New iodotriptycenes, including some chiral derivatives, have been synthesised, and their catalytic potential towards oxidative transformations has been investigated. The enantioselectivities observed in the products using chiral iodotriptycene catalysts are low, probably owing to the large distances between the coordinating groups and the iodine moieties in these compounds.

Introduction

Triptycenes have a bridged bicyclooctatriene core structure and are the simplest members of the iptycene family. These rigid molecules with $D_{3h}$ symmetry provide a large free volume around the three aromatic rings which are at an angle of 120°. Mainly achiral triptycenes have been extensively studied in different areas such as polymer chemistry, materials chemistry, molecular machines, nanosized molecular cages, molecular balances, medicinal chemistry, peptide chemistry, molecular assembly and host–guest chemistry. Triptycenes as structures for catalysts or reagents in organic transformations have not been explored intensively. Some work highlights the use of triptycenes as a ligand/catalyst incorporating metals, mostly pincer-type ligands/complexes in organic transformations such as alkenes and 2-methyl-3-butenenitrile isomerization, chemo-selective transfer-hydrogenation of $\alpha,\beta$-unsaturated ketones, transfer dehydrogenations of alkanes, bis-hydroformylation of butadiene, selective hydrocyanation of butadiene, cyanation of aryl bromides, and cross-coupling reactions of aryl chlorides with phenylboronic acid. Very recently, triptycenyl methyl sulfide has been explored for electrophilic aromatic halogenations with N-halosuccinimides through the formation of sulfonium salt 1 as the active species (Figure 1a). Metal-free trifluoromethylthiolation of aromatic compounds has also been investigated. Mainly achiral triptycenes were explored in different areas of chemicals and material science, although the first synthesis of chiral triptycenes was reported in 1962. Very recently, reviews have been published on chiral triptycenes. Triptycene-based ligands in enantiopure form have been prepared by lithiation of rac-1-bromo-8-diphenyloxophosphinotriptycene and subsequent quenching with enantiomerically pure (1R,2S,5R)-(−)-menthyl (S)-p-toluenesulfinate. The diastereomers were resolved using column chromatography and finally hydrogenated to P,S-symmetry provides a large free volume

Results and Discussion

Initially, the triptycene core structure bearing iodine at position 1 or 2 in one of the aromatic rings was prepared. For this approach, readily available 2-amino-5-iodobenzoic acid 4a was reacted with anthracene 3a to form 2-iodotriptycene 5a in 30% yield (Scheme 1). Similarly, regioisomer 4b was reacted with 3a to form 1-iodotriptycene 5b in 25% yield (Scheme 1). Compounds 5a and 5b were fully characterized, including single-crystal X-ray structures.
The hypervalent iodine(III) compounds 6a and 6b were synthesised in 91 % and 78 % yield, respectively, by reacting 5 with Selectfluor® in the presence of acetic acid and acetonitrile (see Supporting Information).

The 1- and 2-iodo-substituted triptycene compounds 5 were investigated as catalysts in the α-oxoytolsylation of propiophenone. Propiophenone was reacted in presence of para-toluenesulfonic acid, meta-chloroper oxybenzoic acid and 10 mol % of iodotriptycene in acetonitrile at room temperature. Catalyst 5a provided the product in 62 % yield and catalyst 5b showed 76 % yield for the α-oxoyltsylated propiophenone. These results showed that 5a and 5b can act as an iodine catalyst (see below). Catalysts 5a and 5b were recovered in about 50 % from the reaction mixture. These recovered catalysts were reused in this reaction and were found to be similarly efficient.

Encouraged by these initial results, the synthesis of different chiral iodotriptycenes by reacting substituted anthracene derivatives with either 4a or 4b was carried out. The iodotriptycenes 5 obtained as Diels–Alder products are shown in Figure 2.

To obtain 5c (Figure 2), commercially available 1-chloroanthracene 3b was reacted with 4a under the same reaction conditions as described for compound 5a and 5b. The reaction provides a mixture of diastereomers 5c (synanti = 1 : 1.6) in 16 % yield which were separated using preparative thin layer chromatography (TLC). The geometries of the isolated diastereomers were assigned by X-ray crystallographic analysis, which identified the major compound as the anti-product 5c (see Supporting Information). For the compound syn-5c, the enantiomers were separated using chiral HPLC columns to provide (−)syn-5c (ee = 98 %) and (+)syn-5c (ee = 67 %).

To prepare other chiral iodotriptycene derivatives, 2-methoxyanthra n cene 3c and 1-methoxyanthracene 3d were synthesised in a stepwise process (Scheme 2). Compound 9 was prepared using a palladium-catalysed C–H arylation of 2-methylbenzaldehyde 7 with methoxyiodobenzene 8.[20] Compounds 9 were then cyclized to 3c and 3d on a gram scale using boron trifluoromethane. Product 3c was obtained in 32 % yield whereas 3d was only observed in trace amounts due to the formation of a polymeric product (see Supporting Information). Other Lewis acids such as In(OTf)3,[21] Bi(OTf)3, Sc(OTf)3, Cu(OTf)2, and FeCl3 also failed to provide 3d.

As the position of iodine is not very close to the chiral centre in syn-5c, the synthesis of chiral 1-iodosubstituted triptycenes was then envisaged. The use of symmetrical anthracenes will avoid the formation of diastereomers. For this approach, 1,4-dimethoxyanthracene 3e was prepared from 1,4-dihydroxyanthraquinone 12 through methylation and reduction similar to the reaction conditions described for 3d and used in the Diels–Alder reaction to obtain triptycene 5f (Scheme 3) in 11 % yield. Typically, the yields for triptycene products in this step are low, as a controlled addition of anthranilic acid

![Scheme 1. Process to obtain iodotriptycenes 5 the corresponding iodine(III) derivatives 6.](Image 70x633 to 268x775)

![Scheme 2. Synthetic routes to 1- and 2-methoxyanthracene 3c and 3d (TFA: trifluoroacetic; TBAB: tetrabutylammonium bromide).](Image 88x114 to 249x300)

![Figure 2. Syn- and anti-diastereomers of chiral iodotriptycene derivatives 5.](Image 306x123 to 548x249)
derivatives is necessary to reduce benzene dimerization. Owing to the advantages of controlled addition and intense mixing of the substrates and reagents in flow chemistry,\cite{23} this Diels–Alder reaction was performed in a flow system. A 0.25 M solution of 4b in 1,2-dimethoxyethane and a 0.125 M solution of 3e in either 1,2-dimethoxyethane or 1,2-dichloroethane containing isoamyl nitrite were pumped with a flow rate of 0.2 mL min\(^{-1}\) (2.5 min residence time) through a PTFE coil at 90 °C. Interestingly, the reaction efficiency increased with 1,2-dichloroethane as solvent, providing 38% yield of 5f (1,2-dimethoxyethane: 24% yield of 5f). The racemic compound 5f obtained was fully characterised, including X-ray analysis.\cite{23} Crystal structure shows an I···O distance of 4.58 Å. Before separating the enantiomers of 5f, its catalytic activity was investigated in the α-oxytosylation of propiophenone that provided the desired product in 74% yield. However, a separation of the enantiomers of 5f using chiral phase HPLC was not possible due to the very low solubility of 5f in solvents compatible with the chiral column.

To overcome this issue, both methyl groups from 5f were removed using BBr\(_3\), and 5-ido-1,4-dimethoxytripyrene 13 was obtained in 87% yield (Scheme 3). When compound 13 was passed through the HPLC column aiming to separate the enantiomers, it was found to be unstable as it oxidized to the corresponding quinone (see Supporting Information). Therefore, 13 was initially reacted with (1S)-(−)-10-camphorsulfonyl chloride 14 (Scheme 4) to prepare a diastereomeric mixture, but the resulting diastereomers were difficult to isolate and separate. However, when 13 was treated with (1S)-(−)-camphoric chloride 15, the diastereomeric mixture could be separated using preparative TLC (Scheme 4). The camphyl substituents were then removed from the isolated isomers (+)-16 and (−)-16 by treatment with hydrochloric acid in methanol and the methyl groups were installed again using dimethyl sulfate in a one-pot procedure without isolating the intermediate to afford (+)-5f and (−)-5f in 72% and 74% yield, respectively. The absolute configuration of each of the enantiomers was determined by their single-crystal X-ray structures. The HPLC purity was high and the enantiomeric excess was > 99% for both.

Compounds (−)-5f and (+)-5f were subsequently investigated in stereoselective oxidative transformations as shown in Scheme 5. When used in the α-oxytosylation of propiophenone, the product 18 was formed with 68% (71%) yield in only 3% ee. Similarly, the use of (−)-5f and (+)-5f in the dearomatizing cyclization of 19 provided 20 in 38% yield (6% ee) and 32% yield (1% ee), respectively. (−)-5f and (+)-5f were also screened for the dearomatic spirolactonization of 21. (−)-5f provided the product 22 in 23% yield with an enantioinduction of 6% while (−)-5f resulted in a 30% yield with 2% ee. Furthermore, the oxidative rearrangement of 23 was observed with both the catalysts (−)-5f and (+)-5f. (−)-5f showed the formation of the product 24 in 63% yield (1% ee) and (−)-5f in 70% (1% ee). The isolated intermediates (+)-16 and (−)-16 were also investigated for the dearomatizing...
cyclization of 19. However, (+)-16 produced the compound 20 in 28% yield (1% ee) and (−)-16 in 31% yield (5% ee), indicating that these compounds are also not selective catalysts. The absolute configuration of the products 18, 19, 20, 21, 22, and 24 were assigned using data reported in literature.

All the results obtained from the screened reactions show low enantioselectivities for the products (Scheme 5). This could be due to the rather large distance between the iodine and the coordinating methoxy group in 5 of about 4.58 Å. The design of a suitable coordinating ligand in closer proximity to iodine centre is desirable. New chiral iodotriptycene in stereoselective reactions are being explored and will be reported in due course.

**Conclusions**

In conclusion, a reliable approach for the synthesis of iodotriptycenes has been established. Reacting either 3- or 5-idoanthranilic acid with differently substituted anthracenes provides iodotriptycenes. Iodotriptycenes were shown to be efficient catalysts in several oxidative organic transformations. For two chiral triptycene derivatives, the enantiomers were separated and investigated in enantioselective oxidative transformations. The enantioinduction in the products, however, was very low. This investigation provides new and useful information for the synthesis of chiral triptycenes including hypervalent iodine chemistry.

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**Conflict of Interest**

The authors declare no conflict of interest.

**Data Availability Statement**

The data that support the findings of this study are available in the supplementary material of this article.

**Keywords:** iodine(III) reagents · ligand synthesis · oxidation · stereoselective synthesis · triptycenes

[1] a) P. D. Bartlett, M. J. Ryan, S. G. Cohen, J. Am. Chem. Soc. 1942, 64, 2649–2653; b) C.-F. Chen, Y.-X. Ma, SpringerLink, Iodine Chemistry: From Synthesis to Applications, 1st Ed., Springer, Berlin, 2013.

[2] a) C.-F. Chen, Chem. Commun. 2011, 47, 1674–1688; b) C.-F. Chen, Y. Han, Acc. Chem. Res. 2018, 51, 2093–2106; c) J. H. Chong, M. J. MacLachlan, Chem. Soc. Rev. 2009, 38, 3301–3315; d) Y. Han, Z. Meng, Y.-X. Ma, C.-F. Chen, Acc. Chem. Res. 2014, 47, 2036–2039; e) T. R. Kelly, H. De Silva, R. A. Silva, Nature 1999, 401, 150–152; f) Y.-X. Ma, Z. Meng, C.-F. Chen, Org. Lett. 2014, 16, 1860–1863; g) Z. Meng, J.-F. Xiang, C.-F. Chen, Sci. Chem. 2014, 5, 1520–1525; h) A. Ohira, T. M. Swager, Macro-molecules 2007, 40, 19–25; i) T. M. Swager, Acc. Chem. Res. 2008, 41, 1181–1189; j) G. Zhang, D. Presly, F. White, T. M. Oppel, M. Mastrolo, Angew. Chem. Int. Ed. 2014, 53, 1516–1520; Angew. Chem. 2014, 126, 1542–1546.

[3] V. A. Kirkina, G. A. Silantyev, S. De-Botton, O. A. Filipov, E. M. Titova, A. A. Pavlov, N. Belkova, L. M. Epstein, D. Gelman, E. S. Shubina, Inorg. Chem. 2020, 59, 11962–11975.

[4] M. E. Tauchert, D. C. M. Warth, S. M. Braun, I. Gruber, A. Ziesak, F. Rominger, P. Hofmann, Organometallics 2011, 30, 2790–2809.

[5] J. Kisets, D. Gelman, Organometallics 2018, 37, 526–529.

[6] a) D. Bézier, M. Brookhart, ACS Catal. 2014, 4, 3411–3420; b) S. De-Botton, S. Cohen, D. Gelman, Organometallics 2018, 37, 1324–1330.

[7] G. Abkai, S. Schmidt, T. Rosendahl, F. Rominger, P. Hofmann, Organometallics 2013, 33, 3212–3214.

[8] L. Bini, C. Mülker, J. Wilting, L. von Chrzanowski, A. L. Spek, D. Vogt, J. Am. Chem. Soc. 2007, 129, 12622–12623.

[9] O. Grossman, D. Gelman, Org. Lett. 2006, 8, 1189–1191.

[10] O. Grossman, C. Azeraf, D. Gelman, Organometallics 2006, 25, 375–381.

[11] Y. Nishi, M. Ikeda, Y. Hayashi, S. Kawauchi, M. Miura, J. Am. Chem. Soc. 2020, 142, 1621–1629.

[12] a) T. Wirth, Hypervalent Iodine Chemistry in Topics in Current Chemistry, Vol. 373, Springer, Switzerland, 2016; b) A. Dasgupta, C. Thiehoff, P. D. Newman, T. Wirth, R. L. Melen, Org. Biomol. Chem. 2021, 19, 4852–4865; c) H. Zhang, T. Wirth, Chem. Eur. J. 2022, 28, e202200181; d) A. Yoshimura, V. V. Zhdkhanin, Chem. Rev. 2016, 116, 3328–3345; e) A. Parra, Chem. Rev. 2019, 119, 12033–12088; f) E. A. Merritt, B. Olfsson, Angew. Chem. Int. Ed. 2009, 48, 9052–9070; Angew. Chem. 2009, 121, 9214–9234; g) D. Gonzalez Fernandez, F. Benfatti, J. Waser, ChemCatChem 2012, 4, 955–958; h) M. Uyanik, K. Ishiihara, J. Organomet. Chem. 2009, 20, 719–727.

[13] a) O. Cohen, O. Grossman, L. Vaccaro, D. Gelman, J. Organomet. Chem. 2014, 750, 13–16; b) F. K.-C. Leung, F. Ishiwari, Y. Shoji, T. Nishikawa, R. Yoshimura, V. V. Zhdkhanin, Chem. Eur. J. 2020, 26, 1520–1525; h) A. Ohira, T. M. Swager, Angew. Chem. Int. Ed. 2014, 53, 7059–7068; b) G. Preda, A. Nitti, D. Pasini, ChemistryOpen 2020, 9, 719–727.

[14] a) O. Cohen, O. Grossman, L. Vaccaro, D. Gelman, J. Organomet. Chem. 2014, 750, 13–16; b) F. K.-C. Leung, F. Ishiwari, Y. Shoji, T. Nishikawa, R. Yoshimura, V. V. Zhdkhanin, Chem. Eur. J. 2020, 26, 1520–1525; h) A. Ohira, T. M. Swager, Angew. Chem. Int. Ed. 2014, 53, 7059–7068; b) G. Preda, A. Nitti, D. Pasini, ChemistryOpen 2020, 9, 719–727.
[19] a) J. Chmiel, I. Heesemann, A. Mix, B. Neumann, H.-G. Stammler, N. W. Mitzel, *Eur. J. Org. Chem.* 2010, 3897–3907; b) M. E. Rogers, B. A. Averill, *J. Org. Chem.* 1986, 51, 3308–3314.

[20] F.-L. Zhang, K. Hong, T.-J. Li, H. Park, J.-Q. Yu, *Science* 2016, 351, 252–256.

[21] S. M. Rafiq, R. Sivasakthikumaran, J. Karunakaran, A. K. Mohanakrishnan, *Eur. J. Org. Chem.* 2015, 5099–5114.

[22] Y. Kuninobu, T. Tatsuzaki, T. Matsuki, K. Takai, *J. Org. Chem.* 2011, 76, 7005–7009.

[23] T. Wirth, in *Microreactors in Organic Synthesis and Catalysis – 2nd Ed.*, Wiley-VCH, 2013.

[24] S. M. Altermann, R. D. Richardson, T. K. Page, R. K. Schmidt, E. Holland, U. Mohammed, S. M. Paradine, A. N. French, C. Richter, A. M. Bahar, B. Witulski, T. Wirth, *Eur. J. Org. Chem.* 2008, 5315–5328.

[25] A. H. Abazida, B. J. Nachtsheim, *Chem. Commun.* 2021, 57, 8822–8825.

[26] a) T. Dohi, A. Maruyama, N. Takenaga, K. Senami, Y. Minamitsuji, H. Fujioka, S. B. Caemmerer, Y. Kita, *Angew. Chem. Int. Ed.* 2008, 47, 3787–3790; *Angew. Chem.* 2008, 120, 3847–3850; b) T. Dohi, N. Takenaga, T. Nakae, Y. Toyoda, M. Yamasaki, M. Shiro, H. Fujioka, A. Maruyama, Y. Kita, *J. Am. Chem. Soc.* 2013, 135, 4558–4566.

[27] J. Qurban, M. Elsherbini, T. Wirth, *J. Org. Chem.* 2017, 82, 11872–11876.

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