Structural Basis for Regioisomerization in the Alkali-Metal-Mediated Zincation (AMM*Zn*) of Trifluoromethyl Benzene by Isolation of Kinetic and Thermodynamic Intermediates

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Abstract: Performed with a desire to advance knowledge of the structures and mechanisms governing alkali-metal-mediated zincation, this study monitors the reaction between the TMP-dialkylzincate reagent [(TMEDA)Na(TMP)(^{t}Bu)Zn(^{t}Bu)] **1** and trifluoromethyl benzene $C_6H_5CF_3$ **2**. A complicated mixture of products is observed at room temperature. X-ray crystallography has identified two of these products as ortho- and meta-regioisomers of heterotrianionic [(TMEDA)Na(TMP)(C_6H_4-CF_3)Zn(^{t}Bu)], **3**-*ortho* and **3**-*meta*, respectively. Multinuclear NMR data of the bulk crystalline product confirm the presence of these two regioisomers as well as a third isomer, **3**-*para*, in a respective ratio of 20:11:1, and an additional product **4**, which also exhibits ortho-zincation of the aryl substrate. Repeating the reaction at 0 °C gave exclusively **4**, which was crystallographically characterized as [{(TMEDA)$_2$Na}$^+${Zn(C_6H_4-CF_3)(^{t}Bu)$_2$}$^-$]. Mimicking the original room-temperature reaction, this kinetic product was subsequently reacted with TMP(H) to afford a complicated mixture of products, including significantly the three regioisomers of **3**. Surprisingly, **4** adopts a solvent-separated ion pair arrangement in contrast to the contacted ion variants of **3**-*ortho* and **3**-*meta*. Aided by DFT calculations on model systems, discussion focuses on the different basicities, amido or alkyl, and steps, exhibited in these reactions, and how the structures and bonding within these isolated key metallic intermediates (prior to any electrophilic interception step), specifically the interactions involving the alkali metal, influence the regioselectivity of the Zn–H exchange process.

Introduction

Organozinc reagents play a pivotal role in many fundamental organic reactions, being among the most commonly utilized reagents in synthesis.[1] Their main attractions are their marked "soft nucleophilicity" and exceptional functional group tolerance; however, their poor kinetic reactivity has limited their applications in deprotonative metalation (Zn–H exchange reactions).[2] Notwithstanding, recent breakthroughs in the area have established that this drawback can be circumvented by pairing organozinc reagents with a group 1 organometallic compound to form alkali metal zincates.[3] Among these mixed-metal reagents, TMP-dialkyl zincates [MZn(TMP)R$_2$] (M = Li,[4]

Na,[5] K;[6] TMP = 2,2,6,6 tetramethylpiperidide) have risen to prominence as powerful deprotonating agents that allow the direct zincation of aromatic substrates that usually are inert toward conventional organozinc reagents, including benzene,[5] anisole,[4a,b,7] toluene,[8] naphthalene,[9] pyridines,[10] indoles,[11] benzamides,[4a,12] benzonitriles,[13] or anilines[14] to name a few. These deprotonations where the departing hydrogen in the

(3) For recent reviews on the applications of alkali-metal zincates in deprotonative metalation reactions see: (a) Mulvey, R. E. *Organometallics* **2006**, *25*, 1060. (b) Mulvey, R. E.; Mongin, F.; Uchiyama, M.; Kondo, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3802. (c) Mulvey, R. E. *Acc. Chem. Res.* **2009**, *42*, 743.

(4) (a) Kondo, Y.; Shilai, M.; Uchiyama, M.; Sakamoto, T. *J. Am. Chem. Soc.* **1999**, *121*, 3539. (b) Uchiyama, M. M.; Matsumoto, Y.; Nobuto, D.; Furuyama, T.; Yamaguchi, K.; Morokuma, K. *J. Am. Chem. Soc.* **2006**, *128*, 8748. (c) Clegg, W.; Dale, S. H.; Hevia, E.; Honeyman, G. W.; Mulvey, R. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 2370.

(5) Andrikopoulos, P. C.; Armstrong, D. R.; Barley, H. R. L.; Clegg, W.; Dale, S. H.; Hevia, E.; Honeyman, G. W.; Kennedy, A. R.; Mulvey, R. E. *J. Am. Chem. Soc.* **2005**, *127*, 6184.

(6) Conway, B.; Graham, D. V.; Hevia, E.; Kennedy, A. R.; Klett, J.; Mulvey, R. E. *Chem. Commun.* **2008**, 2638.

(7) Clegg, W.; Dale, S. H.; Drummond, A. M.; Hevia, E.; Honeyman, G. W.; Mulvey, R. E. *J. Am. Chem. Soc.* **2006**, *128*, 7434.
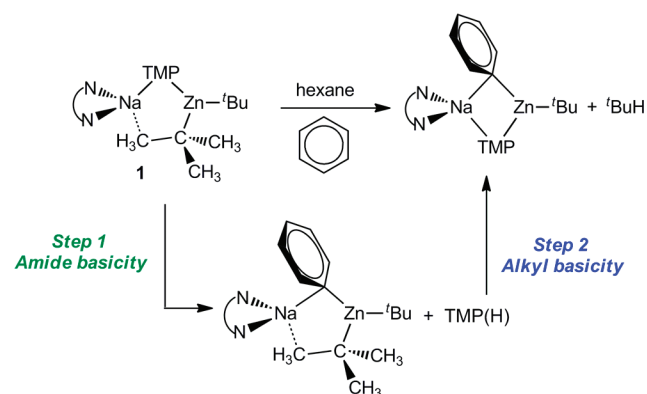
† University of Strathclyde.
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(1) Knochel, P.; Leuser, H.; Gong, L.-Z.; Perrone, S.; Kneisel, F. F. In *Handbook of Functionalised Organometallics*; Knochel, P., Ed.; Wiley-VCH: Weinheim, 2005.

(2) *The chemistry of organozinc compounds*; Rappoport, Z., Marek, I., Eds.; Patai Series; Wiley: Chichester, U.K., 2006.
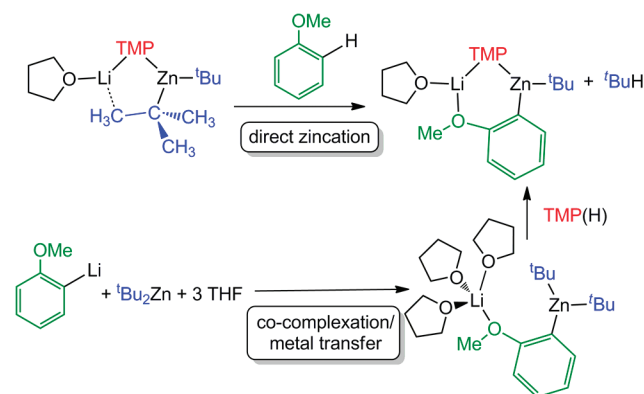
Scheme 1

Scheme 2

molecule is replaced by zinc but that require the presence of an alkali-metal to succeed have been branded as examples of alkali-metal-mediated zincation (AMM*Zn*).[3] The use of this mixed-metal approach has enabled the performing of special metalations exhibiting unique regioselectivities that cannot be reproduced by classical monometallic reagents such as alkyl lithiums or lithium amides. Furthermore, as recently highlighted in *Science*,[15] the synergic entrapment of highly sensitive anions such as α-metalated THF can be accomplished without any ring-opening or cleavage when THF is reacted with the sodium zincate [(TMEDA)Na(TMP)(CH₂SiMe₃)Zn(CH₂SiMe₃)].

First introduced in 2005, another sodium zincate [(TMEDA)-Na(TMP)(ᵗBu)Zn(ᵗBu)] (**1**) is an effective and versatile zincating agent for a wide range of aromatic molecules.[5] Structurally mapping these reactions (by X-ray crystallography) confirmed that these deprotonations are genuine zincations, and also established that heteroleptic base **1** displays overall alkyl basicity (as shown in Scheme 1 for deprotonation of benzene). Thus, one ᵗBu group of **1** is replaced by the deprotonated arene and there is concomitant formation of isobutane. Although informative, these structural studies only provide evidence on the starting material and the final thermodynamic product of the reaction, while any kinetic intermediate remains invisible to this study. Shedding light on these intriguing deprotonations, Uchiyama and Nobuto have recently reported a comprehensive theoretical study which offers an alternative interpretation for the alkyl basicity experimentally observed for **1**.[16] Their findings strongly

suggest that these deprotonations occur via a two-step mechanism where kinetically the sodium zincate acts first as an amide base, deprotonating the aromatic molecule (Scheme 1) to form a bisalkyl(aryl) intermediate and releasing concomitantly TMP(H). In a second step, the intermediate [(TMEDA)Na(aryl)(ᵗBu)Zn-(ᵗBu)] reacts with concomitant TMP(H) giving [(TMEDA)-Na(TMP)(aryl)Zn(ᵗBu)] and isobutane, in agreement with the overall alkyl basicity observed experimentally.

In spite of these insightful theoretical studies, to date the proposed reaction intermediates [(TMEDA)Na(aryl)(ᵗBu)Zn-(ᵗBu)] have not been detected even when the deprotonations are performed at subambient temperatures. In a closely related study for the AMM*Zn* of anisole by the analogous lithium TMP-zincate [(THF)Li(TMP)(ᵗBu)Zn(ᵗBu)],[17] we have prepared the putative intermediate [(THF)₃LiZn(C₆H₄−OMe)(ᵗBu₂)] suggested by the theoretical studies via an indirect route (cocom-plexation of ortho-lithiated anisole with ᵗBu₂Zn, combined with a lithium−zinc transfer, Scheme 2) and explored its reactivity toward TMP(H), mirroring the second step of the theoretically studied process. The outcomes of this study have provided for the first time compelling experimental evidence of the possibility of a two-step mechanism for these TMP-zincates.

Herein we extend our mechanistic and structural studies to the metalation of the aromatic substrate trifluoromethyl benzene (**2**) by the bimetallic base **1**. From a merely electronic point of view, the most acidic sites in **2** should be the *ortho*-protons due to the activating inductive effect of the CF₃ group.[18] However, on the other hand, *ortho*-deprotonation can be disfavored by the steric hindrance exerted by this functional group which is a rather large sterically demanding substituent (intermediate between an ᵢPr and a ᵗBu group).[19] Thus, it can be anticipated that the regioselectivity of these deprotonation reactions will be largely dominated by the counterbalance of these two fundamental effects. Previous studies by Roberts and Curtin have shown that when **2** is treated with ⁿBuLi in refluxing hexane, followed by quenching with carbon dioxide, a 100:40:1 mixture of the *ortho*-, *meta*- and *para*- isomers of the relevant carboxylic acid in a 33−48% yield is obtained.[20] More recently Schlosser has reported the regioselective deprotonation of **2** when reacted with superbasic LICKOR reagent at −75 °C which

(8) Armstrong, D. R.; Garcia-Alvarez, J.; Graham, D. V.; Honeyman, G. W.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E. *Chem.—Eur. J.* **2009**, *15*, 3800.

(9) Clegg, W.; Dale, S. H.; Hevia, E.; Hogg, L. M.; Honeyman, G. W.; Mulvey, R. E.; O'Hara, C. T. *Angew. Chem., Int. Ed.* **2006**, *45*, 6548.

(10) Clegg, W.; Conway, B.; Graham, D. V.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; Russo, L.; Wright, D. S. *Chem.—Eur. J.* **2009**, *15*, 7074.

(11) Conway, B.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E. *Chem. Commun.* **2007**, 2864.

(12) (a) Clegg, W.; Dale, S. H.; Harrington, R. W.; Hevia, E.; Honeyman, G. W.; Mulvey, R. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 2374. (b) Kondo, Y.; Morey, J. V.; Morgan, J. C.; Naka, H.; Nobuto, D.; Raithby, P. R.; Uchiyama, M.; Wheatley, A. E. H. *J. Am. Chem. Soc.* **2007**, *129*, 12734.

(13) (a) Uchiyama, M.; Matsumoto, Y.; Usui, S.; Hashimoto, Y.; Moro-kuma, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 926. (b) Clegg, W.; Dale, S. H.; Hevia, E.; Hogg, L. M.; Honeyman, G. W.; Mulvey, R. E.; O'Hara, C. T.; Russo, L. *Angew. Chem., Int. Ed.* **2008**, *47*, 731.

(14) Armstrong, D. R.; Clegg, W.; Dale, S. H.; Hevia, E.; Hogg, L. M.; Honeyman, G. W.; Mulvey, R. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 3775.

(15) Kennedy, A. R.; Klett, J.; Mulvey, R. E.; Wright, D. S. *Science* **2009**, *326*, 706.

(16) Nobuto, D.; Uchiyama, M. *J. Org. Lett.* **2008**, *73*, 1117.

(17) Clegg, W.; Conway, B.; Hevia, E.; McCall, M. D.; Russo, L.; Mulvey, R. E. *J. Am. Chem. Soc.* **2009**, *131*, 2375.

(18) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon, Elsevier Science Ltd.: Oxford, U.K., 2002.

(19) (a) de Riggi, I.; Virgili, A.; de Moragas, M.; Jaime, C. *J. Org. Chem.* **1995**, *60*, 27. (b) Wolf, C.; König, W. A.; Roussel, C. *Liebigs Ann.* **1995**, 781.

(20) Roberts, J. D.; Curtin, D. Y. *J. Am. Chem. Soc.* **1946**, *68*, 1658.

Scheme 3

3-*ortho*, 3-*meta*, 3-*para*
(20:11:1)
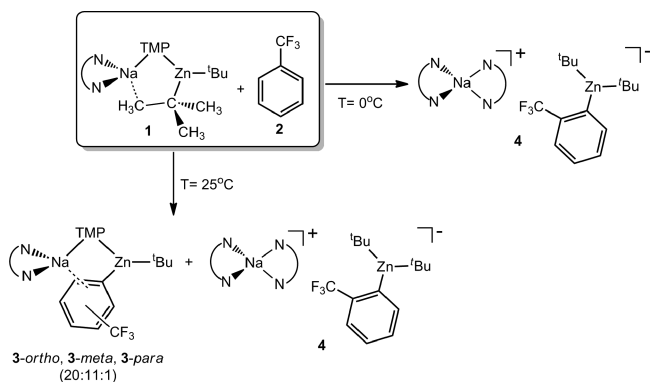
allows the preparation of 2-(trifluoromethyl)benzoic acid in a 94% yield.[21] However, information regarding the characterization or isolation of the relevant metalated intermediates, prior to an electrophilic quenching protocol, has not yet been forthcoming. Starting to fill this important gap of knowledge, in this work we report the first intermediates of AMMZ*n* of trifluoromethyl benzene **2** using sodium zincate **1** which affords a mixture of *ortho*, *meta* and *para* regioisomers of [(TMEDA)-Na(TMP)(C₆H₄—CF₃)Zn(ᵗBu)] (**3**) in a 4.3:2.6:1.0 ratio.[22] Furthermore, this report includes, to the best of our knowledge, the first successful isolation and spectroscopic/crystallographic characterization of a key reaction intermediate, obtained via the actual experimental conditions used to perform direct zincation of trifluoromethyl benzene demonstrating that these direct zincation reactions indeed proceed via a two-step mechanism. The kinetic product surprisingly has the solvent-separated formulation [{(TMEDA)₂Na}⁺{Zn(C₆H₄—CF₃)(ᵗBu)₂}⁻] (**4**). Furthermore, mimicking the second proposed step predicted by the theoretical calculations, we also report the reaction of **4** with TMP(H), in which ¹H NMR monitoring reveals key implications for the final outcome of the reaction, affecting the yield and the regioselectivity of the AMMZ*n* of **2**. In addition, to quantify and provide an explanation for these different regioselectivities encountered, a theoretical study using DFT calculations has been carried out.

Results and Discussion

Sodium TMP-zincate **1** was prepared in situ in hexane solution and reacted with one molar equivalent of trifluoromethyl benzene **2** at room temperature, affording a yellow solution that on cooling deposited colorless crystals. Multinuclear (¹H, ¹³C, and ¹⁹F) NMR spectroscopic analysis of these crystals evidenced that **2** has been deprotonated, affording a complex mixture of products (Scheme 3). ¹H and 2D-[¹H,¹H] COSY NMR spectra from deuterated benzene solution revealed the presence of the three possible regioisomers for the monometalation of **2** (Figure 1a and Table 1). Thus, four multiplets at 7.85, 7.54, 7.19, and 6.98 ppm are observed for the major *ortho*-metalated product (**3**-*ortho*), three multiplets at 7.74, 7.34, and 7.06 ppm and a singlet at 8.14 ppm for the next most abundant *meta*- product (**3**-*meta*), and two doublets at 7.71 and 7.42 ppm for the minor *para*- product (**3**-*para*) (Figure 1a and Table 1) in a 20:11:1

(21) Schlosser, M.; Katsoulos, G.; Takagishi, S. *Synlett* **1990**, 747.
(22) Note that this is the ratio found in solution for the **3**-*ortho*/**3**-*meta*/**3**-*para* products (vide infra) which differs from that found in the isolated crystalline solid (20:11:1). This discrepancy is probably due to the different solubility/crystallization properties of the three distinct isomers.

ratio. In addition, another *ortho*-metalated product, different from **3**-*ortho*, **4** is evident (from four multiplets at 8.06, 7.51, 7.20, and 6.96 ppm) (Figure 1a and Table 1). A ¹⁹F NMR spectrum displayed four different signals at −59.9, −61.5, −61.7, and −61.8 ppm (see Experimental Section) in agreement with the presence in solution of four distinct organometallic species.

X-ray crystallographic studies established the molecular structures of **3**-*ortho* and **3**-*meta*. Thus, in a single crystal a mixture of the *ortho* and *meta* regioisomers of **3** in a respective ratio of 91:9% was found, with the asymmetric unit consisting of one molecule of **3**-*ortho* and one site occupied by a disordered mixture of **3**-*ortho* and **3**-*meta* (Figures 2a and 2b).[23] Exhibiting contacted ion pair structures, both molecules contain a Na-TMP-Zn backbone where TMEDA chelates to sodium and a tert-butyl group binds terminally to zinc. This backbone is also present in the bimetallic base **1**. As previously observed for other products of AMMZ*n*, zinc fills the position previously occupied by a hydrogen atom, adopting a distorted trigonal planar geometry, lying almost coplanar with the aromatic ring and forming a strong Zn—C σ-bond. However, the structures of **3**-*ortho* and **3**-*meta* differ strikingly in the manner in which the metalated arene engages with the alkali-metal. For **3**-*ortho* one fluorine atom of the CF₃ group binds with the sodium center, closing a seven-membered [NaNZnCCCF] ring (Figure 2a) and no interaction exists between the aromatic ring and the alkali metal. In contrast, for **3**-*meta*, sodium π-engages with the aromatic ring, interacting primarily with the *meta*-carbon (that has experienced the metalation and therefore carries most of the developed negative charge), which gives rise to a four-membered [NaNZnC] ring with the CF₃ group situated too far from the alkali metal to form any type of contact. This distinct σ/π bonding mode for Zn and Na respectively has become a general feature observed for AMMZ*n* products derived from nonheteroatom-substituted arenes,[3] as for example in [(TMEDA)-Na(TMP)(*meta*-C₆H₄—CH₃)Zn(ᵗBu)] obtained by reaction of **1** with toluene,[8] which exhibits a structure identical in its key features to that displayed by **3**-*meta*. Unfortunately the disorder and high displacement parameters affect the precision of this structure and thus prevent discussion of the bond lengths or bond angles though the connectivity is definite. That notwith-
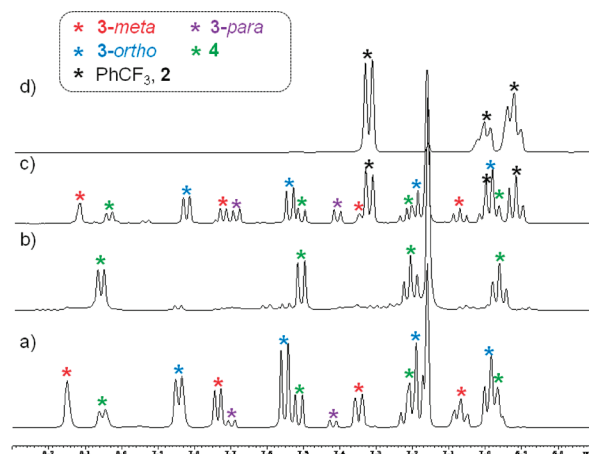

Figure 1. Aromatic region of ¹H NMR spectra for deuterated benzene solutions of (a) crystals obtained from the reaction of [(TMEDA)Na-(TMP)(ᵗBu)Zn(ᵗBu)] (**1**) with 1 equiv of trifluoromethyl benzene (**2**) at room temperature; (b) isolated crystals of **4**, obtained by reaction of [(TMED-A)Na(TMP)(ᵗBu)Zn(ᵗBu)] (**1**) with 1 equiv of trifluoromethyl benzene (**2**) at 0 °C; (c) isolated crystals of **4** on the addition of 1 equiv of TMP(H) after 2 h; (d) trifluoromethyl benzene (**2**).

Table 1. Aromatic Chemical Shifts in the ^1H NMR Spectra of **3**–**4** in C_6D_6 Solution

| compound	$\delta(H_a)$	$\delta(H_b)$	$\delta(H_c)$	$\delta(H_d)$
[Na(TMP)(o-C_6H_4−CF_3)Zn(^tBu)] (**3**-*ortho*)	7.54 (d)	7.19 (t)	6.98 (t)	7.85 (d)
[Na(TMP)(m-C_6H_4−CF_3)Zn(^tBu)] (**3**-*meta*)	7.34 (d)	7.06 (t)	7.74 (d)	8.14 (s)
[Na(TMP)(p-C_6H_4−CF_3)Zn(^tBu)] (**3**-*para*)	7.42 (d)	7.71 (d)	−	−
[{Na(TMEDA)$_2$}{Zn(^tBu)$_2$(o-C_6H_4−CF_3)}] (**4**)	7.51 (d)	7.20 (t)	6.96 (t)	8.06 (d)

standing, **3**-*ortho* and **3**-meta represent to the best of our knowledge the first examples of metalated intermediates of trifluoromethyl benzene to be structurally elucidated. In order to determine the molecular structures of the compounds **3**-*para* and **4** (which are also formed in the reaction of **1** with **2** at room temperature) X-ray crystallographic studies of several crystals were attempted. However the only crystals suitable for these analyses proved to be the same mixture of **3**-*ortho*/**3**-*meta* regioisomers (vide supra).[24]

In an attempt to modulate the regioselectivity of the zincation of **2** and to trap other reaction intermediates that could shed light on the identity of the other metalated species observed (labeled as **4** in Figure 1), trifluoromethyl benzene **2** was reacted with **1** in hexane at the lower temperature of 0 °C (cf. -the earlier preparation at room temperature) for 30 min. The resulting pale yellow solution was placed in the freezer (−30 °C) affording colorless crystals. The comparatively simple ^1H NMR spectrum of these crystals in deuterated benzene solution revealed that under these reaction conditions, compound **4** is the only product obtained whereby substrate **2** has been selectively *ortho*-metalated (four multiplets at 8.06, 7.51, 7.20, and 6.96 ppm) (Figure 1b). Furthermore, the analysis of the aliphatic region of both ^1H and $^{13}C\{^1H\}$ NMR spectra showed relevant resonances for *tert*-butyl and TMEDA ligands (see Experimental Section for details); however, no signals attributable to a TMP group were observed. A $^{19}F\{^1H\}$ NMR spectrum displayed a single resonance at −61.2 ppm.

Determined by X-ray crystallography, the solvent-separated ion pair [{(TMEDA)$_2$Na}$^+${Zn(C_6H_4−CF_3)(^tBu)$_2$}$^-$] (**4**) adopts a significantly different structural motif from that observed for **3**-*ortho* or **3**-*meta* (Figure 3). Thus its anion comprises a

molecule of trifluoromethyl benzene selectively *ortho*-deprotonated and two *tert*-butyl groups bonded to zinc, whereas the cation comprises a sodium center tetrahedrally coordinated by two TMEDA molecules. There is disorder in the positions of the ^tBu groups in the structure of **4** which precludes a detailed discussion of the bond distances and angles. Nevertheless, this bis(alkyl)-aryl sodium zincate represents the first truly kinetic intermediate of an AMMZn reaction of an aromatic molecule to be isolated and structurally defined, which proves unequivocally that these deprotonations must proceed via a two-step mechanism; as previously proposed by theoretical studies (Scheme 1),[16] where TMP-zincate **1** deprotonates arene **2** by sequential combination of amido/alkyl basic behavior. As mentioned in the introduction and within the context of lithium zincates and the deprotonation of anisole, we have recently reported an experimental study which strongly supported this two-step mechanism; however, the putative TMP-free kinetic intermediates have to be prepared using an indirect route (cocomplexation approach) since their formation could not be detected in the actual AMMZn reaction.[17] Compound **4** is isolated in a 22% yield, however, when the reaction is carried out in the presence of a molar equivalent of TMEDA (additional to that in precursor **1**), this yield can be improved to 49%. Note that the isolated crystals of **4** are pure and so it is the only *ortho*-zincated product deposited from the solution. Furthermore, NMR monitoring of the reaction filtrates confirms it is also the major product in the remaining solution with only small amounts of **3**-*ortho*, **3**-*meta*, and **3**-*para* (as a consequence of the second step of the reaction starting to take place).

These results prompted us to pursue the reaction of **4** with the amine TMP(H), in order to replicate the anticipated second
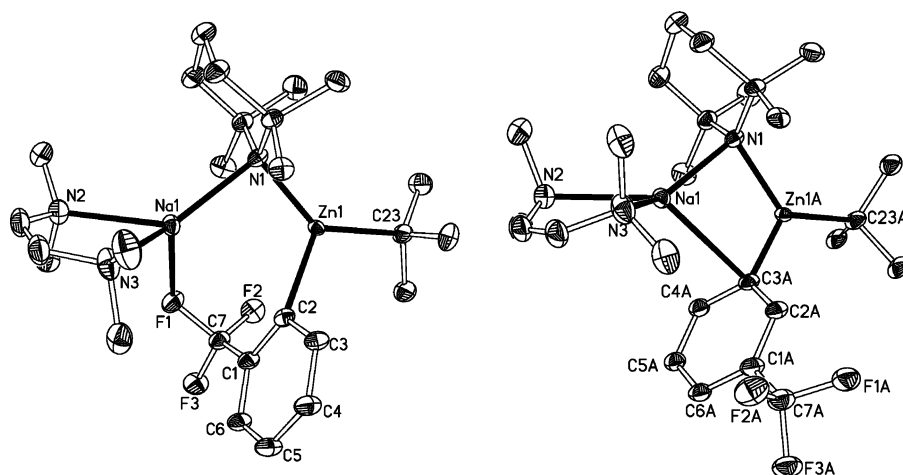
Figure 2. Molecular structures of (a) **3**-*ortho* and (b) **3**-*meta*. Hydrogen atoms and other disorder components are omitted for clarity.
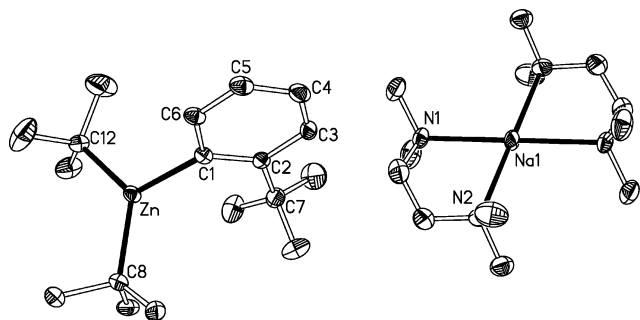
Figure 3. Molecular structure of **4**. Hydrogen atoms and minor disorder components are omitted for clarity.

step of the AMMZ*n*. Thus, isolated crystals of **4** were dissolved in deuterated benzene and a stoichiometric amount of TMP(H) was introduced. ^{1}H NMR monitoring of the reaction provided evidence that the amine had been metalated as shown by the inequivalence of the α-Me groups of TMP (see Experimental Section) and the formation of isobutane coproduct (doublet and multiplet at 0.81 and 1.46 ppm respectively). Furthermore, even more surprisingly, the aromatic region of the spectrum has dramatically changed, revealing the presence of a complex mixture of **3**-*ortho*, **3**-*meta*, and **3**-*para* products, as well as some unreacted **4** and trifluoromethyl benzene (Figure 1c). These results add a new level of complexity to these bimetallic deprotonations, revealing that the second step of the AMMZ*n* process, far from being a simple substitution of a [t]Bu ligand for a TMP ligand, also involves the isomerization of the deprotonated CF₃-aromatic ligand, which has profound consequences for the final regioselectivity of the reaction. To elaborate, upon deprotonation of **2** by zincate **1**, the kinetic product of the reaction **4** (which can be isolated if the reaction is carried out at 0 °C) is initially formed (where **2** is regioselectively deprotonated at the *ortho*-position),[25] and exhibits a solvent-separated ion pair structure that keeps the alkali-metal apart from the zincated aryl molecule. However in the second step, the formation of the contacted ion pair compounds **3** takes place, regenerating TMP anion which by providing a synergic bridge between sodium and zinc, promotes new interactions between sodium and the zincated aryl molecule. This structural reorganization from solvent-separated ions to contacted ions also facilitates a rearrangement of some *ortho*-zincated aryl molecules to *meta* and *para* isomers (Scheme 4 (ii), Figure 1c). Furthermore, the formation of a substantial

amount of free trifluoromethyl benzene **2** (Figure 1c and d) indicates that, when **4** reacts with TMP(H), some of the amine must react in a different way, targeting the metalated aryl anion, to regenerate the starting materials **1** and **2** (Scheme 4, reaction pathway i).[26] We have previously proposed a competitive reaction pathway of this type for the AMMZ*n* of anisole, which can be overcome when an excess of the bimetallic base is employed.[17,27] These findings highlight the critical importance of this second step in the AMMZ*n* of **2**, which greatly affects the final outcome of the metalation, not only by diminishing the yield of **3** but also by altering the regioselectivity of the aromatic deprotonation reaction. It should be stressed that much of this information on how amido(dialkyl)zincates operate would be hidden if the reactions were performed in situ then followed by electrophilic quenching. To explain, when trifluoromethyl benzene **2** is reacted with one molar equivalent of the bimetallic base **1** at room temperature followed by treatment with iodine, a 6:2.3:1 mixture of *ortho*, *meta*, and *para* isomers of iodo-(trifluoromethyl)benzene is obtained in a modest 45% yield. This low yield, which now can be explained in terms of the competitive reaction of TMP(H) (generated in the first step of the reaction) with the metalated arene group of the kinetic intermediate **4**, can be improved to 92% when two equivalents of zincate **1** are employed. In addition, the amount of *ortho*-iodo(trifluoromethyl)benzene observed arises from the combined electrophilic quenching of the two different organometallic compounds **3**-*ortho* and **4**. Furthermore, a comparison of this ratio of products with that observed for the metalated intermediates in the reaction of **4** with one equivalent of TMP(H) (a 6.3:2.6:1 ratio of the metalated products at the *ortho* (combined ratio of **3**-*ortho* and **4**), *meta* (**3**-*meta*) and *para* (**3**-*para*) positions)[28] demonstrates that by reacting **4** with TMP(H), we are genuinely mimicking the second step involved in the AMMZ*n* of **2**. In contrast, if isolated crystals of the kinetic product **4** are reacted with iodine (preventing the second step of the AMMZ*n* to from taking place), *ortho*-iodo(trifluoromethyl)benzene is formed exclusively in almost quantitative yields.

To shed some light upon the unconventional control on the regioselectivity of this reaction, where the second step of the AMMZ*n* seems to play a key role, theoretical calculations at the DFT level using the B3LYP method and the 6-311G** basis set were employed to compute the relative stabilities of the three possible regioisomers of **3**, in which trifluoromethyl benzene **2**
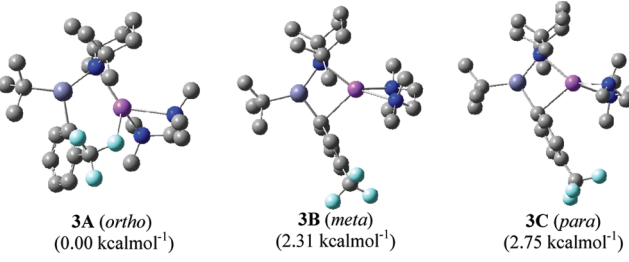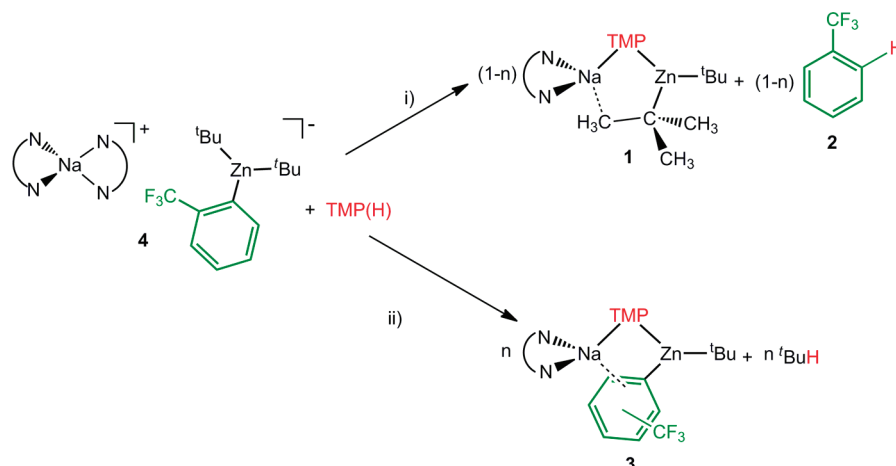
Scheme 4

Table 2. Selected Bond Distances (Å) Calculated for the Three Theoretical Regioisomers **3A−C**

| | **3A** (*ortho*) (0.00 kcal mol^{-1}) | **3B** (*meta*) (2.31 kcal mol^{-1}) | **3C** (*para*) (2.75 kcal mol^{-1}) |

bond distance (Å)	**3A**	**3B**	**3C**
Zn−C$_{metalated}$	2.132	2.101	2.094
Na−C$_{metalated}$	2.860	2.703	2.652
Na$\cdots$FCF$_2$	2.435	4.986	5.464
Na$\cdots$C$_{aryl}$	3.349, 3.741, 4.468, 4.765, 5.083	3.200, 3.565, 3.969, 4.445, 4.621	3.120, 3.231, 3.950, 4.040, 4.439

is deprotonated at the *ortho* (**3A**), *meta* (**3B**), or *para* (**3C**) positions. In support of the experimental findings we find that the *ortho* isomer (**3A**) is energetically the most preferred (relative energy: 0.00 kcal mol^{-1}), closely followed by **3B** (+2.31 kcal mol^{-1}) and then **3C** (+2.75 kcal mol^{-1}). Our theoretical studies also show that the reaction of sodium zincate **1** with **2** to yield **3** is exothermic by −27.16 kcal mol^{-1}. The modest difference in the relative energies obtained for the three possible regioisomers of **3** could explain the experimentally observed isomerization of some of **3**-*ortho* to **3**-*para* and **3**-*meta* (vide supra), which is in sharp contrast with the larger difference in the relative energies when the deprotonation of **2** was modeled using the conventional monometallic reagent *t*BuLi/TMEDA,[29] where the *ortho*-metalated product is the minimum-energy structure (by 7.48 and 10.58 kcal mol^{-1} from the *meta* and *para* isomers respectively).

Scrutinizing the dimensions of **3A−C** (Table 2) reveals that while zinc interacts similarly with the deprotonated aryl in the three regiosiomers (the largest variation between the Zn−C$_{metalated}$ bond distances is only 0.038 Å), there is a significant difference with the contacts formed by the sodium center in **3A** when compared with those in **3B** and **3C**. Thus, for the *meta* and *para* isomers **3B** and **3C**, these interactions are considerably shorter (Na−C bond lengths, **3B**: 2.703, 3.200, 3.534, 3.969, 4.445, and 4.621 Å; **3C**: 2.652, 3.120, 3.231, 3.950, 4.040, and 4.439 Å) than in *ortho* **3A** (2.860, 3.349, 3.741, 4.468, 4.765, and 5.083 Å). Although separately these medium-short Na−C contacts are relatively weak, collectively they must contribute to the overall stability of **3B** and **3C** and maximize the strength of the π-interaction of sodium with the metalated arene. In contrast, for **3A**, where these contacts are much less important, sodium interacts strongly with one fluorine atom of the CF$_3$ group, as evidenced by the short Na−F bond distance (2.435 Å) which is comparable with the values found in the literature for other compounds which display Na$\cdots$F dative bonds[30] and contrasts with the Na$\cdots$F distances calculated for **3B** (4.986 Å) and **3C** (5.464 Å), which are far too elongated to suggest any type of interaction.

Thus, these results clarify the distinct manners in which the metalated trifluoromethyl benzene molecule can interact with the alkali metal (either via Na$\cdots$F dative bonding or a combination of Na$\cdots$C π-interactions) that play a dominant role in the final regioselectivity observed for the AMM*Zn* thermodynamic product [(TMEDA)Na(TMP)(C$_6$H$_4$−CF$_3$)Zn(*t*Bu)] (**3**).

This view of the importance of the alkali metal is supported by previous structural elucidations of key metalated intermediates from the reactions of **1** with other substituted aromatic molecules which show that, when their substituents possess strong Lewis donor groups, as for example in *N,N*-diisopropylbenzamide,[12a] sodium interacts with the basic heteroatom of the functional group and the deprotonation occurs exclusively at the *ortho* position. On the other hand, when the aromatic substrate lacks a heteroatomic functional group that can coordinate strongly to the alkali metal (as in *N,N*-dimethylaniline[14] where the lone pair on the nitrogen is not available for coordination since it is involved in conjugation with the aromatic ring), then the interaction of sodium takes place through metal-π arene interactions directing the deprotonation to the position in the molecule where these π contacts[31] are maximized (in this case the *meta* position). Furthermore, it is only when the latter scenario occurs that unusual regioselectivities are observed for AMM*Zn* reactions, at positions not available for conventional monometallic reagents, where these favorable π-interactions between the metalated substrate and sodium are not feasible.[8,9,14]

In general for substrate **2**, the CF$_3$ substituent can be considered as a weak *ortho*-directing group (in comparison with other more powerful directing groups such as sulfones, tertiary amides or carbamates, to name a few),[32] where the metalation is directed almost entirely by the inductive acidifying effect of the CF$_3$ group. Notwithstanding, the large steric hindrance exerted by this group and the poor donor ability of highly electronegative fluorine atoms to coordinate to the organometallic base can hinder *ortho*-metalation of **2**. Using alkali-metal zincate **1** as a base, we can propose that for formation of kinetic product **4**, which exhibits a solvent-separated ion pair structure, and therefore contains no interactions between sodium and the metalated substrate, the coordination and steric effects of the CF$_3$ group do not greatly influence the regioselectivity of the reaction, which occurs exclusively at the *ortho* position, removing the most acidic proton in **2**. However, for the thermodynamic products, (**3**-*ortho*, **3**-*meta*, and **3**-*para*) which involve the formation of contacted ion pair species, although the acidifying effect of the CF$_3$ group is still dictating the regioselectivity of the reaction with formation of *ortho*-metalated **3**-ortho as the major product, the isomerization of some of this compound to the *meta* and *para* isomers (**3**-*meta* and **3**-*para*), which appear relatively close in stability, must also take place. This could probably be a consequence of the competing Na$\cdots$C π stabilizing interactions of the metalated aryl with the relatively weak Na$\cdots$F dative bond, which experimentally translates into the formation of a 6:2.3:1 ratio mixture of **3**-*ortho*, **3**-*meta*, and **3**-*para*.

Collectively, these results show for the first time that AMM*Zn* reactions can exhibit distinct kinetic/thermodynamic regioselectivities. In the first step of the reaction, which involves the formation of solvent-separated ion pair compounds,[33] steric effects will be of less importance, as the cation species is not covalently bound to the anionic component, and no communication between sodium and zinc is possible. Therefore deprotonation/zincation will occur at the most acidic position (following the same principles as conventional monometallic reagents).[34] However, in the second step, by regenerating the synergic bridge TMP, the regioselectivity of the reaction can change, where the cooperative effect of both metals can induce an isomerization on the metalated aryl product where the interaction between sodium and the metalated arene will be more favored, allowing

unique regioselectivities as for example observed in the direct *meta* metalation of dimethylanilines.[14]

Conclusions

The AMMZ*n* of trifluoromethyl benzene (**2**) by sodium zincate [(TMEDA)Na(TMP)(^{t}Bu)Zn(^{t}Bu)] (**1**) has been structurally mapped by isolation of the kinetic [{(TMEDA)$_2$Na}$^+$-{Zn(C$_6$H$_4$−CF$_3$)(^{t}Bu)$_2$}$^-$] (**4**) and thermodynamic [(TMEDA)-Na(TMP)(C$_6$H$_4$−CF$_3$)Zn(^{t}Bu)] (**3**) products providing the first experimental proof that these bimetallic bases operate by a combination of kinetic amide/thermodynamic alkyl basicity.

(23) The asymmetric unit of these crystals has two independent complexes, one of them is **3**-*ortho* and the other one contains an approximately 5:1 [0.828:0.172(5)] disordered mixture of **3**-*ortho* and **3**-*meta*, giving overall a ratio of almost 11:1 for these two isomers in the crystal structure.

(24) For **3**-*para* a structural motif similar to that observed for **3**-*meta* can be proposed, in which sodium atom will form a π-contact with the *para*-carbon as observed previously for the related product of toluene zincation, [(TMEDA)Na(TMP)(*para*-C$_6$H$_4$-CH$_3$)Zn(^{t}Bu)], ref 8.

(25) It must be noted that ^{1}H NMR spectroscopic monitoring of a solution of isolated crystals of **4** in deuterated benzene over a 4 day period showed no isomerisation of **4** to related *meta* or *para* products.

(26) The presence of free **2** could also be attributed to the partial hydrolysis of the organometallic species **3** or **4** in deuterated benzene solution. However we can rule out this possibility since formation of **2** could not be observed in solutions of compounds **3** and **4** monitored by ^{1}H NMR spectroscopy over 3 days.

(27) Compound **1** reacts with the deuterated solvent C$_6$D$_6$ (ref 5); therefore, although it must be formed in the competing reaction of **4** with TMP(H) that yields to the formation of **2** (reaction pathway i, Scheme 4), it could not be detected.

(28) This ratio has been determined using the integration values of the ^{1}HNMR spectrum of the reaction of **4** with one equivalent of TMP(H) (Figure 1c).

(29) These theoretical calculations have been carried out modeling the monometallic base and the metalated products as dimeric [{^{t}BuLi-(TMEDA)}$_2$] and [{(C$_6$H$_4$-CF$_3$)Li(TMEDA)}$_2$]; see Supporting Information for full details.

(30) For selected examples of structurally characterised compounds which contain Na···F dative interactions, see: (a) Dias, H. V. R.; Jin, W.; Kim, H.-J.; Lu, H.-L. *Inorg. Chem.* **1996**, *35*, 2317. (b) Plenio, H.; Diodone, R. *J. Am. Chem. Soc.* **1996**, *118*, 356. (c) Jolas, J. L.; Hoppe, S.; Whitmire, K. W. *Inorg. Chem.* **1997**, *36*, 3335. (d) Deacon, G. B.; Forsyth, C. M.; Junk, P. C.; Wang, J. *Chem.—Eur. J.* **2009**, *15*, 3082.

(31) For key references to electrostatic π interactions between alkali metals and aromatic molecules, see: (a) Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303. (b) Gokel, G. W.; De Wall, S. L.; Meadows, E. S. *Eur. J. Org. Chem.* **2000**, 2967. (c) Forbes, G C.; Kennedy, A. R.; Mulvey, R. E.; Roberts, B. A.; Rowlings, R. B. *Organometallics* **2002**, *21*, 5115.

(32) For key reviews of DoM see (a) Anctil, E.; Snieckus, V. The Directed ortho Metalation-Cross Coupling Nexus. Synthetic Methodology for Aryl−Aryl and Aryl−Heteroatom−Aryl Bonds. In *Metal-Catalyzed Cross-Coupling Reaction*, 2nd ed.; Diederich, F., de Meijere, A., Eds.; 2004; Vol. 761, p 813. (b) Hartung, C. G.; Snieckus, V. The Directed ortho Metalation Reaction. A Point of Departure for New Synthetic Aromatic Chemistry. In *Modern Arene Chemistry*; Astruc, D., Ed.; Wiley-VCH: New York, 2002; Vol. 330, p 367.

(33) Compound **4** contains two molecules of TMEDA which facilitates the formation of the solvent-separated ion pair structure. In the absence of the additional equivalent of TMEDA (which aids its crystallisation), **4** could exhibit a pseudo solvent-separated ion pair structure, similar to that reported for kinetic intermediate [(PMDETA)Li(C$_6$H$_4$-OMe)Zn(^{t}Bu)$_2$] (prepared by indirect route, Scheme 2, ref 17) where the metals are separated by a large distance (>5. Å).

(34) For selected examples of direct Zn−H exchange reactions using other alkali-metal zincates, see: (a) Wunderlich, S. H.; Knochel, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 7685. (b) Wunderlich, S. H.; Knochel, P. *Org. Lett.* **2008**, *10*, 4705. (c) L'Helgoual'ch, J. M.; Seggio, A.; Chevallier, F. l.; Yonehara, M.; Jeanneau, E.; Uchiyama, M.; Mongin, F. *J. Org. Chem.* **2008**, *73*, 177. (d) Wunderlich, S. H.; Knochel, P. *Chem. Commun.* **2008**, 6387. (e) Dong, Z.; Clososki, G. C.; Wunderlich, S. H.; Unsinn, A.; Li, J.; Knochel, P. *Chem.—Eur. J.* **2009**, *15*, 457. (f) Wunderlich, S. H.; Rohbogner, C. J.; Unsinn, A.; Knochel, P. *Org. Process Res. Dev.* **2010**, *14*, 339.

Thus, in the first step of the reaction arene **1** is selectively *ortho*-deprotonated to give solvent-separated ion pair **4** with concomitant release of TMP(H), which in turn reacts to produce contacted ion pair **3** (affording a mixture of the *ortho*, *meta*, and *para* regioisomers) and isobutane. Simulating the second, multipart-step of the AMMZ*n* process by reacting isolated crystals of **4** with TMP(H) in deuterated benzene and monitoring the reaction by ^{1}H NMR spectroscopy, shows that, far from playing a minor role, this second step, strongly influences the final outcome of the AMMZ*n* process, affecting not only the yield of the reaction but also the final regioselectivity of the metalation. To elaborate, a complex mixture of products is observed in solution that includes unreacted **4**, a mixture of the three possible regioisomers of **3**, *ortho*, *meta*, or *para* (in a 4.3:2.6:1 ratio, resulting from the amination reaction of TMP(H) with one ^{t}Bu group of **4**), and trifluoromethyl benzene **2** (obtained by the competing reaction of the amine with the metalated aryl ligand of **4**).

In addition DFT studies probing the reaction of **1** with **2** to generate **3**, showed that of the three possible regioisomers for this reaction, although the *ortho* structure is energetically the most preferred, the *meta* and *para* isomers are very close in energy (both of them almost equally favored) to it, which could explain the experimentally observed isomerization of some of **3**-*ortho* into **3**-*para* and **3**-*meta*. Analysis of the dimensions of the modeled structures,- suggest that this isomerization could be partly due to the competing Na···C π stabilizing interactions of the metalated aryl present in the *meta* and *para* structures with the Na−F dative bonding displayed in the *ortho*-isomer. These results show that depending on the type of preferred interaction between the alkali-metal and the metalated molecule in the contacted ion pair structures, the kinetic and thermodynamic regioselectivities of the AMMZ*n* can be adjusted.

These findings not only highlight the complexity of these metalation reactions but also draw attention to the significance of structurally identifying the metalated intermediates involved which otherwise, if these reactions were carried out in situ followed by subsequent electrophilic interception, would have remained hidden.

Finally, we believe this study provides a greater understanding of the mechanisms involved in direct zincation of aromatic molecules by TMP-dialkyl zincate bases and may contribute to further advances in the area of alkali-metal-mediated zincation generally, in particular to rationalize the unusual regioselectivities observed when bimetallic base **1** is employed which can be explained in part by the different structures of the kinetic and thermodynamic intermediates. In the former there is no metal−metal communication, whereas in the latter Na and Zn are connected by a TMP bridge that facilitates the interaction of sodium with the deprotonated arene, which seems to play a defining role in the regioselectivity observed in the final AMMZ*n* product.

Experimental Section

General. All reactions were performed under a protective argon atmosphere using standard Schlenk techniques. Hexane, THF and toluene were dried by heating to reflux over sodium benzophenone ketyl and distilled under nitrogen prior to use. [(TMEDA)Na(TMP)-(^{t}Bu)Zn(^{t}Bu)] (**1**)[5] was prepared according to literature methods. NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer, operating at 400.13 MHz for ^{1}H, 376.36 MHz for ^{19}F{^{1}H} and 100.62 MHz for ^{13}C{^{1}H}.

Reaction of [(TMEDA)Na(TMP)(^{t}Bu)Zn(^{t}Bu)] (1) with Trifluoromethyl Benzene (2) at Room Temperature. A Schlenk tube was charged with 2 mmol (0.358 g) of Zn^{t}Bu$_2$, which was dissolved in 10 mL of hexane. In a separate Schlenk tube, 2 mmol of BuNa

(0.16 g) was suspended in 10 mL of hexane and one molar equivalent of TMP(H) (2 mmol, 0.34 mL) was added via syringe. The resultant creamy white suspension was allowed to stir for an hour, after which the hexane solution containing Zn^tBu_2 was added via a syringe. The suspension changed from creamy white to a yellow hue (seemed to be less solid, but required TMEDA for it all to dissolve into solution). This was followed by the addition of a molar equivalent of TMEDA (2 mmol, 0.30 mL). The resultant suspension was heated gently to form a yellow solution which was allowed to cool to ambient temperature. Then, 2 mmol (0.25 mL) of trifluoromethyl benzene was added to the solution and it was allowed to stir at room temperature for 2 h before being moved to the freezer to aid crystallization. A large crop (0.52 g) of colorless crystals formed in solution which were suitable for analysis. Multinuclear (^{1}H, ^{13}C, and ^{19}F) NMR spectroscopy confirmed the presence of a mixture of **3**-*ortho*, **3**-*meta*, and **3**-*para* and **4** in 20: 11:1:8 ratio. ^{1}H NMR (400.13 MHz, 298 K, C_6D_6) δ 8.14 (1H, s, H_d, **3**-*meta*), 8.06 (0.71H, d, H_d, **4**), 7.84 (1.79H, d, H_d, **3**-*ortho*), 7.74 (1.02H, d, H_c, **3**-*meta*), 7.71 (0.19H, d, H_b, **3**-*para*), 7.54 (1.78H, d, H_a, **3**-*ortho*), 7.51 (0.72H, d, H_a, **4**), 7.42 (0.19H, d, H_a, **3**-*para*), 7.34 (1.03H, d, H_a, **3**-*meta*), 7.22- 7.17 (2.09H, m, H_b, **3**-*ortho* and H_b, **4**), 7.06 (1.03H, t, H_b, **3**-*meta*), 7.00−6.96 (2.59H, m, H_c, **3**-*ortho* and H_c, **4**), 2.12−1.75(m(broad), H_γ and H_β TMP), 1.58−1.42 (m (broad, overlapping), CH_3, TMP, CH_3 and CH_2, TMEDA, and CH_3, ^tBu group), 1.21, 1.14, 1.09 (s (broad), CH_3, TMP). (See Table 1 for labeling scheme of aromatic protons.) ^{13}C{^{1}H} NMR (100.62 MHz, 298 K, C_6D_6) δ 171.2, 168.5 (Zn−C_ortho), 141.7, 140.2, 139.3, 138.5, 137.6, 137.7, 137.1, 134.3, 130.1, 129.5, 127.0, 129.5, 125.6, 124.7, 124.03, 123.6, 122.0 (C_aryl), 56.7 (CH_2, TMEDA), 52.4, 52.5 (C_α, TMP), (CH_3, TMEDA), 40.9, 40.2, 39.2 (C_β, TMP), 36.5, 36.0, 35.6, 35.4, 35.3 (CH_3, TMP), 35.1, 35.0, 34.9 (CH_3, ^tBu), 20.4, 20.1(C_γ, TMP) (the relevant resonances for the CF_3, C_ipso, Zn−C_aryl could not be detected). ^{19}F{^{1}H} NMR (298 K, C_6D_6): δ −59.9, −61.5, −61.7, −61.8.

Reaction of [(TMEDA)Na(TMP)(^tBu)Zn(^tBu)] (1) with Trifluoromethyl Benzene (2) at 0 °C. The above-mentioned procedure was repeated to prepare a solution of the base (**1**) (2 mmol) in situ in hexane. The resulting light yellow solution was cooled to 0 °C via an ice bath before trifluoromethyl benzene (0.25 mL, 2 mmol) was added. The yellow solution was immediately transferred to the refrigerator (at 5 °C) to aid crystallization. A crop of colorless prismatic crystals of **4** were deposited from the solution (0.26 g 22%). This yield can be increased to 49% (0.58 g) if an additional molar equivalent of TMEDA is introduced (2 mmol, 0.30 mL). ^{1}H NMR (400.13 MHz, 298 K, C_6D_6) δ 88.06 (1H, d, H_d, **4**), 7.51 (0.1H, d, H_a, **4**), 7.20 (1H, t, H_b, **4**), 6.96 (1H, t, H_c, **4**), 1.85−1.71(32H, m (broad overlap), CH_3 and CH_2, TMEDA), 1.45 (18H, s, CH_3, ^tBu). ^{13}C{^{1}H} NMR (100.62 MHz, 298 K, C_6D_6) δ 140.0, 130.1, 125.5, and 124.01 (C_a, C_b, C_c, and C_d), 57.3 (CH_2, TMEDA), 45.5 (CH_3, TMEDA), 30.9 (CH_3, ^tBu), 21.4 (Zn−C, ^tBu) (the relevant resonances for the remaining quaternary carbons in **4**, CF_3, C_ipso, Zn−C_aryl could not be detected). ^{19}F{^{1}H} NMR (298 K, C_6D_6): δ −61.2.

Table 3. Crystallographic Data

	3	4
Chem form	C_{26}H_{47}F_3N_3NaZn	C_{12}H_{32}N_4Na^+·C_{15}H_{22}F_3Zn^−
Form wt	547.0	580.1
Cryst syst	monoclinic	triclinic
Space group	$P2_1/c$	$P\bar{1}$
a, Å	18.935(4)	10.4379(4)
b, Å	10.6904(9)	10.5920(4)
c, Å	30.382(6)	17.3032(7)
α, deg		88.910(3)
β, deg	103.88(2)	89.721(3)
γ, deg		60.559(2)
V, Å^3	5970.4(18)	1665.65(11)
Z	8	2
Reflns measd	36191	14089
Unique reflns	7682	5341
R_{int}	0.076	0.060
Refined params	831	633
Restraints	1171	1982
R (F, $F^2 > 2\sigma$)	0.102	0.071
R_w (F^2, all data)	0.205	0.202
GoF (F^2, all data)	1.186	1.118
Max, min el dens, e Å^{-3}	0.60, −0.84	1.12, −0.58

X-Ray Crystallography. Data were collected on Nonius KappaCCD (**3**) and Oxford Diffraction Gemini A Ultra (**4**) diffractometers, with MoKα radiation ($\lambda = 0.71073$ Å) at 150 K. Key crystallographic data are given in Table 3. Absorption corrections and frame scaling corrections were applied based on repeated and symmetry-equivalent data. The structures were solved by direct methods and refined on all unique F^2 values, with anisotropic non-H atoms and with constrained riding-model H atoms. Both structures display extensive disorder, which was modeled satisfactorily with the aid of restraints on geometry (similarity of equivalent groups) and displacement parameters. **3** has two independent molecules in the asymmetric unit, one of which shows minor disorder of the single **3**-*ortho* isomer while the other consists of a disorder of the **3**-*ortho* and **3**-*meta* isomers on a common site. The noncentrosymmetric structure of **4** was found to be partially twinned by inversion and has two ion pairs in the asymmetric unit (which is the entire unit cell).

Supporting Information Available: NMR spectra, computational details and CIF files giving crystallographic data for compounds **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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