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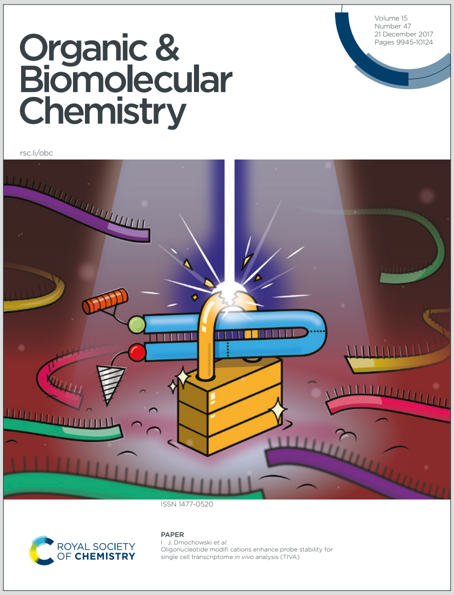

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ARTICLE

Asymmetric Tandem Reaction of Dicyanoalkenes with Conjugated Sulfinyl Imino Esters

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An asymmetric tandem reaction of α,α-dicyanoalkenes and enantiomerically pure α,β-unsaturated *N*-sulfinyl imino esters is reported herein. It involves a four step-protocol that ends up in the generation of a new family of tetracyclic products in a diastereoselective fashion. The overall process takes place in good yields and moderate to good enantioselectivities, and entails the formation of three bonds and four stereocenters. A plausible reaction mechanism has also been proposed.

Introduction

Tandem reactions, categorized as a series of chemical transformations that follow one another in a defined order, have revolutionized the field of organic chemistry. They enable us to create molecular complexity in a single chemical operation, thereby avoiding time-consuming purification and intermediate isolation processes, and approaching the concept of ideal synthesis introduced by Hendrickson several decades ago.[1] It is known that Nature uses this principle in the highly efficient synthesis of biomolecules with extraordinary selectivity. Moreover, the concept of tandem reactions has been around for more than a century, being the Robinson annulation one of the earliest and more emblematic examples.[2] However, it was not until the end of the last century that tandem reactions gained exposure in organic synthesis, standing nowadays at the forefront of chemical synthesis. Additionally, the interest in combining asymmetric processes with tandem reactions is obvious, since multiple stereogenic centers can be created in a single synthetic step.[3]

The ambident character of 1,1-dicyanoalkenes bearing enolizable sites converts them into ideal reagents to be engaged in domino processes, since they can react as nucleophiles through the α- and γ-positions and as electrophiles through the β-position.[4] Reactions that take advantage of the excellent vinylogous donor properties of dicyanoalkenes start by their reaction with an electrophile, ending up with a remaining conjugated malononitrile moiety, suitable for further transformations in a tandem fashion. This reactivity shows the usefulness of the vinylogy principle for the design of tandem protocols. A wide variety of electrophiles have been combined with 1,1-dicyanoalkenes in tandem protocols such as 2-hydroxycinnamaldehydes,[5] enynals,[6] 2,2-disubstituted cyclopentene-1,3-diones,[7] 5-vinyloxazolidine-2,4-diones,[8] nitroalkenes,[9] α-succinimide-substituted allenoates,[10] 3-ethynyl-2-oxoindolin-3-yl acetates,[11] 4-unsaturated isoxazol-5-ones,[12] α-vinyl enals,[13] 2-mercaptoquinoline-3-carbaldehydes,[14] *N*-protected methyleneindolinones,[15] 2-pyrrole benzaldehydes,[16] 3-alkenyl-oxindoles,[17] methylene cyclopropanes,[18] δ-sulfonamido substituted enones,[19] allenylic alcohols,[20] 2-nitrobenzofuranes[21] or trifluoromethyl aryl ketones,[22] rendering new families of heterocycles and carbocycles.

Despite the widespread usage of 1,1-dicyanoalkenes in tandem protocols, their reactivity with conjugated sulfinyl imines as electrophilic partners has only been evaluated by our research group. On the one hand, we found that the reaction of 1,1-dicyanoalkenes with fluorinated conjugated *N-tert*-butylsulfinyl imines in the presence of DBU gave rise to polycyclic trifluoromethyl arenes by means of a new cycloaromatizacion cascade process. This took place in isopropanol with concomitant elimination of both cyano groups and the sulfinyl amine moiety (Scheme 1, **A**).[23] On the other hand, the use of fluorinated conjugated *N-p*-tolylsulfinyl imines in dichloromethane triggered a divergent reactivity pathway that led to tetracyclic compounds through an azetidinimine rearrangement, with elimination of the sulfinyl amine moiety while retaining in this case both cyano groups (Scheme 1, **B**).[24]

In this work, we found that the reaction of 1,1-dicyanoalkenes with conjugated *N*-sulfinyl imino esters follows, again, a different reactivity pathway, rendering a new family of polycyclic heterocycles and increasing the structural diversity of the overall process just by changing the substitution pattern of the starting conjugated sulfinyl imines (Scheme 1, **C**). The optimization of this asymmetric tandem process and the

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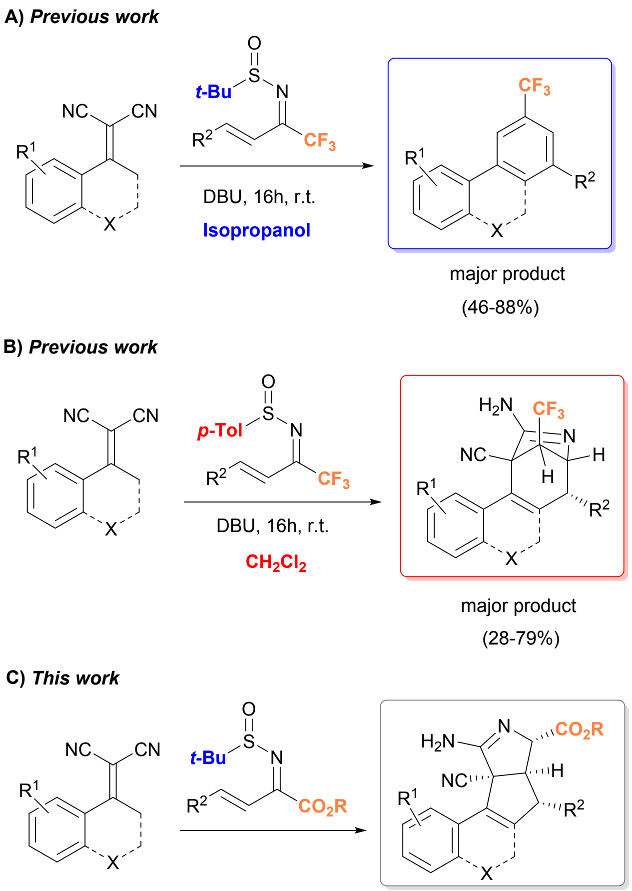
evaluation of its scope are reported herein. A plausible mechanistic explanation of the divergent reactivity observed is also discussed.



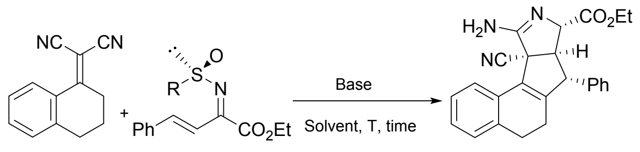
Scheme 1. Divergent reactivity of conjugated sulfinyl imines with 1,1-dicyanoalkenes.

Results and discussion

Our study was initiated with dicyanoalkene **1a**, derived from 1-tetralone, and enantiomerically pure conjugated *N*-*tert*-butyl- and *N*-*p*-tolylsulfinyl α-imino esters **2a**, **b** as model substrates. Previous work from our laboratory demonstrated that DBU was the base of choice to perform the reaction of 1,1-dicyanoalkenes with fluorinated conjugated sulfinyl imines. Therefore, a mixture of compounds **1a** and **2a** was treated with DBU in dichloromethane at room temperature. After 16 hours, the novel tetracyclic derivative **3a** was isolated in 57% yield and 86:14 enantiomeric ratio (Table 1, entry 1). The unexpected formation of compound **3a** reveals a new divergent pathway in the reaction of dicyanoalkenes with conjugated *N*-sulfinyl imino esters, ending up with the creation of three new bonds and four stereocenters in a very selective manner. Other organic and inorganic bases such as Et_3N, Na_2CO_3 or NaH, were also tested in this tandem process with little success (Table 1, entries 2-4). The reaction with *N*-*p*-tolylsulfinyl imino ester **2b** took place less efficiently, affording product **3a** in 36% yield and 77:23 enantiomeric ratio (Table 1, entry 5). The influence of the solvent was examined next. However, the efficiency of the tandem protocol did not improve with any of the different types of solvents tested (Table 1, entries 6-9), when compared with the reaction in dichloromethane.

Moreover, in order to enhance the enantioselectivity, the reaction was performed at low temperature. In this context, starting the process at -78 °C and allowing the reaction mixture to reach room temperature, the enantiomeric ratio of the final product (84:16 er) was comparable to that obtained at room temperature, although with a noticeable drop in yield (Table 1, entry 10). When the reaction was performed at 0 °C, the enantioselectivity of the process increased until 92:8 er, albeit with a poor 39% chemical yield (Table 1, entry 11). Finally, enlarging the reaction time until 48 h, it was possible to increase the final yield to 68%, with an excellent enantiomeric ratio of 93:7 (Table 1, entry 12). In light of this study, we concluded that the optimal conditions for the new asymmetric tandem reaction involved the use of *tert*-butylsulfinyl imine **2a** and DBU as a base, in dichloromethane at 0 °C for 48 h (Table 1, entry 12). These reaction conditions were further applied to other dicyanoalkenes **1** and conjugated sulfinyl imino esters **2** in order to evaluate the scope of our tandem process. The results of this study are summarized in Table 2.

Table 1. Optimization of the conditions for the tandem reaction of dicyanoalkenes **1** with conjugated sulfinyl imino esters **2**.[a]



1a **2a** (R= *t*-Bu) **2b** (R= *p*-Tol) **3a**

Entry	2	Solvent	Base	T (°C)	Time (h)	**3a**(%)[b, c]	er[d]
1	**2a**	CH_2Cl_2	DBU	25	16	57	86:14
2	**2a**	CH_2Cl_2	Et_3N	25	16	—	—
3	**2a**	CH_2Cl_2	Na_2CO_3	25	16	—	—
4	**2a**	CH_2Cl_2	NaH	25	16	18	76:24
5	**2b**	CH_2Cl_2	DBU	25	16	36	77:23
6	**2a**	*i*-PrOH	DBU	25	16	21	79:21
7	**2a**	Toluene	DBU	25	16	29	82:18
8	**2a**	THF	DBU	25	16	25	78:22
9	**2a**	MeCN	DBU	25	16	22	69:31
10	**2a**	CH_2Cl_2	DBU	-78 to rt	16	15	84:16
11	**2a**	CH_2Cl_2	DBU	0	16	39	92:8
12	**2a**	CH_2Cl_2	DBU	0	48	68	93:7

[a] Reactions were performed with **1a** (0.4 mmol), **2a**/**b** (0.2 mmol) and base (0.4 mmol) in the corresponding solvent (0.03M), temperature and time. [b] Isolated yields after flash column chromatography. [c] In all cases, compound **3a** was obtained with excellent diastereoselectivity. [d] Enantiomeric ratios were determined by HPLC analysis on a chiral stationary phase (see Supporting Information for details).

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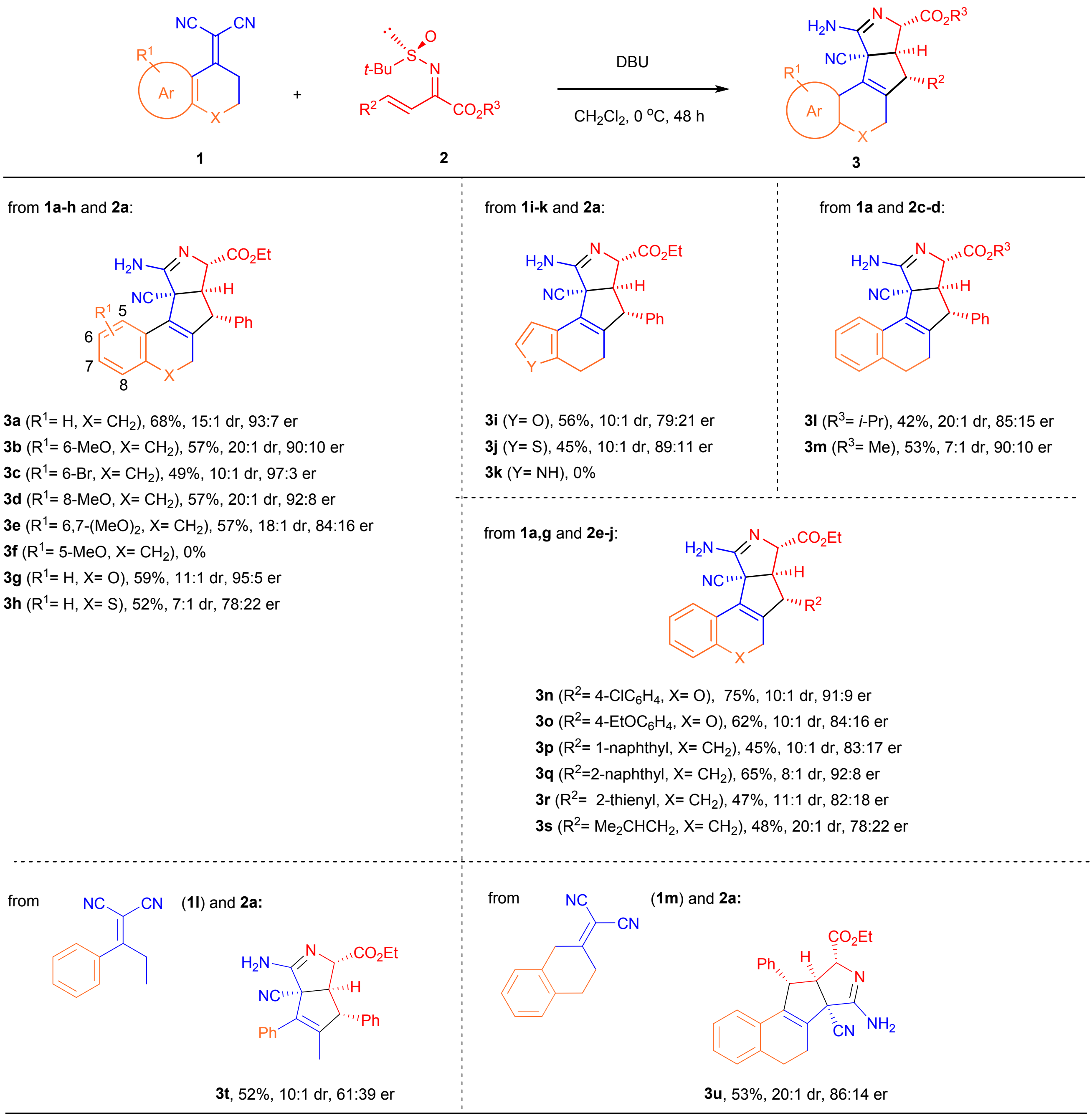
Initially, we evaluated the asymmetric tandem reaction with conjugated sulfinylimine **2a** (R^2= Ph, R^3= Et) and several substituted bicyclic 1,1-dicyanoalkenes **1** derived from 1-tetralone (X= CH_2). Compared to the unsubstituted compound **3a** (R^1= H, 93:7 er), the electron-donating methoxy group at the 6 position produced a slightly lower er value (**3b**, 90:10 er); while the bromine electron-withdrawing group provided the best enantiomeric ratio (**3c**, 97:3 er), and the methoxy group at the 8 position led to comparable results (**3d**, 92:8 er). The presence of two methoxy substituents at the 6 and 7 positions of the starting dicyanoalkene yielded a significant drop in enantioselectivity (**3e**, 84:16 er); while substitution at the 5 position completely prevented the tandem reaction, probably due to steric issues. 1,1-Dicyanoalkenes derived from 4-chromanone (X= O) and 4-thiochromanone (X= S) were also compatible with the reaction, giving rise to the corresponding tetracycles **3g** (95:5 er) and **3h** (78:22 er), respectively, being the latter quite less efficient in terms of enantiocontrol. In all cases, the tandem reaction was highly diastereoselective (up to 20:1 dr) and the final products were obtained in good yields (49-68%) (Table 2), considering that the tandem process comprises four chemical transformations.

Table 2. Scope of the tandem reaction of dicyanoalkenes **1** with conjugated sulfinylimino esters **2**. [a, b, c, d]



from **1a-h** and **2a**:

3a (R^1= H, X= CH_2), 68%, 15:1 dr, 93:7 er
3b (R^1= 6-MeO, X= CH_2), 57%, 20:1 dr, 90:10 er
3c (R^1= 6-Br, X= CH_2), 49%, 10:1 dr, 97:3 er
3d (R^1= 8-MeO, X= CH_2), 57%, 20:1 dr, 92:8 er
3e (R^1= 6,7-$(MeO)_2$, X= CH_2), 57%, 18:1 dr, 84:16 er
3f (R^1= 5-MeO, X= CH_2), 0%
3g (R^1= H, X= O), 59%, 11:1 dr, 95:5 er
3h (R^1= H, X= S), 52%, 7:1 dr, 78:22 er

from **1i-k** and **2a**:

3i (Y= O), 56%, 10:1 dr, 79:21 er
3j (Y= S), 45%, 10:1 dr, 89:11 er
3k (Y= NH), 0%

from **1a** and **2c-d**:

3l (R^3= *i*-Pr), 42%, 20:1 dr, 85:15 er
3m (R^3= Me), 53%, 7:1 dr, 90:10 er

from **1a,g** and **2e-j**:

3n (R^2= 4-ClC_6H_4, X= O), 75%, 10:1 dr, 91:9 er
3o (R^2= 4-$EtOC_6H_4$, X= O), 62%, 10:1 dr, 84:16 er
3p (R^2= 1-naphthyl, X= CH_2), 45%, 10:1 dr, 83:17 er
3q (R^2=2-naphthyl, X= CH_2), 65%, 8:1 dr, 92:8 er
3r (R^2= 2-thienyl, X= CH_2), 47%, 11:1 dr, 82:18 er
3s (R^2= Me_2CHCH_2, X= CH_2), 48%, 20:1 dr, 78:22 er

from (**1l**) and **2a**:

3t, 52%, 10:1 dr, 61:39 er

from (**1m**) and **2a**:

3u, 53%, 20:1 dr, 86:14 er

[a] Unless otherwise noted, reactions were carried out with **1** (0.4-1.0 mmol) and **2** (0.2-0.5 mmol), DBU (2 equiv) in dichloromethane (2 mL) at 0 °C for 48 h. [b] Isolated yields after flash column chromatography. [c] Enantiomeric ratios were determined by HPLC analysis on a chiral stationary phase (see the Supporting Information for details). [d] Diastereoisomeric ratios were determined by ^1H-NMR of the crude reaction mixtures.

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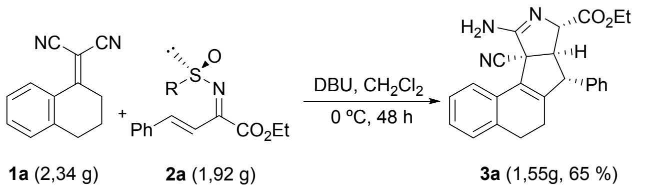
Starting dicyanoalkenes **1** bearing heterocyclic five-membered rings were also examined. In this context, substrates containing a furane and a thiophene moieties behaved as expected, giving rise to tetracycles **3i** and **3j** with moderate er values (79:21 and 89:11, respectively). However, the dicyanoalkene containing a pyrrole moiety did not react with the conjugated sulfinyl imine **2a** (Table 2).

The scope of our tandem protocol with respect to the sulfinyl imine counterpart (**2**) in their reaction with bicyclic dicyanoalkenes **1a** (derived from 1-tetralone) and **1g** (derived from 4-chromanone) was examined next. Regarding the ester substitution (R^3), isopropyl and methyl esters were good partners for the tandem reaction, albeit providing lower er values in the tetracyclic products **3l** (85:15 er) and **3m** (90:10 er) than the ethyl ester derivative (**3a**, 93:7 er). With respect to the β-position (R^2), the tandem protocol was compatible with aromatic substituents bearing both electron-withdrawing (**3n**) and electron-donating (**3o**) substituents, as well as naphthyl groups (**3p**, **q**) and heteroaromatic substituents such as the 2-thienyl group (**3r**). The process was also tolerated with an aliphatic substituent (**3s**) at the R^2 position of the conjugated sulfinyl imino esters **2**. In these cases, the expected tetracyclic products were obtained in good yields (45-75%) and enantioselectivity ranging from 78:22 to 92:8 er (Table 2).

We also tested a monocyclic 1,1-dicyanoalkene derived from propiophenone (**1l**). This reacted with sulfinyl imino ester **2a**, affording the expected product **3t** in good yield but with a dramatic drop in enantioselectivity (61:39 er), compared with the bicyclic dicyanoalkenes. This difference was probably due to the lower conformational flexibility of the bicyclic substrates that confers rigidity to the transition state, allowing for a better enantiocontrol. Finally, dicyanoalkene **1m** (derived from 2-tetralone), which possesses two reactive sites, provided also the desired product **3u**, by means of its reaction, through the most acidic benzylic position, with conjugated sulfinyl imino ester **2a** (Table 2).[25]

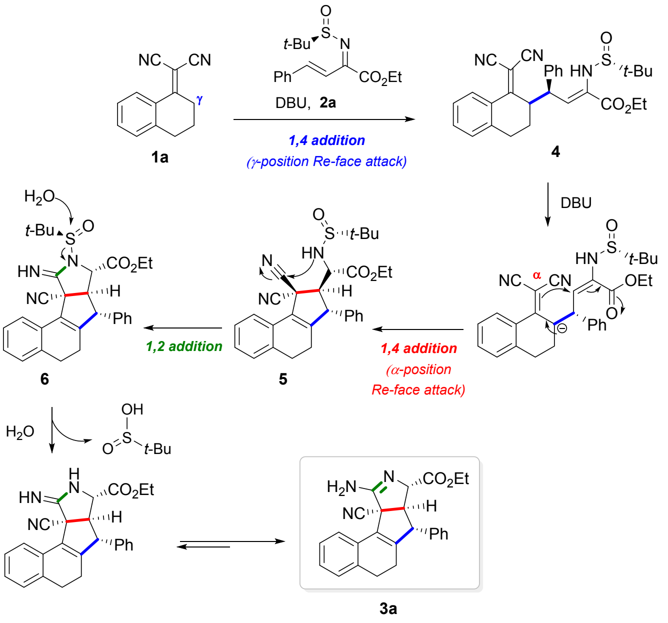
To assess the utility of this tandem protocol, a gram-scale experiment was carried out. Thus, starting from 2.34 g (12 mmol) of 1,1-dicyanoalkene **1a**, and 1.92 g (6 mmol) of conjugated *N*-*tert*-butylsulfinyl imino ester **2a**, 1.55 g of tetracyclic derivative **3a** were obtained, *i.e.* this product was isolated in 65% overall yield after four reaction steps that occurred in a tandem fashion (Scheme 2). Moreover, no erosion of the enantioselectivity was observed.



Scheme 2. Gram-scale experiment with dicyanoalkene **1a** and conjugated sulfinyl imino ester **2a**.

The structure of final products **3** was determined by means of an X-ray diffraction analysis of compound (±)-**3m**.[26] Furthemore, the absolute configuration of the four newly created stereocenters was unequivocally assigned by electronic circular dichroism of compound **3c**, assuming identical stereochemical outcome for all other tetracycles **3**, as displayed in Table 2 (see Supporting Information for details).

Once confirmed the unexpected molecular skeleton of products **3**, a mechanistic proposal to explain their formation has been outlined below in Scheme 3. The tandem reaction would start with the base-mediated conjugated addition of the 1,1-dicyanoalkene **1** through its γ-position to the sulfinyl imino ester **2**, rendering enamino ester **4**. This 1,4-addition reaction would take place by the opposite face of the bulky *terc*-butyl substituent at the sulfinyl group, providing the configuration showed in intermediate **4** at the Ph-containing stereocenter. This stereochemical outcome is based on theoretical calculations performed in our previous work with fluorinated conjugated sulfinyl imines.[23] Then, deprotonation of intermediate **4** would generate an anionic species that, this time, would undergo intramolecular conjugated addition through the α-position of the dicyanoalkene to the conjugated ester moiety, affording the fused five-membered ring **5**. In this case, the nucleophilic addition would take place by the upper face (*Re*-face attack) since the bottom one would be shielded by the phenyl group at the adjacent carbon. Subsequently, the *N*-sulfinyl amine would preferentially react with the upwards nitrile moiety, giving rise to amidine **6**, with four stereocenters. Finally, hydrolysis of the sulfinyl group would deliver the final tetracyclic heterocycle **3** after tautomeric equilibrium (Scheme 3).



Scheme 3. Mechanistic proposal for the formation of tetracyclic products **3**.

Conclusions

In conclusion, the reaction of 1,1-dicyanoalkenes **1** with enantiomerically pure conjugated *N*-sulfinyl α-imino esters **2** has been studied in this work. Thus, in the presence of DBU as a base, enantiomerically enriched tetracyclic compounds **3** were formed in good yields by means of a tandem process

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involving four chemical steps, with concomitant elimination of the sulfinyl group that acted as a chiral inducer. The conformational constraint imposed by the bicyclic dicyanoalkene counterpart allowed a good stereochemical control of the process, rendering the final products with moderate to good enantiomeric ratios and high diastereoselectivity.

This work complements our previous studies regarding the divergent reactivity showed by 1,1-dicyanoalkenes and conjugated *N*-sulfinyl ketimines, which allowed us to synthesize structurally diverse collections of compounds and represented an example of diversity-oriented synthesis.

Experimental Procedure

General procedure for the synthesis of rearranged polycycles 3. To a stirred solution of imine **2** (1 equiv.) and dicyanoalkene **1** (2 equiv.) in DCM (0.03 M), 2 equivalents of DBU was added. After stirring for 48h at 0 °C, the solvents were evaporated under vacuum and the crude product purified by means of flash column chromatography on silica gel using mixtures of *n*-hexane and ethyl acetate as eluents.

Ethyl (7*R*,7*aR*,8*S*,10*aS*)-10-amino-10a-cyano-7-phenyl-5,6,7,7a,8,10a-hexahydrobenzo[6,7]indeno[1,2-c]pyrrole-8-carboxylate (3a). Starting from imine **2a** (61 mg, 0.2 mmol) and dicyanoalkene **1a** (78 mg, 0.4 mmol), following the general procedure indicated before, **3a** was obtained as a separable mixture of diastereoisomers as a brown solid (54.mg, 68%,.15:1 d.r., 93:7 e.r.) after purification by column chromatography with Hex:EtOAc (1:1) as eluent. The e.r. value was determined by HPLC analysis using a Chiralpak AY-H column (hexane:isopropanol 95:5); flow rate = 1.0 mL/min, tmajor= 46.1 min, tminor= 35.9 min. M.p.= 194.3 – 195 °C. $[\alpha]^{25}_{D}$ = +50.6 (c 0.1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.27 (m, 4H), 7.25 – 7.18 (m, 4H), 4.52 (d, *J* = 4.5 Hz, 1H), 4.26 – 4.19 (m, 2H), 4.03 (d, *J* = 3.1 Hz, 1H), 3.63 (dd, *J* = 4.5, 3.1 Hz, 1H), 2.95 – 2.76 (m, 2H), 2.17 (dd, *J* = 10.4, 5.5 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 162.4, 147.4, 140.2, 136.6, 130.3, 129.6, 129.2 (2C), 128.8, 128.2, 127.7, 127.7 (2C), 127.1, 122.2, 118.9, 75.4, 62.8, 61.6, 60.6, 58.4, 28.3, 23.7, 14.2. HRMS (ESI/Q-TOF) m/z calculated for $C_{25}H_{24}N_3O_2^+$ $[M+H]^+$: 398.1863 found 398.1859.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: detailed experimental procedures, compound characterization, NMR spectra and copies of HPLC chromatograms.

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Notes and references

1 J. B. Hendrikson, *J. Am. Chem. Soc.* **1975**, *97*, 5784.
2 [W. S. Rapson and R. Robinson. *J. Chem. Soc.* **1935**, 1285.
3 For recent reviews regarding asymmetric tandem reactions, see: (*a*) H. Pellissier, *Adv. Synth. Catal.* **2023**, *365*, 620; (*b*) H. Pellissier, *Adv. Synth. Catal.* **2023**, *365*, 768; (*c*) L. Bai and X. Jiang, *Chem. Catal.* **2023**, *3*, 100752; (*d*) L. Zou, Y. Gao, Q. Zhang, X.-Y. Ye, T. Xie, L.-W. Ye and Y. Wang, *Chem. Asian J.* **2023**, *18*, e202300617; (*e*) R. Westphal, E. V. Filho, F. Medici, M. Benaglia and S. J. Greco, *Synthesis* **2022**, *54*, 2927; (*f*) R.-X. Liang and Y.-X. Jia, *Acc. Chem. Res.* **2022**, *55*, 734; (*g*) R. K. Maurya, D. Sharma, Kumari, S. R. Chatterjee, M. Khatravath and R. Dandela, *ChemistrySelect* **2022**, *7*, e202201408; (*h*) Y. Hussain, Tamanna, M. Sharma, A. Kumar and P. Chauan, *Org. Chem. Front.* **2022**, *9*, 572; (*i*) B. Delayre, Q. Wang and J. Zhu, *ACS Cent. Sci.* **2021**, *7*, 559; (*j*) M. Zhang, Y. Gong, W. Zhou, Y. Zhou and X.-L. Liu, *Org. Chem. Front.* **2021**, *8*, 3968; (*k*) Y.-X. Song and D.-M. Du, *Adv. Synth. Catal.* **2021**, *363*, 4667; (*l*) F.-L. Hong and L.-W. Ye, *Acc. Chem. Res.* **2020**, *53*, 2003; (*m*) H. Pellissier, *Adv. Synth. Catal.* **2020**, *362*, 2289; (*n*) H. Pellissier, *Adv. Synth. Catal.* **2019**, *361*, 173; (*o*) H. A. Döndas, M. de Retamosa and J. M. Sansano, *Organometallics* **2019**, *38*, 1828; (*p*) C. S. Evans and L. O. Davis, *Molecules* **2018**, *23*, 33; (*q*) P. Chauan, S. Mahajan and D. Enders, *Acc. Chem. Res.* **2017**, *50*, 2809.
4 For reviews on the chemistry of dicyanoalkenes, see: (*a*) B. Farajpour and A. Alizadeh, *Org. Biomol. Chem.* **2022**, *20*, 8366; (*b*) C. Curti, A. Sartori, L. Battistini and F. Zanardi, *Synlett* **2018**, *29*, 266; (*c*) L. Battistini, C. Curti, G. Rassu, A. Sartori and F. Zanardi, *Synthesis* **2017**, *49*, 2297; (*d*) J. Kaur, P. Chauhan and S. S. Chimni, *Org. Biomol. Chem.* **2016**, *14*, 7832; (*e*) M. Sánchez-Roselló, C. del Pozo and S. Fustero, *Synthesis* **2016**, *48*, 2553; (*f*) H.-L. Cui and Y.-C. Chen, *Chem. Commun.* **2009**, 4479.
5 H.-C. Wu, C. Wang, Y.-H. Chen and Y.-K. Liu, *Chem. Commun.* **2021**, *57*, 1762.
6 Y. Hayashi, X. Han and N. Mori, *Chem. Eur. J.* **2023**, *29*, e202301093.
7 K. Choudhary, H. Joshi, S. Rohilla and V. K. Singh, *Chem. Eur. J.* **2024**, *30*, e202304078.
8 K. Li, S. Zhen, W. Wang, J. Du, S. Yu, Y. Wu and H. Guo, *Chem. Sci.*, **2023**, *14*, 3024.
9 L.-F. Cao, Y. Yin, Y.-L. Xie and J.-W. Xie, *ChemistrySelect* **2024**, *9*, e202401711.
10 Z. Gao, X. Zhou, L. Xie, X. Wang, S. Wang, H. Liu and H. Guo, *J. Org. Chem.* **2024**, *89*, 7169.
11 S. Lu, Y. Zhao, S. Xie, W. Li and S.-W. Li, *New. J. Chem.* **2023**, *47*, 21155.
12 Y. Wang, C. Niu, D.-H. Xie and D.-M. Du, *Org. Biomol. Chem.* **2021**, *19*, 8572.
13 Y. Gao, X. Song, R.-J. Yan, W. Du and Y.-C. Chen, *Org. Biomol. Chem.* **2021**, *19*, 151.
14 W.-B. Yao, X.-S. Xie, J.-N. Liu and J.-W. Xie, *Org. Biomol. Chem.* **2022**, *20*, 1982.

View Article Online
DOI: 10.1039/D6OB00277C

15 H. Mei, L. Lin, B. Shen, X. Liu and X. Feng, *Org. Chem. Front.* **2018**, *5*, 2505

16 M. Guo, F. Dong, X. Yin, L. Xu, L. Wang and S.-S. Li, *Org. Chem. Front.* **2021**, *8*, 2224.

17 S. Lu, Z. Zhao, Y. Ren, G. Du, J. Zhao and S.-W. Li, *Org. Chem. Front.* **2022**, *9*, 3446.

18 I. Suzuki, S. Tsunoi and Y. Shibata, *Org. Lett.* **2017**, *19*, 2690.

19 M. Liu, L. Zhou, W. Shi, Y. Hu, J. Liao, Z. Duan, W. Wang, Y. Wu, B. Zheng and H. Guo, *Org. Lett.* **2021**, *23*, 7703.

20 Z. Duan, M. Liu, B. Zheng, Y. Tang, J. Du, L. Wang, S. Yu, Y. Wu and H. Guo, *Org. Lett.* **2023**, *25*, 3298.

21 J.-R. Zhuo, B.-X. Quan, J.-Q. Zhao, M.-L. Zhang, Y.-Z. Chen, X.-M. Zhang and W.-C. Yuan, *Tetrahedron* **2020**, *76*, 131115.

22 J. Wang, C.-F. Gao, H. Zhou, F. Li, J. Nie, J.-A. Ma and F. G. Zhang, *Adv. Synt. Catal.* **2025**, *early view.* doi/10.1002/adsc.70090.

23 A. Sanz-Vidal, D. Gaviña, L. Sotorríos, E. Gómez-Bengoa, F. López-Ortiz, M. Sánchez-Roselló, C. del Pozo, *Chem. Commun.* **2021**, *57*, 8023.

24 D. Gaviña, M. Escolano, L. Sotorríos, E. Gómez-Bengoa, F. López-Ortiz, M. Sánchez-Roselló, C. del Pozo, *Adv. Synth. Catal.* **2024**. *366*, 970.

25 Compounds **3** were obtained as inseparable mixtures of diastereoisomers.

26 CCDC 2513043 contain the supplementary crystallographic data for compound **3m**. These data can be obtained free of charge from: The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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The data supporting this article have been included as part of the Supplementary Information.