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Novel Chiral 1,3-Diamines by a Highly Modular Umpolung Strategy Employing a Diastereoselective Fluorination–Nucleophilic Aromatic Substitution Sequence

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Dedicated to the memory of our friend and colleague Prof. Dr. Birgit Drießen-Hölscher

Keywords: Amines / Chirality / Aromatic substitution / Nucleophilic substitution / Halogenation / Chromium / Asymmetric synthesis / Umpolung

A new highly modular synthesis for the rare class of chiral 1,3-diamines has been devised. It is accessible through nucleophilic aromatic *ipso*-substitution of fluorine in [(*R*,*R*)-1-fluoro-2-{(1-dimethylamino)ethyl}benzene]tricarbonylchromium and related complexes by secondary as well as primary amines. The precursor is accessible by a new diastereoselective electrophilic fluorination using *N*-fluorobenzenesulfonimide (NFSI), and the method is of potential interest for the synthesis of fluorinated pharmaceuticals. The protocol allows for the straightforward, modular synthesis of a broad library of diamines. A stock of 21 diamines has been synthesized. Primary amines bearing a stereogenic α-center can be introduced without loss of optical purity, yielding planar-chiral diamines with two stereogenic centers in close proximity. An extended number of X-ray structures of these diamines is presented and discussed along with NMR experiments which show them to be "chiral proton-donors". The 1,3-diaminoarene moiety can easily be liberated from the chromium complex by decomplexation with I_2 as exemplified in four examples. The new methodology adds a powerful tool to the synthesis of organic diamines, and opens a new way to the formerly difficult-to-access class of chiral 1,3-diamines.

Introduction

Since the discovery by Alfred Werner that chelating diamines can enhance the kinetic stability of metal complexes[1] and the first isolation of chiral-at-metal complexes, chelating ligands, especially diamines, have become an integral part of coordination chemistry. Applications of chelating ligands range from detergents to biochemistry, from cancer therapy to metallurgy to new polymerization methods. Chiral derivatives have also found entry into homogeneous catalysis as rivals to phosphane ligands. A survey of the known and widely applied ligands shows most of them to be either 1,2-diamines or 1,4-diamines, the majority of which display C_2-symmetry, for example, diaminocyclohexane (dach),[2] diphenylethylenediamine (dpen)[3] or diaminobis(naphthalene) (binam).[4] A search using SciFinder, on the other hand, gives just 3 hits when inquiring for "chiral 1,3-diamines": a ferrocene derivative,[5] a class of anilines[6] useful as a chiral proton source, and some diaminopropanes derived from chiral aziridines.[7]

Chiral diamines have gained considerable importance in pharmaceutical chemistry, mostly 1,2-diamines, as in the synthesis of tamiflu;[8a,8b] in addition, examples of 1,3-diamines of pharmaceutical importance are known.[8c]

Chiral fluorinated compounds have gathered importance in chemistry in recent years,[9] as intermediates for further functionalization as well as target structures in pharmacological research.[10] Fluorine groups can replace C–H groups with relatively inert moieties with respect to human metabolism, increase lipophilicity (especially Ar–F) and acidity, act as bioisosteric mimics for other potentially more labile groups, contribute to peptidomimetics, and be valuable analytical probes involving the ^{19}F nucleus. In 1970, not more than 2% of pharmaceuticals contained fluorine compared to 18% in 2006. In the same year, 9 out of 31 drugs approved in the U.S.A. contained fluorine. Because the fluorine atom has to be introduced stereoselectively, en-

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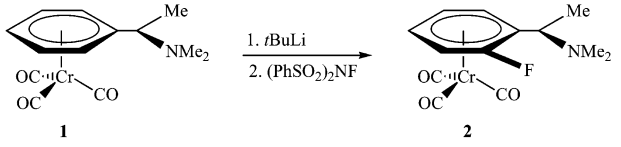
antio- and diastereoselective fluoro-functionalization remains a field of continuing chemical research.[11]

We have recently investigated the chemistry of chiral diphosphanes (the "Daniphos" ligands),[12] based on an optically active [η^6-arene]tricarbonylchromium backbone,[13] and have found many applications for them in homogeneous catalysis, where they rival the better-known and industrially important Josiphos ligands.[12j,12k,12m] Both ligand classes are based on the same structural principle of combining central and planar chirality and reveal C_1-symmetry. We have now found a new highly modular method to prepare C_1-symmetric chiral 1,3-diamines based on the same chiral organometallic framework.

Results and Discussion

In some of our recent contributions, we reported on the synthesis and application of the modularly built planar-chiral Daniphos ligand for stereoselective catalysis.[12] The starting material for the synthesis of Daniphos is [(*R*)-(1-phenyl)ethyldimethylamine]tricarbonylchromium (**1**).[14] Our approach to chiral 1,3-diphosphanes or similar derivatives employed a successive electrophilic exchange of the ring proton in the 2-position followed by a nucleophilic exchange of the dimethylamino group via a chloro intermediate. This method was only limited by the availability of suitable electrophiles or nucleophiles, and enabled us to build a whole library of new ligands.[12j,12l] This methodology has also been successfully applied by Bolm and Knochel to other organometallic frameworks.[15]

We have now discovered that after diastereoselective electrophilic fluorination[11] employing *N*-fluoro-benzenesulfonimide (NFSI), the resulting 2-fluoro derivative **2** can be isolated in good yields (77%) (Scheme 1).



Scheme 1. Diastereospecific electrophilic *ortho*-fluorination.

The reaction proved to be diastereoselective—the other diastereomer could not be detected. The ^{19}F NMR spectrum of the crude reaction mixture showed only a single resonance at δ = –135.5 ppm (Figure 1). The fluoroarene complex was characterized by X-ray structure analysis (Figure 2; single crystals were obtained by slow evaporation of an ethereal solution).

The crystal structure of **2** contains two independent molecules in the asymmetric unit. These molecules are related to each other by pseudosymmetry, which confirms the envisaged course of the reaction, displaying the *ortho*-fluorinated complex in the expected (*R*,*R*)-configuration. The C–F bond lengths are 134.0(8) and 135.3(9) pm, which are typical values for fluoroarene chromium tricarbonyl complexes.[16,17] The fluoro substituent is situated almost in the

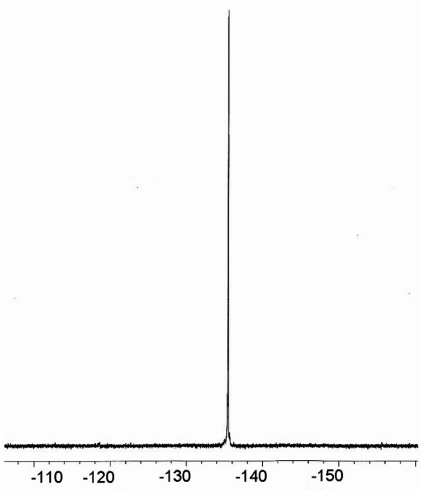


Figure 1. ^{19}F NMR spectrum of the crude reaction mixture of the electrophilic fluorination.

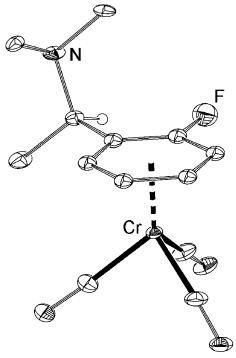
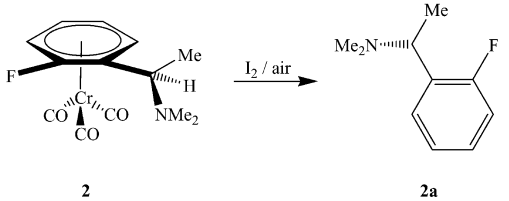


Figure 2. Displacement ellipsoid plot (30% probability) of one independent molecule in the asymmetric unit of fluoroarene complex **2**.

best plane defined by coordinated arene [2.2(3) pm and 0.3(4) pm].

Fluorinated compound **2** was easily decomplexed from the chromium tricarbonyl fragment by reaction with iodine in air in an ethereal solution, yielding the free *ortho*-fluorinated benzylamine in 76% yield (Scheme 2).

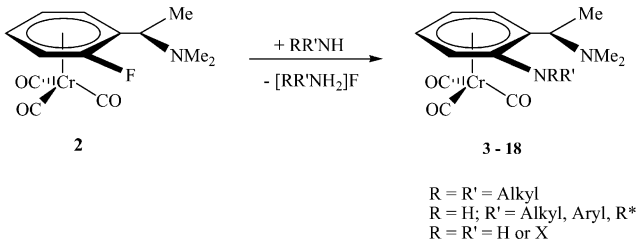


Scheme 2. Liberation of the *ortho*-fluorinated benzylamine.

(Fluorobenzene)tricarbonylchromium complexes are well known to undergo nucleophilic exchange reactions on the arene ring (S_NAr reactions) by common nucleophiles like amines, alkoxides, phosphides or nucleophilic carbon equivalents. The substitution reaction is facilitated by the electron-withdrawing nature of the chromium tricarbonyl moiety, which switches the nucleophilic nature of the aromatic

ring to an electrophilic character.[18] An elegant recent example by Imamoto demonstrated that an optically active BH_3-protected secondary phosphide could be attached to benzenetricarbonylchromium in this manner.[19] By the time Imamoto's paper appeared, we had also found that compound **2** could be employed for the synthesis of planar-chiral 1,3-P,N-ligands by nucleophilic substitution with lithium phosphides, especially those bearing unusual phosphane moieties which cannot be introduced via the classic electrophilic route[12] due to the lack of availability of the appropriate chlorophosphane (e.g. the phobane isomers). Essential for this finding was the *ipso*-specific course of the reaction (vide infra).[20]

Even more interesting was the discovery that amines can react in a similar manner. Simple stirring of **2** in an excess of amine at room temperature generates the 2-substituted arenetricarbonylchromium complexes in a straightforward and almost quantitative manner (Scheme 3). The reaction was performed without solvent in order to facilitate an easy procedure and a quantitative and benign reaction; precious chiral amines were recovered after completion of the reaction by a trap-to-trap distillation. Both secondary and primary amines, as well as some inorganic derivatives such as ethanolamine, hydroxylamine and hydrazine, could be used, and we have not yet found any limitation to this reaction.[21] In summary, the reaction sequence lithiation–fluorination–substitution represents an example of an Umpolung strategy, in which the original reactivity of the arene is reversed.



Scheme 3. Substitution of the fluorine for an amine.

To date, 18 diamines (plus another 3, see below) have been synthesized; they are depicted in Figure 3.

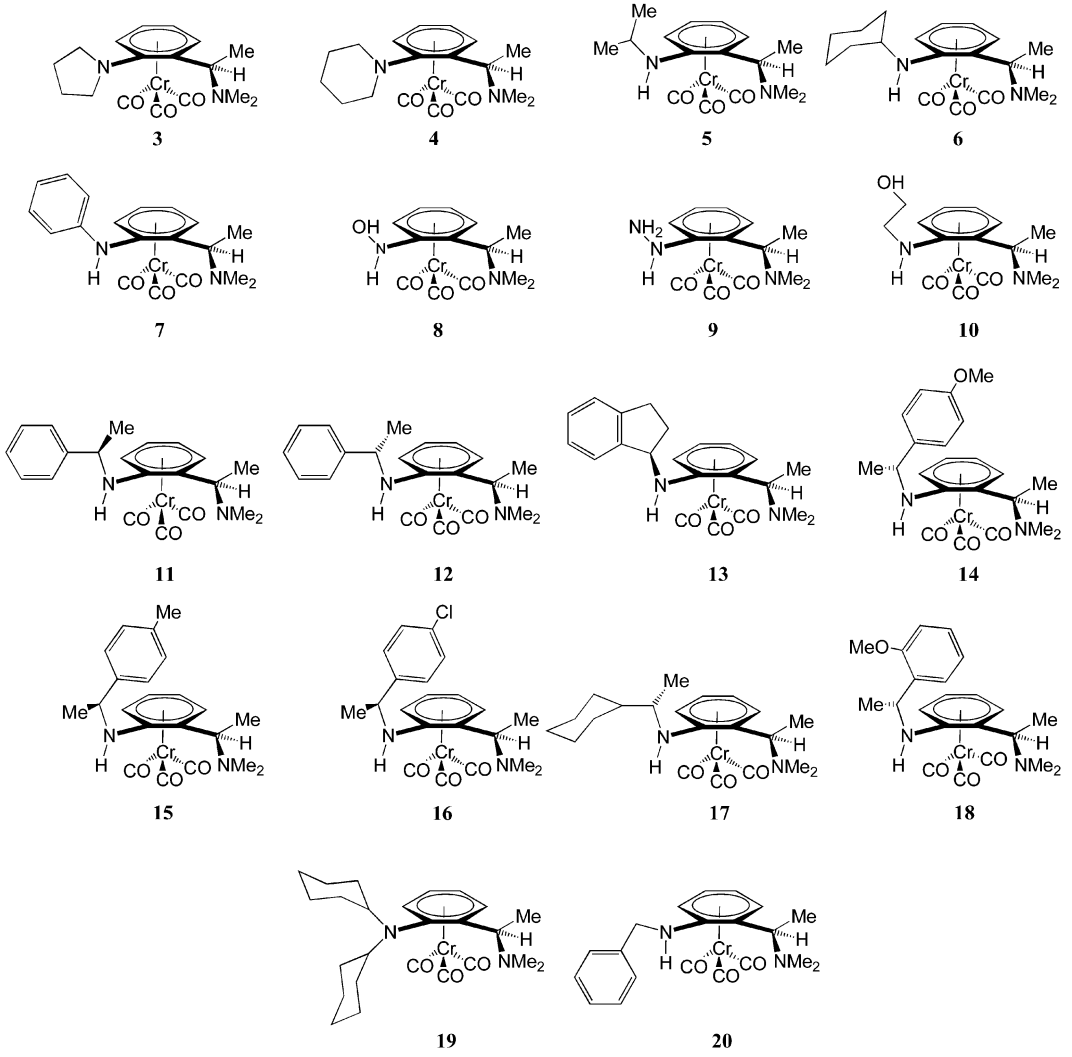


Figure 3. Depiction of the diamines derived from complex **2**.

The library of diamines includes simple alkyl- and aryl-substituted candidates (**3**–**7**), as well as derivatives bearing chiral sidechains in the amino groups (**11**–**18**). Compounds **8**–**10** incorporate unusual amines (ethanolamine, hydroxylamine, hydrazine), two of them (**8** and **10**) bearing ambident nucleophiles, which were found to coordinate via the more nucleophilic N-atom, obeying Kornblum's rule. We also tried to introduce amino groups with sterically demanding substituents like *tert*-butyl and (*R*)-1-(*tert*-butyl)ethyl, but even after repeated attempts, no diamine product could be detected. With these moieties, the tolerance of steric bulk in the *ortho*-position is over-extended, an observation which we also had made in the preparation of the analogous diphosphanes, where we found it still possible to introduce diisopropylphosphane but not bis(*tert*-butyl)phosphane.

Because NFSI is a relatively expensive reagent, we searched for a potentially cheaper alternative. We reasoned that the nucleophilic substitution should also be possible via a chloro-substituted chromium complex. Therefore an appropriate chlorinating agent for the lithiated chromium complex was needed, and we envisioned the use of hexachloroethane. The *ortho*-chlorination worked excellently, giving the *ortho*-chlorinated complex **21** in 96% yield as a single diastereomer (Scheme 4), yet the subsequent substitution with isopropylamine failed under standard reaction conditions, as well as at elevated temperature and prolonged reaction time (65 °C, 24 h, Scheme 5).

An X-ray analysis of compound **21** was conducted (single crystals were grown from an ethereal solution); a displacement ellipsoids plot is depicted in Figure 4.

Complex **21** crystallizes in the orthorhombic space group $P2_12_12_1$ with similar lattice parameters as its related F-substituted complex **2**, which crystallizes in the subspace group $P2_1$ of the former with two independent molecules in the asymmetric unit. Despite their resemblance with regard to unit cell parameters (see Table 2), no obvious analogous packing is observed. This might be ascribed to the fact that the free electron pair of the nitrogen atom of the complex **2** points almost exactly in the direction of the C_{ipso}–C_α bond,

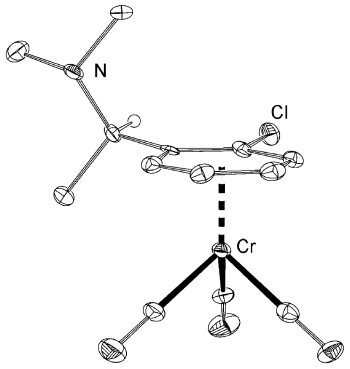


Figure 4. Displacement ellipsoid plot (30% probability) of chloroarene complex **21**.

whereas that of complex **21** is pointing in the opposite direction of the chlorine atom, whereby the two molecules exhibit significant conformational differences. The torsion angles between C^1–N–C^2 and C^3 of complexes **21** and **2** have been calculated to be 179° in the case of the chloro derivative and –65.3° and –61.7° for the fluoro derivative (for the two independent molecules in the asymmetric unit cell), respectively (Figure 5). The C–Cl bond length in complex **21** is 1.739(5) pm.

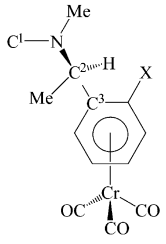
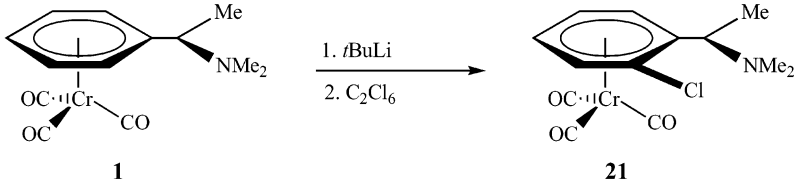
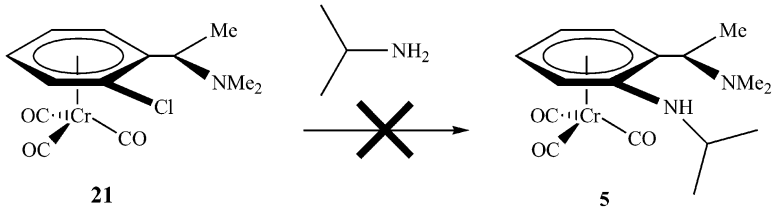


Figure 5. Assignment of atoms for the calculation of the torsion angles in the halo derivatives.

Not less than ten of the diamines have also been characterized by X-ray crystallography as well. In all cases, the course of the substitution reaction was specifically *ipso* with



Scheme 4. Diastereospecific *ortho*-chlorination.



Scheme 5. Failed amination with chloro complex **21**.

regard to the fluorine atom, and no side products of possible *cine*- and *tele*-substitutions were observed.[22] Some representative examples of these X-ray structures are shown in Figure 6.

An interesting difference emerged between the structures similar to complex **3**, with two tertiary amines, which showed no interaction between the 2 nitrogen atoms, and those like complex **6**, with the combination of a tertiary and a secondary amino group, in which a hydrogen bond appears to be formed between the NH group and the dimethylamino group. This causes the side chain bearing the dimethylamino group to undergo a conformational rotation towards the inner sphere of the complex, a phenomenon which we also observed for the diphosphane class of compounds on coordination to a metal centre forming a six-membered chelate.[12h]

An interesting case in this respect is also complex **10**, incorporating the ethanolamine moiety. In the analysis of its ^{1}H NMR spectrum, it was found that for one methylene group, each proton showed an independent resonance at δ = 3.33 and 3.21 ppm respectively. It seems likely that the hydrogen bond formed by NH-group induces a hindrance with respect to the free rotation of that methylene group on the NMR time scale, resulting in a different environment for each proton (which in fact cannot be due to diastereotopicity of the protons, as the other set of diastereotopic methylene protons shows only one resonance at δ = 2.57 ppm). In the solid, the ethanolamine side group is disordered over two different conformations, which both allow for the intramolecular hydrogen bond. In Figure 6 the major conformer is shown. In the cases of the secondary-tertiary diamines forming such a hydrogen bond, it seems justified to speak of a "chelated hydrogen", resembling another example of the rare class of a "chiral hydrogen", similar to the one recently described by Johnston.[23] In order to further investigate this aspect, we carried out a protonation experiment with the isopropyl-substituted diamine **5** using trifluoromethane sulfonic acid. We anticipated that

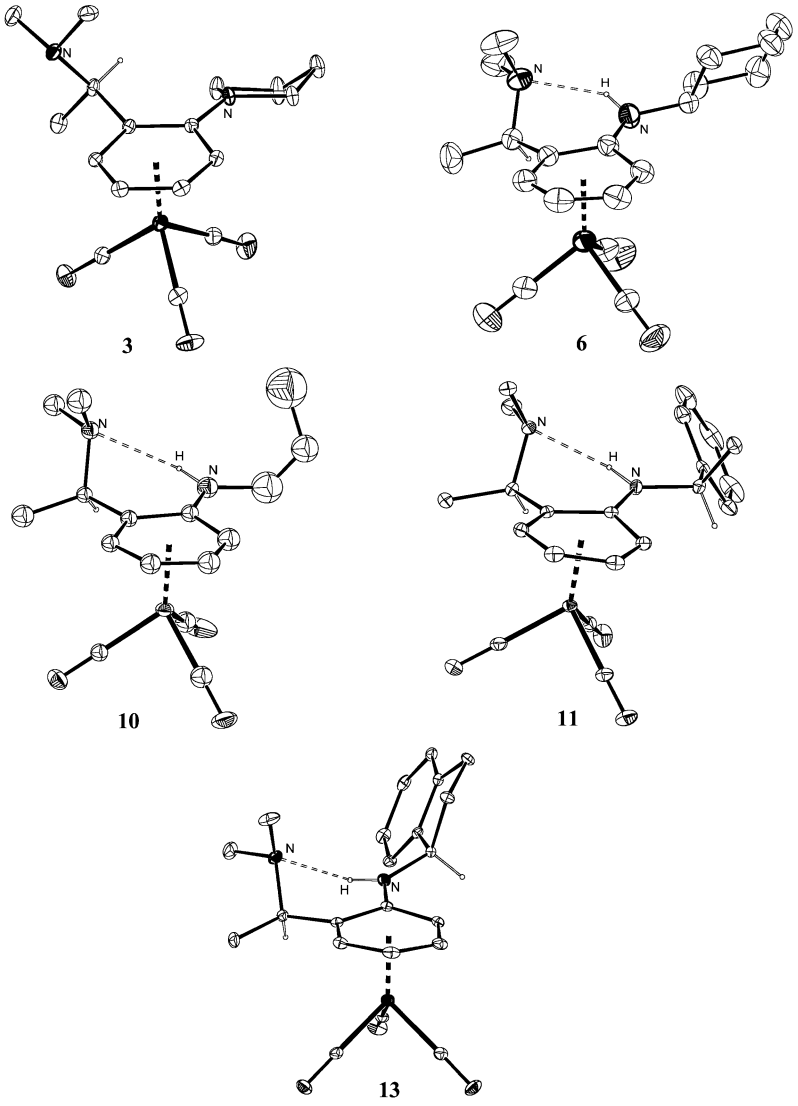
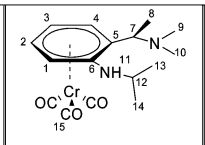
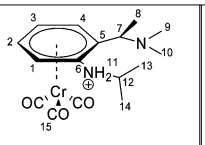


Figure 6. X-ray structures of compounds **3**, **6**, **10**, **11** and **13**.

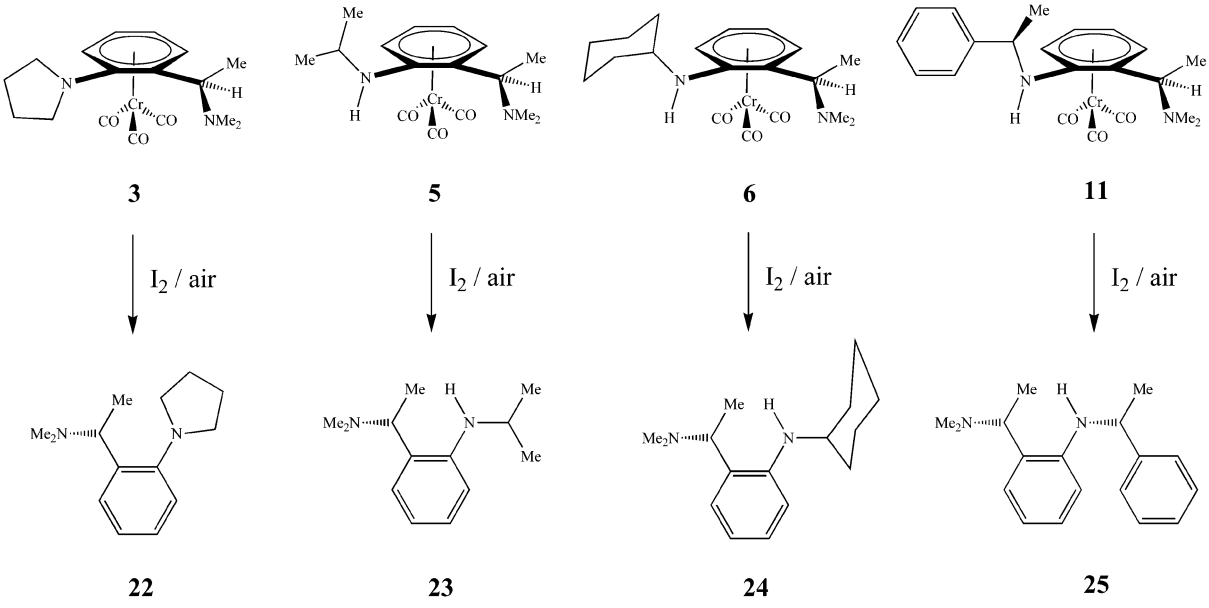
this additional proton should be captured between the two amino groups to form the ammonium cation, and therefore cause significant changes in the ^{1}H NMR spectrum. An evaluation of the ^{1}H NMR spectra of the unprotonated and protonated species showed remarkable differences. In Table 1, a detailed comparison is presented of the NMR spectra of compound **5** in its unprotonated and protonated forms, respectively.

Table 1. NMR spectroscopic data of compound **5** (unprotonated and protonated as [**5**H]O_3SCF_3).

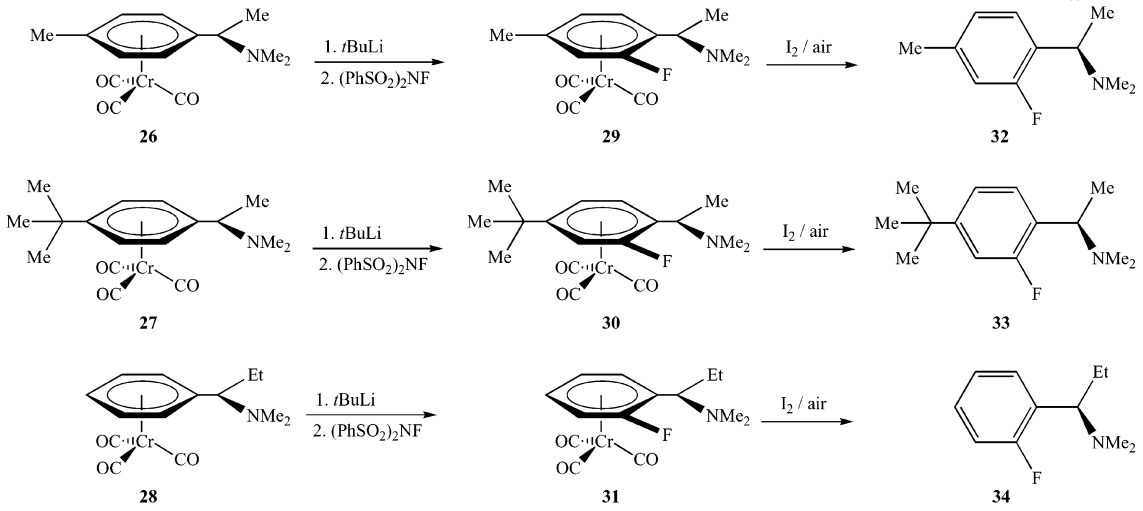
	 Unprotonated form			 Protonated form			
Proton	δ / ppm	mult.	J / Hz	δ / ppm	mult.	J / Hz	$\Delta\delta$ / ppm
H-8	1.157	d	6.4	1.789	d	6.7	0.632
H-13\14	1.230	d	5.9	1.209	d	6.1	–0.021
H-13\14	1.260	d	6.1	1.284	d	6.1	0.024
				2.852	d	4.8	0.618
H-9\10	2.234	s	–	2.893	d	4.6	0.659
H-12	3.502	q	6.4	3.605	m	–	1.103
H-7	3.871	q	6.8	4.784	m	–	0.913
H-3	4.794	t	6.2	4.997	t	6.2	0.203
H-4	4.872	d	6.8	5.048	d	7.0	0.176
H-2	5.651	t	6.6	5.873	t	6.6	0.222
H-1	5.719	d	6.4	6.076	d	6.4	0.357
				5.103	d	6.5	(–1.505)
H-11	6.608	d	5.1	9.182	s	–	–2.574

As expected, the most pronounced effects occur for those protons in close proximity to the protonated nitrogens. The NH proton (11-H) is shifted downfield by almost 2.6 ppm, while the CH protons on the side chains (7-H and 12-H) are both shifted by roughly 1 ppm. Also, the protons on the methyl group of the chiral α-chain (8-H) undergo a downfield shift of 0.6 ppm. The most interesting effect, however, is associated with the two methyl groups of the NMe_2-moiety: while in the unprotonated form they can freely rotate and thus give only one resonance in the NMR, in the protonated form of the molecule, their free rotation is stopped by the hydrogen bond formed by the additional proton and its positive charge. The two methyl groups become fixed in their positions and therefore chemically inequivalent and magnetically anisochronous, which results in an independent resonance for each methyl group. Moreover, both signals are shifted more than 0.6 ppm downfield. This phenomenon of hydrogen bonding and consecutive conformative adjustment of the side chain was already observed in the solid state of these diamines (compare the X-ray structures mentioned above), yet in solution it proved not to be strong enough to maintain this rigidity. An additional proton and its positive charge amplified this effect in order to yield a fixed side chain in solution as well as in the solid state. This finding strengthens the argument for a "chelated proton" mentioned above.

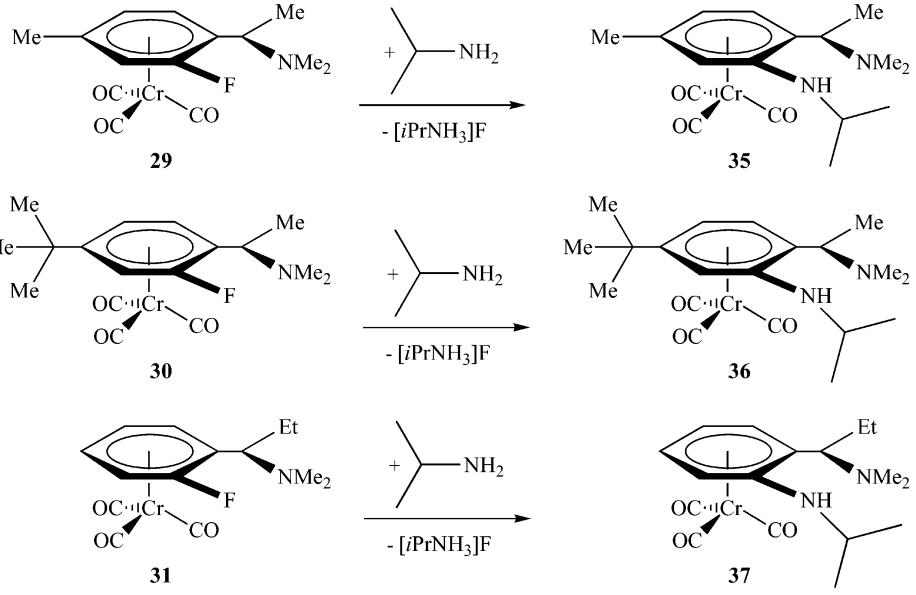
Especially interesting in terms of applications in transition-metal catalyzed transformations or organocatalysis are the derivatives bearing an α-chiral side chain in the substituted amine. They combine two stereogenic centers with planar chirality in the same molecule, along with the advantage of an easy and straightforward modular synthesis of the whole diamine. This reveals a promising prospect for a future application in asymmetric catalysis. The employment



Scheme 6. Decomplexation to liberate the free diamines **22**–**25**.



Scheme 7. Diastereoselective *ortho*-fluorination of alternative chromium complexes and liberation of the free fluorinated benzylamines.



Scheme 8. Amination of alternative *ortho*-fluorinated chromium complexes to form diamines with different substitution patterns on the aromatic ring and the chiral side chain.

of these compounds in organocatalytic aldol reactions[24,25] and other enamine/iminium catalytic transformations is currently investigated in our labs. It should be noted that diamines of this kind represent the first example of a planar-chiral organocatalyst next to the impressive example of a planar-chiral nucleophilic catalyst presented by Fu[26].

As representative examples compounds **3**, **5**, **6** and **11** were decomplexed by reaction with iodine in air in order to liberate the free organic diamines **22**–**25** (Scheme 6).

In order to prove the general applicability of our new method, some additional benzylamine(tricarbonyl)chromium complexes[12l,12n,12o] were subjected to the same synthetic protocol. This allows for the stereoselective synthesis of *ortho*-fluorinated benzylic amines as well as diamines bearing additional substituents on the aromatic ring and in the side chain bearing the stereogenic carbon atom (Scheme 7 and Scheme 8). Again, our method proved to be highly effective with regard to stereoselectivity (no other diastereomer was detectable in the fluorination or the substitution reaction) and yield (*ortho*-fluorination: 90–93%, decomplexation: 89–97%, amination: 87–89%, 70–80% overall).

Conclusions

Starting from the readily available precursor [(*R*)-(1-phenyl)ethyldimethylamine]chromium tricarbonyl and related benzylamine complexes, the *ortho*-fluoro derivative was synthesized by a new diastereospecific electrophilic fluorination protocol. Successive decomplexation delivered the free *ortho*-fluorinated benzylamines. This new method exhi-

bits great potential for the use in the stereoselective synthesis of fluorinated pharmaceuticals. The new protocol was used to generate a library of a new class of the rare chiral 1,3-diamines by a straightforward, high-yield and stereoconservative nucleophilic aromatic substitution reaction employing various kinds of primary, secondary and "inorganic" amines. Chiral amines can also be employed without loss of optical purity, yielding a new valuable class of planar-chiral diamines with two stereogenic centers in close proximity. The whole reaction sequence represents an example of an Umpolung strategy. The resulting diamines can be synthesized in a highly modular way, allowing for the synthesis of a broad library of diamines, which exhibit a valuable prospect for the use in asymmetric catalysis, both transition-metal-mediated and organocatalytic.

Experimental Section

General Remarks: All manipulations were carried out under nitrogen using standard Schlenk techniques. Solvents were dried and deoxygenated by standard procedures. Chromatography was carried out with Merck alumina 90. NMR spectra were recorded with a Varian Mercury 200 (^{1}H: 200 MHz, ^{13}C: 50 MHz, ^{19}F: 188 MHz), a Varian Unity 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) or a Bruker 400 MHz (^{1}H: 400 MHz, ^{13}C: 100 MHz) spectrometer at ambient temperature. IR spectra were recorded with a Perkin–Elmer FT-IR model 1720 X spectrometer. Mass spectra were obtained with a Finnigan MAT 95 spectrometer, using the CI (isobutane as reactand gas) and EI recording techniques. Complexes **1** and **26**–**28** were synthesized according to the literature.[12] $(PhSO_2)_2NF$ was purchased from ABCR; amines were commercially available used without further purification. Chiral amines were generously donated by BASF AG (Dr. Ditrich).

[(*R*,*R*)-1-Fluoro-2-(1-dimethylaminoethyl)benzene]tricarbonylchromium (2): In a Schlenk tube, [(*R*)-(1-phenyl)ethyldimethylamine]tricarbonylchromium (**1**, 5.35 g, 18.8 mmol) was dissolved in ether (150 mL), cooled to –80 °C, and *t*BuLi (1.5 M, 15 mL, 22.6 mmol, 1.15 equiv.) was added dropwise over 1 h. The solution was stirred for 1 h, after which it was warmed to –60°C, and a yellowish precipitate occurred. The solution was re-cooled to –80 °C, and the precipitate was redissolved by adding THF (20 mL) dropwise. A solution of *N*-fluorobenzenesulfonimide (7.13 g, 22.6 mmol, 1.15 equiv.) dissolved in THF (40 mL) was added dropwise over 0.5 h. The solution was warmed to room temperature overnight. The resulting precipitate was filtered through celite, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (alumina/diethyl ether). The product was recrystallized from diethyl ether at –30 °C. Yield 4.40 g (14.5 mmol, 77%). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1978, 1818 (CO) cm^{-1}. MS (CI): *m*/*z* (%) = 304 (81) [M + 1$^{+\cdot}$]. ^{1}H NMR (200 MHz, C_6D_6): δ = 0.92 (d, 3 H, CHC*H*$_3$), 1.84 (s, 6 H, N*Me*$_2$), 3.65 (q, 1 H, C*H*CH$_3$), 3.81 (dd, 1 H, H_{ar}), 4.38 (m, 2 H, H_{ar}), 4.81 (d, 1 H, H_{ar}) ppm. ^{13}C NMR (200 MHz, C_6D_6): δ = 12.22 (CH*C*H$_3$), 40.60 (N*Me*$_2$), 61.47 (*C*HCH$_3$), 84.87 (C_{ar}), 91.83 (C_{ar}), 93.36 (C_{ar}^{ipso}), 93.51 (C_{ar}), 95.65 (C_{ar}), 138.06 (C_{ar}^{ipso}), 232.28 (*C*O) ppm. ^{19}F NMR (188 MHz): δ = –132.5 ppm. $C_{13}H_{14}CrFNO_3$ (303.23): calcd. H 4.65, C 51.49; found H 4.67, C 51.74.

1-F-2-[(*R*)-Me$_2$NCHMe]C$_6$H$_4$ (2a): Compound **5** (180 mg, 0.594 mmol) was dissolved in ether and some crystals of iodine were added. The solution was stirred under air overnight. The slurry was filtered through a pad of Celite. The ether was evaporated, and the clean product was obtained as a colourless oil. Yield 75 mg (0.449 mmol, 76%). MS (EI): *m*/*z* (%) = 167 (9) [M$^{+\cdot}$]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (d, *J* = 6.8 Hz, 3 H, CH*Me*), 2.21 (s, 6 H, NMe$_2$), 3.74 (q, *J* = 6.8 Hz, 1 H, C*H*Me), 7.01 (m, 1 H, H_{ar}), 7.11 (td, *J* = 7.5, 1.3 Hz, 1 H, H_{ar}), 7.20 (m, 1 H, H_{ar}), 7.39 (td, *J* = 7.5, 2.0 Hz, 1 H, H_{ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5 (CH*Me*), 42.8 (NMe$_2$), 57.4 (d, J_{CF} = 1.8 Hz, *C*HMe), 115.3 (d, J_{CF} = 23.5 Hz, C_{CF}^{ortho}), 123.9 (d, J_{CF} = 3.4 Hz, C_{ar}), 128.2 (d, J_{CF} = 7.5 Hz, C_{CF}^{meta}), 128.8 (d, J_{CF} = 5.0 Hz, C_{ar}), 130.20 (d, J_{CF} = 13.8 Hz, C_{CC}^{ipso}), 160.66 (d, J_{CF} = 245.0 Hz, C_{CF}^{ipso}) ppm. ^{19}F NMR (188 MHz, $CDCl_3$): δ = –118.49 ppm. $C_{10}H_{14}FN$ (167.21): calcd. H 8.44, C 71.83; found H 8.38, C 71.11.

General Procedure for the Substitution of Fluorine by an Amino Group: In a small Schlenk tube, fluoro complex **2** (1.0 mmol, 303 mg) was dissolved in the respective amine (2 mL). For complexes **11**–**13**, a mixture of H_2O/THF was added until all solids were dissolved. The solutions were degassed by three freeze/purge cycles, and were allowed to stir at room temperature for three days. All liquids were removed under reduced pressure (in cases where chiral amines were used they could be easily recovered by condesation into a cooling trap), and the residue was purified by column chromatography (alumina/ether). The resulting diamines were easily be recrystallized from ether, with slow evaporation yielding single crystals suitable for X-ray analysis in most cases. All compounds melted at a melting point higher than 150 °C with decomposition.

(*R*,*R*)-[η^6-(Me$_2$NCHMe)C$_6$H$_4$N(CH$_2$)$_4$]Cr(CO)$_3$ (3): Yield 344 mg (0.97 mmol, 97%). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 1896, 1975 (CO) cm^{-1}. MS (CI): *m*/*z* (%) = 354 (17) [M$^{+\cdot}$], 355 (7) [M + 1$^{+\cdot}$]. ^{1}H NMR (500 MHz, C_6D_6): δ = 1.23 (d, *J* = 6.8 Hz, 3 H, CH*Me*), 1.40 (m, 4 H, C*H*$_2$), 1.87 (s, 6 H, N*Me*$_2$), 2.78–2.95 (br. m, 4 H, NC*H*$_2$), 3.50 (q, *J* = 6.6 Hz, 1 H, C*H*Me), 4.29 (m, 1 H, H_{ar}) 4.34 (m, 1 H, H_{ar}), 4.87 (m, 1 H, H_{ar}), 5.39 (m, 1 H, H_{ar}) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 15.56 (CH*Me*), 25.63 (2 C, *C*H$_2$), 41.37 (N*Me*$_2$), 52.25 (2 C, N*C*H$_2$), 57.94 (*C*HMe), 80.69 (C_{ar}), 83.23 (C_{ar}), 96.15 (C_{ar}), 97.24 (C_{ar}), 102.13 (C_{ar}^{ipso}), 132.38 (C_{ar}^{ipso}), 235.14 (*C*O) ppm. $C_{17}H_{22}CrN_2O_3$ (360.4): calcd. H 6.27, C 57.62; found H 6.29, C 57.84.

X-ray Structure Determinations: Crystal data and details of the structure determinations are listed in Table 2. Data collections were performed with a Bruker Smart CCD (Mo-K_α radiation, λ = 0.71073 Å, graphite monochromator) area detector. All data were collected at 110 K except for **6**, which was collected at 293 K. The structures were solved by direct methods (SHELXS-97)[27] and refined by full-matrix least-squares procedures based on F^2 with all measured reflections (SHELXL-97)[28] The SADABS[29] program was used for absorption correction of the structures. All non-hydrogen atoms with the exception of the disordered ethanolamines in **10** were refined anisotropically. All H atom positions were introduced at their idealized positions [*d*(CH) = 0.98 Å, *d*(NH) = 0.95 Å] and were refined using a riding model. The absolute configuration was confirmed by evaluation of the Flack[30] parameter. The crystal structure of **2** is highly pseudosymmetric, the match of electron density corresponding with its centrosymmetric space group is 84%. The crystal structure of **10** presents disorder for the ethanolamine fragment, which can occupy two different positions in the solid state.

CCDC-615999 (for **2**), -616000 (for **3**), -616001 (for **6**), -616002 (for **10**), -616003 (for **11**), -616004 (for **13**), and -679639 (for **21**) contain the supplementary crystallographic data for this paper. These data

Table 2. Experimental X-ray diffraction parameters and crystal data.

Complex	**2**	**3**	**6**	**10**	**11**	**13**	**21**
Empirical formula	$C_{13}H_{14}CrFNO_3$	$C_{17}H_{22}CrN_2O_3$	$C_{19}H_{26}CrN_2O_3$	$C_{15}H_{21}CrN_2O_4$	$C_{21}H_{24}CrN_2O_3$	$C_{22}H_{24}CrN_2O_3$	$C_{13}H_{14}CrClNO_3$
Formula weight	303.25	354.37	382.41	345.34	404.42	416.43	319.70
Crystal size [mm]	0.05 × 0.25 × 0.24	0.17 × 0.17 × 0.67	0.22 × 0.29 × 0.52	0.21 × 0.21 × 0.75	0.07 × 0.13 × 0.60	0.30 × 0.57 × 0.63	0.12 × 0.15 × 0.54
Crystal habit, color	plate, light yellow	rod, light yellow	block, light yellow	rod, light yellow	plate, light yellow	rod, light yellow	rod, light yellow
Crystal system	monoclinic	orthorhombic	orthorhombic	orthorhombic	monoclinic	orthorhombic	orthorhombic
Space group	$P2_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_1$	$P2_12_12_1$	$P2_12_12_1$
a [Å]	6.7652(9)	8.5469(16)	9.471(3)	6.5545(13)	8.4286(16)	8.3252(15)	7.125(11)
b [Å]	13.6312(19)	16.907(3)	12.081(4)	12.428(3)	9.6196(18)	10.2597(19)	12.79(2)
c [Å]	14.708(2)	23.850(5)	17.375(5)	19.735(4)	12.639(2)	23.991(4)	15.39(2)
α [°]							
β [°]	92.294(3)				92.062(4)		
γ [°]							
V [Å^3]	1355.3(3)	3446.4(11)	1988.0(11)	1607.6(5)	1024.1(3)	2049.2(6)	1402(4)
D [g cm^{-3}]	1.486	1.366	1.278	1.427	1.312	1.350	1.514
Z	4	8	4	4	2	4	4
μ (Mo-K_α) [mm^{-1}]	0.858	0.679	0.594	0.730	0.581	0.583	1.008
F(000)	624	1488	808	724	424	872	656
θ range [°]	2. 40–27.45	2.41–27.45	2.05–28.40	2.06–5.00	2.66–28.33	2.16–28.47	2.65–25.99
Reflections collected	17491	56050	41536	15396	7071	37365	15603
R_{int}	0.0836	0.0474	0.0397	0.0397	0.0179	0.0470	0.0869
Unique refl. in refin.	6181	7861	4976	2829	4989	5155	2741
Refl. with $I > 2\sigma(I)$	4177	7138	4607	2687	4712	5002	2479
Param. refined	253	421	229	201	248	256	175
$R1$ [$2\sigma(I)$]	0.0696	0.0418	0.0448	0.0550	0.0368	0.0290	0.0546
$R1$ (all data)	0.1098	0.0487	0.0487	0.0578	0.0393	0.0301	0.0620
wR_2	0.1500	0.1120	0.1123	0.1457	0.0951	0.0771	0.1106
Flack parameters	–0.02(4)	–0.013(16)	–0.01(2)	0.02(4)	0.000(16)	0.009(13)	0.09(4)
Goodness of fit	1.052	1.036	1.089	1.029	1.053	1.064	1.084
Diff. peak/hole [e/Å^3]	0.66/–0.47	–0.23/0.52	–0.19/0.41	–0.49/1.49	–0.23/0.43	–0.36/0.42	–0.43/0.49

can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see also the footnote on the first page of this article): Experimental, spectroscopic and analytical details for compounds **4**–**37**, solid-state structures of compounds **4**, **5**, **12** and **14**.

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