Pummerer-like Reactions

Resolution of [4]Heterohelicenium Dyes with Unprecedented Pummerer-like Chemistry**

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Helicenes and heterohelicenes, which present fascinating left- and right-handed chiral helical structures (of *M* and *P*

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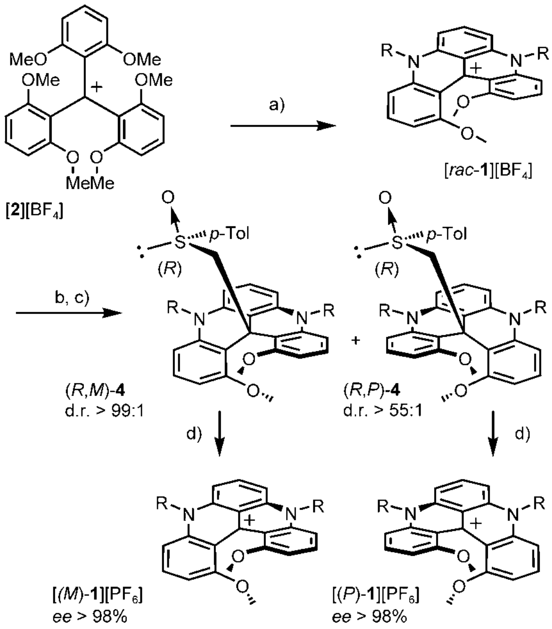
configuration, respectively),[1] have been intensively studied owing to their excellent ability to self-assemble[2] as well as their chiroptical, photochromic, nonlinear optical,[3] and DNA-intercalating properties.[4] Furthermore, they are useful for applications in asymmetric molecular recognition[5] and synthesis[6] as well as in polymer and material sciences.[7,8] For many of these applications, the (hetero)helicenes must be isolated with high enantiomeric purity. The most efficient syntheses of nonracemic helicenes reported to date are based on resolutions of racemic derivatives.[9,10] Several enantio- or diastereoselective approaches have also been described, and in some cases high levels of asymmetric inductions have been achieved.[1d,11]

The 1,13-dimethoxyquinacridinium cation **1a** has previously been reported (Scheme 1, R = *n*Pr).[12] This cationic dye is prepared in one step and with good yield by the reaction of primary propylamine and the readily available salt of **2**. The molecular framework of **1** contains four *ortho*-condensed aromatic rings. Owing to the steric repulsion between the two methoxy substituents, these derivatives adopt a twisted helical conformation. As such, compounds of type **1** may be regarded as [4]heterohelicenium derivatives.[13,14]



Scheme 1. Synthesis of [(*M*)-**1**][PF$_6$] and [(*P*)-**1**][PF$_6$]. a) RNH$_2$ (R = *n*Pr (**a**), *n*Oct (**b**), *i*Pr (**c**), *c*Hex (**d**)), *N*-methylpyrrolidine (NMP), 1.5 h, 110 °C; b) (+)-(*R*)-**3**, LDA, THF, 0 °C, 1:1 mixture of diastereomers; c) column chromatography (SiO$_2$); d) aq HPF$_6$, acetone. Tol = tolyl.

Recently it was shown that cation **1a** demonstrates high configurational stability, even more so than [6]helicene.[15] The hexafluorophosphate salt of **1a** was obtained in enantioenriched form (*ee* > 96 %) by ion-pairing association with enantiopure BINPHAT (BINPHAT = bis(tetrachlorobenzenediolato)mono([1,1′]binaphthalenyl-2,2′-diolato)-phosphate(v)) anion,[16] selective precipitation of one diastereomeric salt (benzene/THF), and ion metathesis with KPF$_6$. However, the moderate yields at the precipitation stage (30 %), the low diastereomeric purity in the mother liquor (*de* = 41 %), and the fact that the process cannot be applied to lipophilic cations such as **1b** (R = *n*Oct) prompted us to look for a more effective resolution procedure. Herein we report a short and general protocol for the resolution of cationic dyes of type **1** using 1) the addition of an enantiopure sulfoxide moiety,[17] 2) a facile chromatographic separation of the neutral diastereomers ($\Delta R_f \approx 0.3$), and 3) an unprecedented Pummerer-like C–C bond-fragmentation reaction that generates both enantiomers with high enantiomeric purity (*ee* > 98 %).

Procedures involving preparative chromatographic resolution have often freed chemists from being dependent on crystallization.[18] These procedures are usually performed with covalent diastereomer mixtures prepared by reactions of racemic substrates with classical enantiopure resolving agents (acids, alcohols, amines, etc.). In helicene chemistry, several such examples make use of aminohydroxybornane[10a] and camphanates.[10b,c,19] However, as cations **1** are devoid of functional handles for attaching these resolving agents, an alternative procedure had to be found.

Siegel, Krebs, Laursen, and co-workers have shown that reactive carbanions can attack the center of structurally related carbenium ions to generate rigid neutral molecular cavities by the formation of a covalent C–C bond between the reactants.[20] In the case of [**1a**][PF$_6$], reaction with acetonitrile in the presence of NaH was documented, and the product of CH$_2$CN addition was isolated.[15] For the resolution of cations of type **1**, we expected that the addition of a reactive enantiopure carbanionic moiety would result in two neutral diastereomeric structures, which could then be separated by chromatography.

(+)-(*R*)-Methyl-*p*-tolylsulfoxide ((+)-(*R*)-**3**) was selected for its ready availability,[21] known carbanionic chemistry,[22] and, once introduced, efficiency in chromatographic separation of diastereomers.[23] Treatment of (+)-(*R*)-**3** with lithium diisopropylamide (LDA) at 0 °C in THF and subsequent addition of [*rac*-**1a**][BF$_4$] resulted in the formation of two neutral diastereomeric adducts, (*R*,*M*)-**4a** and (*R*,*P*)-**4a**, in good overall yield (Scheme 1, Table 1).[24,25]

Thin layer chromatographic plates (SiO$_2$, Et$_2$O) of the 1:1 mixture of (*R*,*M*)-**4a** and (*R*,*P*)-**4a** displayed two spots with very different R_f values ($\Delta R_f = 0.36$). Preparative chromatography under analogous conditions afforded two separated fractions in good yields (Table 1). The electronic circular dichroism spectra of the first and second eluted compounds, $[\alpha]_D^{20} = -700$ and $+820$, respectively (CH$_2$Cl$_2$, $c = 0.056$ g/100 mL), displayed symmetrical curves except in the region below 250 nm due to the contribution from the CD-active (*R*)-tolylsulfoxide (Figure 1). At higher wavelengths, only negative or positive Cotton effects were observed for (−)-**4a** and (+)-**4a**, respectively; this spectral region is only related to valence transitions in the helical chromophore of compounds **4a**.

The next question concerned the removal of the chiral auxiliary. Sulfoxide groups are usually removed by treatment with Raney nickel to cleave C–S bonds adjacent to the sulfoxide moiety.[22b] In the case of **4a**, this would mean leaving an extra methyl group on the skeleton of the addition

Table 1: Synthesis of the sulfoxide diastereomers **4**: Results of the Pummerer-like reaction and resulting enantiopure carbenium ions **1**.

			Sulfoxides					Derived carbenium salts		
compound	R	R_f[a]	yield [%]	d.r.[b]	$[\alpha]_D^{20}$	config.	compound	yield [%]	config.	$[\alpha]_{365}^{20}$ [c]
(−)-**4a**	*n*Pr	0.63	39	>99:1	−710	*R*,*M*	(−)-[**1a**][PF_6]	94	*M*	−12500
(+)-**4a**	*n*Pr	0.27	39	55:1	+820	*R*,*P*	(+)-[**1a**][PF_6]	92	*P*	+13200
(−)-**4b**	*n*Oct	0.92	44	>99:1	−680	*R*,*M*	(−)-[**1b**][PF_6]	92	*M*	−12200
(+)-**4b**	*n*Oct	0.59	44	>99:1	+800	*R*,*P*	(+)-[**1b**][PF_6]	92	*P*	+12200
(−)-**4c**	*i*Pr	0.56	43	>99:1	−610	*R*,*M*	(−)-[**1c**][PF_6]	80	*M*	−10000
(+)-**4c**	*i*Pr	0.28	41	>99:1	+880	*R*,*P*	(+)-[**1c**][PF_6]	82	*P*	+10200
(−)-**4d**	*c*Hex	0.82	44	>99:1	−480	*R*,*M*	(−)-[**1d**][PF_6]	88	*M*	−7500
(+)-**4d**	*c*Hex	0.43	43	61:1	+550	*R*,*P*	(+)-[**1d**][PF_6]	94	*P*	+8700

[a] Et_2O as eluent. [b] Determined by HPLC (see Supporting Information). [c] Cations **1** are dyes that absorb light efficiently in most of the visible region. Very dilute solutions and restricted wavelengths were required to measure the specific optical rotations.

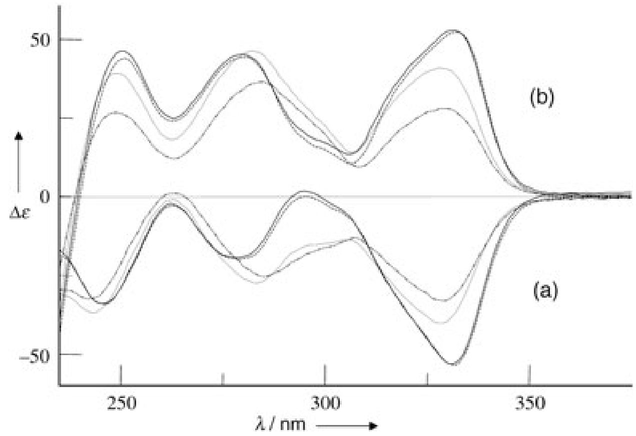
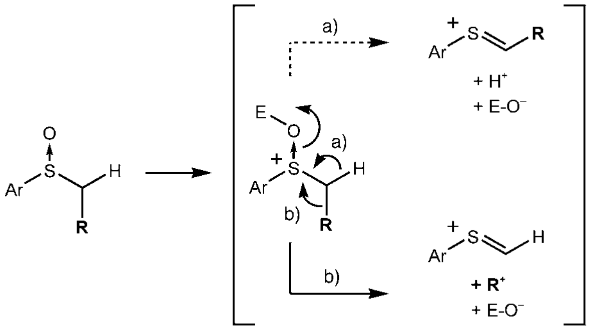


Figure 1. Superposition of the CD spectra of the first (a) and second (b) eluted diastereomers—that is, compounds of (−)-(*R*,*M*) and (+)-(*R*,*P*) configuration, respectively—for derivatives **4a** (——), **4b** (-----), **4c** (•••••), and **4d** (–•–•).

adducts, and then carbenium ion **1a** would not be generated. However, it is known that treatment of aryl alkyl sulfoxides with strong acids or anhydrides results in aldehyde moieties and/or derivatives.[26] This Pummerer reaction proceeds by protonation or esterification of the oxygen atom of the sulfoxide (Scheme 2). Subsequent cleavage of the S–O and β-C–H bonds results in the formation of a thionium moiety that can be trapped to generate a variety of functional groups (route a). To our knowledge, β-C–C bond fragmentation (route b) instead of β-C–H bond cleavage has not been reported. This is probably due to the strong electrofugal character of H^+. As nitrogen-containing carbenium ions obtained by the reaction of amines with cation **2** show high chemical stability ($pK_{R+} \geq 19$),[12] we considered that the traditional pathway of the Pummerer reaction could be overcome as cation **1a** could be a better leaving group than H^+ (route b).



Scheme 2. The Pummerer reaction of a branched aryl alkyl sulfoxide with an electrophile E^+ along the classical (a) and nonclassical pathways (b).

The colorless compounds (−)-**4a** and (+)-**4a** were treated with aqueous HPF_6 in acetone at room temperature. The immediate formation of a deep green color indicated the presence of cation **1a**. Addition of water and partial concentration under vacuum resulted in the precipitation of salts (−)-[**1a**][PF_6] and (+)-[**1a**][PF_6]. Further purification of the isolated salts on SiO_2 afforded the compounds in good overall yields and with high enantiomeric purity (Table 1).[27]

The generality of the resolution procedure was then tested on derivatives from linear (**1b**, R = *n*Oct) and branched (**1c**, R = *i*Pr; **1d**, R = *c*Hex) primary amines (Scheme 1). These compounds were prepared by the addition of $n\text{OctNH}_2$, $i\text{PrNH}_2$, and $c\text{HexNH}_2$ to [**2**][BF_4] in NMP at 110 °C (yield: 80, 58, and 48 %, respectively). Addition of (+)-(*R*)-**3** to the BF_4^- salts of *rac*-**1b**, *rac*-**1c**, and *rac*-**1d** proceeded as for *rac*-**1a** and formed compounds **4b, 4c**, and **4d** in good yields (78–88 %). In all cases, 1:1 mixtures of diastereomers were obtained (as determined by ^1H NMR spectroscopy and HPLC), which were separated by column chromatography (SiO_2) in satisfying yields and with good diastereomeric excess (Table 1). The first and second eluted fractions were all levogyre and dextrogyre, respectively, and presented CD spectra similar to that of (−)-**4a** and (+)-**4a** (Figure 1). In the case of [*rac*-**1a**][BF_4], the addition of (+)-(*R*)-**3** was scaled-up to 10 mmol of cation **1a** (5.0 g); the addition and separation proceeded with no loss of efficiency.

X-ray-quality crystals of diastereomerically pure (+)-**4c** were obtained, and the absolute *R*,*P* configuration was determined from the crystal structure analysis (Figure 2).[28] As all the second eluted chromatographic fractions of diastereomeric compounds **4a**–**d** demonstrate analogous chiroptical properties (Figure 1), the *R*,*P* configuration determined for (+)-**4c** can also be assigned to (+)-**4a**, (+)-**4b**, and (+)-**4d**. Consequently, the first eluted derivatives (−)-**4a**–**d** are all of *R*,*M* configuration. Previously, an absolute *M* configuration was determined for (−)-[**1a**][PF_6] by vibrational circular dichroism analysis.[15] Evidently, upon removal

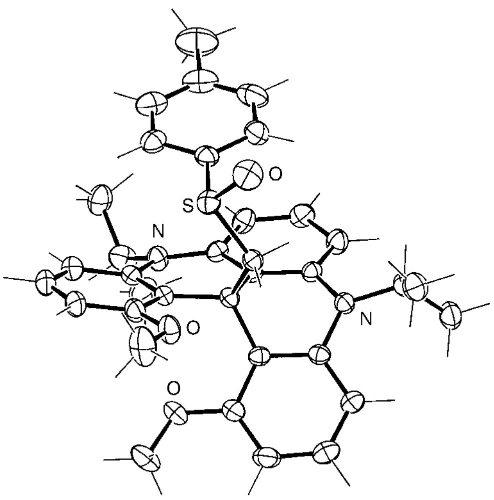


Figure 2. X-ray crystal structure of (+)-(*R*,*P*)-**4c**. Ellipsoids are represented at the 40% probability level.

of the central sulfoxide moiety, the sense of helicity of the skeleton remains. This means that the fragmentation occurs with retention of configuration, for example, from (−)-(*R*,*M*)-**4a** to (−)-[(*M*)-**1a**][PF_6].

Finally, treatment of (*R*,*M*)-**4b–d** with HPF_6 in acetone afforded salts (−)-[**1b**][PF_6], (−)-[**1c**][PF_6], and (−)-[**1d**]-[PF_6] in excellent yields. Analogous results were obtained for the diastereomeric (*R*,*P*) series in favor of the dextrogyre salts (Table 1). In the case of the more hindered compounds **4c** and **4d**, simply increasing the reaction times and the amount of Brønsted acid (50.0 equiv) was sufficient for the reactions to proceed to completion. Interestingly, a comparison of the CD spectra of salts (−)-[**1**][PF_6] showed that the CD properties of the carbenium ions depend on the nature of the side-chain residues. The branched compounds (−)-**1c** and (−)-**1d** display stronger Cotton effects (4×, $\Delta\varepsilon_{620} \approx 7.5$) at higher wavelength than the linear derivatives (−)-**1a** and (−)-**1b**. This result opens interesting prospects for future applications.[19]

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[1] For general references, see a) W. H. Laarhoven, W. J. C. Prinsen, *Top. Curr. Chem.* **1984**, *125*, 63–130; b) K. P. Meurer, F. Vögtle, *Top. Curr. Chem.* **1985**, *127*, 1–76; c) T. J. Katz, *Angew. Chem.* **2000**, *112*, 1997–1999; *Angew. Chem. Int. Ed.* **2000**, *39*, 1921–1923; d) A. Urbano, *Angew. Chem.* **2003**, *115*, 4116–4119; *Angew. Chem. Int. Ed.* **2003**, *42*, 3986–3989; e) C. Diedrich, S. Grimme, *J. Phys. Chem. A* **2003**, *107*, 2524–2539; f) S. D. Peyerimhoff, *Interactions in Molecules: Electronic and Steric Effects*, Wiley-VCH, Weinheim, **2003**, pp. 363.

[2] Y. Kitahara, K. Tanaka, *Chem. Commun.* **2002**, 932–933.

[3] C. Wachsmann, E. Weber, M. Czugler, W. Seichter, *Eur. J. Org. Chem.* **2003**, 2863–2876; J. E. Field, T. J. Hill, D. Venkataraman, *J. Org. Chem.* **2003**, *68*, 6071–6078; T. Verbiest, S. Sioncke, A. Persoons, L. Vyklicky, T. J. Katz, *Angew. Chem.* **2002**, *114*, 4038–4040; *Angew. Chem. Int. Ed.* **2002**, *41*, 3882–3884; T. B. Norsten, A. Peters, R. McDonald, M. T. Wang, N. R. Branda, *J. Am. Chem. Soc.* **2001**, *123*, 7447–7448; F. Furche, R. Ahlrichs, C. Wachsmann, E. Weber, A. Sobanski, F. Vögtle, S. Grimme, *J. Am. Chem. Soc.* **2000**, *122*, 1717–1724.

[4] Y. Xu, Y. X. Zhang, H. Sugiyama, T. Umano, H. Osuga, K. Tanaka, *J. Am. Chem. Soc.* **2004**, *126*, 6566–6567; S. Honzawa, H. Okubo, S. Anzai, M. Yamaguchi, K. Tsumoto, I. Kumagai, *Bioorg. Med. Chem.* **2002**, *10*, 3213–3218.

[5] L. Owens, C. Thilgen, F. Diederich, C. B. Knobler, *Helv. Chim. Acta* **1993**, *76*, 2757–2774; E. Murguly, R. McDonald, N. R. Branda, *Org. Lett.* **2000**, *2*, 3169–3172.

[6] I. Sato, R. Yamashima, K. Kadowaki, J. Yamamoto, T. Shibata, K. Soai, *Angew. Chem.* **2001**, *113*, 1130–1132; *Angew. Chem. Int. Ed.* **2001**, *40*, 1096–1098; M. T. Reetz, S. Sostmann, *Tetrahedron* **2001**, *57*, 2515–2520; M. T. Reetz, E. W. Beuttenmuller, R. Goddard, *Tetrahedron Lett.* **1997**, *38*, 3211–3214; A. Terfort, H. Gorls, H. Brunner, *Synthesis* **1997**, 79–86.

[7] M. Miyasaka, A. Rajca, *Synlett* **2004**, 177–181.

[8] See also: R. El Abed, B. Ben Hassine, J.-P. Genêt, M. Gorsane, A. Marinetti, *Eur. J. Org. Chem.* **2004**, 1517–1522; P. M. Donovan, L. T. Scott, *J. Am. Chem. Soc.* **2004**, *126*, 3108–3112; M. C. Carreño, S. García-Cerrada, A. Urbano, *Chem. Eur. J.* **2003**, *9*, 4118–4131; F. Teplý, I. G. Stará, I. Starý, A. Kollárovic, D. Saman, S. Vyskocil, P. Fiedler, *J. Org. Chem.* **2003**, *68*, 5193–5197; T. Sooksimuang, B. K. Mandal, *J. Org. Chem.* **2003**, *68*, 652–655; K. Paruch, L. Vyklicky, D. Z. Wang, T. J. Katz, C. Incarvito, L. Zakharov, A. L. Rheingold, *J. Org. Chem.* **2003**, *68*, 8539–8544; M. d. M. Real, J. Pérez Sestelo, L. A. Sarandeses, *Tetrahedron Lett.* **2002**, *43*, 9111–9114; D. C. Harrowven, M. I. T. Nunn, D. R. Fenwick, *Tetrahedron Lett.* **2002**, *43*, 7345–7347; M. C. Carreño, S. García-Cerrada, A. Urbano, *Chem. Commun.* **2002**, 1412–1413; F. Teplý, I. G. Stará, I. Starý, A. Kollárovic, D. Saman, L. Rulisek, P. Fiedler, *J. Am. Chem. Soc.* **2002**, *124*, 9175–9180; S. D. Han, A. D. Bond, R. L. Disch, D. Holmes, J. M. Schulman, S. J. Teat, K. P. C. Vollhardt, G. D. Whitener, *Angew. Chem.* **2002**, *114*, 3357–3361; *Angew. Chem. Int. Ed.* **2002**, *41*, 3223–3227; M. C. Carreño, S. García-Cerrada, A. Urbano, *J. Am. Chem. Soc.* **2001**, *123*, 7929–7930; F. Dubois, M. Gingras, *Tetrahedron Lett.* **1998**, *39*, 5039–5040.

[9] M. S. Newman, D. Lednicer, *J. Am. Chem. Soc.* **1956**, *78*, 4765–4770; H. Wynberg, M. B. Groen, H. Schadenberg, *J. Org. Chem.* **1971**, *36*, 2797–2809; D. A. Lightner, D. T. Hefelfinger, T. W. Powers, G. W. Frank, K. N. Trueblood, *J. Am. Chem. Soc.* **1972**, *94*, 3492–3497; R. H. Martin, M. J. Marchant, *Tetrahedron* **1974**, *30*, 343–345; F. Mikes, G. Boshart, E. Gil-Av, *J. Chem. Soc. Chem. Commun.* **1976**, 99–100; C. Stammel, R. Fröhlich, C. Wolff, H. Wenck, A. de Meijere, J. Mattay, *Eur. J. Org. Chem.* **1999**, 1709–1718; K. Tanaka, H. Osuga, H. Suzuki, Y. Shogase, Y. Kitahara, *J. Chem. Soc. Perkin Trans. 1* **1998**, 935–940.

[10] a) K. Tanaka, Y. Kitahara, H. Suzuki, H. Osuga, Y. Kawai, *Tetrahedron Lett.* **1996**, *37*, 5925–5928; b) T. Thongpanchang, K. Paruch, T. J. Katz, A. L. Rheingold, K.-C. Lam, L. Liable-Sands, *J. Org. Chem.* **2000**, *65*, 1850–1856; c) D. Nakano, R. Hirano, M. Yamaguchi, C. Kabuto, *Tetrahedron Lett.* **2003**, *44*, 3683–3686.

[11] A. Sudhakar, T. J. Katz, *J. Am. Chem. Soc.* **1986**, *108*, 179–181; T. J. Katz, A. Sudhakar, M. F. Teasley, A. M. Gilbert, W. E. Geiger, M. P. Robben, M. Wuensch, M. D. Ward, *J. Am. Chem. Soc.* **1993**, *115*, 3182–3198; K. Tanaka, H. Osuga, H. Suzuki, *Tetrahedron: Asymmetry* **1993**, *4*, 1843–1856; I. G. Stará, I. Starý, M. Tichý, J. Závada, V. Hanus, *J. Am. Chem. Soc.* **1994**, *116*, 5084–5088; H. Osuga, H. Suzuki, K. Tanaka, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 891–897; Y. Ogawa, M. Toyama, M. Karikomi, K. Seki, K. Haga, T. Uyehara, *Tetrahedron Lett.* **2003**, *44*, 2167–2170; R. El Abed, B. Ben Hassine, J.-P. Genêt, M. Gorsane, J. Madec, L. Ricard, A. Marinetti, *Synthesis* **2004**, 2513–2516.

[12] B. W. Laursen, F. C. Krebs, *Angew. Chem.* **2000**, *112*, 3574–3576; *Angew. Chem. Int. Ed.* **2000**, *39*, 3432–3434; B. W. Laursen, F. C. Krebs, *Chem. Eur. J.* **2001**, *7*, 1773–1783.

[13] The [4]helicene derivatives can be configurationally stable if correctly substituted; see M. S. Newman, R. M. Wise, *J. Am. Chem. Soc.* **1956**, *78*, 450–454; M. C. Carreño, S. García-Cerrada, M. J. Sanz-Cuesta, A. Urbano, *Chem. Commun.* **2001**, 1452–1453; Y. Saiki, K. Nakamura, Y. Nigorikawa, M. Yamaguchi, *Angew. Chem.* **2003**, *115*, 5348–5350; *Angew. Chem. Int. Ed.* **2003**, *42*, 5190–5192; Y. Saiki, H. Sugiura, K. Nakamura, M. Yamaguchi, T. Hoshi, J. Anzai, *J. Am. Chem. Soc.* **2003**, *125*, 9268–9269, and references therein.

[14] Nitrogen-containing cationic heterohelicenes have been described: K. Sato, S. Okazaki, T. Yamagishi, S. Arai, *J. Heterocycl. Chem.* **2004**, *41*, 443–447, and references therein.

[15] C. Herse, D. Bas, F. C. Krebs, T. Bürgi, J. Weber, T. Wesolowski, B. W. Laursen, J. Lacour, *Angew. Chem.* **2003**, *115*, 3270–3274; *Angew. Chem. Int. Ed.* **2003**, *42*, 3162–3166.

[16] J. Lacour, A. Londez, C. Goujon-Ginglinger, V. Buß, G. Bernardinelli, *Org. Lett.* **2000**, *2*, 4185–4188; J. Lacour, V. Hebbe-Viton, *Chem. Soc. Rev.* **2003**, *32*, 373–382.

[17] I. Fernández, N. Khiar, *Chem. Rev.* **2003**, *103*, 3651–3705.

[18] J. Jacques, A. Collet, S. H. Wilen, *Enantiomers, Racemates, and Resolutions*, 2nd ed., Krieger, Melbourne, USA, **1994**.

[19] J. E. Field, G. Muller, J. P. Riehl, D. Venkataraman, *J. Am. Chem. Soc.* **2003**, *125*, 11808–11809.

[20] M. Lofthagen, R. V. Clark, K. K. Baldridge, J. S. Siegel, *J. Org. Chem.* **1992**, *57*, 61–69; B. W. Laursen, F. C. Krebs, M. F. Nielsen, K. Bechgaard, J. B. Christensen, N. Harrit, *J. Am. Chem. Soc.* **1998**, *120*, 12255–12263.

[21] K. K. Andersen, *Tetrahedron Lett.* **1962**, 93–95; K. K. Andersen, *J. Org. Chem.* **1964**, *29*, 1953–1956; P. Pitchen, H. B. Kagan, *Tetrahedron Lett.* **1984**, *25*, 1049–1052; P. Pitchen, E. Dunach, M. N. Deshmukh, H. B. Kagan, *J. Am. Chem. Soc.* **1984**, *106*, 8188–8193; G. Solladié, J. Hutt, A. Girardin, *Synthesis* **1987**, 173.

[22] a) G. Solladié, *Synthesis* **1981**, 185–196; b) M. C. Carreño, *Chem. Rev.* **1995**, *95*, 1717–1760; c) C.-C. Wang, H.-C. Huang, D. B. Reitz, *Org. Prep. Proced. Int.* **2002**, *34*, 271–319, and references therein.

[23] M. R. Naimi-Jamal, J. Ipaktschi, M. R. Saidi, *Eur. J. Org. Chem.* **2000**, 1735–1739, J. Yoon, D. J. Cram, *J. Am. Chem. Soc.* **1997**, *119*, 11796–11806; A. Albinati, P. Bravo, F. Ganazzoli, G. Resnati, F. Viani, *J. Chem. Soc. Perkin Trans. 1* **1986**, 1405–1415; J. G. Hansen, M. Johannsen, *J. Org. Chem.* **2003**, *68*, 1266–1274; P. Macours, J. C. Braekman, D. Daloze, *Tetrahedron* **1995**, *51*, 1415–1428.

[24] (R,P) and (R,M) indicate that the diastereomers contain a sulfoxide moiety of R configuration and are derived from the P and M enantiomers of compounds **1**, respectively.

[25] The ^{1}H NMR spectrum of the crude reaction mixture showed two sets of related signals in a 1:1 ratio; this ratio was confirmed by chiral stationary phase (CSP) HPLC analysis (Chiralpak AD-H, Daicel, *n*-hexane/*i*PrOH). See Supporting Information for details.

[26] K. Bur Scott, A. Padwa, *Chem. Rev.* **2004**, *104*, 2401–2432; A. Padwa, A. G. Waterson, *Curr. Org. Chem.* **2000**, *4*, 175–203.

[27] The high enantiomeric purity of (−)-[**1a**][PF$_6$] and (+)-[**1a**][PF$_6$] was verified by ^{1}H NMR spectroscopy using [Bu$_4$N][Δ-BINPHAT] as an NMR chiral solvating agent. The enantiomeric ratio (e.r.) of [**1a**][PF$_6$] to [**1d**][PF$_6$] is therefore assumed to be identical to the diastereomeric ratios of the precursors **4a–d**.

[28] Crystal data for (+)-(R,P)-**4c** ($C_{35}H_{38}N_2O_3S$): $M_r = 566.8$, $\mu = 0.148\ \text{mm}^{-1}$, $d_x = 1.273\ \text{g cm}^{-3}$, monoclinic space group $P2_1$, $Z = 2$, $a = 11.2301(10)$, $b = 10.5366(7)$, $c = 12.5563(10)$ Å, $\beta = 95.509(10)°$, $V = 1478.9(2)$ Å^3. A colorless prism ($0.19 \times 0.22 \times 0.34\ \text{mm}^3$) was mounted on a quartz fiber with protection oil. The cell dimensions and intensities were measured at 200 K on a Stoe IPDS diffractometer with graphite-monochromated Mo$_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). Of 20736 measured reflections, 6497 were unique and 3869 were observed ($|F_o| > 4\sigma(F_o)$); R_{int} for 14219 equivalent reflections 0.058. Data were corrected for Lorentz and polarization effects and for absorption ($T_{min,max} = 0.9629, 0.9745$). The structure was solved by direct methods (SIR97), all other calculations were performed with XTAL system and ORTEP programs. Full-matrix least-squares refinement based on F using weight of $1/(\sigma^2(F_o) + 0.00025(F_o^2))$ gave final values $R = 0.040$, $\omega R = 0.036$, and $S = 1.46(2)$. The maximum Δ/σ on the last cycle was 0.91×10^{-4}. Flack parameter $x = 0.01(12)$. Hydrogen atoms were placed in calculated positions. The ECD spectrum of the crystal analyzed by X-ray diffraction was totally superposable to the spectrum of bulk (+)-**4c**. CCDC-252698 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.