either MA or dimer to give, respectively, methyl propionate or dimethyl adipate.

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Supplementary Material Available: A listing of the synthetic procedures used to prepare **2**, **4**, **6**, and **7**, ^1H and ^{13}C NMR spectral data for **2**, **4**, **6**, and **7**, microanalytical data for **4**, **6**, and **7**, details of kinetic calculations, and crystal data and an ORTEP diagram for **7a** (9 pages). Ordering information is given on any current masthead page.

Stereochemistry of Chiral, Nonracemic Lithium Salts of Acyclic α-Sulfonyl Carbanions: The Asymmetric Induction Exerted by the Lithium-Coordinated Sulfonyl Group

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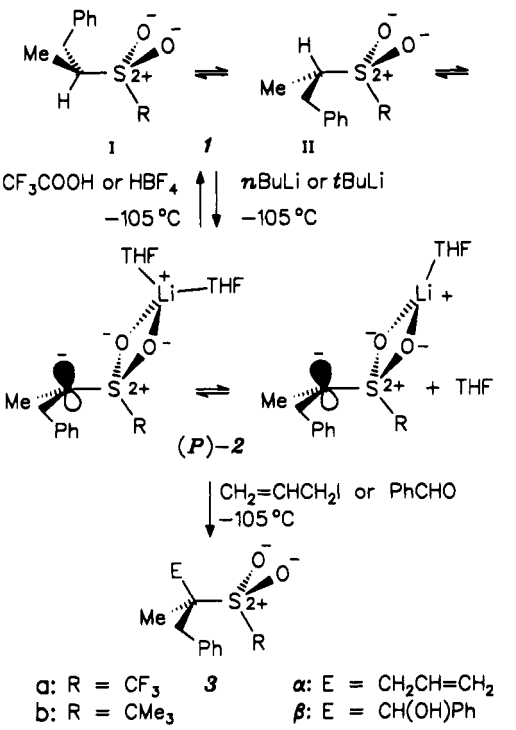
We have recently described the synthesis of the lithio (trifluoromethyl)sulfone (*M*)-(−)-**2a**[1,2] (Scheme I), which has an extrapolated half-life for racemization of 30 days at −78 °C. It belongs to the exceedingly small group[3] of functionalized chiral, nonracemic organolithium compounds which are configurationally stable on a synthetic time scale while lacking elements of auxiliary chirality. The attainment of (*M*)- and (*P*)-**2a**[1,2,4] allowed for the first time the study of the asymmetric induction exerted by the sulfonyl group at the α-C atom in lithium salts of acyclic α-sulfonyl carbanions. The stereochemistry of deuteration and protonation of transient chiral, nonracemic acyclic α-sulfonyl carbanions has been studied through base-catalyzed H/D-exchange, retro-aldol, and decarboxylation reactions of optically active sulfones.[5]

We report herein on the synthesis and racemization kinetics of a new chiral, nonracemic lithio sulfone, the lithio *tert*-butylsulfone (*P*)-(+)-**2b** (Scheme I), and on the stereochemistry of the formation and protonation as well as alkylation of (*P*)-(+)-**2a** and (*P*)-(+)-**2b**.

(*P*)-**2b** was generated by deprotonation of the sulfone (*S*)-**1b**[4] (≥99% ee[6a]) in THF at −105 °C with *n*-BuLi in THF[7] and its

Scheme I



racemization in the presence of DMPU (4 equiv)[8] monitored polarimetrically at low temperatures as a function of time.[4] The process was found to follow pseudo-first-order kinetics. This allowed for a determination of the activation parameters $\Delta G^{\ddagger}_{298}$ = 13.0 ± 0.3 kcal mol^{-1}, $\Delta H^{\ddagger}$ = 13.2 ± 0.3 kcal mol^{-1}, and $\Delta S^{\ddagger}$ = 0.6 ± 1.2 cal mol^{-1} K^{-1}, which translate into an extrapolated half-life of 3 h at −105 °C. A comparison with the activation parameters $\Delta G^{\ddagger}_{298}$ = 17.3 ± 0.3 kcal mol^{-1}, $\Delta H^{\ddagger}$ = 16.7 ± 0.3 kcal mol^{-1}, and $\Delta S^{\ddagger}$ = −1.9 ± 1.1 cal mol^{-1} K^{-1} for the racemization of (*M*)-**2a** in THF[1] reveals, besides a very small entropic contribution in both cases, a lower barrier to Cα–S bond rotation in (*P*)-**2b**, which we ascribe to a reduced n_C–σ^*_{SR} hyperconjugation as well as Coulombic interaction.[1,9] Restricted Cα–S bond rotation due to torsional as well as electronic effects, not restricted inversion of the α-C atom, is decisive for the configurational stability of (*P*)-**2b**. This follows, among other conclusions, from the similar activation parameters obtained by ^1H DNMR spectroscopy for the enantiomerization of (±)-lithium 1-(*tert*-butylsulfonyl)-1,2-diphenylethanide,[9] whose α-C atom is planar,[4] and of *rac*-**2b**,[4] whose α-C atom is most probably pyramidal.[10]

Deprotonation of the sulfones (*S*)-**1a**[1,4] (≥98% ee[6b]) and (*S*)-**1b**[4] (≥99% ee[6a]) in THF at −105 °C with *n*-BuLi (1 equiv) in *n*-hexane or THF[7] (3 min[11]) led to the lithio sulfones (*P*)-**2a** and (*P*)-**2b**, respectively. They gave, upon protonation at −105 °C with CF_3COOH (4 equiv) in THF,[7] with overall retention of configuration, (*S*)-**1a** (97%) of 82% ee[6c] and (*S*)-**1b** (98%) of 90% ee,[6a,c]

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(7) The solution was precooled to about −80 °C.

(8) Racemization of (*P*)-**2a** and (*P*)-**2b** in THF is slower in the presence of *N*,*N*'-dimethyl-*N*,*N*'-propyleneurea (DMPU) (Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385 and references cited therein), thereby allowing in the latter case for a determination of the temperature dependency of k_{rac} at experimentally more convenient temperatures.[1,4]

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(11) Quantitative deprotonation of (*S*)-**1a** and (*S*)-**1b** after the time given was ascertained in each case by deuteration.

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respectively. Addition of (*S*)-**1a** and (*S*)-**1b** in THF[7] to *t*-BuLi (1 equiv) in THF at −105 °C and protonation of thus formed (*P*)-**2a** (3 min[11]) and (*P*)-**2b** (10 min[11]), respectively, at −105 °C with CF_3COOH in THF[7] led to (*S*)-**1a** (96%) with 87% ee[6c] and (*S*)-**1b** (98%) with 92% (93%[12]) ee,[6a,c] respectively. Thus deprotonation of (*S*)-**1a** and (*S*)-**1b** with *t*-BuLi in THF seems to be slightly more selective than with *n*-BuLi in THF/*n*-hexane. Allylation of (*P*)-**2a** and (*P*)-**2b**, which were generated as described above with *t*-BuLi, with allyl iodide (2 equiv) in THF[7] at −70 and −100 °C, respectively, gave after a reaction time of 300 min and 10 min, respectively, the homoallylic sulfones (*R*)-**3a**α (79%) with ≥95% ee[6d] and (*R*)-**3b**α (80%) with 92% (95%[12]) ee,[6a] respectively. Hydroxyalkylation of (*P*)-**2b**, generated from (*S*)-**1b** with *t*-BuLi at −105 °C (10 min[11]), with benzaldehyde (2 equiv) in THF[7] at −105 °C (10 min) delivered the hydroxy sulfones (*S*,*R*)-**3b**β and (*S*,*S*)-**3b**β (84%; 3:2), each with 92% (95%[12]) ee.[6a] The (*R*) configuration at the α-C atom was provisionally assigned to the sulfones **3a**α and **3b**α and the (*S*) configuration to the sulfone **3b**β since the alkylation of (*P*)-**2a** and (*P*)-**2b** should proceed with the same sense of asymmetric induction as the protonation (vide infra).

The above enantioselectivities are composites and stem from the two stereoselective processes deprotonation and either protonation or alkylation. It follows, from cryoscopy,[1,9] $^6Li\{^1H\}$ NOE spectroscopy,[1] ab initio calculations,[13,14] X-ray structure analysis,[1,4,9,10,15,16] and other studies[17] of α-sulfonyl carbanion salts, that (*P*)-**2a** and (*P*)-**2b** are most probably monomeric contact ion pairs in THF at low temperatures endowed with (a) a chiral conformation, which is due to a stabilization by $n_C-\sigma^*_{SR}$ hyperconjugation[13] and a minimization of torsional strain, (b) a pyramidalized and hence chiral α-C atom, and (c) *a THF-solvated Li atom which is bound to the O atoms but not to the* α*-C atom* as depicted in Scheme I. Enantioselective formation of (*P*)-**2a** and (*P*)-**2b** can be attributed to a preferential intermolecular deprotonation of (*S*)-**1a** and (*S*)-**1b**, respectively, in conformation II (Scheme I) primarily for steric and electronic[13,14] reasons. It remains to be determined if and to what extent selectivity is due to a prior coordination of *n*-BuLi or *t*-BuLi to the sulfonyl group (O–Li)[18] of (*S*)-**1a** and (*S*)-**1b** followed by an intramolecular deprotonation in conformation II[5] as proposed for other systems.[19] Enantioselective protonation and alkylation of (*P*)-**2a** and (*P*)-**2b** occurs preferentially syn to the O atoms and can be attributed to two major factors whose individual contribution is not apparent yet: (1) steric hindrance by the CR_3 group and (2) the pyramidalization of the α-C atom,[20,21] which originates from a relief of torsional strain between the alkyl groups and the O atoms in conjunction with a shallow pyramidalization potential.[10b,14] From crystal structure analysis of a monomeric and several dimeric α-sulfonyl carbanion salts containing THF[4,9] or other ethers as ligands,[10a,15,22] however, a severe shielding of the α-C atom by the syn-positioned THF molecule in disolvated (*P*)-**2a**/**b**·2THF is perceptible. Therefore it seems likely that monosolvated (*P*)-**2a**/**b**·THF (Scheme I), which could be in a fast equilibrium with (*P*)-**2a**/**b**·2THF, is the decisive species. In this case, however, intramolecular protonation and alkylation via prior coordination of the electrophile to the Li atom[23] could be the preferred reaction path. In order to probe this possibility in the case of the protonation, (*P*)-**2b** generated from (*S*)-**1b** with *n*-BuLi in THF at −105 °C was treated at −105 °C with HBF_4 in Et_2O.[7] Here, too, (*S*)-**1b** was isolated but with the slightly lower ee value of 82%.[6b]

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Thermodynamic Analysis of β-Turn Formation in Pro-Ala, Pro-Gly, and Pro-Val Model Peptides in Methylene Chloride

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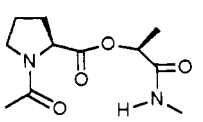
β-turns constitute the smallest common element of protein secondary structure[1] accounting for up to one-third of the residues in globular proteins.[2] Information on the intrinsic stability of such turns in various environments should provide insight on the origin of protein folding patterns. Although turn conformations have been detected within small linear peptides in numerous solvents,[3] only a few attempts have been made to quantify the extent of turn formation.[4] Thermodynamic relationships between folded and open peptide conformations have been explored computationally,[5] but not experimentally. We report a thermodynamic assessment of β-turn formation in Pro-Ala, Pro-Gly, and Pro-Val model peptides in methylene chloride solution.[6]

Figure 1 shows the temperature dependences of the amide proton chemical shifts ($\Delta\delta NH/\Delta T$) of Ac-L-Pro-L-Ala-NHMe (**1**) and two reference compounds, depsipeptides Ac-L-Pro-L-Lac-NHMe (**2**)[7] and c-$C_5H_9C(=O)$-Lac-NHMe (**3**), in CD_2Cl_2.



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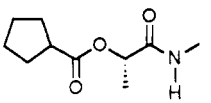

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(6) Abbreviations: Ala = alanine residue, Gly = glycine residue, Lac = lactic acid reside, Pro = proline residue, c-$C_5H_{11}C(=O)$ = cyclopentylcarbonyl.

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