics XXXX, XXX, XXX−XXX

Et_2TlCl. ^1H NMR (400 MHz, CD_3OD, δ/ppm): 2.36 (bd, 2H, J_{Tl-H} = 274.3 Hz), 1.61 (bd, 12H, J_{Tl-H} = 572.3 Hz). $^{13}C\{^1H\}$ NMR (400 MHz, CD_3OD, δ/ppm): 163.3 (q, J_{C-F} = 34.9 Hz), 118.6 (q, J_{C-F} = 292.7 Hz), 59.7 (bd, J_{Tl-C} = 1857.2 Hz), 22.3 (bs). $^{19}F\{^1H\}$ NMR (400 MHz, CD_3OD, δ/ppm): −76.88. ^{205}Tl NMR (400 MHz, CD_3OD, δ/ppm): 3125.96 (m). HRMS (ESI): calcd for $C_6H_{14}Tl^+$ 291.0834, found 291.0842. Anal. Calcd for $C_8H_{14}F_3O_2Tl$: C, 23.81; H, 3.50; N, 0.00. Found: C, 24.13; H, 3.72; N, 0.00.

General Protocol for Metal− Alkyl Functionalization Studies. Unless otherwise mentioned here, in a typical study, a J. Young NMR tube (containing a C_6D_6 coaxial for locking and shimming) was charged, in an open atmosphere, with 0.5 mL of a 25 mM solution of metal alkyl in HTFA (see Table 1) and an equimolar amount of methylene chloride or dimethyl sulfone (as an internal standard). A T_0 ^1H NMR of the reaction mixture was taken. Subsequently, 0.5 mL of a 250 mM solution of oxidant ($Tl(TFA)_3$ or $Pb(TFA)_4$) was added (10 equiv based on metal alkyl) and the J. Young tube was resealed. Upon initial mixing, a ^1H NMR spectrum was taken. Product formation was monitored as a function of time. Reported product distributions are an average of three functionalization studies. See Table 1 for the results. The metal alkyls used in these studies are all presumed to be highly toxic. It is an absolute necessity to avoid exposure in all circumstances. Proper PPE should be worn at all times and proper sanitation procedures followed carefully.

$Et_2Tl(TFA)$ Functionalization Oxygen Dependence Study. This study was carried out analogously to the functionalization study of $Et_2Tl(TFA)$ with $Tl(TFA)_3$, except that all solutions were degassed by a series of three freeze−pump−thaw cycles prior to use. Schlenk techniques were used to charge all reagents to a J. Young tube that was under argon to ensure that the environment was oxygen-free. It was found that the functionalization reaction did not display a dependence on O_2.

General Considerations for High-Temperature Functionalization Studies. The metal alkyls used in all of these studies are highly toxic, and extreme care should be taken to avoid contact in all circumstances. With that said, extra precautions must be taken when performing chemistry with these molecules when the solvent temperature is substantially higher than its boiling point. The use of proper PPE is absolutely a requirement, and it is necessary to use equipment that can handle the high pressures associated with boiling solvents in a sealed vessel. As such, a specialized reactor had to be designed to conduct these high-temperature functionalization studies.

Functionalization of $Et_2Tl(TFA)$ at 75 °C. A 0.5 mL portion of a 20 mM stock solution of $Et_2Tl(TFA)$ in HTFA was placed in a microwave vial containing a stir bar and an additional 0.5 mL of HTFA. The vial was sealed and heated to 75 °C with stirring. When the temperature was reached, 0.2 mL of a 1 M stock solution of $Tl(TFA)_3$ in HTFA was added. The reaction mixture was stirred for 15 min at 75 °C and then removed from the heat and cooled to RT. A 0.1 mL portion of a 300 mM solution of AcOH in HTFA was added as an internal standard. Approximately 0.3 mL was transferred to an NMR tube, and the reaction mixture was analyzed by ^1H NMR using a benzene-d_6 coaxial for locking and shimming. The ratio of EtTFA to $EG(TFA)_2$ was found to be 2.1:1.

Functionalization of $Et_2Tl(TFA)$ at 100 °C. A 0.5 mL portion of a 20 mM stock solution of $Et_2Tl(TFA)$ in HTFA was added to a microwave vial containing a stir bar and an additional 0.5 mL of HTFA. The vial was sealed and heated to 100 °C with stirring. When the temperature was reached, 0.2 mL of a 1 M stock solution of $Tl(TFA)_3$ in HTFA was added. The reaction mixture was stirred for 15 min at 100 °C and then removed from the heat and cooled to RT. A 0.1 mL portion of a 300 mM solution of AcOH in HTFA was added as an internal standard. Approximately 0.3 mL was transferred to an NMR tube, and the reaction was analyzed by ^1H NMR using a benzene-d_6 coaxial for locking and shimming. The ratio of EtTFA to $EG(TFA)_2$ was found to be 2.0:1.

Reaction of $Tl(TFA)_3$ with Ethylene (C_2H_4). Ethylene reactions were conducted at 180 °C following a procedure described previously[15], with the only difference being that 500 psig of ethylene (C_2H_4) was utilized as the gas. ^1H NMR analysis indicated quantitative generation of $EG(TFA)_2$ post reaction (250 mM).

Room-Temperature Oxidation of Ethylene Mediated by $Tl(TFA)_3$. A glass-lined, stainless steel, high-pressure reactor was charged with 2 mL of a 250 mM solution of $Tl(TFA)_3$ in HTFA. The reactor was sealed and pressure degassed five times with 500 psig of argon. It was subsequently charged with 500 psig of ethylene with stirring and sealed. The reaction mixture was stirred at room temperature for 20 min, at which point the pressure was released. The reactor was opened, and 0.2 mL of a 250 mM solution of methylene chloride in HTFA was added as an internal standard. The reaction mixture was analyzed by ^1H NMR using a C_6D_6 coaxial for locking and shimming. The results revealed a species analogous to that seen in the functionalization of $Et_2Tl(TFA)$, and this species was observed to quantitatively collapse to $EG(TFA)_2$.

Room-Temperature Oxidation of Ethylene Mediated by $Pb(TFA)_4$. A procedure analogous to that one above was used, with the exception of using $Pb(TFA)_4$ in place of $Tl(TFA)_3$. An analogous species that quantitatively collapsed to $EG(TFA)_2$ was observed in this case as well.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.0c00120.

NMR spectral data of new compounds and crude reaction mixtures (PDF)

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Organometallics XXXX, XXX, XXX−XXX

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■ REFERENCES

(1) *U. S. Crude Oil and Natural Gas Proved Reserves*; U.S. Energy Information Administration: 2013; pp 1−49.
(2) Gunsalus, N. J.; Koppaka, A.; Park, S. H.; Bischof, S. M.; Hashiguchi, B. G.; Periana, R. A. Homogeneous Functionalization of Methane. *Chem. Rev.* **2017**, *117* (13), 8521−8573.
(3) Olah, G. A.; Goeppert, A.; Prakash, G. K. S. *Beyond Oil and Gas: The Methane Economy*; Wiley-VCH: Weinheim, Germany, 2006.
(4) Periana, R. A.; Taube, D. J.; Evitt, E. R.; Loffler, D. G.; Wentrcek, P. R.; Voss, G.; Masuda, T. A Mercury-Catalyzed, High-Yield System for the Oxidation of Methane to Methanol. *Science* **1993**, *259* (5093), 340−343.
(5) Mukhopadhyay, S.; Bell, A. T. Catalyzed sulfonation of methane to methanesulfonic acid. *J. Mol. Catal. A: Chem.* **2004**, *211* (1−2), 59−65.
(6) Periana, R. A.; Taube, D. J.; Gamble, S.; Taube, H.; Satoh, T.; Fujii, H. Platinum catalysts for the high-yield oxidation of methane to a methanol derivative. *Science* **1998**, *280* (5363), 560−564.
(7) Gol'dshleger, N. F.; Es'kova, V. V.; Shteinman, A. A.; Shilov, A. E. Reactions of Alkanes in Solutions of Chloride Complexes of Platinum. *Russ. J. Phys. Ch. Ussr.* **1972**, *46* (5), 785−786.
(8) Zerella, M.; Bell, A. T. Pt-catalyzed oxidative carbonylation of methane to acetic acid in sulfuric acid. *J. Mol. Catal. A: Chem.* **2006**, *259* (1−2), 296−301.
(9) Periana, R. A.; Mironov, O.; Taube, D.; Bhalla, G.; Jones, C. J. Catalytic, oxidative condensation of CH_4 to CH_3COOH in one step via CH activation. *Science* **2003**, *301* (5634), 814−818.
(10) Gretz, E.; Oliver, T. F.; Sen, A. Carbon-Hydrogen Bond Activation by Electrophilic Transition-Metal Compounds - Palladium-(II)-Mediated Oxidation of Arenes and Alkanes Including Methane. *J. Am. Chem. Soc.* **1987**, *109* (26), 8109−8111.
(11) Tellers, D. M.; Bergman, R. G. C-H bond activation by a rare cationic iridium dinitrogen complex. An important electronic effect in the chemistry of the hydridotris(pyrazolyl)borate ligand. *J. Am. Chem. Soc.* **2000**, *122* (5), 954−955.
(12) Wong-Foy, A. G.; Bhalla, G.; Liu, X. Y.; Periana, R. A. Alkane C-H activation and catalysis by an O-donor ligated iridium complex. *J. Am. Chem. Soc.* **2003**, *125* (47), 14292−14293.
(13) Koppaka, A.; Park, S. H.; Hashiguchi, B. G.; Gunsalus, N. J.; King, C. R.; Konnick, M. M.; Ess, D. H.; Periana, R. A. Selective C-H Functionalization of Methane and Ethane by a Molecular Sb-V Complex. *Angew. Chem., Int. Ed.* **2019**, *58* (8), 2241−2245.
(14) Jones, C. J.; Taube, D.; Ziatdinov, V. R.; Periana, R. A.; Nielsen, R. J.; Oxgaard, J.; Goddard, W. A. Selective oxidation of methane to methanol catalyzed, with C-H activation, by homogeneous, cationic gold. *Angew. Chem., Int. Ed.* **2004**, *43* (35), 4626−4629.
(15) Hashiguchi, B. G.; Konnick, M. M.; Bischof, S. M.; Gustafson, S. J.; Devarajan, D.; Gunsalus, N.; Ess, D. H.; Periana, R. A. Main-Group Compounds Selectively Oxidize Mixtures of Methane, Ethane, and Propane to Alcohol Esters. *Science* **2014**, *343* (6176), 1232−1237.
(16) Konnick, M. M.; Bischof, S. M.; Yousufuddin, M.; Hashiguchi, B. G.; Ess, D. H.; Periana, R. A. A Mechanistic Change Results in 100 Times Faster CH Functionalization for Ethane versus Methane by a Homogeneous Pt Catalyst. *J. Am. Chem. Soc.* **2014**, *136* (28), 10085−10094.
(17) Kurosawa, H.; Okawara, R. Preparation and Properties of Monoalkylthallium Derivatives. *J. Organomet. Chem.* **1967**, *10* (2), 211−217.
(18) Uemura, S.; Toshimitsu, A.; Okano, M. Preparation of Some Alkylthallium(III) Dichlorides and Their Reactions with Potassium and Copper Halides. *Bull. Chem. Soc. Jpn.* **1976**, *49* (10), 2762−2764.
(19) Gardner, H. C.; Kochi, J. K. Charge-Transfer Spectra and Alkylation of Tetracyanoethylene with Organometallic Derivatives of Lead, Tin, and Mercury. *J. Am. Chem. Soc.* **1976**, *98* (9), 2460−2469.
(20) Ingold, C. K. Organo-Metal Substitutions. *Helv. Chim. Acta* **1964**, *47* (5), 1191−1203.
(21) Kochi, J. K. Electron-Transfer Mechanisms for Organometallic Intermediates in Catalytic Reactions. *Acc. Chem. Res.* **1974**, *7* (10), 351−360.
(22) Schrauzer, G. N.; Weber, J. H.; Beckham, T. M.; Ho, R. K. Y. Alkyl Group Transfer from Cobalt to Mercury - Reaction of Alkylcogalamins, Oximes and of Related Compounds with Mercuric Acetate. *Tetrahedron Lett.* **1971**, *12* (3), 275−277.
(23) Chen, X.; Li, J. J.; Hao, X. S.; Goodhue, C. E.; Yu, J. Q. Palladium-catalyzed alkylation of aryl C-H bonds with sp^3 organotin reagents using benzoquinone as a crucial promoter. *J. Am. Chem. Soc.* **2006**, *128* (1), 78−79.
(24) Kalman, J. R.; Morgan, J.; Pinhey, J. T.; Sternhell, S. Electrophilic metal-alkyl bond cleavage in tetraorganosilicon and tetraorganotin compounds by lead tetracarboxylates and aryllead tricarboxylates. *Tetrahedron* **1999**, *55* (12), 3615−3624.
(25) Neumann, W. P. Tin for Organic-Synthesis.6. The New Role of Organotin Reagents in Organic-Synthesis Part 1: Stannyl Groups as Leaving Groups in Electrophilic Substitutions Part 2: Polymer-Supported Organotin Reagents for Organic-Synthesis. *J. Organomet. Chem.* **1992**, *437* (1−2), 23−39.
(26) Sasin, R.; Sasin, G. S. Reactions of Tetraethyltin with Organic Acids. *J. Org. Chem.* **1955**, *20* (6), 770−773.
(27) Kurosawa, H.; Yasuda, K.; Okawara, R. Structure of Dimethylthallium Compounds Soluble in Non-Polar Solvents. *Bull. Chem. Soc. Jpn.* **1967**, *40* (4), 861−864.
(28) Marko, I. E.; Southern, J. M. Triorganothallium Reagents in Organic-Chemistry.1. A Simple, Efficient, and Versatile Preparation of Ketones from Acid-Chlorides. *J. Org. Chem.* **1990**, *55* (10), 3368−3370.
(29) Ross, S. D.; Finkelstein, M. Trifluoroacetates of Ethylene Glycol. *J. Org. Chem.* **1957**, *22* (7), 847−848.
(30) Kaplan, E. D.; Thornton, E. R. Secondary Deuterium Isotope Effects. *β*-Kinetic Effects in Sn2 Reactions of N, N-Dimethylaniline and Dimethylphenylphosphine with Methyl *p*-Toluenesulfonate and Comparison with Observed and Calculated Vibrational Frequencies of Deuterated and Undeuterated Dimethylaniline and Trimethylanilinium Ion. *J. Am. Chem. Soc.* **1967**, *89* (25), 6644−6651.
(31) Saunders, W. H. Calculations of Isotope Effects in Elimination-Reactions - New Experimental Criteria for Tunneling in Slow Proton Transfers. *J. Am. Chem. Soc.* **1985**, *107* (1), 164−169.
(32) Leffek, K. T.; Matheson, A. F. Secondary Kinetic Isotope-Effects in Bimolecular Nucleophilic Substitutions.VI. Effect of Alpha and Beta Deuteration of Alkyl-Halides in Their Menschutkin Reactions with Pyridine in Nitrobenzene. *Can. J. Chem.* **1972**, *50* (7), 986−991.
(33) Leffek, K. T.; Matheson, A. F. Secondary Kinetic Isotope-Effects in Bimolecular Nucleophilic Substitutions.V. Role of Solvent in Reaction between Methyl-Iodide and Pyridine. *Can. J. Chem.* **1972**, *50* (7), 982−985.
(34) Konnick, M. M.; Hashiguchi, B. G.; Devarajan, D.; Boaz, N. C.; Gunnoe, T. B.; Groves, J. T.; Gunsalus, N.; Ess, D. H.; Periana, R. A. Selective CH Functionalization of Methane, Ethane, and Propane by a Perfluoroarene Iodine(III) Complex. *Angew. Chem., Int. Ed.* **2014**, *53* (39), 10490−10494.
(35) Mckillop, A.; Hunt, J. D.; Zelesko, M. J.; Fowler, J. S.; Taylor, E. C.; Mcgilliv, G.; Kienzle, F. Thallium in Organic Synthesis. XXII. Electrophilic Aromatic Thallation Using Thallium(III) Trifluoroacetate - Simple Synthesis of Aromatic Iodides. *J. Am. Chem. Soc.* **1971**, *93* (19), 4841−4844.

https://dx.doi.org/10.1021/acs.organomet.0c00120
Organometallics XXXX, XXX, XXX−XXX

(36) Bell, H. C.; Kalman, J. R.; Pinhey, J. T.; Sternhell, S. Chemistry of Aryllead(IV) Tricarboxylates - Synthesis. *Aust. J. Chem.* **1979**, *32* (7), 1521−1530.
(37) Gilman, H.; Jones, R. G. Reactions of Metallic Thallium and Metallic Lead with Organic Halides. *J. Am. Chem. Soc.* **1950**, *72* (4), 1760−1761.
(38) Duhamel, L.; Plaquevent, J. C. 4-Phenylbenzylidene Benzylamine - a New and Convenient Reagent for the Titration of Solutions of Lithium Alkyls and Metal Amides. *J. Organomet. Chem.* **1993**, *448* (1−2), 1−3.
(39) Hinton, J. F. Thallium NMR Spectroscopy. *Bull. Magn. Reson.* **1992**, *13* (3−4), 90−108.

https://dx.doi.org/10.1021/acs.organomet.0c00120
Organometallics XXXX, XXX, XXX−XXX