Chemical Science

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: P. Tian, V. Saraiva Câmara, M. Valentine, A. P. Tinkler, A. E. Crumpton and E. A. Anderson, *Chem. Sci.*, 2026, DOI: 10.1039/D6SC01387B.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemical-science

View Article Online
DOI: 10.1039/D6SC01387B

ARTICLE

Enantioselective Titanium-Catalyzed Cycloadditions of Thiophene-*S*,*S*-Dioxides with Indenes

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Peilin Tian,[a‡] Viktor S. Camara,[a,b‡] Margarita Valentine,[a] Andrew P. Tinkler,[a] Agamemnon Crumpton,[a] and Edward A. Anderson*[a]

Asymmetric inverse electron-demand Diels-Alder (IEDDA) cycloadditions of thiophene *S*,*S*-dioxides (TDOs) remain largely unexplored. Here we report the development of highly enantioselective titanium-catalyzed IEDDA reactions between TDOs and indenes which enables the asymmetric construction of complex carbocyclic frameworks. In combination with $TiCl_2(O^iPr)_2$, two chiral ligand classes proved capable of promoting this transformation, with BINOL-based catalysts offering optimal selectivity. The transformation exhibits broad substrate scope and high functional group tolerance, and is amenable to gram-scale synthesis; the chiral ligand can be readily recovered and recycled with no deterioration in yield or enantioselectivity. The resulting adducts are versatile synthetic intermediates, undergoing facile derivatization via reduction, esterification, Suzuki coupling, and further Diels-Alder transformations.

Introduction

Polycyclic molecules are ubiquitous throughout organic chemistry, especially in the context of the complex three-dimensional scaffolds found in bioactive natural products.[1-4] For example, 6/5/6 all-carbon fused ring systems comprising one benzene ring and two saturated rings are a common structural motif that features in the cores of lucidomone, dysanbiol, ussuriedinone and hypoxylonol C (Figure 1a).[5-9] The stereocontrolled construction of such tricyclic frameworks poses a significant synthetic challenge that could be met by the implementation of stereoselective Diels-Alder reactions, due to the ability of such processes to effect the atom-economical formation of six-membered rings with control over multiple stereocenters.[10-12]

Despite the long history of Diels-Alder chemistry, the development of asymmetric inverse-electron demand Diels-Alder (IEDDA) reactions remains less established compared to normal electron-demand variants, with a-pyrones being the most explored substrate class to date.[13-23] In contrast, thiophene *S*,*S*-dioxides (TDO) have received considerably less attention, despite their established utility as electron-deficient dienes for non-asymmetric IEDDA processes, in which TDOs display high reactivity due to their non-aromatic nature and intrinsically *s-cis* constrained diene. Upon (4+2) cycloaddition, TDOs afford sulfone-bridged adducts that readily undergo cheletropic extrusion of SO_2,[24, 25] providing an entropic driving force that typically renders the cycloaddition irreversible. Accordingly, TDOs have been applied in cycloadditions with partners such as alkynes, alkenes and furans,[26-32] and in natural product synthesis contexts for the construction of the aromatic cores of the dictyodendrins[33] and the illudalane sesquiterpenes.[34]

Despite their promise as dienes for IEDDA chemistry, the use of TDOs in asymmetric transformations remains challenging, with few examples achieving high levels of stereocontrol in the generation of new stereogenic centers. In 2023, Aggarwal *et al*. described the IEDDA reaction of a TDO with a chiral bicyclic dihydrofuran (Figure 1b), which afforded the corresponding chlorocyclohexadiene (bearing two new stereogenic centers) with excellent diastereoselectivity (>95:5 *dr*), although ultimately these stereocenters were ablated through aromatization.[35] This transformation nonetheless served as the key step in a synthesis of the antiplatelet pharmaceutical beraprost, with the diastereoselectivity of the cycloaddition being governed by the *cis*-fused-nature of the bicyclic enol ether. More recently, our group reported the development of intermolecular asymmetric (4+2) cycloadditions between indoles and enantioenriched thiophene *S*,*S*-dioxides bearing an inexpensive, readily available camphorsultam sidechain, which produced tricyclic indolines as single diastereomers in high yield.[36] This functional group tolerant methodology was applied to a wide range of substituted indoles, and was furthermore employed in the total synthesis of eight *Strychnos* alkaloids.

Both of these transformations relied on substrate stereoinduction, as catalytic asymmetric IEDDA/cheletropic extrusions of TDOs had yet to be developed. During the preparation of this manuscript, Cai *et al.* presented a catalytic

[a] Dr. P.Tian, Dr. V. S. Camara, M. Valentine, A. P. Tinkler, Dr. A. Crumpton and Prof. E. A. Anderson, Chemistry Research Laboratory, Department of Chemistry, University of Oxford, 12 Mansfield Road, Oxford, OX1 3TA, UK. E-mail: edward.anderson@chem.ox.ac.uk.
[b] Dr. V. S. Camara, Department of Physical Chemistry, Institute of Chemistry of São Carlos, University of São Paulo, CEP 13560-970, São Carlos, Brazil..
§ These authors contributed equally to this work.

View Article Online
DOI: 10.1039/D6SC01387B

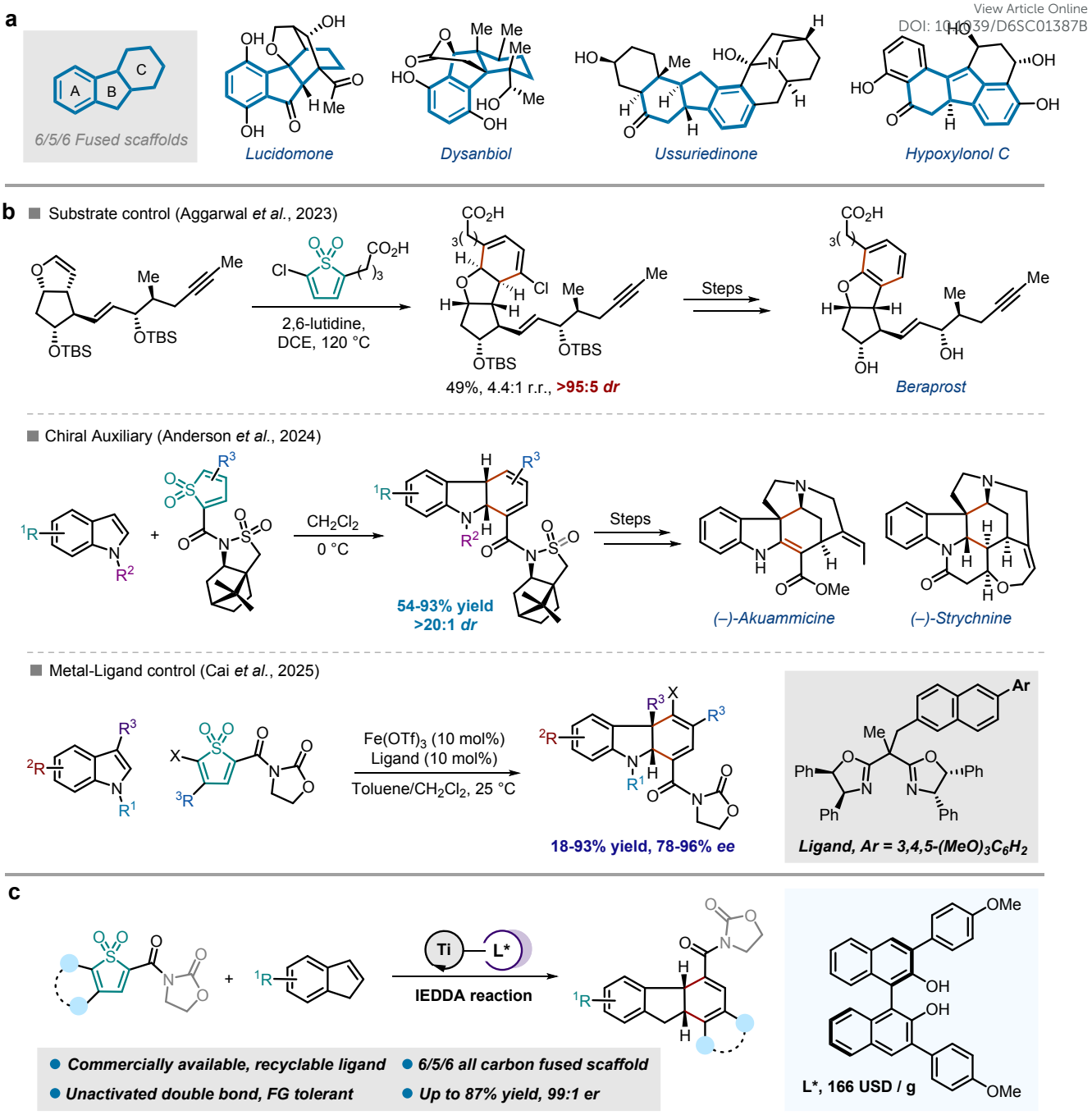


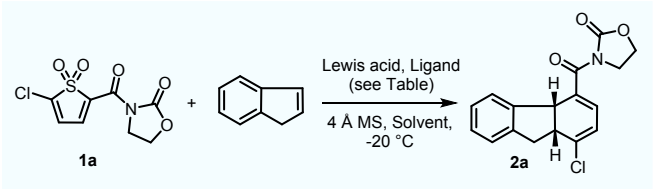
Figure 1. a Natural products containing a 6/5/6 all carbon fused scaffolds; **b** Examples of asymmetric IEDDA/cheletropic extrusion reactions using TDOs as the diene. **c** Enantioselective titanium/BINOL-catalyzed IEDDA using TDOs and indenes (this work).

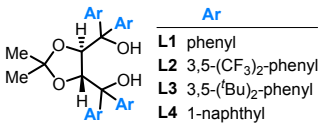
asymmetric IEDDA between TDOs and indoles using a chiral Fe(III)/bis-oxazoline catalyst. This elegant reaction could be employed across a range of indoles bearing electron-rich and electron-poor substituents at various positions of the indole ring. However, the methodology was limited to *N*-alkyl indoles, and also required substitution at the indole C3 position; otherwise, a competing Michael addition of the indole to the TDO was observed.[37] Here, we report a complementary asymmetric IEDDA/cheletropic extrusion of TDOs and indenes, where incorporation of an *N*-acyloxazolidinone moiety onto the TDO scaffold enabled coordination to a chiral titanium Lewis acid-ligand complex that is readily prepared from a common titanium salt and commercially available ligands (Figure 1c).

Results and discussion

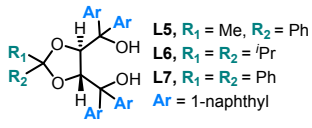
Our investigations began with the reaction between thiophene *S,S*-dioxide **1a** and two equivalents of indene in the presence of

Table 1. Optimization of asymmetric IEDDA/cheletropic extrusion of **1a** and indene.

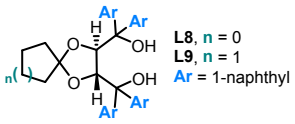




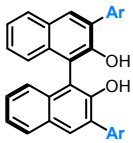
Ar	
L1	phenyl
L2	3,5-$(CF_3)_2$-phenyl
L3	3,5-$(^tBu)_2$-phenyl
L4	1-naphthyl



L5, R_1 = Me, R_2 = Ph	
L6, R_1 = R_2 = ^{i}Pr	
L7, R_1 = R_2 = Ph	
Ar = 1-naphthyl	



L8, n = 0	
L9, n = 1	
Ar = 1-naphthyl	



Ar	
L10	phenyl
L11	1-naphthyl
L12	9-anthryl
L13	3,5-$(CF_3)_2$-phenyl
L14	3,5-dimethylphenyl
L15	4-methoxyphenyl

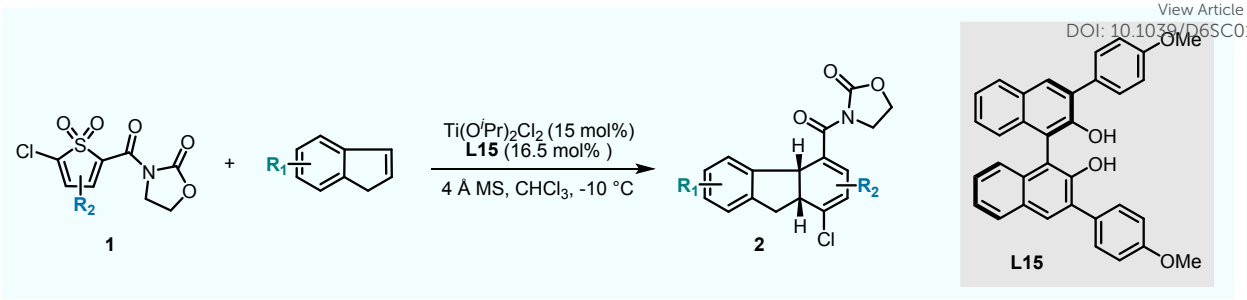
Entry [a]	Lewis acid	Ligand	Solvent	Yield (%)	*er* [b]
1	$TiCl_2(O^iPr)_2$	**L1**	Toluene	37	37:63
2	$TiCl_2(O^iPr)_2$	**L2**	Toluene	41	20:80
3	$TiCl_2(O^iPr)_2$	**L3**	Toluene	27	39:61
4	$TiCl_2(O^iPr)_2$	**L4**	Toluene	35	10:90
5	$TiCl_2(O^iPr)_2$	**L4**	$PhCF_3$	41	16:84
6	$TiCl_2(O^iPr)_2$	**L4**	CH_2Cl_2	52	18:82
7	$TiCl_2(O^iPr)_2$	**L4**	$CHCl_3$	58	10:90
8	$TiCl_2(O^iPr)_2$	**L4**	Et_2O	39	16:84
9	$TiCl_2(O^iPr)_2$	**L5**	$CHCl_3$	51	8:92
10	$TiCl_2(O^iPr)_2$	**L6**	$CHCl_3$	53	6:94
11	$TiCl_2(O^iPr)_2$	**L7**	$CHCl_3$	41	6:94
12	$TiCl_2(O^iPr)_2$	**L8**	$CHCl_3$	37	12:88
13	$TiCl_2(O^iPr)_2$	**L9**	$CHCl_3$	43	10:90
14	$TiCl_2(O^iPr)_2$	**L10**	$CHCl_3$	76	97:3
15[c]	$Yb(OTf)_3$	**L10**	$CHCl_3$	65	50:50
16[c]	$Mg(OTf)_2$	**L10**	$CHCl_3$	72	50:50
17[c]	$Eu(OTf)_3$	**L10**	$CHCl_3$	75	50:50
18	$TiCl_2(O^iPr)_2$	**L11**	$CHCl_3$	67	67:33
19	$TiCl_2(O^iPr)_2$	**L12**	$CHCl_3$	61	50:50
20	$TiCl_2(O^iPr)_2$	**L13**	$CHCl_3$	83	97:3
21	$TiCl_2(O^iPr)_2$	**L14**	$CHCl_3$	77	99:1
22	$TiCl_2(O^iPr)_2$	**L15**	$CHCl_3$	85	99:1
23[d]	$TiCl_2(O^iPr)_2$	**L15**	$CHCl_3$	75	98:2
24[d, e]	$TiCl_2(O^iPr)_2$	**L15**	$CHCl_3$	81	98:2
25[f]	$TiCl_2(O^iPr)_2$	**L15**	$CHCl_3$	69	96:4

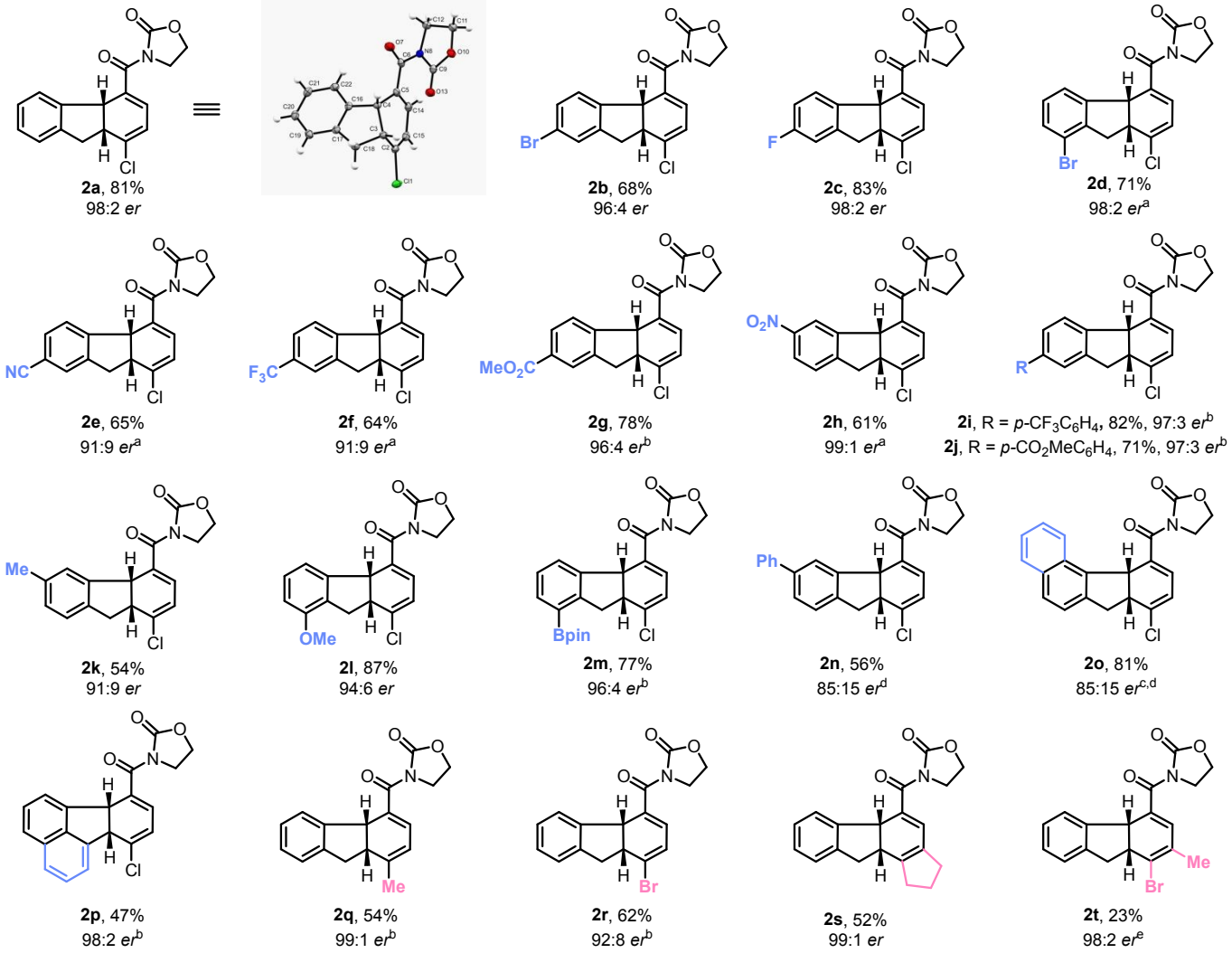
[a] Reaction conditions: **1a** (0.1 mmol), indene (0.2 mmol), Lewis acid (20 mol %), ligand (22 mol %) in solvent (1.0 mL) at -20 °C. [b] *er* values were determined by HPLC on a chiral stationary phase. [c] The reaction employed 25 mol% of $^iPr_2EtN$. [d] 15 mol% $TiCl_2(O^iPr)_2$ / 16.5 mol% **L15**. [e] The reaction was performed at -10 °C. [f] 10 mol% $TiCl_2(O^iPr)_2$ / 11 mol% **L15**.

$TiCl_2(O^iPr)_2$ (20 mol%) and TADDOL[38-42] ligand **L1** (22 mol%) in toluene at -20 °C (Table 1, Entry 1). The desired cycloadduct **2a** was obtained in 37% yield and 63:37 *er*. Encouraged by this result, we examined the influence of the aryl substituents on the TADDOL 'arms' (Entries 2-4).[43, 44] Electronic effects exerted only a minor influence on the enantioselectivity, however the introduction of the bulky 1-naphthyl group in **L4** offered a pronounced improvement (Entry 4), delivering the product in 90:10 *er*, albeit in only 35% yield.A solvent screen (Entries 5-8) led to an improved 58% yield in chloroform while maintaining 90:10 *er*. The conformation of the five-membered cyclic acetal moiety in the TADDOL ligand has also been found to impact enantioselectivity,[38] and we thus investigated the influence of the substituents on this ring (**L5**-**L9**, Entries 9-13). When both substituents were isopropyl (**L6**, Entry 10) or phenyl (**L7**, Entry 11), the reaction reached its highest enantioselectivity (up to 94:6 *er*), although the isolated yields remained modest. Hypothesizing that the moderate yield results from the relatively slow reaction rate and consequently incomplete conversion, we sought to increase the Lewis acidity of the metal center, and therefore evaluated BINOL[15, 17, 45] as an alternative ligand. Replacing TADDOL with BINOL **L10** (Entry 14) resulted in a marked enhancement of both yield (76%) and enantioselectivity (97:3 *er*). Several metal triflates including $Yb(OTf)_3$,[15] $Mg(OTf)_2$[46] and $Eu(OTf)_3$[47] were examined, but all afforded only moderate yields and no enantioselectivity. Given the superior performance of the Ti-based conditions, we returned to this system and screened other BINOL derivatives. Bulky substituents (**L11**, Entry 18 and **L12**, Entry 19) proved detrimental to enantioselectivity, whereas electron-withdrawing groups (3,5-CF_3, **L13**, Entry 20) maintained high selectivity (97:3 *er*). Remarkably, electron-rich aryl substituents such as 3,5-dimethylphenyl (**L14**, Entry 21) and 4-methoxyphenyl (**L15**, Entry 22) delivered **2a** in 77% and 85% yield respectively, both with 99:1 *er*. Reducing the loading to 15 mol% had minimal impact on enantioselectivity (98:2 *er*) but slightly reduced the yield (75%, Entry 23). Increasing the temperature to –10 °C restored the yield to 81% while maintaining 98:2 *er* (Entry 24). A further reduction to 10% catalyst loading led to a slight erosion in enantioselectivity and yield (Entry 25, 69%, 96:4 *er*). It is worth noting that molecular sieves[48] were crucial for maintaining high enantioselectivity; in their absence, the enantiomeric ratio dropped dramatically.

Under the optimized reaction conditions (Table 1, Entry 24), we examined the scope of this transformation (Scheme 1). A series of indene derivatives bearing electron-withdrawing substituents[16] were well tolerated, affording the desired products in good to excellent yields (**2b**-**2h**, 52-83%) with high enantiomeric ratios (91:9 to 98:2 *er*), including bromo, fluoro, cyano, trifluoromethyl, ester and nitro groups. Importantly, these substituents were accommodated regardless of their position on the indene ring (C5, C6, or C7). The transformation proved sensitive to temperature: substrates bearing weakly electron-withdrawing groups (Br, F) proceeded efficiently at –10 °C, while more electron deficient indenes (with substituents such as esters, CN, CF_3 or NO_2) required elevated temperatures (between room temperature and 35 °C). Electron-donating groups such as methyl and methoxy (**2k**, **2l**) were also tolerated,

View Article Online
DOI: 10.1039/D6SC01387B





Scheme 1: Substrate scope of catalytic asymmetric IEDDA between TDOs and indenes. Reaction conditions: **1a** (0.10 mmol), indene (0.20 mmol), $TiCl_2(O^iPr)_2$ (0.015 mmol), **L15** (0.0165 mmol), 4 Å MS (50 mg), dry $CHCl_3$ (1 mL, 0.1 M), -10 °C. [a] Reaction performed at 35 °C. [b] Reaction performed at 25 °C. [c] Reaction performed at -20 °C. [d] $TiCl_2(O^iPr)_2$ (0.025 mmol), **L15** (0.0275 mmol) were used. [e] Using **L13** as ligand. *Er* values were determined by HPLC on a chiral stationary phase. The absolute configuration of **2a** was determined by X-ray crystallography (CCDC 2512830)

affording high yields and enantiomeric ratios (54%, 91:9 *er* and 87%, 94:6 *er* respectively); the slightly reduced selectivities compared to the electron-poor substrates could be ascribed to minor levels of non-asymmetric background reaction. A sensitive boronic ester-substituted indene also performed well, affording **2m** in 77% yield and 96:4 *er*, enabling further potential derivatization *via* Suzuki cross-coupling. Structurally complex substrates including phenyl-substituted indene, 3*H*-cyclopenta[a]naphthalene, and acenaphthylene (**2n**-**2p**) were well tolerated, furnishing the corresponding products in moderate to good yields (50-81%) and with good to excellent levels of enantioenrichment (85:15 to 98:2 *er*). The successful and selective reaction of acenaphthylene (98:2 *er*) in particular highlights the robustness of the reaction toward sterically and electronically diverse substrates. Finally, the use of other TDOs was examined: methyl substitution on the TDO scaffold

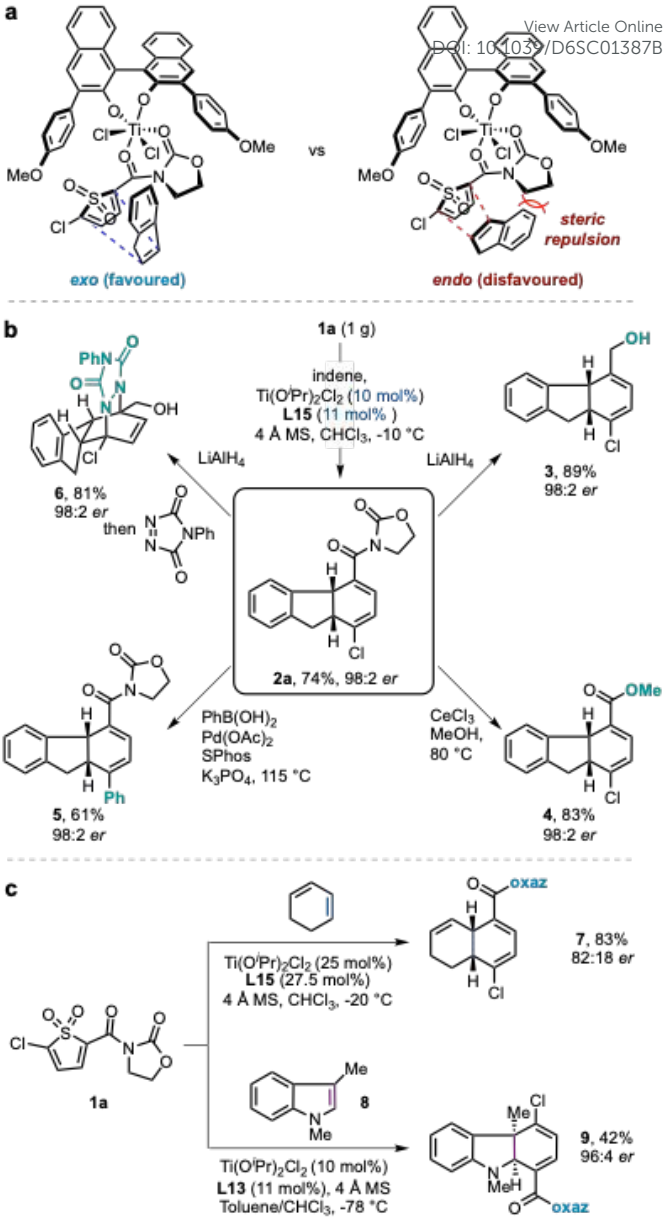
View Article Online
DOI: 10.1039/D6SC01387B

afforded **2q** in 54% yield and 99:1 *er*, while 5-bromo substitution provided **2r** in 62% yield and 92:8 *er*. Pleasingly, a bicyclic TDO substrate reacted smoothly under the optimized conditions, delivering **2s** in 52% yield with excellent enantioselectivity (99:1 *er*). A trisubstituted TDO was also tolerated, with **2t** isolated with an excellent *er* of 98:2. The absolute configurations of all products were assigned by analogy to the single-crystal X-ray diffraction structure of cycloaddition product **2a** (CCDC 2512830).

To rationalise the stereochemical outcome, we propose the transition state model shown in Scheme 2a, in which enantioselectivity is primarily governed by steric effects. Based on established structures of Ti(IV)(BINOL) complexes,[49, 50] we propose an octahedral geometry where the BINOL and acyloxazolidinone adopt the depicted configuration. The oxazolidone ring is located in a relatively hindered region (proximal to one of the *para*-methoxylphenyl (PMP) BINOL sidechains) and the thiophene *S*,*S*-dioxide rotates to π-stack with the opposing PMP group. This arrangement blocks the 'back' face of the TDO (as drawn), such that the indene dienophile approaches from the front face in either an *exo* or *endo* fashion. The conformation of the oxazolidinone is such that it also protrudes towards the front face, which sterically disfavours the *endo* orientation of the indene. This interaction is absent in the *exo* orientation, which is the one that leads to the experimentally observed product.

To demonstrate the practicality of the methodology, a gram-scale synthesis of **2a** was carried out (Scheme 2b), which afforded the cycloadduct in 74% yield with 98:2 *er*. On this larger scale, the reaction concentration could be doubled, and the catalyst loading reduced to 10 mol% without compromising the enantioselectivity. Furthermore, 88% of the ligand could be recovered by column chromatography, and the recycled ligand was successfully reused to catalyze the reaction without any loss in enantioselectivity.[51] With quantities of **2a** in hand, further transformations were explored: for example, **2a** could be readily reduced to the allylic alcohol **3** in 89% yield, or the oxazolidinone motif could be converted into the corresponding methyl ester **4** in 83% yield under Lewis acidic promotion ($CeCl_3$, MeOH).[37] The chlorine substituent present in **2a** provides additional opportunities for derivatization; for example, Suzuki–Miyaura coupling[37] afforded the arylated diene **5** in 61% yield. Additionally, the diene unit in **2a** underwent Diels–Alder reaction with PTAD[52] (4-phenyl-1,2,4-triazoline-3,5-dione) to furnish the polycyclic bridged adduct **6** in 81% yield.

Finally, to further explore the scope of the asymmetric cycloaddition, other dienophiles were investigated (Scheme 2c). Cyclohexadiene proved a viable substrate,[18] undergoing asymmetric Diels–Alder reaction with TDO **1a** to give the *cis*-fused decalin derivative **7** in 83% yield with 82:18 *er*. It is interesting that cyclohexadiene was observed to act exclusively as a dienophile rather than a diene in this process, which may derive from its ability to engage in an ambimodal transition state, as found for our earlier studies with furan dienophiles.[34] Inspired by our previous studies on auxiliary-controlled asymmetric Diels–Alder reactions of TDOs and indoles, we further sought to develop a catalytic asymmetric variant.[36]



Scheme 2. Proposed asymmetric induction model, synthetic transformations and investigation of other dienophile substrates.

However, attempts using unsubstituted indole predominantly afforded a Michael addition product between C3 of the indole and C3 of the TDO, rather than the desired Diels–Alder adduct. Ultimately, *N*-methyl-3-methylindole was employed as the substrate and, after a brief ligand screen, BINOL ligand **L13** (substituted with 3,5-bis(trifluoromethyl) groups) was found to afford the highest enantioselectivity, providing indoline product **9** in 42% yield with 96:4 *er*. Notably, substitution at the N1 and C3 positions of indole is essential to suppress the undesired Michael addition pathway, which is consistent with the findings reported by Cai and co-workers.[37]

Conclusions

In summary, we have developed a highly enantioselective

View Article Online
DOI: 10.1039/D6SC01387B

titanium-catalyzed Diels-Alder reaction of thiophene dioxides with indenes employing commercially-available BINOL derivatives as ligands, providing a broad range of polycyclic products in high yields and excellent enantioselectivities. The reaction exhibits broad substrate scope and functional group tolerance, enabling the asymmetric construction of complex carbocyclic frameworks. The practicality of the methodology was demonstrated by gram-scale synthesis and efficient ligand recycling. Furthermore, the resulting products could be readily diversified through reduction, esterification, Suzuki cross coupling, and Diels-Alder chemistry, and the reaction itself could be expanded to encompass cyclohexadiene and indole derivatives as dienophiles. Overall, this work provides a new catalytic platform for asymmetric inverse electron-demand Diels-Alder reactions based on underexplored TDOs, highlighting the untapped potential of this heterocycle in asymmetric synthesis.

Author contributions

PT, VS and EA conceptualised the project. PT, VS, MV and AP carried out the investigation and developed the methodology. AC acquired the X-ray crystal structures of **1a** and **2a**. All authors conducted the formal analysis and curated the data. EA and PT supervised the project. EA and PT wrote the original draft and edited the manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article has been included as part of the Supplementary information: experimental procedures, NMR data and crystallographic data (.cif). See DOI: https://doi.org/10.1039/xxxxx.

Acknowledgements

E.A.A. and P.T. thank the EPSRC for support (EP/X028674/1). V.S.C. thanks the São Paulo Research Foundation (FAPESP) for financial support (2024/07727-8). M.V. thanks the EPSRC for a studentship.

Notes and references

1. P. S. Baran, *J. Am. Chem. Soc.*, 2018, **140**, 4751–4755.
2. Y. Stöckl, T. Fellmeth, F. Bauer, B. Wank, W. Frey, B. Claasen, A. Zens, A. Köhn and S. Laschat, *Eur. J. Org. Chem.*, 2022, e202101416.
3. C. G. Zhao, Z. Q. Ye, Z. X. Ma, S. A. Wildman, S. A. Blaszczyk, L. H. Hu, I. A. Guizei and W. P. Tang, *Nat. Commun.*, 2019, **10**, 4015.
4. S. P. Yin, Z. Liu, J. J. Shen, Y. W. Xia, W. H. Wang, P. Y. Gui, Q. Jia, K. Kachanuban, W. M. Zhu and P. Fu, *Nat. Commun.*, 2022, **13**, 5169.
5. X. Z. Liao, R. Wang, X. Wang and G. Li, *Nat. Commun.*, 2024, **15**, 2647.
6. X. Liang, H. N. Jiang, J. T. Yang, Y. J. Duan, K. Wei and Y. R. Yang, *Org. Lett.*, 2025, **27**, 10619–10624.
7. Z. Xu, W. Peng, J. Huang, J. Shen, J. J. Guo and A. Hu, *Nat. Commun.*, 2024, **15**, 9748.
8. W. H. Jiao, J. X. Li, H. Y. Liu, X. C. Luo, T. Y. Hu, G. H. Shi, D. D. Xie, H. F. Chen, B. H. Cheng and H. W. Lin, *Org. Lett.*, 2023, **25**, 6391–6395.
9. M. Konya, K. Shimoyama, S. Arima, T. Fukuda, R. Uchida, H. Tomoda and T. Nagamitsu, *Org. Lett.*, 2020, **22**, 5131–5134.
10. K. C. Nicolaou, S. A. Snyder, T. Montagnon and G. Vassilikogiannakis, *Angew. Chem. Int. Ed.*, 2002, **41**, 1668–1698.
11. A. Rana, A. Mishra and S. K. Awasthi, *RSC Adv.*, 2025, **15**, 4496–4525.
12. A. A. Sara, Um-E-Farwa, A. Saeed and M. Kalesse, *Synthesis*, 2022, **54**, 975–998.
13. C. J. F. Cole, L. Fuentes and S. A. Snyder, *Chem. Sci.*, 2020, **11**, 2175–2180.
14. G. H. Huang, R. Guillot, C. Kouklovsky, B. Maryasin and A. de la Torre, *Angew. Chem. Int. Ed.*, 2022, **61**.
15. X. W. Liang, Y. L. Zhao, X. G. Si, M. M. Xu, J. H. Tan, Z. M. Zhang, C. G. Zheng, C. Zheng and Q. Cai, *Angew. Chem. Int. Ed.*, 2019, **58**, 14562–14567.
16. Y. Lu, M. M. Xu, Z. M. Zhang, J. Zhang and Q. Cai, *Angew. Chem. Int. Ed.*, 2021, **60**, 26610–26615.
17. X. G. Si, Z. M. Zhang, C. G. Zheng, Z. T. Li and Q. Cai, *Angew. Chem. Int. Ed.*, 2020, **59**, 18412–18417.
18. M. M. Xu, L. M. Yang, K. Tan, X. Y. Chen, Q. T. Lu, K. N. Houk and Q. Cai, *Nat. Catal.*, 2021, **4**, 892–900.
19. G. H. Huang, C. Kouklovsky and A. de la Torre, *Chem. Eur. J.*, 2021, **27**, 4760–4788.
20. G. H. Huang, C. Kouklovsky and A. de la Torre, *J. Am. Chem. Soc.*, 2022, **144**, 17803–17807.
21. Y. Wang, H. M. Li, Y. Q. Wang, Y. Liu, B. M. Foxman and L. Deng, *J. Am. Chem. Soc.*, 2007, **129**, 6364–6365.
22. F. Q. Zhang, B. T. Ren, Y. Q. Zhou, Y. B. Liu and X. M. Feng, *Chem. Sci.*, 2022, **13**, 5562–5567.
23. H. B. Yu, Y. G. Chen, Y. Tian, M. S. Xie and H. M. Guo, *ACS Catal.*, 2024, **14**, 8930–8938.
24. A. M. Moiseev, E. S. Balenkova and V. G. Nenajdenko, *Russ. Chem. Bull.*, 2006, **55**, 712–717.
25. J. Nakayama, *Bull. Chem. Soc. Jpn.*, 2000, **73**, 1–17.
26. J. Nakayama, S. Yamaoka, T. Nakanishi and M. Hoshino, *J. Am. Chem. Soc.*, 1988, **110**, 6598–6599.
27. M. S. Raasch, *J. Org. Chem.*, 1980, **45**, 867–870.
28. D. B. Xia, X. Guo, L. Chen, M. Baumgarten, A. Keerthi and K. Müllen, *Angew. Chem. Int. Ed.*, 2016, **55**, 941–944.
29. D. Wang, C. X. Zhao, Y. M. Zhu, X. Y. Zhang, X. Y. Wang and P. An, *Chem. Eur. J.*, 2024, **30**, e202402723.
30. B. R. Boswell, C. M. F. Mansson, G. E. Cabrera, C. R. Hansen, A. G. Oliver and N. Z. Burns, *J. Am. Chem. Soc.*, 2023, **145**, 5631–5636.
31. C. Niu, Y. Zhou, Q. Chen, Y. Zhu, S. Tang, Z. X. Yu and J. Sun, *Org. Lett.*, 2022, **24**, 7428–7433.

View Article Online
DOI: 10.1039/D6SC01387B

32. X. Y. Ji, E. M. El-Labbad, K. L. Ji, D. S. Lasheen, R. A. T. Serya, K. A. Abouzid and B. H. Wang, *Org. Lett.*, 2017, **19**, 818–821.
33. A. Kabuki and J. Yamaguchi, *Synthesis*, 2022, **54**, 4963–4970.
34. K. H. K. Park, N. Frank, F. Duarte and E. A. Anderson, *J. Am. Chem. Soc.*, 2022, **144**, 10017–10024.
35. Z. S. Wang, S. H. Bennett, B. Kicin, C. C. Jing, J. A. Pradeilles, K. Thai, J. R. Smith, P. D. Bacos, V. Fasano, C. M. Saunders and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2023, **145**, 14124–14132.
36. K. H. Park, J. Park, N. Frank, H. W. Zhang, P. L. Tian, Y. Biddick, F. Duarte and E. A. Anderson, *Nat. Chem.*, 2026, **18**, 782–789.
37. S. X. Feng, Q. T. Lu, Y. Lu, L. X. Cui, L. M. Yang, A. S. Baghel and Q. Cai, *Angew. Chem. Int. Ed.*, 2025, **64**, e202512345.
38. K. Narasaka, N. Iwasawa, M. Inoue, T. Yamada, M. Nakashima and J. Sugimori, *J. Am. Chem. Soc.*, 1989, **111**, 5340–5345.
39. K. Narasaka and I. Yamamoto, *Tetrahedron*, 1992, **48**, 5743–5754.
40. K. V. Gothelf and K. A. Jorgensen, *J. Org. Chem.*, 1995, **60**, 6847–6851.
41. M. S. Andrä, J. Thiemermann, J. Schnaubelt, D. Lentz, R. Zimmer and H. U. Reissig, *Eur. J. Org. Chem.*, 2017, 124–130.
42. D. Seebach, A. K. Beck and A. Heckel, *Angew. Chem. Int. Ed.*, 2001, **40**, 92–138.
43. M. Hou, M. M. Xu, B. C. Yang, H. B. He and S. H. Gao, *Org. Lett.*, 2021, **23**, 7487–7491.
44. K. Mikami, M. Terada, Y. Motoyama and T. Nakai, *Tetrahedron Asymm.*, 1991, **2**, 643–646.
45. H. F. Du, J. Long, J. Y. Hu, X. Li and K. L. Ding, *Org. Lett.*, 2002, **4**, 4349–4352.
46. H. F. Du, X. Zhang, Z. Wang, H. L. Bao, T. P. You and K. L. Ding, *Eur. J. Org. Chem.*, 2008, 2248–2254.
47. G. Desimoni, G. Faita, M. Mella, F. Piccinini and M. Toscanini, *Eur. J. Org. Chem.*, 2007, 1529–1534.
48. G. H. Posner, H. Y. Dai, D. S. Bull, J. K. Lee, F. Eydoux, Y. Ishihara, W. Welsh, N. Pryor and S. Petr, *J. Org. Chem.*, 1996, **61**, 671–676.
49. J. Balsells, T. J. Davis, P. Carroll and P. J. Walsh, *J. Am. Chem. Soc.*, 2002, **124**, 10336–10348.
50. Y. Hayashi, N. Yamamura, T. Kusukawa and T. Harada, *Chem. Eur. J.*, 2016, **22**, 12095–12105.
51. See the Supporting Information for details.
52. Y. C. Lai, S. E. Mallakpour, G. B. Butler and G. J. Palenik, *J. Org. Chem.*, 1985, **50**, 4378–4381.

View Article Online
DOI: 10.1039/D6SC01387B

The data supporting this article has been included as part of the Supplementary information: experimental procedures, NMR data and crystallographic data (.cif). See DOI: https://doi.org/10.1039/xxxxx.