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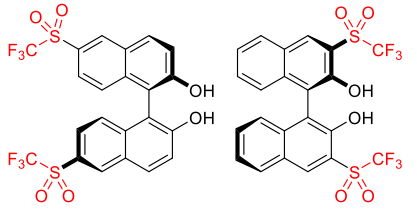
Supporting information for this article is given via a link at the end of the document.

Abstract:

A multi-gram scale synthesis of ferrocenetriflone was optimised from ferrocenesulfonyl fluoride and Me_3SiCF_3 (Ruppert reagent). Enantioselective deprotolithiations were then optimised using alkyllithiums in the presence of catalytic (+)-sparteine to afford 2-substituted ferrocene triflones in 79-84% *ee*. The use of chiral lithium amides in the presence of *in situ* traps was also optimised and was found to outperform alkyllithium·chiral diamine chelates for the first time in the ferrocene series, with 89-93% *ee*. Crystallisation of derivatives afforded enantiopure compounds that were engaged in deprotolithiation-electrophilic trapping sequences, a halogen 'dance' reaction and transition metal-promoted coupling to afford a wide range of variously polysubstituted ferrocene triflones.

As a potent lipophilic[1] and electron-withdrawing substituent (Hammett σ_p = 0.96 and σ_m = 0.83),[2] the trifluoromethylsulfonyl group (or triflyl; SO_2CF_3) can modulate the properties of compounds for applications. In medicinal chemistry, for example, it is a key component of ABT-263 and BM-957, two structurally related inhibitors of B-cell lymphoma 2 (Bcl-2) pro-survival proteins.[3] In addition, the radiolabelled $SO_2CF_2{}^{18}F$ group has recently been introduced as a new tracer for positron emission tomography.[4] The triflyl group is also capable of stabilising carbanions, as demonstrated with tetratriflylpropene used in Brønsted and Lewis acid catalysis,[5] as well as promoting intramolecular charge transfer in two-photon fluorophores used for the detection of micropolarity changes.[6]

However, while enantiopure fluorinated catalysts[7] and fluorinated and trifluoromethylated drugs[8] have been studied and developed, enantiopure trifluoromethylsulfones remain little studied to date.[9] Furthermore, while several synthetic methods have been developed in recent years to reach and functionalise (hetero)aromatic triflones,[10] examples of enantiopure aryltriflone derivatives are currently limited to structures based on BINOL possessing axial chirality.[11] (*R*)-BINOL-6,6'-bistriflone and -3,3'-bistriflone (Figure 1) are representative examples of such compounds, capable of efficiently catalysing Zr-mediated Mannich-type reactions[11a, 11b] and In-mediated allylation of imines,[11c] respectively. Given the importance of planar chirality in the discovery of new catalysts and materials,[12] it is somewhat surprising that no aromatic triflones with planar chirality have been reported to date.



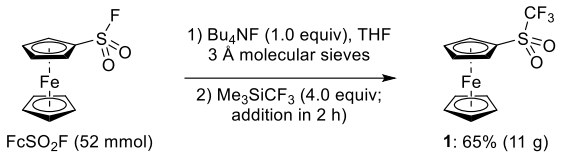
(*R*)-BINOL-6,6'-bistriflone (*R*)-BINOL-3,3'-bistriflone

Figure 1. Enantiopure aromatic triflones used as catalysts.

As a strong electron-withdrawing substituent,[13] the triflyl group can promote specific aromatic *ortho*-functionalisation reactions, as shown by Shibata and co-workers during the deprotolithiation of benzenetriflone using lithium amides followed by electrophilic trapping.[14] Butenschön's group recently followed a similar approach in the ferrocene series for the synthesis of racemic 2-methylferrocenetriflone.[15] Drawing on our expertise in alkyllithium-chiral diamine chelates and chiral lithium amides, we report here the first enantioselective functionalisations of

ferrocenetriflone, and thus the possibility of accessing a whole library of new non-racemic planar-chiral derivatives.

In 2021, Butenschön's group reported the synthesis of ferrocenyl (Fc) triflone (**1**) from $FcSO_2F$ in 46% yield by treatment with Me_3SiCF_3 (Ruppert reagent) at room temperature in the presence of a catalytic amount of $(Me_2N)_3S(Me_3SiF_2)$.[15] In the benzene series, the latter could be replaced by the less expensive Bu_4NF, although used in a stoichiometric quantity.[16] Thus, by slowly adding an excess of Me_3SiCF_3 to a solution of $FcSO_2F$ and Bu_4NF in tetrahydrofuran (THF) containing molecular sieves, we were able to isolate the expected product **1** in an improved 65% yield (11 g in a single batch). However, as full conversion could not be achieved under these conditions, **1** was successfully separated from the residual $FcSO_2F$ by selective hydrolysis of the latter using NaOH (Scheme 1). Although K_3PO_4 had been used for the same purpose by Butenschön's group,[15] we often encountered reproducibility issues during large scale reactions and therefore preferred the more basic NaOH.



Scheme 1. Optimised synthesis of ferrocenetriflone (**1**).

Although the directing group properties of the triflyl substituent have already been reported,[14-15] we were keen to further evaluate the pK_a values of **1**. Therefore, they were calculated within the density functional theory (DFT) framework, and were found comparable to those of $FcSO_2F$.[17] The electron-withdrawing character of the triflyl substituent was also highlighted by the redox potential of the ferrocene core. Indeed, with a recorded $E_{1/2}$ value of +0.54 V *vs.* FcH/FcH$^+$, it appeared to be one of the most powerful electron-withdrawing groups in the ferrocene series, almost comparable to fluorosulfonyl (Figure 2).

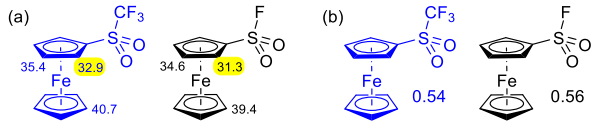


Figure 2. (a) Calculated pK_a values of **1** and $FcSO_2F$. (b) Measured $E_{1/2}$ values (in V) of **1** and $FcSO_2F$ (potential values from DPV experiments, referenced to Ag/AgCl and recalculated to FcH/FcH$^+$).

To achieve original enantiopure ferrocene triflone derivatives, we then evaluated the asymmetric deprotolithiation of **1**, initially using alkyllithium·chiral diamine chelates.[18] Indeed, good to excellent enantioselectivities were recorded using such chelates, prepared from (*R*,*R*)-*N*,*N*,*N'*,*N'*-tetramethylcyclohexane-1,2-diamine [(*R*)-TMCDA] or (−)-sparteine, to deprotometallate hindered $FcC(O)NR_2$,[19] $FcCH_2NMe_2$[20] and $FcNMe_2{\cdot}BF_3$[21] (Figure 3).

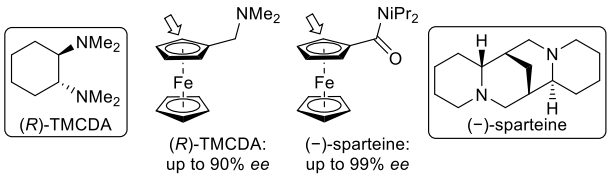
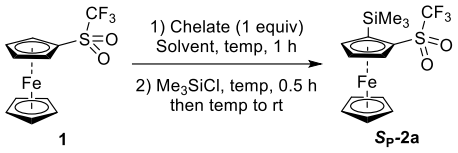


Figure 3. Successful examples of enantioselective deprotometallation promoted by alkyllithium·chiral diamine chelates.

Inspired by the work of Strohmann and co-workers,[20] we first assessed the ability of the BuLi·(*R*)-TMCDA chelate to carry out the enantioselective deprotolithiation of **1**. After 1 h contact at –80 °C in Et_2O, the addition of Me_3SiCl afforded the 2-silylated derivative **2a** in low yield and enantioselectivity (Table 1, entry 1). It was possible to double the yield using the more hindered *s*BuLi, but without any major change in *ee* (entry 2). We then evaluated the use of (+)-sparteine which could provide a better chiral environment around the base. Pleasingly, both yield and *ee* increased using this chiral diamine in Et_2O (entries 3 and 4). Switching to *tert*-butyl methyl ether (TBME) gave better results (entry 5) and lowering the temperature to –100 °C gave product **2a** in a good 84% *ee* (in favour of the S_P enantiomer; entry 6). As demonstrated by O'Brien and co-workers[19c] and further studied by Stohmann,[20] Metallinos and co-workers,[21] the use of a catalytic amount of chiral diamine can still provide an enantioenriched product with very good results. In our case, the use of 0.4 equivalent of (+)-sparteine gave **2a** in a reduced 51% yield, but with an almost unchanged *ee* of 80% (entry 7).

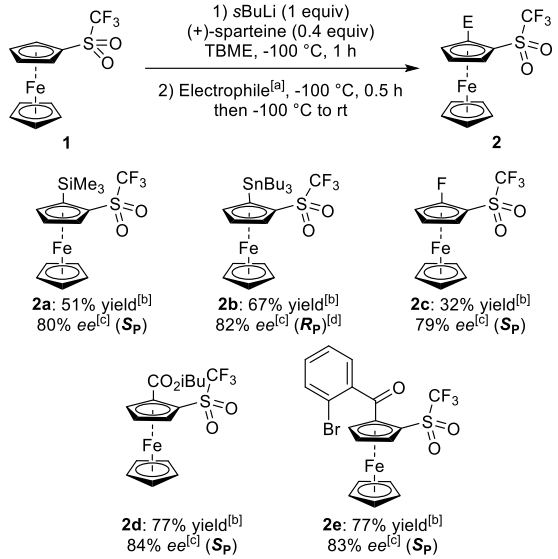
Table 1. Enantioselective deprotolithiation of compound **1** using alkyllithium·chiral diamine chelates.



Entry	Chelate	Solvent	temp (°C)	Yield (%)[a]	*ee* (%)[b]
1	BuLi·(*R*)-TMCDA	Et_2O	–80	23	4
2	*s*BuLi·(*R*)-TMCDA	Et_2O	–80	42	0
3	BuLi·(+)-sparteine	Et_2O	–80	84	26
4	*s*BuLi·(+)-sparteine	Et_2O	–80	78	59
5	*s*BuLi·(+)-sparteine	TBME	–80	86	67
6	*s*BuLi·(+)-sparteine	TBME	–100	85	84
7	*s*BuLi·(+)-sparteine[c]	TBME	–100	51	80

[a] Isolated yield. [b] Determined by HPLC analysis (see Supporting Information for details). [c] 0.4 equivalent of (+)-sparteine was used.

These results represent a marked improvement over the asymmetric deprotolithiation of other sulfur-containing prochiral ferrocenes such as *O*-isopropylferrocenesulfonate (58% *ee*)[22] and (fluorosulfonyl)ferrocene (20% *ee*).[17b] Therefore, we decided to briefly evaluate the scope of electrophiles compatible with this catalytic functionalisation promoted by (+)-sparteine. While the use of Bu_3SnCl afforded the stannylated product **2b** in increased yield, switching to *N*-fluorobenzenesulfonimide (NFSI) led to **2c** with a similar enantioselectivity but in a lower 32% yield (Scheme 2). Isobutyl chloroformate and 2-bromobenzoyl chloride were ultimately used as electrophiles to obtain ester **2d** and ketone **2e**, both isolated in similar yields and enantioselectivities. Pleasingly, it was possible to crystallise the latter by diffusion and isolate the enantiopure ***S*P-2e** in 53% yield, thus unambiguously validating its structure (Figure 4).



Scheme 2. Use of sBuLi·(+)-sparteine chelate to access enantioenriched 2-substituted ferrocene triflones. [a] Electrophiles used: Me_3SiCl (**2a**), Bu_3SnCl (**2b**), NFSI (**2c**), $iBuCO_2Cl$ (**2d**), $2\text{-}BrC_6H_4COCl$ (**2e**). [b] Isolated yield. [c] Determined by HPLC analysis (see Supporting Information for details). [d] Configuration established by Sn/Li exchange followed by trapping with $ClSiMe_3$, and comparison with **2a** by HPLC analysis (see Supporting Information for details).

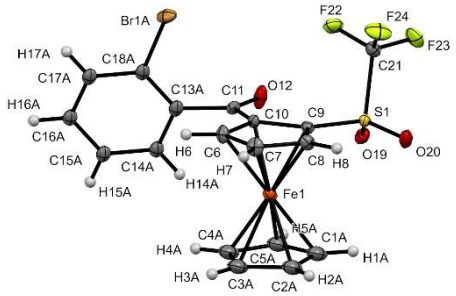


Figure 4. Molecular structure of ***S*P-2e** (thermal ellipsoids shown at the 30% probability level).[23]

In addition to alkyllithium·chiral diamine chelates, chiral lithium amides, in the presence of *in situ* traps,[24] have also been used to prepare enantioenriched 1,2-disubstituted ferrocenes. This approach was first documented by Simpkins from $FcP(O)Ph_2$,[25] and later thoroughly studied by our group from $FcC(O)NR_2$,[26] $FcS(O)_2OiPr$[22b] and $FcCO_2R$[27] (*ee* values of up to 80% from the latter substrate, Figure 5). We were therefore keen to involve ferrocenetriflone (**1**) in this approach.

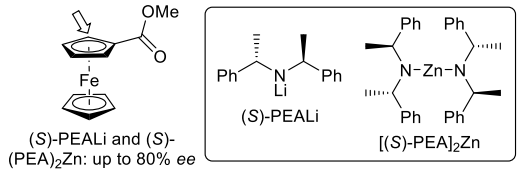
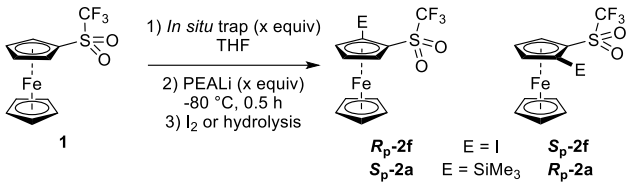


Figure 5. Successful example of enantioselective deprotolithiation promoted by lithium amide-*in situ* trap pair.

To this end, we first used 1 equivalent of lithium di[(*R*)-1-phenylethyl]amide] [(*R*)-PEALi] as a chiral base in the presence of the putative zinc diamide [{(*R*)-PEA}$_2$Zn], obtained *in situ* from the corresponding PEALi and $ZnCl_2$·TMEDA (TMEDA = *N*,*N*,*N'*,*N'*-tetramethylethylenediamine) in a 2:1 ratio.[24] After slow warming and iodolysis,[22b, 26-27] a promising 51% *ee* was obtained for compound **2f**, but with a rather disappointing 10% yield (Table 2, entry 1). Slightly better results were noticed using the other enantiomer of the chiral amine (entry 2). However, when $ZnCl_2$·TMEDA was used as an *in situ* trap instead of zinc diamides, the *ee* of **2f** reached 93%, although it was isolated in a moderate 29% yield (entry 3). As previously proposed,[27] competitive deprotometallation by mixed lithium amido-ferrocenyl zincates formed during the reaction could explain the lower enantioselectivities using [{(*R*)-PEA} ($_2$Zn].

To avoid these issues, we investigated the use of Me_3SiCl as an *in situ* trap. In combination with [(*R*)-PEALi], after 1 h at –80 °C, silane **2a** was isolated in 40% yield and 79% *ee* (entry 4). As already observed above, switching to [(*S*)-PEALi] had a slight effect on the reaction outcome (entry 5). However, increasing the amount of base to 2 equivalents and working at –90 °C improved both yield (55%) and enantioselectivity (89% *ee*; entry 6). Pleasingly, we were able to grow crystals suitable for X-ray diffraction analysis, confirming the absolute configuration of the ***R*P-2a** structure (Figure 6).

Table 2. Enantioselective deprotolithiation of compound **1** using chiral lithium amides in the presence of *in situ* traps.



Entry	PEALi and *in situ* trap (ratio)	E (**Cpd**)	Yield (%)[a]	*ee* (%)[b]
1[c]	[(*R*)-PEALi] and [{(*R*)-PEA}$_2$Zn] (1:1)	I (**2f**)	10	51 (R_P)[d]
2[c]	[(*S*)-PEALi] and [{(*S*)-PEA}$_2$Zn] (1:1)	I (**2f**)	22	61 (S_P)[d]
3[e]	[(*S*)-PEALi] and $ZnCl_2$·TMEDA (1:3)	I (**2f**)	29	93 (S_P)[d]
4	(*R*)-PEALi and Me_3SiCl (1.2:1.2)	$SiMe_3$ (**2a**)	40	79 (S_P)
5	(*S*)-PEALi and Me_3SiCl (1.2:1.2)	$SiMe_3$ (**2a**)	48	79 (R_P)
6[e]	(*S*)-PEALi and Me_3SiCl (2:2)	$SiMe_3$ (**2a**)	55	89 (R_P)

[a] Isolated yield, except for entry 2. [b] Determined by HPLC analysis (see Supporting Information for details). [c] Slow warming from –80 to –10 °C. [d] Configuration in analogy to that of **2b** (see Supporting Information for details). [e] –90 °C instead of –80 °C.

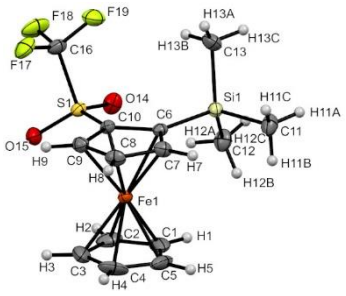


Figure 6. Molecular structure of ***R*$_P$-2a** (thermal ellipsoids shown at the 30% probability level).[23]

A computational analysis was then carried out to rationalise the high enantioselectivity observed in this asymmetric deprotolithiation using (*R*)- and (*S*)-PEALi. Thus, using ferrocenetriflone (**1**) as a model substrate, DFT calculations at the B3LYP/LANL2DZ (for Fe) & 6-31+G** (for the other atoms) levels were performed (Figure 7).[28] First of all, we were able to rule out a possible coordination of the lithium atom by a fluorine of the triflone group. We were then pleased to find that the activation energy leading to (R_P)-2-lithioferrocenetriflone was 2.4 kcal/mol higher than that leading to its isomer (S_P), in good agreement with the experimental results.[29] In addition, from the calculated ΔG value,[28] we estimated the ee of the deprotolithiation to 97% at -90 °C, in good agreement with the experimental results.

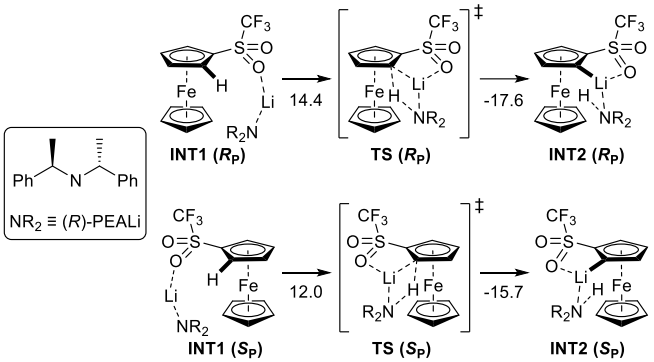
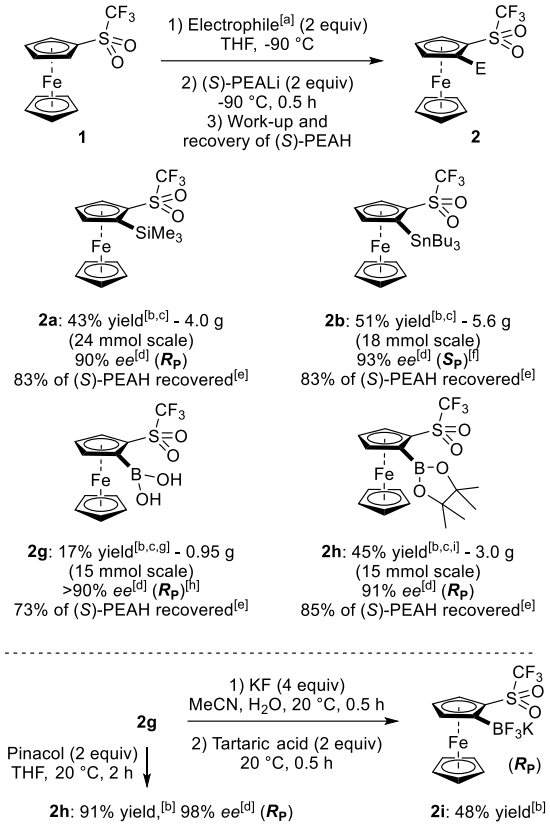


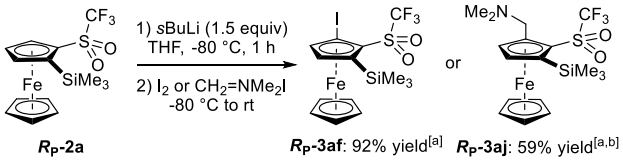
Figure 7. DFT calculation of deprotolithiation of **1** using (*R*)-PEALi at the B3LYP/Lanl2DZ level (for Fe) & 6-31+G** (other atoms) level (Δ*G* in kcal/mol).

As the enantiomeric excesses obtained with the chiral lithium amide-*in situ* trap tandems were slightly better than those recorded with the alkyllithium·(+)-sparteine chelates, we then investigated the applicability of the first approach (Scheme 3). However, our main limitation lies in the ability of the electrophile to react more rapidly with deprotolithiated species than with lithium amides, as observed with Me_3SiCl.[30] Therefore, based on literature precedents, we then chose Bu_3SnCl[31] and $B(OiPr)_3$[32] as *in situ* traps in combination with (*S*)-PEALi (2 equiv) in THF at –90 °C. Under these conditions, stannane **2b** was isolated in moderate 51% yield but with a 93% *ee* while boronic acid **2g** was only obtained in 17% yield due to purification problems. However, a one-pot esterification with pinacol afforded the derivative **2h** in better 45% yield and 91% *ee*. To evaluate the robustness of our approach, all these reactions were carried out on a gram scale without any problems. Moreover, while it requires the use of 2 equivalents of (*S*)-PEAH, we were able to recycle around 80% of the chiral amine each time. Boronic acid **2g** was subsequently converted to its pinacol ester **2h** for *ee* determination and to its potassium trifluoroborate salt **2i** (Scheme 3, bottom).[33] We were pleased to find possible to crystallise the 2-silylated compound **2a** (90% *ee*) from a hexane solution to give the enantiopure product (> 99.5% *ee*) in 65% yield, paving the way for libraries of enantiopure ferrocenetriflone derivatives.



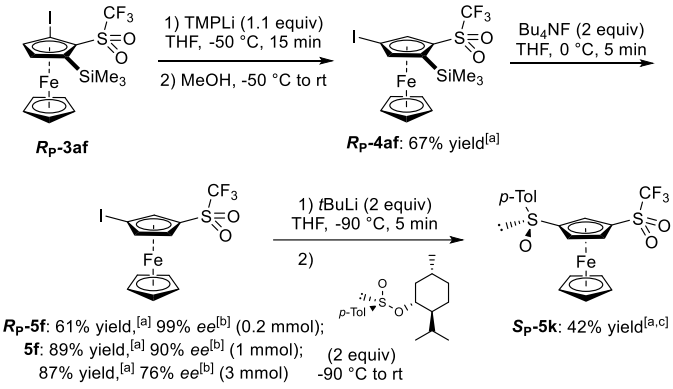
Scheme 3. Use of (*S*)-PEALi in the presence of different *in situ* electrophilic traps to access non-racemic 2-substituted ferrocene triflones. [a] Electrophiles used: Me_3SiCl (**2a**), Bu_3SnCl (**2b**), $B(OiPr)_3$ (**2g** and **2h**). [b] Isolated yield. [c] The rest was mainly starting **1**. [d] Determined by HPLC analysis (see Supporting Information for details). [e] After treatment and distillation ($[\alpha]_D^{20}$ identical to that of a commercial sample). [f] Configuration established by Sn/Li exchange followed by trapping with Me_3SiCl, and comparison with **2a** by HPLC analysis (see Supporting Information for details). [g] After hydrolysis. [h] Determined by conversion to **2h** (see Scheme 3, bottom). [i] Yield given after *in situ* conversion to the pinacol ester.

To progress towards polysubstituted ferrocenes, we selected the enantiopure compound ***R*P-2a** and carried out deprotolithiation using *s*BuLi in THF at –80 °C for 1 h. After addition of iodine or $CH_2{=}NMe_2I$ (Eschenmoser salt), the 2,5-disubstituted ferrocene triflones ***R*P-3af** (Figure 8, left) and ***R*P-3aj** were isolated in 92% and 59% yield, respectively (Scheme 4).



Scheme 4. Synthesis of enantiopure 2,5-disubstituted ferrocene triflones from ***R*P-2a**. [a] Isolated yield. [b] > 99% enantiomeric purity shown by NMR, using (*R*)-*tert*-butylphenylphosphinothioic acid as a chiral resolving agent[34] (see Supporting Information for details).

To obtain isomeric 2,4-disubstituted ferrocene triflones, we next considered the halogen 'dance' reaction[35] from ***R*P-3af**, which contains both triflyl as a strong directing group and a trimethylsilyl to protect its adjacent position. As with the other iodoferrocene derivatives,[36] the reaction was carried out using lithium 2,2,6,6-tetramethylpiperidide (TMPLi) in THF at –50 °C prior to methanolysis (Scheme 5). As already observed for the fluorosulfonyl analogue,[17a] a short reaction time (15 min) was advantageously applied to limit competitive iodine/lithium exchange.[17b] This afforded the first enantiopure 2,4-disubstituted ferrocene triflone ***R*P-4af** (Figure 8, right), isolated in 67% yield. Its desilylation using Bu_4NF provided the expected 3-substituted ferrocene triflone ***R*P-5f**, although partial racemisation was noticed from a scale of 1 mmol. This compound can be further functionalised to give a pure 3-substituted ferrocenetriflone stereoisomer, as shown in the synthesis of ***S*P-5k**. Indeed, halogen/lithium exchange was first carried out using *t*BuLi in THF[17b, 37] at –90 °C and the lithiated derivative was trapped with (−)-menthyl (*S*)-4-toluenesulfinate,[38] leading to the expected sulfoxides ***S*P-5k** and ***R*P-5k** in yields of 42% and 9%, respectively.



Scheme 5. Synthesis of enantiopure 2,4-disubstituted and 3-substituted ferrocene triflones from ***R*P-3af**. [a] Isolated yield. [b] Determined by HPLC analysis (see Supporting Information for details). [c] ***R*P-5k** was also isolated in 9% yield.

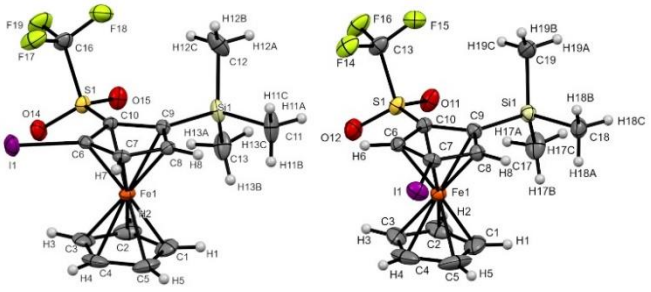
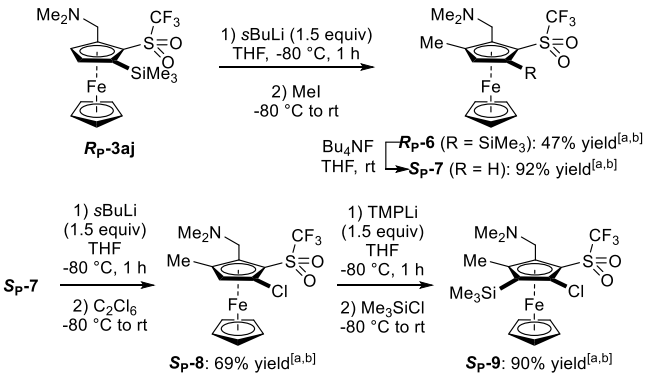


Figure 8. Molecular structures of ***R*P-3af** and ***R*P-4af** (thermal ellipsoids shown at the 30% probability level).[23]

To progress towards an enantiopure hetero-1,2,3,4,5-pentasubstituted ferrocene triflone, we performed another deprotometallation-trapping sequence from ***R*P-3aj** to the methylated derivative ***R*P-6** (47% yield; Scheme 6). To allow further functionalisation, the trimethylsilyl group was first removed (compound ***S*P-7**) and a further deprotometallation-trapping sequence was then carried out to afford the chlorinated derivative ***S*P-8** in 69% yield. To avoid competitive halogen/metal exchange, the final deprotolithiation was carried out using TMPLi in THF at –80 °C. After trapping with Me_3SiCl, the pentasubstituted ferrocene ***S*P-9** was isolated in an excellent 90% yield. Crystals suitable for X-ray diffraction analysis could be grown, confirming the expected structure (Figure 9).



Scheme 6. Synthesis of enantiopure 2,3-disubstituted, 2,3,5-trisubstituted and 2,3,4,5-tetrasubstituted ferrocene triflones from ***R*P-3aj**. [a] Isolated yield. [b] > 99% enantiomeric purity shown by NMR, using (*R*)-*tert*-butylphenylphosphinothioic acid as a chiral resolving agent[34] (see Supporting Information for details).

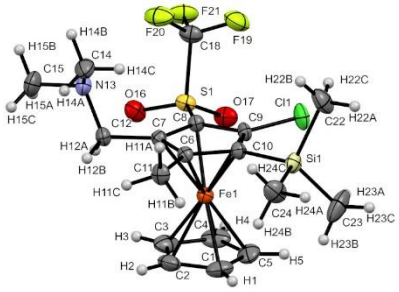
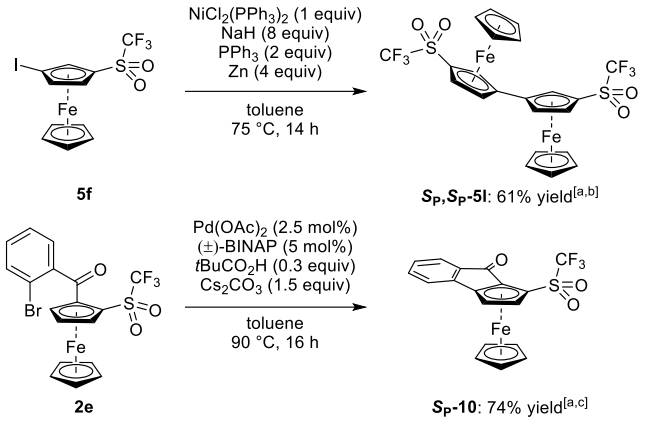


Figure 9. Molecular structure of ***S*P-9** (thermal ellipsoids shown at the 30% probability level).[23]

Finally, we were eager to engage some of our original ferrocenetriflones in metal-promoted transformations. Biferrocene derivatives represent an important family of compounds for studies in molecular electronics.[39] As they are usually prepared from iodoferrocene derivatives, we engaged the 1,3-disubstituted ferrocene **5f** (90% *ee*) in a nickel-promoted Ullmann-type homocoupling (Scheme 7).[40] Pleasingly, we found that the stereopure 1,1'-biferrocene-3,3'-bistriflone ***S*P,*S*P-5l** could be isolated to 61%, its structure being unambiguously validated by X-ray diffraction analysis (Figure 10, top).

Over the past decade, C-H bond activation has become a popular approach to obtain enantioenriched derivatives containing a fused ferrocene.[41] To progress towards an original fused ferrocene triflone, cyclisation was finally attempted from the enantiopure compound **2e**. We therefore adapted a protocol from Gu, You and co-workers,[42] and succeeded in obtaining enantiopure ***S*p-10** in 74% yield (Figure 10, bottom).



Scheme 7. Transition metal-promoted functionalisations of ferrocenetriflone derivatives. [a] Isolated yield. [b] ***meso*-5l** was also isolated in 4% yield. [c] > 99% *ee* determined by HPLC analysis (see Supporting Information for details).

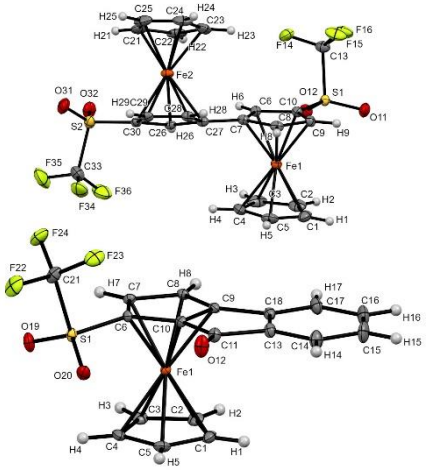


Figure 10. Molecular structure of ***S*P,*S*P-5l** and ***S*P-10** (thermal ellipsoids shown at the 30% probability level).[23]

Here, we report how a multigram scale synthesis of ferrocenetriflone enabled an in-depth study of its enantioselective deprotolithiation. The use of *s*BuLi in combination with the catalytic (+)-sparteine afforded the expected 2-substituted derivatives in good yields and enantioselectivities of up to 84%, mirroring the best results in the asymmetric deprotometallation of ferrocenes. Most importantly, for the first time in the ferrocene series, we found that chiral lithium amides, in combination with *in situ* traps, led to better stereocontrol, increasing the *ee* up to 93%, in good agreement with DFT calculations. Further functionalisations were achieved by combining deprotolithiation-

electrophilic trapping sequences, a halogen 'dance' reaction and transition metal catalysis to generate a library of variously substituted ferrocene triflones. Given the growing application of compounds containing a triflone function in molecular chemistry, we hope that this study will encourage the development of this original motif.

Supporting Information

The authors have cited additional references within the Supporting Information.[43]

Experimental Section

Typical procedure for the asymmetric deprotolithiation using catalytic chiral diamine. The protocol was adapted from previously reported procedures.[19a, 22b] *s*BuLi (1.0 M in cyclohexane; 1.2 mL, 1.2 mmol) was added dropwise to a solution of (+)-sparteine (0.11 mL, 0.11 g, 0.48 mmol) in TBME (3.5 mL) at –80 °C. After 0.5 h of stirring, the reaction mixture was cooled to –100 °C and a solution of ferrocenetriflone (**1**; 0.38 g, 1.2 mmol) in TBME (2 mL) was added over 10 min using a syringe pump. After addition, the reaction mixture was stirred at –100 °C for 1 h. Me_3SiCl (0.15 mL, 0.13 g, 1.2 mmol) was then added and the reaction mixture was stirred at –100 °C for 0.5 h. The reaction mixture was warmed to rt out of the cooling bath and stirred for 0.5 h. Aqueous HCl (1 M) was added, and the reaction mixture was extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtrated over cotton wool, and concentrated under reduced pressure to give the crude product. Purification by column chromatography over silica gel (eluent: petroleum ether-EtOAc 95:5) afforded 2-(trimethylsilyl)ferrocenetriflone (**2a**) in 51% yield (0.24 g) and 80% *ee* (in favour of the S_P enantiomer) as an orange solid: Rf (eluent: petroleum ether) 0.54; mp 90-92 °C; IR (ATR) ν 760, 832, 858, 957, 1004, 1042, 1067, 1111, 1144, 1185, 1209, 1247, 1274, 1356, 1414, 1711, 2902, 2957 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.34 (s, 9H, $SiMe_3$), 4.49 (s, 5H, Cp), 4.58 (dd, 1H, *J* = 2.6 and 1.4 Hz, H3), 4.78 (t, 1H, *J* = 2.6 Hz, H4), 4.95-4.96 (m, 1H, H5) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 0.73 ($3CH_3$), 71.4 (5CH, Cp), 75.4 (CH, C4), 76.1 (CH, C5), 77.2 (C, C2, *C*-$SiMe_3$), 80.8 (CH, C3), 81.0 (q, C, *J* = 2.2 Hz, C1, *C*-SO_2CF_3), 119.5 (q, C, *J* = 326 Hz, CF_3) ppm; $^{19}F\{^1H\}$ NMR ($CDCl_3$) δ –78.6 ppm. Anal. Calcd for $C_{14}H_{17}F_3FeO_2SSi$ (390.27): C, 43.09; H, 4.39; S, 8.21. Found: C, 43.05; H, 4.57; S, 8.15%. The *ee* value was determined by HPLC analysis on a Chiralpak-IB column using hexane-iPrOH (99:1) as the eluent at 0.5 mL.min^{-1} and 10 °C, λ = 254 nm, t (minor, ***R*$_P$-2a**) = 10.80 min, t (major, ***S*$_P$-2a**) = 11.66 min. 39% of starting **1** were also recovered.

Typical procedure for the deprotolithiation using (*S*)-PEALi in the presence of an *in situ* trap and recovery of the chiral amine. The protocol was adapted from previously reported procedures.[24a, 25-27] To a solution of ferrocenetriflone (**1**; 7.6 g, 24 mmol) and Me_3SiCl (6.1 mL, 48 mmol) in THF (96 mL) at –90 °C was added dropwise a solution of (*S*)-PEALi [prepared by adding BuLi (1.4 M in hexane; 34 mL, 48 mmol) to (*S*)-PEAH (11 mL, 48 mmol) in THF (96 mL) at –15 °C and stirring at this temperature for 5 min before cooling to –90 °C]. After 0.5 h at this temperature, 5% aqueous H_3PO_4 (100 mL) was added, and the reaction mixture was warmed to rt and stirred for 0.5 h. Extraction with Et_2O (2 x 100 mL), washing the combined organic layers with 5% aqueous H_3PO_4 (2 x 50 mL), drying over $MgSO_4$ and removal of the solvents under reduced pressure led to the crude. Purification by column chromatography over silica gel (eluent: petroleum ether-EtOAc 95:5) afforded **2a** in 43% yield (4.0 g) and 90% *ee* (in favour of the S_P enantiomer) as an orange solid, as above ($[\alpha]_D^{20}$ +111 (*c* 1.0, $CHCl_3$)). 48% of starting **1** were recovered. To recover the chiral amine, the combined aqueous acidic phases were basified until pH 11 with 20% aqueous NaOH. After extraction using Et_2O (3 x 50 mL), the combined organic layers were dried over K_2CO_3, and the solvent was removed under reduced pressure to give the crude amine. This was purified by Kugelrohr distillation (200 °C, 5.5 mbar) to give pure (*S*)-PEAH in 83% recovery (9.0 g) as a colourless oil: ^1H NMR ($CDCl_3$) δ 1.29 (d, 6H, *J* = 6.7 Hz, Me), 3.52 (q, 2H, *J* = 6.7 Hz, C*H*Me), 7.22-7.29 (m, 6H, Ph), 7.31-7.37 (m, 4H, Ph); $[\alpha]_D^{20}$ –157 (*c* 0.024, EtOH).

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Triflone • Chirality • Ferrocene • Substituent effect • Lithium amide

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[23] Deposition numbers 2364199 (for **2aa**), 2364200 (for $\boldsymbol{S_P}$**-2e**), 2364201 (for $\boldsymbol{R_P}$**-2a**), 2364202 (for $\boldsymbol{R_P}$**-3af**), 2364203 (for $\boldsymbol{R_P}$**-4af**), 2364204 (for $\boldsymbol{R_P}$**-5f**), 2364205 (for $\boldsymbol{S_P}$**-9**), 2364206 (for $\boldsymbol{S_P,S_P}$**-5l**), 2364207 (for $\boldsymbol{S_P}$**-10**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

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