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Synthesis of 2,6-Diaminotriptycene Conjugates with Chiral Auxiliaries: Towards the Scalable Resolution of Crucial Triptycene Intermediates

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Abstract: Triptycenes are tridimensional molecular scaffolds with interesting properties for applications in materials science: molecular rigidity and preorganization, tailorable chromophores, and, with an appropriate substitution pattern, chirality. The separation of the two enantiomers of chiral triptycenes has been the subject of increasing interest in recent years, with limited success. Here, we report the synthesis and characterization of a series of new organic compounds, in which a chiral triptycene scaffold, derivatized in the 2 and 6 positions with amino groups, has been functionalized with different enantiopure chiral auxiliaries, forming diastereoisomeric couples. The properties of such compounds, in terms of the optimization of their chromatographic separation, are elucidated with the aid of computational calculations of preferred conformations and molecular polarities.

Keywords: triptycenes; chirality; chiral auxiliaries; high performance chromatography

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1. Introduction

Asymmetry, when inserted into supramolecular or nano-aggregate systems, can give rise to sophisticated optical properties (electronic circular dichroism (ECD), vibrational circular dichroism (VCD), and circularly polarized luminescence (CPL)), which can be manipulated for a series of applied outputs [1–6]. Many examples have been reported in the last decade concerning the use of chiral π-conjugated synthons, in which the chiroptical output can be expressed in the chromophore region [7]. In this context, the relevance of chiral synthons with C_2 symmetry, such as binaphthyls, is now fully recognized [8]; they have been used as chiral subcomponents to dictate the stereochemical outcome of self-assembled helicates, and for water-soluble enantiomeric macrocycles having excellent enantioselectivity in water [9,10].

Triptycenes are instead an intriguing class of organic molecules with several unusual characteristics [11–15]. When decorated with an appropriate substitution pattern, triptycenes can be chiral, and can express chirality robustly, efficiently, and with relevance to chiroptical spectroscopies (Figure 1) [16–18].

The field of chiral triptycene-containing supramolecular systems is "opening up" as researchers exploit their unique properties to develop new chiral materials and supramolecules. Selected chiral triptycenes have recently been successfully incorporated into nanostructures as metallamacrocycles, π-conjugated oligomers or polymers, and supramolecular receptors [18–24]; the applications of chiral triptycenes are still relatively unexplored, due to the lack of useful strategies to obtain these synthons in enantiopure form on a large scale.

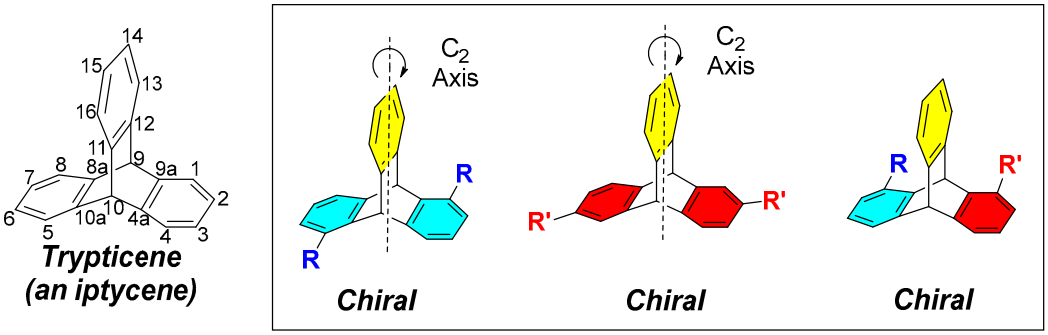


Figure 1. The structure of triptycene (**left**), and some of the substitution patterns affording chiral triptycene derivatives (**right**).

Potential strategies for obtaining enantiopure chiral triptycenes are crystallization of diastereomeric salts, enantioselective synthesis, chiral HPLC, and resolution with chiral auxiliaries. Crystallization of diastereomeric salts has been used in the past to obtain the first chiral triptycenes [17,25–27], as well as in one more recent report [28]. Only two examples of enantioselective synthesis of chiral triptycenes have been reported to date, and although good enantiomeric excesses could be obtained, the syntheses were complex and the allowed structural variability (necessary for implementation in supramolecular systems) was limited [29,30]. In the majority of recent reports, resolution of chiral triptycenes was accomplished using chiral HPLC, with consequently limited the scalability of the resolution process [19–22,31–33].

Functionalization using chiral auxiliaries is probably the most promising approach to obtain large quantities of pure enantiomers of triptycene derivatives. It has been used in two cases: the resolution of triptycene-containing homochiral macrocycles [34] and the resolution of a chiral triptycene derivative [35]. In the latter case, recently reported by Mastalerz and coworkers, the separation of triptycenes enantiomers was performed using (*R*)-methoxy phenylacetic acid as the chiral auxiliary (Figure 2).

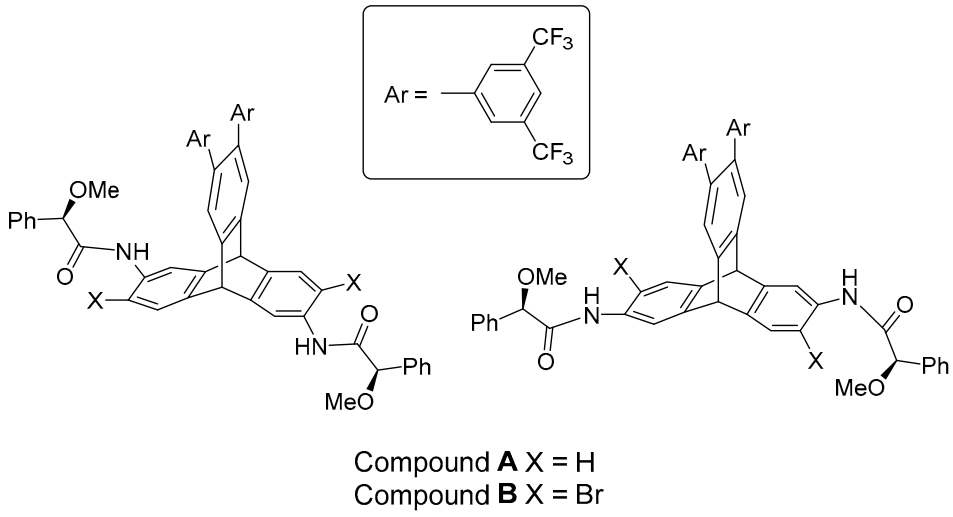


Figure 2. The chiral auxiliary approach for the scalable separation of enantiomers reported by Mastalerz and coworkers.

The separation of diastereoisomers using column chromatography could be achieved only on the derivative bearing bulky, polarizable bromine atoms on the 2,6-positions of the triptycene scaffold (compound **B**); in this case, the difference between the retention factors (DR_f = 0.1) allowed a relatively large scale enantioseparation (>1 g). However, when work-

ing on the synthetically more accessible compound **A** (Figure 2) (bearing hydrogen atoms instead of bromine atoms) the chromatographic separation ($DR_f < 0.05$) was inefficient.

2,6-Diaminotriptycene and 2,6-dinitrotriptycene are easily achievable on a >10 g scale. We believe that these synthons will play a pivotal role in the future, as amine groups can provide extensive structural variability, giving access to numerous derivatives, such as iodine, chlorine, bromine, and fluorine, just to mention some. From these derivatives, it will be possible to develop several new chiral functional materials, exploit new or known synthetic protocols, and take advantage of the peculiar properties of the triptycene skeleton, as highlighted in recent reviews [12,36–38].

We have shown how it is possible to obtain the resolution of compounds related to 2,6-diaminotriptycene on an analytical scale via chiral HPLC, and studied them as probes to study enantiorecognition properties of chiral stationary phases [39,40]. A practical, scalable resolution procedure would, however, be advantageous, and open new and exciting horizons in a variety of multidisciplinary fields, ranging from the construction of a new class of chiral macrocycles, chiral organic nanotubes, to high-performance chiral polymers with unique 3D-nanostructures. We recently reported the fusion of non-planar π-conjugated triptycene synthon with quinacridone chromophore, which is potentially generalizable to chiral small molecules or one-handed helical ladder polymers [41].

In this contribution, we report our efforts towards the resolution of the crucial chiral synthon 2,6-diaminotriptycene through a scalable chiral auxiliary approach.

2. Materials and Methods

2.1. General Experimental

Racemic mixtures of simple triptycene were synthetized following a previously reported procedure [41,42]. **Tripty-NO_2** and **Tripty-NH_2** were synthesized as reported previously [21,43]. All commercially available reagents and solvents were purchased from Sigma-Aldrich (Burlington, MA, USA), Fluorochem (Glossop, UK), TCI (Tokyo, Japan), and Alfa Aesar (Ward Hill, MA, USA). They were all used as received. Anhydrous solvents, such as THF and dichloromethane, were obtained using conventional methods through distilling with drying agents (Na for THF and CaH_2 for dichloromethane). Flash chromatography was carried out using Merck silica gel 60 (Merck Millipore, Burlington, MA, USA) (pore size 60 Å, 270–400 Mesh). ^{1}H and ^{13}C NMR spectra were recorded from solutions in deuterated solvents using 300 Bruker or 400 Bruker spectrometers (Bruker, Billerica, MA, USA) with the residual solvent as the internal standard. Mass spectra of pure compounds were recorded using an Electron Spray Ionization Agilent Technologies mass spectrometer (Agilent Technologies, Inc., Santa Clara, CA, USA), using direct exposure probe mass spectrometry. Chromatographic conditions for Section 3.2 are reported in the Supporting Information Section.

2.2. Synthetic Procedures

Synthesis of 1a. DCC (131 mg, 0.633 mmol, 3 eq) and *N*-hydroxy succinimide (73 mg, 0.633 mol, 3.00 eq) were added in small portions to a vigorously stirred solution of *N*-Boc-protected *L*-tryptophan (193 mg, 0.633 mmol, 3.00 eq) and racemic 2,6-diaminotriptycene (**Tripty-NH_2**) (60 mg, 0.211 mmol, 1.00 eq) in dry DCM (10 mL). The mixture was stirred at room temperature for 16 h, filtered on celite, and then concentrated in vacuo. The crude product was purified via silica gel flash column chromatography (EtOAc/hexane 1/1, Rf 0.30) as the eluent mixture to give the product **1a** (76 mg, 43%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.76 (s, 2 H), 9.92 (s, 2 H), 7.76 (s, 2 H), 7.62 (d, *J* = 7.9 Hz, 2 H), 7.43 (dd, *J* = 5.4, 3.3 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.1 Hz, 2 H), 7.12–6.94 (m, 8 H), 6.87 (d, *J* = 7.9 Hz, 2 H), 5.56 (d, *J* = 8.0 Hz, 2 H), 5.54 (s, 2 H), 4.31 (dd, *J* = 7.6, 7.6 Hz, 2 H), 3.14–2.78 (m, 2 H), 1.31 (s, 18 H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.88, 156.60, 155.21, 145.90, 145.34, 140.16, 135.98, 135.90, 127.26, 124.91, 123.75, 123.56, 123.47, 120.83, 118.55, 118.14, 115.56, 111.24, 109.86, 78.03, 52.17, 47.49, 33.33, 30.67. ESI-MS: 857.3 $[M + 1]^+$. Anal. calcd. for $C_{52}H_{52}N_6O_6$: C, 72.9; H, 6.1. Found: C, 73.1; H, 6.0.

Synthesis of 1b. A mixture of (1*S*)-(−)-camphanic chloride (152 mg, 0.703 mmol, 2.50 eq), 2,6-diaminotriptycene (**Tripty-NH_2**) (80 mg, 0.281 mmol, 1.00 eq), and NEt_3 (97.8 uL, 0.703 mmol, 2.50 eq) in anhydrous CH_2Cl_2 (10 mL) was stirred at room temperature overnight. At this point water was added and the mixture was extracted 3 times using CH_2Cl_2. The combined organic layers were washed with water, dried over Na_2SO_4, and concentrated in vacuo. The resulting solid was purified via silica gel flash chromatography with hexane/ethyl acetate 3/1 (Rf 0.35) as the eluent mixture to give 133 mg (73%) of the product **1b** as a white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.74 (s, 2 H), 7.86 (s, 2 H), 7.45–7.43 (m, 2 H), 7.38 (d, *J* = 7.96 Hz, 2 H), 7.25–7.21 (m, 2 H), 7.02–6.99 (m, 2 H), 5.57 (s, 2 H), 2.50–1.16 (m, 26 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.92, 165.15, 145.60, 145.20, 141.17, 134.64, 124.96, 123.52, 123.40, 117.50, 117.28, 91.78, 59.74, 54.53, 53.54, 52.15, 29.30, 28.38, 20.75, 16.47, 16.26, 14.08, 9.55. ESI-MS: 645.5 $[M + 1]^+$. Anal. calcd. for $C_{40}H_{40}N_2O_6$: C, 74.5; H, 6.2. Found: C, 74.1; H, 6.4.

Synthesis of 1c. DCC (174 mg, 0.844 mmol, 3 eq) and *N*-hydroxy succinimide (97 mg, 0.844 mol, 3.00 eq) were added in small portions to a vigorously stirred solution of *N*-Boc protected (S)-2-phenylglycine (212 mg, 0.844 mmol, 3 eq) and racemic 2,6-diaminotriptycene (**Tripty-NH_2**) (80 mg, 0.281 mmol, 1.00 eq) in dry DCM (10 mL). The mixture was stirred at room temperature for 16 h, filtered on celite, and then concentrated in vacuo. The crude product was purified via silica gel flash column chromatography (EtOAc/hexane 4/1, Rf 0.37) as the eluent mixture to give the product **1c** (147 mg, 69%) as a white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.13 (s, 2 H), 7.74 (d, *J* = 5.29 Hz, 2 H), 7.46–7.38 (m, 6 H), 7.34–7.26 (m, 8 H), 7.06 (d, *J* = 7.91 Hz, 2 H), 6.98–6.96 (m, 2 H), 5.57 (d, *J* = 7.87 Hz, 2 H), 5.52 (s, 2 H), 5.30 (d, *J* = 7.77 Hz, 2 H), 1.38 (s, 18 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.87, 156.61, 155.04, 146.00, 145.18, 140.36, 138.10, 135.67, 128.32, 127.67, 127.25, 124.90, 123.67, 123.45, 115.26, 78.45, 59.73, 58.39, 55.83, 52.07, 47.50, 33.34, 29.59, 28.13, 25.31, 24.44. ESI-MS: 752.0 $[M + 1]^+$. Anal. calcd. for $C_{46}H_{46}N_4O_6$: C, 73.6; H, 6.2. Found: C, 73.9; H, 6.4.

Synthesis of 1d. A mixture of 2,6-diaminotriptycene (**Tripty-NH_2**) (90 mg, 0.316 mmol, 1.00 eq), (-)-menthyl chloroformate (460 mg, 2.10 mmol, 6 eq), and dry pyridine (170 µL, 2.10 mmol, 6.00 eq) in dry CH_2Cl_2 (10 mL) was stirred at room temperature for 5 h. The mixture was quenched with water and NaOH (1 M). The aqueous layer was extracted three times using diethyl ether, and the combined organic phases were washed with water and then dried over Na_2SO_4. The solvents were removed in vacuo and the residue was purified via silica gel flash column chromatography using hexane/ethyl acetate 9/1 (Rf 0.40) as the eluent mixture to give 164 mg (yield 80%) of product **1d** as a white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.48 (s, 2 H), 7.60 (s, 2 H), 7.43–7.39 (m, 2 H), 7.30 (dd, J_1 = 8.11 Hz, J_2 = 2.31 Hz, 2 H), 7.01–6.97 (m, 4 H), 5.47 (s, 2 H), 4.53 (dt, J_1 = 8 Hz, J_2 = 4.20 Hz, 2 H), 2.12–0.72 (m, 38 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.31, 146.08, 145.43, 145.41, 139.14, 139.13, 136.26, 124.81, 123.55, 123.36, 114.17, 114.10, 73.30, 55.82, 52.12, 46.86, 41.12, 33.75, 30.92, 29.58, 25.71, 22.99, 21.91, 20.52, 16.18. ESI-MS: 666.4 $[M + 1 + H_2O]^+$. Anal. calcd. for $C_{42}H_{52}N_2O_4$: C, 77.7; H, 8.1. Found: C, 73.9; H, 8.3.

Synthesis of 1e. DCC (131 mg, 0.633 mmol, 3 eq) and *N*-hydroxy succinimide (73 mg, 0.633 mol, 3.00 eq) in small portions were added to a vigorously stirred solution of (S)-mandelic acid (96 mg, 0.633 mmol, 3.00 eq) and racemic 2,6-diaminotriptycene (**Tripty-NH_2**) (60 mg, 0.211 mmol, 1.00 eq) in acetone (10 mL). The mixture was stirred at room temperature for 16 h, filtered on celite and then concentrated in vacuo. The crude product was purified via silica gel flash column chromatography (EtOAc/hexane 1/1, Rf 0.43) as the eluent mixture to give the product **1e** (55 mg, 48%) as a white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.80 (s, 2 H), 7.83 (s, 2 H), 7.47 (d, *J* = 7.17 Hz), 7.41–7.39 (m, 2 H), 7.34–7.26 (m, 6 H), 6.96–6.98 (m, 2 H), 6.35 (d, *J* = 4.64 Hz), 5.50 (s, 2 H), 5.05 (d, *J* = 4.58 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.95, 145.81, 140.83, 140.40, 135.41, 128.01, 127.52, 126.49, 124.88, 123.51, 123.45, 115.85, 115.73, 73.88, 55.83, 52.14. ESI-MS: 553.3 $[M + 1]^+$. Anal. Calcd. for $C_{36}H_{28}N_2O_4$: C, 78.2; H, 5.1. Found: C, 77.9; H, 5.0.

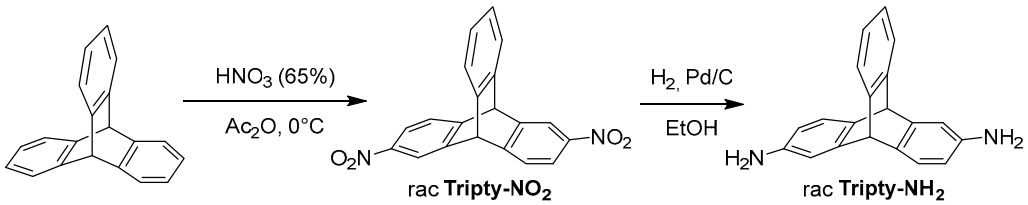
Calculations. All calculations were carried out using the Gaussian 16 program package [44] using B3LYP as a hybrid functional for DFT calculation [45,46]. The chosen basis

set was identical to all atoms as 6–31 g(d) [47–49]. With optimized structures, single points calculations were performed using the M06-2X functional [50]. Moreover, a different basis set was chosen for all atoms: def2SVPP [51,52]. The role of the dichloromethane solvent was simulated using the SMD solvation model [53]. All data reported below are referred to this level of theory, and discussions are based on the values of Gibbs relative energies in kcal/mol. Boltzmann population analysis was performed at 298.15 K.

3. Results

3.1. Synthesis

A racemic mixture of 2,6-diaminotripticene (**Tripty-NH_2**) was synthesized using procedures described by Swager and coworkers, as follows [21,43]. Briefly, synthesis starts from anthracene, which, via a Diels–Alder reaction with benzyne (generated in situ from anthranilic acid), yields unfunctionalized triptycene (Scheme 1). Triptycene is nitrated by treatment with HNO_3 in Ac_2O to give a racemic mixture of 2,6-dinitrotriptycene, which is readily reduced to **Tripty-NH_2**.

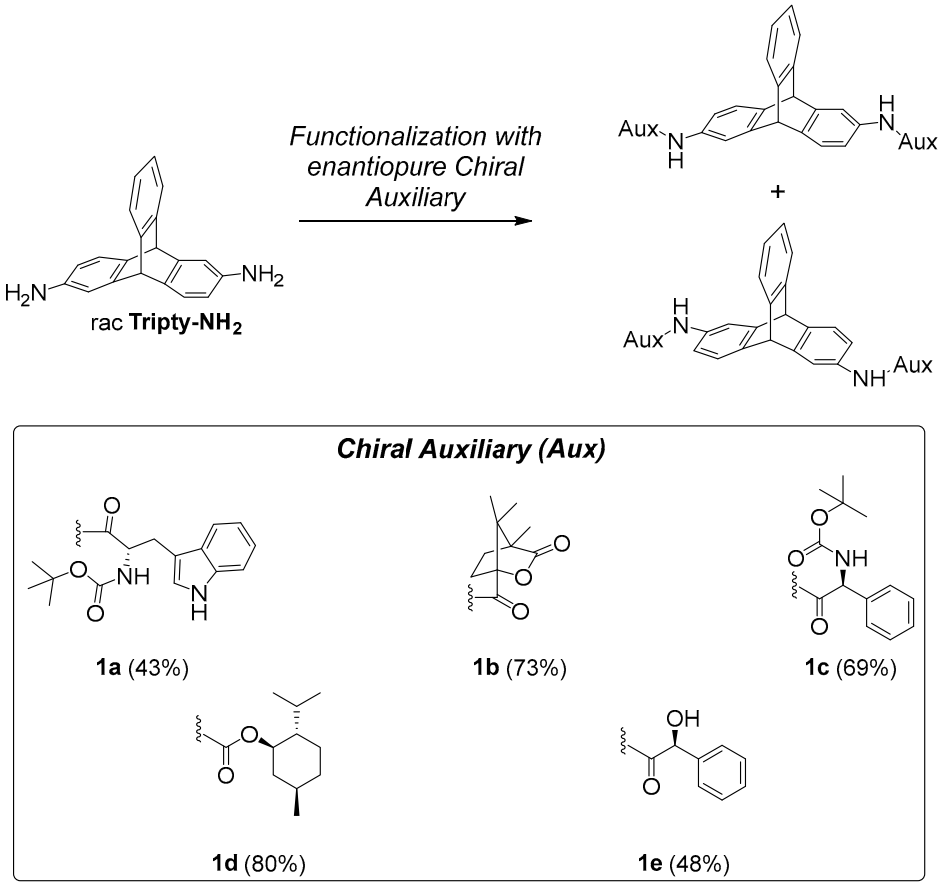


Scheme 1. Synthesis of 2,6-dinitrotriptycene **Tripty-NO_2** and its derivatives.

Initial attempts to resolve a racemic mixture of **Tripty-NH_2** involved crystallization tests with enantiopure chiral acids such as *L*-tartaric acid, (*S*)-camphosulfonic acid, and (*S*)-mandelic acid. Tests were performed by dissolving the triptycene derivative with two equivalents of the enantiopure acids in low-polarity organic solvents, such as chloroform or dichloromethane, and leaving the solution to crystallize via slow evaporation. Amorphous powders were obtained in all attempts.

We therefore turned our attention to the covalent functionalization of racemic **Tripty-NH_2** with enantiopure chiral auxiliaries. This strategy should yield a mixture of two different diastereoisomers; once separated via column chromatography, hydrolysis and detachment of the chiral auxiliaries on the isolated single diastereoisomers afford the pure enantiomers of **Tripty-NH_2**. The racemic mixture of **Tripty-NH_2** was successfully functionalized with five different enantiopure chiral auxiliaries (Scheme 2), which were selected based on their use as chiral auxiliaries in the literature and their commercial availability, as follows [54–57]: Boc-protected *L*-tryptophan, (1*S*)-(−)-camphanic chloride, Boc-protected (*S*)-2-phenylglycine, (-)-menthyl chloroformate, and (*S*)-mandelic acid.

All compounds (**1a**–**1e**) were obtained in fair to good yields using known coupling procedures and reagents for the formation of amide (**1a**–**1c** and **1e**) or carbamate (**1d**) functionalities. In more detail, in the cases of **1a**, **1d**, and **1e**, coupling was conducted using DCC, *N*-hydroxysuccinimide using carboxylic acid functionalities on the chiral auxiliary [58,59]; products were obtained in these cases in fair, similar yields. In the cases of **1b** and **1e**, acid chloride or carbamoyl chloride were used, respectively, because of their commercial availability, with substantial improvements in isolated yields.



Scheme 2. Synthesis of **1a**: Boc-protected *L*-tryptophan, DCC, *N*-hydroxysuccinimide, DCM, 0 °C; **1b**: (1*S*)-(−)-camphanic chloride, NEt_3, DCM, 0 °C; **1c**: *N*-Boc protected (*S*)-2-phenylglycine, DCC, *N*-hydroxysuccinimide, DCM, 0 °C; **1d**: (-)-menthyl chloroformate, NEt_3, DCM, 0 °C; and **1e**: (S)-mandelic acid, DCC, *N*-hydroxysuccinimide, DCM, 0 °C. Yields of isolated products are reported in parentheses.

All compounds were initially purified via column chromatography using hexanes/EtOAc mixtures in order to correctly identify the desired products via NMR spectroscopy and mass spectrometry; such products were isolated by collecting all chromatographically homogeneous material (single spots in TLC, in the eluent mixture used for the column). All other byproducts were analyzed to ascertain that one of the two diastereoisomers of the target compound was not left behind due to potentially large differences in retention times. Partial ^{1}H NMR spectra of conjugates **1a**–**1e** revealed no splitting of the proton resonances associated with bridgehead carbon atoms at ca. 5.5 ppm, which are the two formal centers of asymmetry in the triptycene scaffold (Figure 3). This observation hinted at a not optimal effect of the chiral auxiliaries, whose chiral centers were probably too far apart from the bridgehead carbon atoms, and thus exerted little shielding or deshielding effects on these protons.

We screened several eluent mixtures via TLC to verify whether a tangible difference in retention times could be obtained for any of the purified diastereomeric couples (**1a**–**e**), but no positive results were obtained.

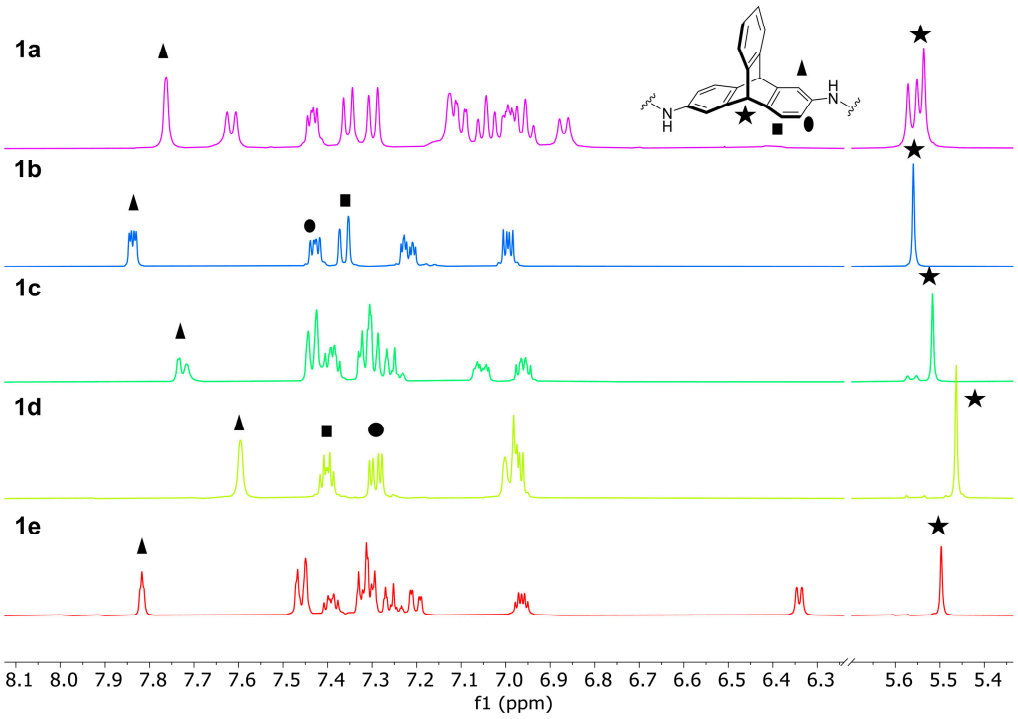


Figure 3. Partial ^{1}H NMR spectra of compounds **1a**–**1e** (300 or 400 MHz, DMSO-d_6 at 298 K).

3.2. Chromatographic Separation of Diastereoisomers

In order to explore the possibility of addressing the chromatographic separations of the diastereoisomeric couples of conjugates **1a**–**e** in a scalable way, we initially checked the ability to resolve the mixtures using an achiral RP-18 stationary phase. Conjugates **1a**–**e** were tested using an UHPLC equipped with a high performance column (see SI for instrument details and column features), but only one (conjugate **1d**) showed a small separation with a low analyte concentration (Figure S1). The difference in retention times was not practically useful in a preparative UHPLC column. Due to the low separation tendency and poor interaction with C18 on the achiral phase, we decided to use chiral stationary phases. Three different types of stationary phases were tested, as described in the Supporting Information Section. Due to the large variability of polysaccharide-based stationary phases, and based on previous work published by some of us [39], all conjugates were tested on all stationary phases. The standard conditions employed (nHeptane/IPA and nHexane/IPA as eluents) and the use of SFC (supercritical fluid chromatography: CO_2/IPA) did not show a significant increase in separation. Only OD3-type cellulose tris(3,5-dimethylphenylcarbamate) coated on 3 µm silica-gel showed some effectiveness in separating **1b** (Figure S2). Using this stationary phase, the other conjugates did not show suitable results for preparative applications.

3.3. Computational Investigation

A comprehensive analysis of the structures generated in the reaction was performed using DFT calculations (see Supporting Information). Conjugate **1d** was selected as the most straightforward example to analyze. All conformational rotamers for product **1d** and its diastereomer **1d′** were thoroughly explored. The most stable conformations for the two diastereomeric products are presented in Figure 4; a comprehensive overview of all conformations is available in the Supporting Information.

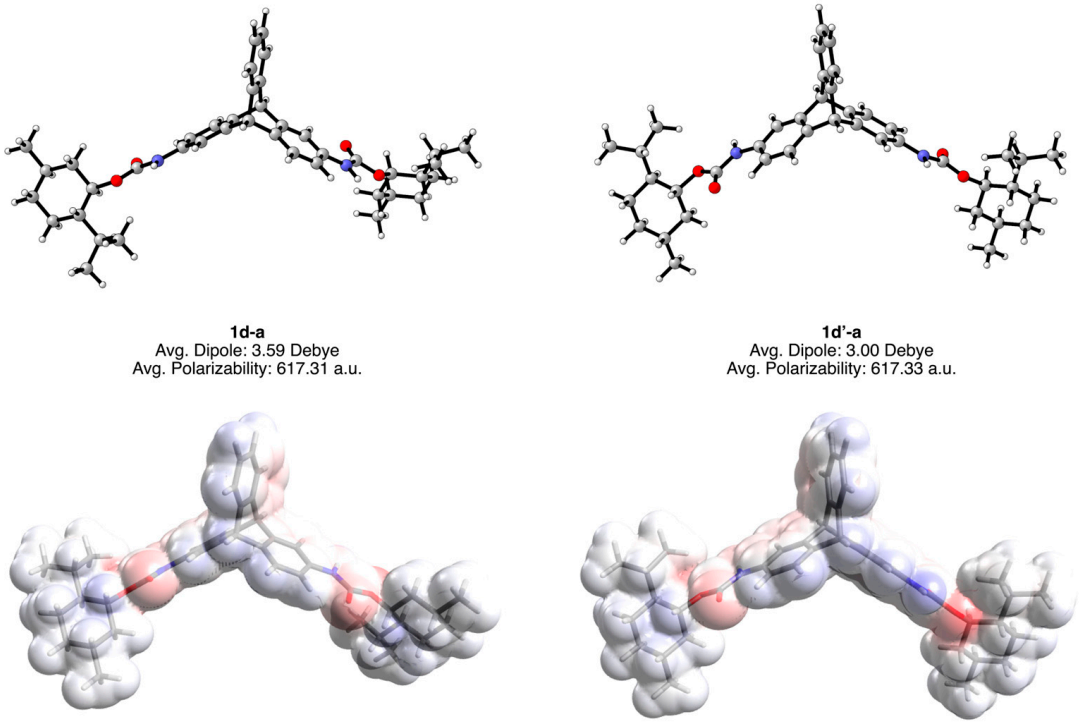


Figure 4. Most stable conformers for **1d** and **1d′** diastereomers. The Boltzmann weighted molecular dipole is reported below each structure, together with the weighted polarizability and the map of electrostatic potential (MEP). [SMD(DCM)-M06-2X/def2svpp//B3LYP/6-31g(d)]. Red and blue colors indicate the different electron densities (most electron density resides in the more red areas, the least electron density resides in the blue areas).

The two systems were too similar in geometry to exert an efficient separation through a chromatographic column. The molecular dipoles of both systems were very similar (i.e., 3.59 Debye for **1d** and 3.00 Debye for **1d′** weighted values, in accordance with Boltzmann population analysis (see SI for more details)) and the polarizability appeared nearly identical, with a value close to 617 a.u. in both cases. The analysis of the map of electrostatic potential (MEP) displays the same orientation of polar surfaces in both systems. A parallel investigation was conducted on products **1a**, **1b**, **1c**, and **1e**, but no system was identified with a stronger difference in terms of molecular dipole; in **1a** chiral auxiliaries consistently occupied the space around the triptycene core (see Supporting Information), but chromatographic results showed no separation during all conditions performed. The conformational study showed us that, although chiral auxiliaries are bulky in space, they do not lead to situations in which the dipole moment and polarization of the molecule are sharply varied. Hence, this results in a lack of resolving ability on the part of the interactions with the stationary phase in the column.

4. Conclusions and Outlook

We successfully synthesized a library of conjugates formed via the coupling of 2,6-diaminotriptycene with a series of enantiopure derivatives belonging to the natural chiral pool, generating either amide or carbamate derivatives in fair to good isolated yields. The stereogenic centers of the chiral auxiliaries were located in all cases at a distance greater than 4 Angstrom from the stereocenter of the triptycene moieties, in their more stable conformations, as shown using calculations. The conjugates appeared to operate in a completely independent way: the nonpolar portion of the π-extended synthon was chemically linked to an enantiopure side chain, which in some cases satisfied the requirements, but in others was unsuitable for interacting efficiently with the stationary phase. Carbamate-containing compound **1d** showed the best performance in achiral HPLC conditions, probably suggest-

ing a higher flexibility of this functionality with respect to amides. This study is for us, and hopefully for other research groups involved in the use of chiral triptycenes, a starting point for the elaboration of novel strategies for a more effective utilization of a chiral auxiliary strategy for the enantioseparation of 2,6-diaminotriptycene. Potential strategies involving a functionalization of the 1,5-positions of the triptycene scaffolds may be much more powerful for addressing a large scale enantioseparation. Sugars have been recently shown to effectively perform as chiral auxiliaries. Their large number of stereogenic centers, together with their easy accessibility and low cost, can be the key for the scalable resolution of triptycene derivatives [60,61].

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/sym16010116/s1: Figures S1 and S2, and Table S1: additional details for chromatographic analyses; Figures S3 and S4, Table S2: additional details for computational analyses; Figures S5–S20: copies of the NMR; and mass spectra of the newly reported compounds.

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