Unexpected behaviour of tosylated and acetylated imidazolinium salts

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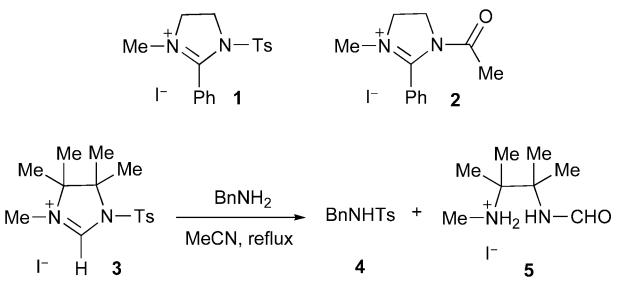
Tosylated and acetylated imidazolinium salts revealed an unexpected reactivity when treated with methyl iodide or benzyl bromide. Moreover an unprecedented acid-catalysed rearrangement for an acetylated imidazolinium salt was observed during an anion metathesis.

Introduction

Tetrahydrofolate coenzymes, which are part of a one-carbon fragment biochemical transfer,[1,2] can be mimicked by several simple imidazolinium salts.[3,4] For example, the imidazolinium iodide salt analogues **1**, **2** and **3** (Scheme 1) were first prepared from the corresponding imidazolines and MeI by Pandit's group.[5]



Scheme 1

The much hindered tosylated analogue **3** revealed a different behaviour than less hindered salts. When heated with an amine, *e.g.* benzylamine, the tosyl group was attacked by the nucleophile and the imidazoline ring left the molecule and was isolated as the hydrolytic product **5**.[5] This observation is very rare for imidazolinium analogues, however very well known for tosylated imidazolium salts, like 1-(toluenesulfonyl)-3-methylimidazolium triflate, which has been used as a tosylating reagent for alcohols[6] and amines.[7,8] The resulting imidazol ring in this reaction is not hydrolysed.

Moreover, a few chiral imidazolinium salts have recently been reported as chiral ionic liquids.[9,10] However, the examples of this emerging class of chiral ionic liquids remain few compared to other types of chiral ionic liquids.[11,12] In addition it is possible to apply 2-phenyl substituted imidazolinium salts as ionic liquids with strong bases.[13]

Recently, we have reported the application of some achiral imidazolinium salts as catalysts for the aza Diels–Alder reaction.[14] The salts may be considered as part of the limited number of metal-free Lewis acids[15–21] and could contribute to the important research field of organocatalysis.[22,23] In order to apply chiral analogues of the salts as catalysts, we were interested in preparing chiral analogues of **1** and **2**, since the electron withdrawing groups could increase the catalytic activity of these salts. Here we would like to discuss some unexpected results along the synthetic route towards some of the desired chiral tosyl and acetyl substituted imidazolinium salts, which, to the best of our knowledge, have not been reported so far.

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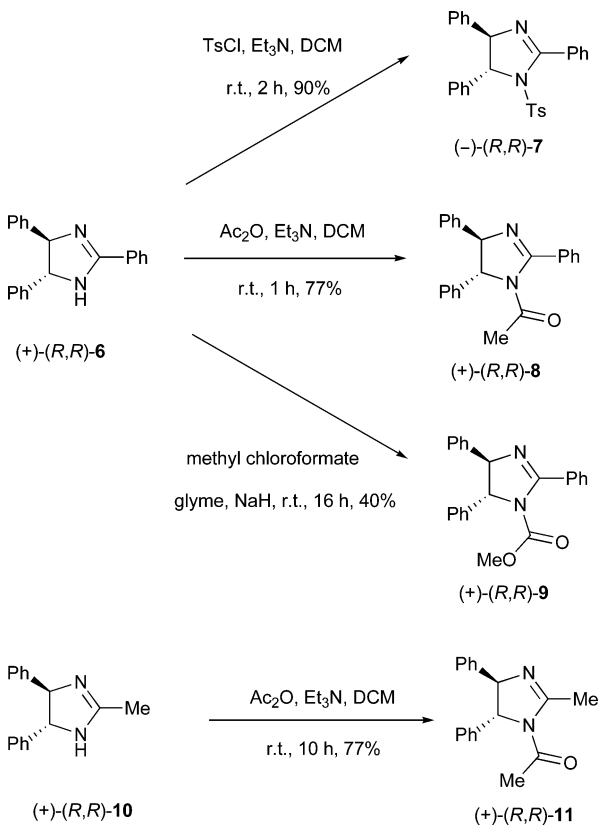
Results and discussion

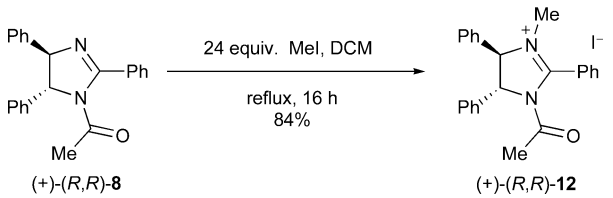
First the precursors for the desired salts were prepared. Therefore, (+)-(*R*,*R*)-**6**,[24] prepared from (+)-(*R*,*R*)-1,2-diphenyl-1,2-ethylenediamine,[25] was treated with tosyl chloride or acetic acid anhydride in the presence of triethylamine to give the imidazoline derivatives (−)-(*R*,*R*)-**7** and (+)-(*R*,*R*)-**8** in 90 and 77% yield, respectively (Scheme 2). In addition imidazoline (+)-(*R*,*R*)-**9** was synthesised in 40% yield, by the reaction of methyl chloroformate with (+)-(*R*,*R*)-**6** in the presence of sodium hydride (Scheme 2).



Scheme 2

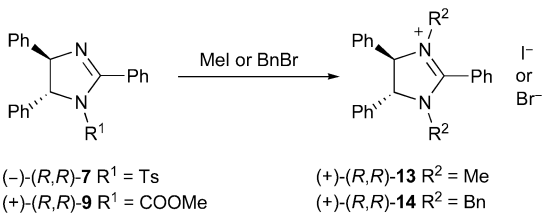
Moreover, imidazoline (+)-(*R*,*R*)-**11** was obtained *via* an acetylation of (+)-(*R*,*R*)-**10**,[26] derived from (+)-(*R*,*R*)-1,2-diphenyl-1,2-ethylenediamine,[25] in 77% yield (Scheme 2).

In order to transform imidazoline **8** into the desired salt **12** the method reported for salts **1** and **2** was applied.[5] An excess of methyl iodide was refluxed with **3** in dichloromethane for 16 h. Therefore (+)-(4*R*,5*R*)-1-acetyl-2,4,5-triphenyl-*trans*-4,5-dihydroimidazole (**8**) yielded (+)-(4*R*,5*R*)-1-acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium iodide (**12**) in 84% (Scheme 3).



Scheme 3

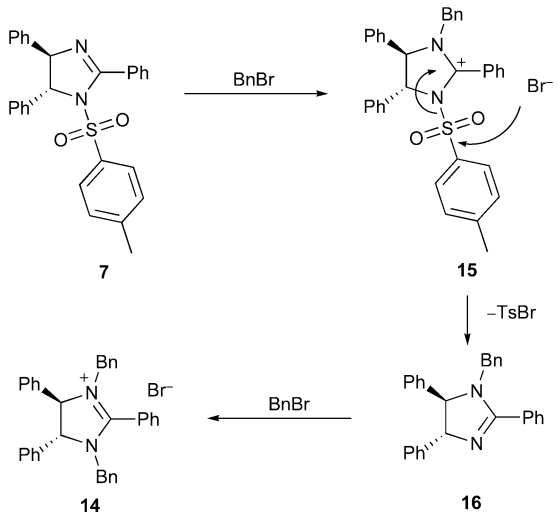
Additionally, imidazolines **7** and **9** were treated the same way. However, in both cases not the expected salts were found as the major products. Instead the dimethylated salt **13** was observed (Scheme 4). In the crude NMR mainly the dimethylated product **13** was detected besides the starting material and the desired product. The latter could be isolated neither *via* column chromatography nor by recrystallisation. When the reaction was performed in dichloromethane at 85 °C in a sealed vessel, only **13** was obtained from **7** and **9** in quantitative yield. The replacement of methyl iodide with dimethyl sulfate resulted in both cases in a complex mixture of compounds. When **11** was treated with methyl iodide only a complex mixture of compounds was found.



Scheme 4

After these unexpected results 3 equiv. of benzyl bromide was used in the reaction with **7** and **9**, respectively (Scheme 4). A reaction in refluxing dichloromethane was not observed. When the reaction was performed at 85 °C in a sealed tube, mainly the dibenzylated product **14** was found next to some starting material. In acetonitrile a total conversion to **14** took place. The bromide salt **14** was isolated in a yield of 74% after recrystallisation. A repeat of the reaction in acetonitrile and 1 equiv. of benzyl bromide resulted in the isolation of the starting material and **14** in a ratio of 1 : 1 by NMR.

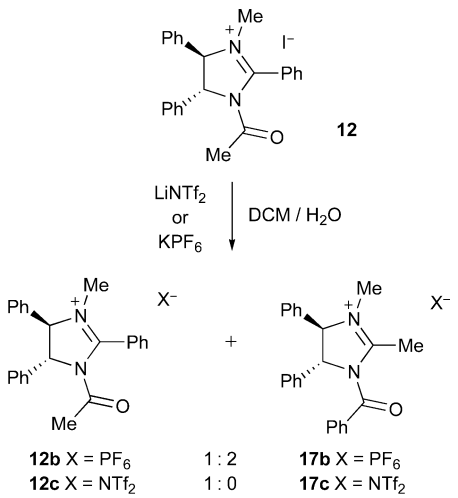
These results may be explained by the following proposed mechanism (Scheme 5), taking the behaviour of salt **3** (Scheme 1) into consideration. In the first step the desired product, *e.g.* **15** is formed. Taking the nucleophilicity of halide anions in polar aprotic solvents into account, the bromide anion of salt **15** can attack at the sulfonyl group in a bimolecular substitution reaction. The formation of tosyl bromide is assisted by the generation of the very good leaving group, the imidazole **16**. In the last step **16** can



Scheme 5

react with another benzyl bromide molecule to the dibenzylated product **14**. The starting material **7** reacts with benzyl bromide far slower then **16**, due to the electron withdrawing tosyl group, which explains, that even when just 1 equiv. of benzyl bromide was used **14** and **7** were observed. When the reaction was repeated with 0.9 equiv. of benzyl bromide and stopped after 6 h, it was possible to isolate **16** in 5% yield through column chromatography. For the reactions involving **9** and methyl iodide a similar mechanism could be assumed.

In order to transform salt **12** into analogues with different anions, **12** was stirred in the presence of 1.5 equiv. of KPF_6 or $LiNTf_2$ in a mixture of dichloromethane and water. The organic phase was separated and washed three times with water. The more lipophilic ion pair remains in the organic solvent. In the case of $LiNTf_2$ the expected salt **12c** was isolated in pure form in 90% yield (Scheme 6). However, the corresponding PF_6^- salt was isolated in only 48% yield. The result of the simple anion exchange was quite amazing. In the NMR spectra all aliphatic signals were twice as much as required and it was found that the unexpected product (+)-(4*R*,5*R*)-1-benzoyl-2,3-dimethyl-4,5-diphenyl-*trans*-imidazolinium hexafluorophosphate (**17b**) was



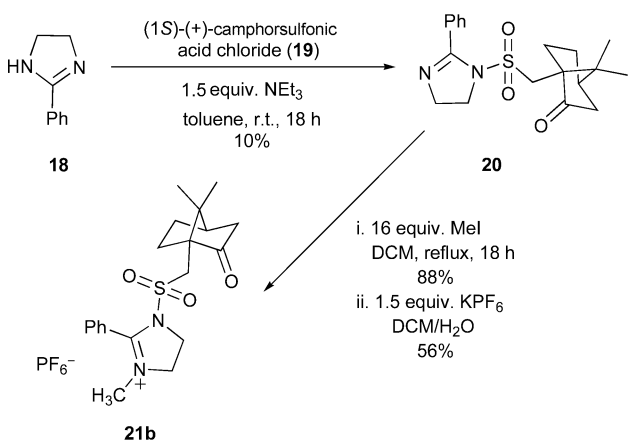
Scheme 6

present. The ratio of the two products was calculated according to the ^{1}H NMR spectra with **12b** : **17b** = 1 : 2.

After the discovery of the unexpected rearrangement product **17b**, further experiments were carried out to find mechanistic clues to describe the reaction in detail. A possible reason for the result may be due to the use of KPF_6. Considering that potassium hexafluorophosphate contains traces of HF and can slowly decompose further in water, a catalytic amount of acid was used to influence the 1 : 2 ratio of the mixture **12b** : **17b**. Manipulation of the mixture **12b** : **17b** = 1 : 2 with a catalytic amount of aqueous HCl in dichloromethane shifted the equilibrium to **12b** : **17b** = 1 : 3. The reduced solubility of HCl in dichloromethane could explain the poor movement of the ratio. Therefore, the next reaction was carried out with a solution of trifluoroacetic acid in dichloromethane. Now the generation of the rearrangement product **12b** : **17b** was more favoured and appeared according to ^{1}H NMR spectra in a ratio of 1 : 6 after 24 h. No total conversion of **12b** to **17b** was obtained, probably an equilibrium exists, wherein an excess of **17b** is thermodynamically favoured. In view of the empiric support, that the rearrangement is catalysed by acidic conditions, a last procedure was tested. (+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium trifluoromethanesulfonimide **12c** was stirred with a catalytic amount of trifluoroacetic acid in dichloromethane. The expected mixture of **12c** : **17c** occurred in a ratio of 1 : 4 after 24 h.

Two possible mechanisms are imaginable: first a rearrangement *via* non-ring opening. After the formation of an enol a four membered ring could be formed followed by a 1,3-phenyl shift. Advantages of this proposed mechanism are no ring openings, permanently just one charge in the molecule, which can be stabilised by tautomerism, and the necessity of a catalytic amount of acid to form an enol in the first step. On the other hand, there is also a disadvantage: constitution of the positively charged [3.2.0]-system in the transition state. The second possible mechanism would be a ring opening of the cation, followed by the formation of the new salt with the former carbonyl carbon atom at the C-2 position.

Finally, in order to explore the behaviour of an aliphatic sulfone rest group, (1*S*)-(+)-camphorsulfonyl-(2-phenyl-4,5-dihydro)-imidazole (**20**) was prepared in a low yield (Scheme 7) from 2-phenyl-4,5-dihydroimidazole (**18**)[5] and (1*S*)-(+)-camphorsulfonic acid chloride (**19**) under basic conditions. The imidazoline **20** was then treated with methyl iodide and after an anion exchange the expected product **21b** was isolated. No side reactions were observed (Scheme 7).



Scheme 7

In conclusion, we have reported some unexpected behaviour of tosylated and acetylated imidazolinium salts, which may be important to consider for the preparation of new imidazolinium based ionic liquids and tetrahydrofolate coenzyme model compounds.

Experimental

General experimental

All reactions were conducted under a protective atmosphere of dry nitrogen. Dichloromethane and acetonitrile were distilled from calcium hydride. All other chemicals, whose preparation is not described below, were bought from Aldrich, Fluka, Merck or Lancaster and were used without further purification. 2-Phenyl-4,5-dihydroimidazole (**18**),[5] (+)-(4*R*,5*R*)-2,4,5-triphenyl-*trans*-4,5-dihydro-1*H*-imidazole[24] (**6**) and (+)-(4*S*,5*S*)-2-methyl-4,5-diphenyl-*trans*-4,5-dihydro-1*H*-imidazole[26] (**10**) were prepared according to literature procedures. Reactions were monitored by TLC with Merck Silica gel 60 F_{254} plates or with neutral aluminium oxide 60 F_{254} plates. Flash column chromatography[27] was performed on Sorbisil C-60 or active neutral aluminium oxide 90. Infrared spectra were recorded on a Vector 22 FT-IR from Bruker. NMR spectra were performed in $CDCl_3$ at ambient temperature on a Bruker AMX 400 and a Bruker AC 200F. The following symbols are used to analyse the ^{13}C-spectra: +: primary or tertiary carbon, −: secondary carbon, q: quaternary carbon. Mass spectra were recorded on MS 5889 B from Hewlett Packard. Electron spray mass spectrometry was performed directly on a MS LC/MSD 1100 MSD from Hewlett Packard. High resolution mass spectra were recorded by Dr Dräger at the Institute of Organic Chemistry, University of Hanover. Elemental analyses were carried out by the Institute of Pharmaceutical Chemistry, Technical University of Braunschweig and are reported as the average of two runs. Optical rotations were measured on a Perkin-Elmer 243 B polarimeter. Melting points were taken with an apparatus after Dr Tottoli and are uncorrected.

(+)-(4*R*,5*R*)-1-(Toluene-4-sulfonyl)-2,4,5-triphenyl-*trans*-4,5-dihydroimidazole (7). (+)-(4*R*,5*R*)-2,4,5-Triphenyl-*trans*-4,5-dihydro-1*H*-imidazole (**6**) (2.5 g, 8.4 mmol) and triethylamine (1.15 mL, 8.4 mmol) were dissolved in dry dichloromethane (20 mL). After adding tosyl chloride (1.76 g, 9.2 mmol) the resulting mixture was stirred for 2 h at r.t. The precipitate was filtered off and the filtrate was washed with dilute sodium bicarbonate solution and dried (Na_2SO_4). Evaporation yielded a thick oil, which was purified by column chromatography on silica with petroleum ether–ethyl acetate (5 : 1) as the eluent to give the title compound **7** as a white solid (3.4 g, 7.5 mmol, 90%). $[\alpha]_D^{24}$ = −150 (c = 1.02, CH_2Cl_2), mp 122 °C; MS (EI), m/e 453 (M + 1, 10%), 297 (70), 91 (100); IR (KBr) 3443w, 1634s, 1368s, 1175s, 761s cm^{-1}; ^{1}H NMR (200 MHz) δ 7.87–7.82 (m, 2 H, Ar–H), 7.56–7.40 (m, 8 H, Ar–H), 7.25–7.05 (m, 7 H, Ar–H), 6.83–6.78 (m, 2 H, Ar–H), 5.10 (s, 2 H, C–H), 2.40 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 159.9 (q, N*C*N), 144.7 (q, Ar), 142.5 (q, Ar), 141.8 (q, Ar), 134.9 (q, Ar), 131.4 (+, Ar), 130.5 (q, Ar), 130.0 (+, Ar), 129.7 (Ar), 129.3 (+, Ar), 128.7 (+, Ar), 128.3 (+, Ar), 128.0 (+, Ar), 127.9 (+, Ar), 127.4 (+, Ar), 126.2 (+, Ar), 126.0 (+, Ar),

77.4 (+, C(5)–H), 72.6 (+, C(4)–H), 21.7 (+, Me). Anal. calcd for $C_{27}H_{24}O_2N_2S_1$: C, 73.61; H, 5.49; N, 6.36. Found: C, 73.87; H, 5.32; N, 6.33%.

(+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-*trans*-4,5-dihydroimidazole (8). (+)-(4*R*,5*R*)-2,4,5-Triphenyl-*trans*-4,5-dihydro-1*H*-imidazole (**6**) (1.0 g, 3.36 mmol) was dissolved in dry dichloromethane (12 mL). Acetic anhydride (0.32 mL, 3.36 mmol) and triethylamine (0.32 mL, 3.36 mmol), dissolved in dichloromethane (2 mL), were added to the mixture and left to stir for 1 h at r.t. The mixture was washed with water and dried (Na_2SO_4). After evaporation of the solvent, the crude product was purified by column chromatography on Al_2O_3 using petroleum ether–ethyl acetate (4 : 1) as the eluent to give the title compound **8** as a colourless oil (0.88 g, 2.6 mmol, 77%). $[a]_D^{24} = 42$ ($c = 1.12$ in CH_2Cl_2); MS (EI), *m/e* 340 (*M*, 5%), 193 (100), 91 (40); IR (KBr) 3445m, 3029m, 1696s, 1622m, 1321s, 1273m, 1024m, 760s, 697s cm^{-1}; ^1H NMR (200 MHz) δ 7.81–7.76 (m, 2 H, Ar–H), 7.52–7.28 (m, 13 H, Ar–H), 5.19 (dd, $J = 3.2$ Hz, $J = 11.5$ Hz, 2 H, C–H), 1.89 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 168.6 (q, C=O), 160.1 (q, N*C*N), 141.9 (q, Ar), 141.2 (q, Ar), 131.9 (q, Ar), 130.8 (+, Ar), 129.4 (+, Ar), 129.1 (+, Ar), 128.4 (+, Ar), 128.2 (+, Ar), 128.0 (+, Ar), 126.1 (+, Ar), 125.5 (+, Ar), 77.1 (+, C(5)–H), 70.6 (+, C(4)–H), 25.0 (+, Me). HRMS (ESI) found: $M + H$ 341.1658. $C_{23}H_{21}N_2O$ requires: 341.1654.

(+)-(4*R*,5*R*)-2,4,5-Triphenyl-*trans*-4,5-dihydroimidazole-1-carboxylic acid methyl ester (9). A sodium hydride solution (60% in petroleum) (0.17 g, 4.4 mmol) was washed with glyme (3 × 5 mL) and then additional glyme (20 mL) was added. A glyme solution (15 mL) of (+)-(4*R*,5*R*)-2,4,5-triphenyl-*trans*-4,5-dihydro-1*H*-imidazole (**6**) (1 g, 3.36 mmol) was slowly added and the mixture was stirred for 2 h. Methyl chloroformate (0.34 mL, 4.36 mmol) was then added quickly. The mixture was stirred at r.t. for 19 h, filtered and the filtrate was evaporated in vacuum. Purification by column chromatography on Al_2O_3 using petroleum ether–ethyl acetate (5 : 1) as the eluent afforded the title compound **4** as a colourless oil (0.48 g, 1.3 mmol, 40%). $[a]_D^{24} = 63$ ($c = 1.03$ in $CHCl_3$); MS (EI), *m/e* 356 (*M*, 50%), 193 (100); IR (KBr) 2962s, 1735m, 1331m, 1262s, 1101s, 1022s, 801s cm^{-1}; ^1H NMR (200 MHz) δ 7.83–7.78 (m, 2 H, Ar–H), 7.53–7.29 (m, 13 H, Ar–H), 5.18 (d, $J = 4.3$ Hz, 1 H, C–H), 5.16 (d, $J = 4.3$ Hz, 1 H, C–H) 3.55 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 160.1 (q, C=O), 152.8 (q, N*C*N), 142.6 (q, Ar), 141.8 (q, Ar), 131.5 (q, Ar), 130.7 (+, Ar), 129.3 (+, Ar), 129.1 (+, Ar), 128.8 (+, Ar), 128.2 (+, Ar), 128.0 (+, Ar), 126.3 (+, Ar), 125.8 (+, Ar), 77.5 (+, C(5)–H), 70.6 (+, C(4)–H), 53.3 (+, Me). HRMS(ESI) found: $M + H$ 357.1611. $C_{23}H_{21}N_2O$ requires: 357.1603.

(+)-(4*S*,5*S*)-1-Acetyl-2-methyl-4,5-diphenyl-*trans*-4,5-dihydroimidazole (11). (+)-(4*S*,5*S*)-2-Methyl-4,5-diphenyl-*trans*-4,5-dihydro-1*H*-imidazole (**10**) (2 g, 8.5 mmol) was dissolved in absolute ethanol (15 mL). Acetic anhydride (0.8 mL, 8.5 mmol) and triethylamine (1.2 mL, 8.5 mmol) dissolved in dichloromethane (2 mL) were added to the mixture, after which the resulting solution was stirred for 10 h at r.t. After evaporation of the solvent the residue was purified by column chromatography on Al_2O_3 using petroleum ether–ethyl acetate (3 : 1) as the eluent to give the crude product as a yellow solid. Recrystallisation in ethanol gave the title compound **11** as a white solid (1.8 g, 6.5 mmol, 77%). $[a]_D^{24} = 136$ ($c = 1.14$ in CH_2Cl_2), mp 133 °C; MS (EI), *m/e* 278 (*M*, 10%), 236 (10), 148 (30), 131 (100), 106 (70), 89 (60); IR (KBr) 1684s, 1641m, 1379s, 1332s, 760s, 700s cm^{-1}; ^1H NMR (200 MHz) δ 7.47–7.31 (m, 6 H, Ar–H), 7.23–7.17 (m, 4 H, Ar–H), 4.86 (dd, $J = 1.9$ Hz, $J = 5.1$ Hz, 2 H, C–H), 2.69 (d, $J = 1.1$ Hz, 3 H, N=C–Me), 1.88 (s, 3 H, CO–Me); ^{13}C NMR (50 MHz) δ 169.1 (q, C=O), 159.5 (q, N*C*N), 141.93 (q, Ar), 141.91 (q, Ar), 129.6 (+, Ar), 129.0 (+, Ar), 128.3 (+, Ar), 127.9 (+, Ar), 126.1 (+, Ar), 125.2 (+, Ar), 77.8 (+, C(5)–H), 70.7 (+, C(4)–H), 25.0 (+, N=C–*Me*), 19.3 (+, CO*Me*). Anal. calcd for $C_{18}H_{18}O_1N_2$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.50; H, 6.57; N, 10.11%.

(+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium iodide (12). Compound **8** (1 g, 2.9 mmol) was dissolved in dry dichloromethane (22 mL). Methyl iodide (2.2 mL) was added and the mixture was refluxed. After 1 h another portion of methyl iodide (2.2 mL) was added and the mixture was refluxed overnight. Evaporation yielded the desired product **12** as a yellowish solid (1.2 g, 2.5 mmol, 84%). $[a]_D^{24} = 66$ ($c = 0.51$ in CH_3CN), mp 155 °C; ESI, *m/e* 355 (M^+, 100%); IR (KBr) 3048s, 3015s, 1747s, 1622s, 1497s, 1449s, 1427s, 1276s, 1225s, 756s, 701s cm^{-1}; ^1H NMR (200 MHz) δ 7.71–7.31 (m, 15 H, Ar–H), 6.01 (d, $J = 11.4$ Hz, 1 H, C–H), 5.79 (d, $J = 11.4$ Hz, 1 H, C–H), 3.03 (s, 3 H, N–Me), 1.86 (s, 3 H, CO–Me); ^{13}C NMR (50 MHz) δ 168.7 (q, C=O), 166.27 (q, N*C*N), 135.5 (q, Ar), 133.3 (+, Ar), 132.1 (q, Ar), 130.6 (+, Ar), 129.9 (+, Ar), 129.7 (+, Ar), 129.53 (+, Ar), 129.47 (+, Ar), 128.2 (+, Ar), 123.5 (q, C^+), 75.8 (+, C(5)–H), 71.7 (+, C(4)–H), 35.1 (+, N–*Me*), 26.4 (+, CO*Me*). HRMS (ESI) found: M^+ 355.1826. $C_{24}H_{23}N_2O$ requires: 355.1810.

(+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium trifluoromethanesulfonimide (12c). Salt **12** (0.2 g, 0.41 mmol) was dissolved in dry dichloromethane (5 mL). 2 equiv. (0.24 g, 0.83 mmol) of *N*-lithiotrifluoromethanesulfonimide were added and the mixture was stirred for 2 h at room temperature. After adding water (5 mL) and additional stirring for 1 h, the phases were separated and the organic layer was washed three times with water, dried (Na_2SO_4) and evaporated under vacuum. Drying on the vacuum line at 40 °C (oil bath temperature) yielded the title compound **12c** as a yellowish solid (238 mg, 0.4 mmol, 90%). $[a]_D^{24} = 115$ ($c = 0.35$ in CH_2Cl_2), mp 50–51 °C; ESI, *m/e* 355 (M^+, 100%); IR (KBr) 3068w, 2360s, 2342s, 1744s, 1624s, 1502m, 1458m, 1352s, 1195s, 1132m, 1057m cm^{-1}; ^1H NMR (200 MHz) δ 7.72–7.68 (m, 3 H, Ar–H), 7.53–7.36 (m, 12 H, Ar–H), 5.69 (d, $J = 9.7$ Hz, 1 H, C–H), 5.28 (d, $J = 9.6$ Hz, 1 H, C–H), 2.95 (s, 3 H, N–Me), 1.80 (s, 3 H, CO–Me); ^{13}C NMR (50 MHz) δ 168.1 (q, C=O), 166.5 (q, N*C*N), 136.2 (q, Ar), 133.7 (+, Ar), 132.6 (q, Ar), 130.9 (+, Ar), 129.9 (+, Ar), 129.8 (+, Ar), 129.4 (+, Ar), 129.2 (+, Ar), 128.3 (+, Ar), 123.1 (q, Ar), 120.2 (q, $J = 65.0$ Hz, *C*F_3), 75.9 (+, C(5)–H), 71.0 (+, C(4)–H), 34.3 (+, N–*Me*), 25.3 (+, CO*Me*); HRMS(ESI) found: M^+ 355.1820. $C_{24}H_{23}N_2O$ requires: 355.1810.

(+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium hexafluorophosphate (12b) and (+)-(4*R*,5*R*)-1-benzoyl-2,3-methyl-4,5-diphenyl-*trans*-imidazolinium hexafluorophosphate (17b). Salt **12** (0.2 g, 0.41 mmol) was dissolved in dry dichloromethane (5 mL). 1.5 equiv. potassium hexafluorophosphate (0.11 g, 0.62 mmol) were added and the mixture was

stirred for 24 h at room temperature. After adding water (5 mL) the stirring was continued for another hour. The phases were separated by using a pipette and the organic layer was washed with water (2 × 2 mL), dried (Na_2SO_4) and evaporated under reduced pressure. Crystallisation in methanol yielded white crystals (88 mg, 0.2 mmol, 48%). The ratio (**17b** : **12b** = 2 : 1) was determined by ^{1}H NMR. Enrichment of **12b** could be obtained after two recrystallisations in diethyl ether–hexane (**17b** : **12b** = 1 : 4). ^{1}H NMR (200 MHz) δ 7.76–7.21 (m, 22.5 H, Ar–H of **12b** + **17b**), 5.73 (d, J = 10.0 Hz, 0.5 H, C–H of **12b**), 5.60 (d, J = 11.6 Hz, 1 H, C–H of **17b**), 5.34 (d, J = 10.0 Hz, 0.5 H, C–H of **12b**), 5.23 (d, J = 11.4 Hz, 1 H, C–H of **17b**), 3.14 (s, 3 H, N–Me of **17b**), 2.96 (s, 1.5 H, N–Me of **12b**), 2.46 (s, 3 H, C$^+$–Me of **17b**), 1.80 (s, 1.5 H, CO–Me of **12b**). ^{13}C NMR (50 MHz) δ 168.1 (q, C=O, **12b** + **17b**), 168.0 (q, N*C*N, **17b**), 166.5 (q, N*C*N, **12b**), 136.2 (q, Ar, **12b**), 134.5 (q, Ar, **17b**), 134.1 (q, Ar, **17b**), 133.7 (+, Ar, **12b**), 132.6 (q, Ar, **12b**), 132.5 (+, Ar, **17b**), 131.0 (+, Ar, **12b**), 130.7 (q, Ar, **17b**), 130.0 (+, Ar, **17b**), 129.9 (+, Ar, **12b**), 129.7 (+, Ar, **12b**), 129.5 (+, Ar, **17b**), 129.3 (+, Ar, **12b**), 129.2 (+, Ar, **12b** + **17b**), 128.5 (+, Ar, **12b** + **17b**), 127.8 (+, Ar, **17b**), 123.1 (q, Ar, **17b**), 122.9 (q, Ar, **12b**), 75.8 (+, C(5)–H, **12b**), 75.2 (+, C(5)–H, **17b**), 72.3 (+, C(4)–H, **17b**), 71.0 (+, C(4)–H, **12b**), 34.3 (+, N–*Me*, **12b**), 33.3 (+, N–*Me*, **17b**), 25.3 (+, CO*Me*, **12b**), 16.0 (+, C*Me*, **17b**).

(+)-(4*R*,5*R*)-1,3-Dibenzyl-2,4,5-triphenyl-*trans*-imidazolinium bromide (14). Compound **7** (1 g, 2.2 mmol) was dissolved in dry acetonitrile (10 mL). 2 equiv. freshly distilled benzyl bromide (0.53 mL, 4.4 mmol) were added and the mixture was refluxed for 22 h. The colour was changing from colourless to yellow. After evaporation of the solvent the residue was dried at 60 °C under high vacuum to remove traces of benzyl bromide. Crystallization in ethyl acetate yielded the title compound **14** as a white solid (920 mg, 1.6 mmol, 74%). $[a]_D^{24}$ = 132 (c = 0.50 in $CHCl_3$), mp 217 °C; ESI, m/e 479 (M^+, 100%); IR (KBr) 3030m, 3003m, 1560s, 1454s, 1286s, 751s, 736m, 698s cm^{-1}; ^{1}H NMR (200 MHz) δ 8.31–8.26 (m, 2 H, Ar–H), 7.70 (dd, J = 1.1 Hz, J = 2.4 Hz, 3 H, Ar–H), 7.45–7.34 (m, 10 H, Ar–H), 7.22 (dd, J = 1.0 Hz, J = 2.4 Hz, 6 H, Ar–H), 6.82 (dd, J = 2.2 Hz, J = 3.5 Hz, 4 H, Ar–H), 5.26 (s, 2 H, C–H), 4.69 (d, J = 15.3 Hz, 2 H, Bn–H), 4.42 (d, J = 15.3 Hz, 2 H, Bn–H); ^{13}C NMR (50 MHz) δ 167.8 (q, NCN), 133.7 (q, Ar), 133.3 (+, Ar), 132.6 (q, Ar), 130.3 (+, Ar), 130.2 (+, Ar), 129.8 (+, Ar), 129.1 (+, Ar), 129.0 (+, Ar), 128.8 (+, Ar), 128.6 (+, Ar), 122.3 (q, Ar), 73.0 (+, C(4,5)–H), 51.1 (−, CH_2). Anal. calcd for $C_{35}H_{31}N_2Br_1$: C, 75.13; H, 5.58; N, 5.01. Found: C, 74.86; H, 5.63; N, 4.74%.

(+)-(4*R*,5*R*)-1,3-Dibenzyl-2,4,5-triphenyl-*trans*-imidazolinium trifluoromethanesulfonimide (14c). Salt **14** (1 g, 1.8 mmol) was dissolved in dry dichloromethane (8 mL). 2 equiv. *N*-lithiotrifluoromethanesulfonimide (1.22 g, 3.6 mmol) were added and the mixture was stirred for 3.5 h at r.t. After adding water (8 mL) stirring was continuing for another hour, the phases were separated by using a pipette and the organic layer was washed with water (3 x 2 mL), dried (Na_2SO_4) and evaporated in vacuum. Drying under high vacuum yielded the title compound **14c** as a white solid (1.18 g, 1.6 mmol, 83%). $[a]_D^{24}$ = 7 (c = 0.98 in CH_2Cl_2), mp 217 °C; ESI, m/e 479 (M^+, 100%); IR (KBr) 1591m, 1557s, 1458s, 1348s, 1323s, 1193s, 1142s, 1059s, 699s cm^{-1}; ^{1}H NMR (200 MHz) δ 8.01 (dd, J = 1.3 Hz, J = 1.6 Hz, 2 H, Ar–H), 7.90–7.78 (m, 3 H, Ar–H), 7.44 (dd, J = 0.9 Hz, J = 2.4 Hz, 6 H, Ar–H), 7.31 (dd, J = 1.1 Hz, J = 2.3 Hz, 6 H, Ar–H), 7.14 (dd, J = 2.3 Hz, J = 3.5 Hz, 4 H, Ar–H), 6.90 (dd, J = 2.2 Hz, J = 3.4 Hz, 4 H, Ar–H), 4.82 (s, 2 H, C–H), 4.73 (d, J = 15.0 Hz, 2 H, Bn–H), 4.15 (d, J = 15.0 Hz, 2 H, Bn–H); ^{13}C NMR (50 MHz) δ 166.8 (q, NCN), 134.3 (q, Ar), 134.1 (+, Ar), 131.5 (+, Ar), 131.0 (q, Ar), 130.5 (+, Ar), 130.2 (+, Ar), 129.5 (+, Ar), 129.4 (+, Ar), 129.1 (+, Ar), 128.4 (+, Ar), 127.5 (+, Ar), 121.5 (q, Ar), 71.5 (+, C(4,5)–H), 50.3 (−, CH_2). Anal. calcd for $C_{37}H_{31}N_3O_4S_2F_6$: C, 58.49; H, 4.11; N, 5.53. Found: C, 58.16; H, 4.07; N, 5.39%.

(4*R*,5*R*)-1-Benzyl-4,5-dihydro-2,4,5-triphenyl-1*H*-imidazole (16). Compound **7** (0.158 g, 0.35 mmol) was dissolved in dry acetonitrile (5 ml). Benzyl bromide (0.9 equiv.) was added, and the mixture was refluxed for 6 h. After evaporation of the solvent under reduced pressure, the residue was columned with ethyl acetate to give the title compound **16** as a colourless oil (7 mg, 0.018 mmol, 5%). ESI m/e 389.2 (M^+ + H, 100%); MS (EI), m/e 388 (M, 11%), 297 (M^+ − Bn, 20), 193 (100), 91 (Bn, 93); IR ($CHCl_3$) 3091m, 3036m, 1478s, 1036s, 637s cm^{-1}; ^{1}H NMR (200 MHz) δ 7.86–7.81 (m, 2 H, Ar–H), 7.52–7.48 (m, 3 H, Ar–H), 7.40–7.20 (m, 10 H, Ar–H), 7.14–7.09 (m, 2 H, Ar–H), 6.98–6.93 (m, 2H, Ar–H), 5.01 (d, J = 8.4 Hz, 1 H, C–H), 4.73 (d, J = 15.6 Hz, 1 H, Bn–H), 4.35 (d, J = 8.5 Hz, 1 H, C–H), 3.94 (d, J = 15.6 Hz, 1 H, Bn–H); ^{13}C NMR (50 MHz) δ 166.0 (N*C*N), 143.8 (Ar), 141.8 (Ar), 136.4 (Ar), 130.2 (Ar), 128.9 (Ar), 128.74 (Ar), 128.69 (Ar), 128.5 (Ar), 128.4 (Ar), 128.0 (Ar), 127.8 (Ar), 127.5 (Ar), 127.2 (Ar), 127.2 (Ar), 127.0 (Ar), 126.8 (Ar), 72.6 (CH), 49.6 (Bn).

(1*S*)-(−)-Camphorsulfonyl-(2-phenyl-4,5-dihydro)-imidazole (20). 2-Phenyl-4,5-dihydroimidazole (**18**) (0.8 g, 5.5 mmol) was dissolved in dry toluene (3 mL) and 1.5 equiv. triethylamine (8.25 mmol, 0.034 mL) were added. After addition of 1.2 equiv. (1*S*)-(+)-camphorsulfonic acid chloride (**19**) (6.6 mmol, 1.65 g) the solution turned into a yellowish cloudy mixture, which was stirred at r.t. for 18 h. The reaction mixture was washed with 5% aqueous HCl (3 × 2 mL) and 10% aqueous $NaHCO_3$ solution (2 × 2 mL), dried (Na_2SO_4) and evaporated under vacuum. The mixture was purified by column chromatography on SiO_2 using petroleum ether–ethyl acetate (1 : 2) as the eluent to give the crude product as a colourless oil. Recrystallisation in petroleum ether–dichloromethane gave the white pure product **20** (200 mg, 0.6 mmol, 10%). $[a]_D^{24}$ = −22 (c = 1.0 in CH_2Cl_2), mp 91–95 °C; MS (EI), m/e 379 (M + H_2O, 100%); IR (KBr) 3285s, 2955s, 1742s, 1726m, 1632s, 1544s, 1328s, 1144s, 697m cm^{-1}; ^{1}H NMR (200 MHz, DMSO–D_2O) δ 8.54 (t, J = 5.4 Hz, 1 H), 7.81–7.76 (m, 2 H, Ar–H), 7.56–7.39 (m, 3 H, Ar–H), 3.38 (m, 2 H), 3.19–3.13 (m, 2 H), 2.87 (d, J = 14.9 Hz, 1 H), 2.32–2.20 (m, 2 H), 2.01 (t, J = 4.3 Hz, 1 H), 1.89–1.80 (m, 2 H), 1.56–1.27 (m, 2 H), 0.93 (s, 3 H, Me), 0.70 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 168.1 (q, C=O), 134.2 (q, Ar), 131.7 (+, Ar), 128.6 (+, Ar), 127.2 (+, Ar), 59.2 (q, C(1)), 49.6 (−, CH_2), 49.0 (q, C(7)), 43.4 (−, CH_2), 43.0 (−, CH_2), 42.8 (+, C(4)), 40.5 (−, CH_2), 27.1 (−, C(6)), 26.3 (−, C(5)), 19.9 (+, Me), 19.5 (+, Me). HRMS(ESI) found: M + H_2O + Na 401.1524. $C_{19}H_{26}N_2O_4SNa$ requires: 401.1511.

(1*S*)-(+)-Camphorsulfonyl-(2-phenyl-3-methyl)-imidazolinium iodide (21). (1*S*)-(−)-Camphorsulfonyl-(2-phenyl)-imidazole (**20**) (1.15 g, 3.2 mmol) was dissolved in dry dichloromethane (15 mL). Methyl iodide (51.2 mmol, 16 equiv., 3.2 mL) was added and the mixture was refluxed overnight. The solvent and the excess of methyl iodide were removed on the vacuum line to yield

a yellowish foam (1.3 g, 2.6 mmol, 88%). **21** was used without further purification in the anion exchange, since it was highly hygroscopic.

(1*S*)-(+)-Camphorsulfonyl-(2-phenyl-3-methyl)-imidazolinium hexafluorophosphate (21b). (1*S*)-(+)-Camphorsulfonyl-(2-phenyl-3-methyl)-imidazolinium iodide (**21**) (0.4 g, 0.78 mmol) was dissolved in dry dichloromethane (6 mL) and 1.5 equiv. potassium hexafluorophosphate (0.22 g, 1.17 mmol) was added. The mixture was stirred at r.t. overnight, quenched with water (6 mL) and stirred for an additional hour. The organic phase was washed with water (3 x 4 mL), dried (Na_2SO_4) and evaporated. Recrystallisation in ethyl acetate gave **21b** as a white solid (0.230 g, 0.4 mmol, 56%). $[\alpha]_D^{24} = 6$ ($c = 1.05$ in CH_3CN), mp 166 °C; MS (EI), *m/e* 375 (M^+, 10%); IR (KBr) 2969m, 2929m, 1738s, 1639s, 1504m, 1445m, 1374s, 1176s, 1035m, 840s cm^{-1}; ^1H NMR (200 MHz, DMSO) δ 7.69–7.66 (m, 5 H, Ar–H), 4.52–4.16 (m, 4 H), 3.79 (d, $J = 3.8$ Hz, 1 H), 3.40 (d, $J = 2.0$ Hz, 1 H), 3.00 (s, 3 H, N–Me), 2.44–2.32 (m, 1 H), 2.05–1.89 (m, 4 H), 1.37 (d, $J = 2.0$ Hz, 2 H), 0.83 (s, 3 H, Me), 0.75 (s, 3 H, Me); ^{13}C NMR (50 MHz) δ 213.9 (q, C=O), 164.9 (q, NCN), 133.0 (+, Ar), 128.9 (+, Ar), 121.5 (q, Ar), 58.2 (q, C(1)), 51.9 (−), 48.2 (q, C(7)), 47.9 (−), 42.0 (−, C(4)), 41.9 (+, C(3)), 35.5 (+, NMe), 26.2 (−, C(6)), 24.9 (−, C(5)), 19.2 (+, Me), 19.1 (+, Me). HRMS (ESI) found: *M* 375.1756. $C_{20}H_{27}N_2O_3S$ requires: 375.1742.

Investigation of the rearrangement

Conversion of the NTf_2 salt 12c with TFA. (+)-(4*R*,5*R*)-1-Acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium trifluoromethanesulfonimide (**12c**) (46 mg, 0.07 mmol) was dissolved in dry dichloromethane (1.2 mL). 20% trifluoroacetic acid in dichloromethane (0.05 mL) was added and the mixture was stirred for 24 h at r.t. After adding water (1 mL), the mixture was shaken strongly, the phases were separated and the organic layer was washed with water (2 × 1 mL), dried (Na_2SO_4) and evaporated under vacuum. Drying under high vacuum yielded a mixture consisting of the starting material **12c** and the rearrangement product **17b** as a yellowish oil (40 mg, 0.06 mmol, 87%). The rearrangement product was obtained in 78% yield according to the ^1H NMR spectra, where a ratio **12c** : **17c** = 4 : 1 was determined.

Manipulation of the PF_6 salt mixture 12b : 17b with aqueous HCl. The mixture of (+)-(4*R*,5*R*)-1-acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium hexafluorophosphate (**12b**) and (+)-(4*R*,5*R*)-1-benzoyl-2,3-methyl-4,5-diphenyl-*trans*-imidazolinium hexafluorophosphate (**17b**) (20 mg, 0.04 mmol) in a ratio 1 : 2 was dissolved in dry dichloromethane (0.6 mL). 1 N aqueous hydrochloric acid (0.02 mL) was added and the mixture was stirred for 24 h at room temperature. After adding water (1 mL) the mixture was strongly shaken, the phases were separated and the organic layer was washed with water (2 × 0.5 mL), dried (Na_2SO_4) and evaporated under vacuum. Evaporation of the remaining solvent under high vacuum yielded a colourless oil (20 mg, 0.04 mmol, 100%). The ratio of the rearrangement products increased from 1 : 2 up to a ratio of 1 : 3 according to the ^1H NMR spectra.

Manipulation of the PF_6 salt mixture 12b : 17b with TFA. The mixture of (+)-(4*R*,5*R*)-1-acetyl-2,4,5-triphenyl-3-methyl-*trans*-imidazolinium hexafluorophosphate (**12b**) and (+)-(4*R*,5*R*)-1-benzoyl-2,3-methyl-4,5-diphenyl-*trans*-imidazolinium hexafluorophosphate (**17b**) (12 mg, 0.02 mmol) with a ratio of 1 : 2 was dissolved in dry dichloromethane (0.3 mL). 20% trifluoroacetic acid in dichloromethane (0.01 mL) was added and the mixture was stirred for 24 h at r.t. After adding water (1 mL) the mixture was shaken strongly, the phases were separated and the organic layer was washed with water (2 × 0.5 mL), dried (Na_2SO_4) and evaporated under vacuum. Evaporation of the remaining solvent under high vacuum yielded a colourless oil (12 mg, 0.02 mmol, 100%). The ratio of the rearrangement products increased from 1 : 2 up to 1 : 6 according to the ^1H NMR spectra.

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