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Substituted proline derivatives as organocatalysts in the Michael reaction

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Abstract: Chiral, polysubstituted proline esters, obtained *via* cycloaddition reactions of azomethine ylides, were studied as organocatalysts in the Michael reaction of aldehydes/ketones and vinylsulphones. Under optimised reaction conditions employing 10 mol % of the catalyst in wet CH_2Cl_2, the yields of the products were generally good while the enantioselectivity varied, reaching up to 52 %.

Keywords: Michael reaction; organocatalysis; proline derivatives.

INTRODUCTION

Proline derived compounds have been extensively utilized in organocatalytic processes and have found wide application in many synthetically useful transformations.[1] Various derivatives, exemplified by the structures in Fig. 1, were synthesised and used with high degrees of chemical and stereochemical efficiency.

Proline compounds have most frequently been employed in organocatalytic transformations involving aldehydes and ketones activating them *via* two general modes, enamine or iminium ion formation. While the enamine formation is usually involved in the α-functionalisation of aldehydes/ketones, the iminium ion is implicated in nucleophilic additions on α,β-unsaturated aldehydes/ketones and related reactions.[2] Even though many organocatalysts of this structure are known, most of them are obtained *via* transformations of the carboxylic group of the parent molecule, while very few examples possess further substituents attached to the ring carbons.

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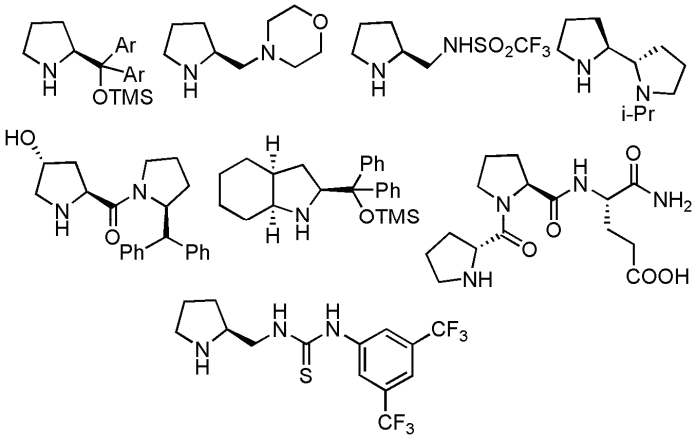


Fig. 1. Proline-derived catalysts.

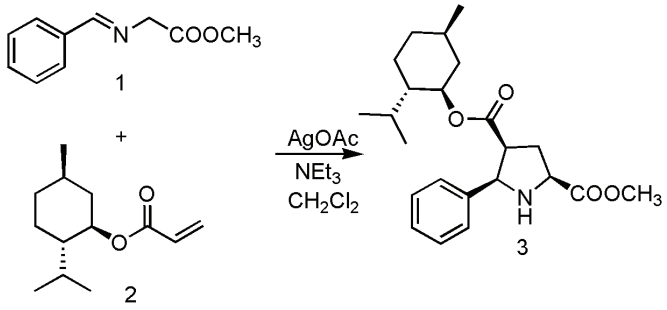
Our work in this area was initiated with the aim of investigating the effect of additional substituents on the organocatalytic efficiency of proline-derived compounds. It was hoped that a range of substituted prolines would be accessible in a straightforward manner *via* highly stereoselective 1,3-dipolar cycloaddition reactions of azomethine ylides.[3] This mild methodology has been extensively investigated in recent decades and a variety of processes employing either chiral auxiliaries or chiral Lewis acids were developed for the stereoselective synthesis of proline derivatives.[4] The substitution pattern of the proline product can be controlled by structural variations of the reacting imine (1,3-dipole) and alkene (dipolarophile).

RESULTS AND DISCUSSION

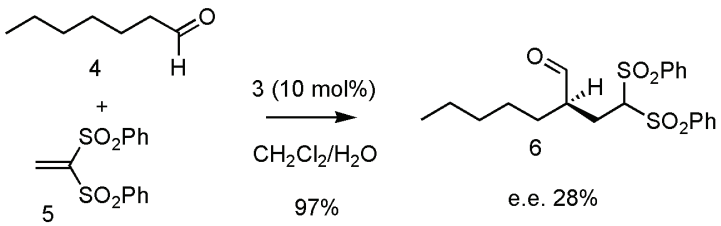
In an initial study and synthesis of substituted proline derivatives, the chiral auxiliary approach using menthyl acrylate was exploited, as outlined in Scheme 1.[5] Thus, the cycloaddition of imine **1** and (–)-menthyl acrylate **2** in the presence of AgOAc afforded the proline derivative **3** as a single diastereomer in 42 % yield. The Ag-catalysed 1,3-dipolar cycloadditions of aminoester derived imines are known to produce all-*cis* prolines and this structural feature was envisaged to be beneficial for organocatalytic processes involving these compounds, due to one face of the pyrrolidine skeleton being better shielded.

Proline ester **3** (10 mol %) was used as a catalyst for the Michael reaction of aldehyde **4** and vinyl sulphone **5**.[6] The reaction was realised in CH_2Cl_2 saturated with H_2O at room temperature. The presence of H_2O proved to be essential and significantly improved the reaction yield (97 *versus* 28 %). Unfortunately, although the product was isolated almost quantitatively, the observed *e.e.* was rather low (28 %), Scheme 2. The absolute stereochemistry of the product was

determined by comparison of the observed and the literature values of $[\alpha]_D$ for compound **6**.[7]



Scheme 1. Synthesis of catalyst **3**.



Scheme 2. Michael reaction catalysed by proline derivative **3**.

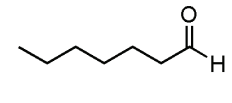
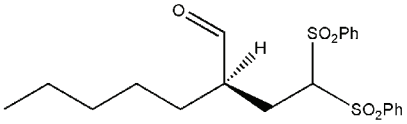
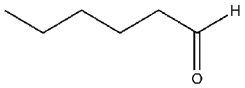
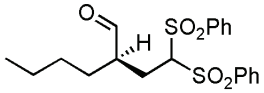
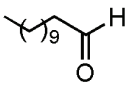
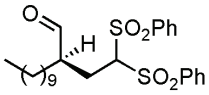
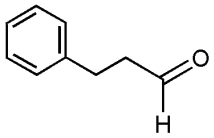
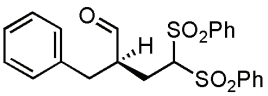
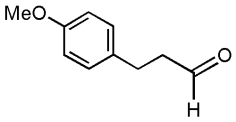
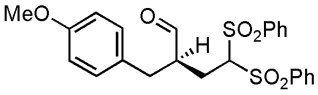
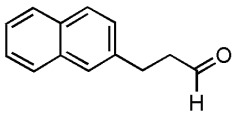
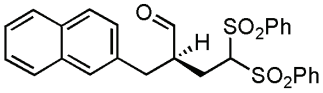
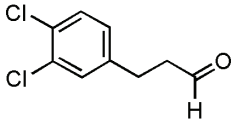
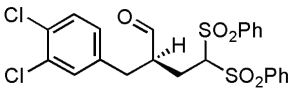
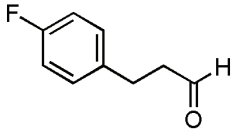
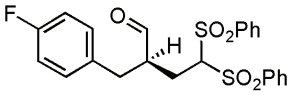
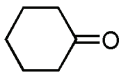
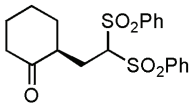
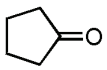
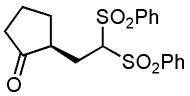
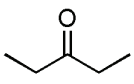
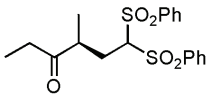
In order to explore the general potential of proline ester **3** as an organocatalyst, a series of reactions were performed using various aldehydes and ketones in place of **4** under the conditions described above, Table I.

The majority of aldehydes (entries a–h, Table I) afforded the products in excellent yields, but with low enantioselectivity. Ketones (entries i–k, Table I) furnished the Michael addition products, generally, in lower yields than the aldehydes but with marginally better stereoselectivity, except in the case of cyclohexanone (entry i, Table I).

With the aim of improving these initial results, the synthesis of a range of related proline catalysts was instigated. The initial focus was on the proline C(5)--substituent originating from the imine, a dipole precursor in the cycloaddition reactions of azomethine ylides. Compounds **17**–**25** were prepared using Ag--catalysed, 1,3-dipolar cycloadditions as outlined in Scheme 1 (Fig. 2). While the two esters at C(2) and C(4) were kept constant, the substituent at C(5) was varied, except in the case of the proline derivative **21**, which possessed an additional substituent at C(2).

Replacing catalyst **3** in the reaction outlined in Scheme 2 with the proline derivative **17** (entry a, Table II) resulted in a slight improvement of enantioselectivity. The introduction of an *ortho* substituent on the C(5) phenyl (entries b, c and

TABLE I. Variation of the aldehydes/ketones

Entry	Aldehyde/ketone	Product	Cmpd.	Yield/*e.e.*, %[a,b]
a			**6**	97/28 (*R*)[c]
b			**7**	99/28
c			**8**	70/20
d			**9**	99/22
e			**10**	98/24
f			**11**	99/12
g			**12**	98/18
h			**13**	77/32
i			**14**	42/11(*S*)[c]
j			**15**	56/33
k			**16**	51/44

[a]Isolated yields after column chromatography; [b]*e.e.* was determined by chiral HPLC (see experimental); [c]the configuration was determined by comparison of $[\alpha]_D$ with literature results

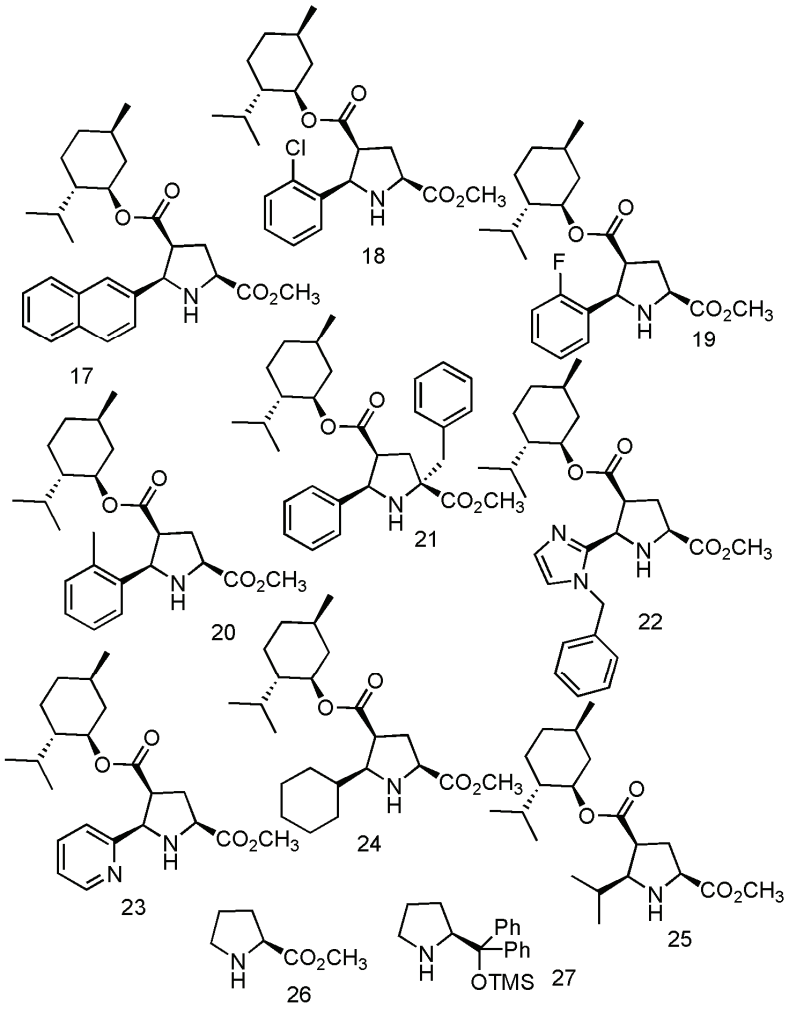


Fig. 2. Variations of the C(5) substituent.

d, Table II) lowered the *e.e.* A similar effect was observed with the catalyst **21** possessing an additional substituent at C(2) (entry e, Table II). An increased steric demand resulted not only in a depleted *e.e.*, but also in a lower chemical yield of the product. The presence of a C(5)-heterocyclic substituent (entries f and g, Table II) did not result in any significant improvement in the enantioselectivity. Compounds possessing an aliphatic substituent at C(5) (entries h and i, Table II) were also briefly tested. They proved to be slightly more efficient, with the iopropyl derived **25** affording the Michael adduct in almost quantitative yield and 42 % *e.e.* Contrary to the other organocatalysts, prolines **24** and **25**, possessing an aliphatic substituent at C(5), afforded product **6** with the *S* con-

figuration.[7] For comparison, the reaction described in Scheme 2 was performed employing proline ester **26** (entry j, Table II) and commercially available **27** (entry k, Table II). While the majority of substituted proline derivatives proved to be more efficient than the parent ester **26**, catalyst **27** showed a significantly better enantioselectivity than the synthesised prolines.

TABLE II. Michael reaction with catalysts **17**–**27** and product **6**

Entry	Catalyst	Yield, %[a]	*e.e.*, %[b]
a	**17**	99	38 (*R*)
b	**18**	99	1
c	**19**	99	10 (*R*)
d	**20**	97	10 (*R*)
e	**21**	24	22 (*R*)
f	**22**	99	10 (*R*)
g	**23**	99	34 (*R*)
h	**24**	70	34 (*S*)
i	**25**	93	42 (*S*)
j	**26**	99	10 (*R*)
k	**27**	77	78 (*R*)

[a]Isolated yields after column chromatography; [b]*e.e.* was determined by chiral HPLC (see experimental)

Further attempts were made to modify the C(2) ester functionality in order to explore the effect of this substituent on the stereoselectivity. Compounds **28**–**31** (Fig. 3) were synthesised and used as organocatalysts replacing **3** in the reaction outlined in Scheme 2.

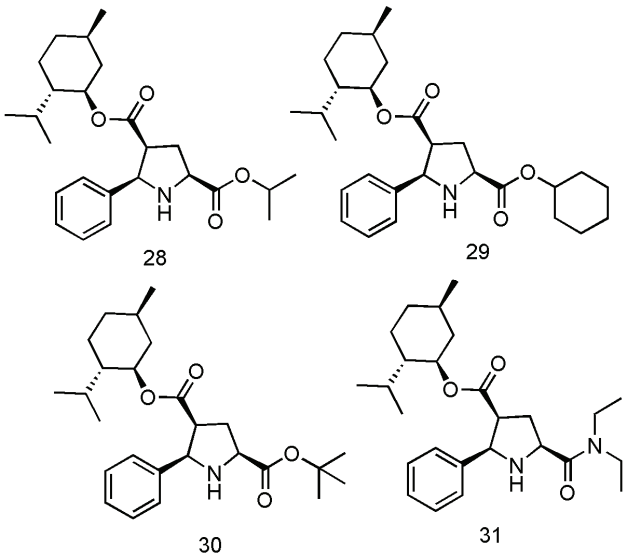


Figure 3. Variations of the C(2) substituent.

Substituting the methyl ester with isopropyl (compound **28**) influenced the stereoselectivity, increasing *e.e*. to 42 % (entry a, Table III). Extension of the ester *via* the introduction of the cyclohexyl moiety (compound **29**) in place of the isopropyl moiety maintained the *e.e*. on the same level (entry b, Table III). This result suggested that substituents at the C-atoms not directly bonded to the ester oxygen would not influence the reaction pathway significantly. Therefore the *t*-butyl derivative **30** was synthesised and employed to furnish product **6** in 52 % *e.e*. (entry c, Table III). Finally, catalyst **31** with a C(2)-amide functionality was briefly studied but the observed *e.e*. (entry d, Table III) was in the range of that obtained with the *t*-butyl compound **30** (entry c, Table III).

TABLE III. Michael reaction with catalysts **28**–**31** and product **6**

Entry	Catalyst	Yield, %[a]	*e.e*., %[b]
a	**28**	93	42 (*R*)
b	**29**	92	41 (*R*)
c	**30**	97	52 (*R*)
d	**31**	93	47 (*R*)

[a]Isolated yields after column chromatography; [b]*e.e*. was determined by chiral HPLC (see experimental)

Although the observed results at this point were not of synthetic significance, attempts were made to rationalise them, in the hope of obtaining some directions for further, rational optimisation of the catalyst properties. In organocatalytic reactions of aldehydes/ketones promoted by secondary amines, such as the one outlined in Scheme 2, the first step is the formation of the enamine. Often, the formed enamino moiety is not planar, with the N-atom being significantly pyramidalized.[8] This places the N-lone pair pseudo-axially, although its localization may depend on steric repulsion between the pseudo-equatorial *N*-substituent and the neighbouring C(2)/C(5) substituents. The intermediate *trans*-**32**, formed in the reaction outlined in Scheme 2, may exist in two forms, **32a** (s-*trans*, related to the C(2)-ester) and **32b** (s-*cis*, related to the C(2)-ester), Fig. 4. Assuming that in both cases the top face of the enamine is better shielded due to the orientation of the pyrrolidine substituents, it is reasonable to expect that the **32a**/**32b** equilibrium has an influence on the reaction stereoselectivity. The energy difference between the two was calculated using computational methods. Two rotamers, **32a** and **32b**, were optimized using DFT with B3LYP hybrid functional and the def2-SVP basis set, in vacuum and the difference in their stability was calculated.[9] The calculated energy difference between **32a** and **32b** was not significant (ΔE = –0.25 kJ/mol), favouring slightly rotamer **28b**. For comparison, ΔE for the pair **33a**/**33b**, obtained for the more efficient pyrrolidine catalyst **27**, suggested a noteworthy difference between the two. The slightly better efficiency of the pyrrolidines **28**–**31** (Table II) that have bulky ester moieties, which are likely to influence the ratio of two rotamers, may suggest that the

equilibrium is, at least, one of the factors contributing to the observed stereoselectivity. A further study of these polysubstituted prolines is on-going.

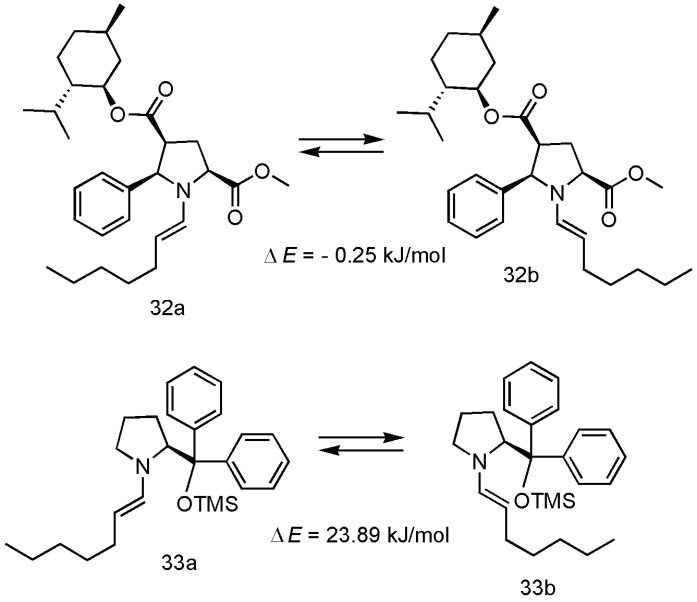


Fig. 4. The enamine equilibrium.

EXPERIMENTAL

The NMR spectra were recorded on a Bruker Avance III (500 MHz) or a Varian Gemini 2000 (200 MHz) spectrometer. The chemical shifts are given in parts per million (δ) downfield from tetramethylsilane as the internal standard, Deuterochloroform or DMSO-d_6 were used as solvents. The mass spectral data were recorded using an Agilent MSD TOF spectrometer coupled with Agilent 1200 HPLC or an Agilent Technologies 5975C MS coupled with Agilent Technologies 6890N GC. The IR spectra were recorded on an IR Thermo Scientific NICOLET iS10 (4950) spectrometer. Silica gel 60 (230–400 mesh was employed for the flash chromatography while thin layer chromatography was realised using alumina plates with 0.25 mm silica layer (Kieselgel 60 F_{254}, Merck). The solvents were purified by distillation before use. The enantiomeric excess was determined by HPLC using a CHIRALPAK IA column. Compounds **3**, **17** and **21** were synthesised according to the literature procedures.[10,11]

General procedure for the cycloaddition reactions

A mixture of the imine (l eq.), triethylamine (0.25 eq.), (–)-menthyl acrylate (1.1 eq.) and AgOAc (0.5 eq.) in dry CH_2Cl_2 was stirred under nitrogen atmosphere for 48 h at room temperature. After solvent evaporation, the residue was purified by flash column chromatography (SiO_2). No attempts were made to optimise the reaction conditions.

*(2S,4S,5R)-4-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl]-2-methyl 5-(2-chlorophenyl)-pyrrolidine-2,4-dicarboxylate (**18**)*. Flash chromatography (SiO_2, 1:1*V/V* petroleum ether–diethyl ether) afforded the product as a colourless oil in 24 % yield.

(2S,4S,5R)-4-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl]-2-methyl 5-(2-fluorophenyl)-pyrrolidine-2,4-dicarboxylate (***19***). Flash chromatography (SiO_2, 1:1*V/V* petroleum ether–diethyl ether) afforded the product as a white solid (m.p. 82–83 °C) in 32 % yield.

(2S,4S,5R)-4-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl]-2-methyl 5-o-tolylpyrrolidine-2,4-dicarboxylate (***20***). Flash chromatography (SiO_2, 1:1*V/V* petroleum ether–diethyl ether) afforded the product as a white solid (m.p. 66–67 °C) in 31 % yield.

(2S,4S,5R)-4-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl]-2-methyl 5-(1-benzyl-1H-imidazol-2-yl)pyrrolidine-2,4-dicarboxylate (***22***). Flash chromatography (SiO_2, EtOAc) afforded the product as a yellow oil in 29 % yield.

(2S,4S,5R)-4-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl]-2-methyl 5-(pyridin-2-yl)pyrrolidine-2,4-dicarboxylate (***23***). Flash chromatography (SiO_2, EtOAc) afforded the product as a white solid (m.p. 104–105 °C) in 38 % yield.

(2S,4S,5S)-4-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl]-2-methyl 5-cyclohexylpyrrolidine-2,4-dicarboxylate (***24***). Flash chromatography (SiO_2, 1:1*V/V* petroleum ether–diethyl ether) afforded the product as a white solid (m.p. 106–107 °C) in 33 % yield.

(2S,4S,5S)-4-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl]-2-methyl 5-isopropylpyrrolidine-2,4-dicarboxylate (***25***). Flash chromatography (SiO_2, diethyl ether) afforded the product as a white amorphous solid (m.p. 51–53 °C) in 20 % yield.

(2S,4S,5R)-2-Isopropyl-4-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl] 5-phenylpyrrolidine-2,4-dicarboxylate (***28***). Flash chromatography (SiO_2, 1:1*V/V* petroleum ether–diethyl ether) afforded the product as a white solid (m.p. 124–126 °C) in 24 % yield.

(2S,4S,5R)-2-Cyclohexyl-4-[(1R,2S,5R)-2-isopropyl 5-methylcyclohexyl] 5-phenylpyrrolidine-2,4-dicarboxylate (***29***). Flash chromatography (SiO_2, 1:1*V/V* petroleum ether–diethyl ether) afforded the product as a white solid (m.p. 126–127 °C) in 54 % yield.

*(2S,4S,5R)-2-*tert*-Butyl-4-[(1R,2S,5R)-2-isopropyl 5-methylcyclohexyl] 5-phenylpyrrolidine-2,4-dicarboxylate* (***30***). Flash chromatography (SiO_2, 1:1*V/V* petroleum ether–diethyl ether) afforded the product as a white solid (m.p. 134–135 °C) in 24 % yield.

*(2R,3S,5S)-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl] 5-(*N,N*-diethylcarbamoyl)-2-phenylpyrrolidine-3-carboxylate* (***31***). Flash chromatography (SiO_2, EtOAc) afforded the product as a yellow amorphous solid (m.p. 103–104 °C) in 29 % yield.

The spectroscopic data for the cycloaddition products **18**–**31** are given in the Supplementary material to this paper.

General procedure for catalytic conjugate addition of aldehydes to 1,1-bis(phenylsulphonyl)-ethylene

To a mixture of catalyst (2 mg, 0.005 mmol) and 1,1-bis(phenylsulphonyl)ethylene (15 mg, 0.05 mmol) in 1.0 mL of CH_2Cl_2 (saturated with H_2O) was added the corresponding aldehyde (0.15 mmol) and the mixture was stirred for 2 h at room temperature. After solvent evaporation, the residue was purified by flash column chromatography (SiO_2).

(R)-2-[2,2-Bis(phenylsulphonyl)ethyl]heptanal[7] (***6***). Flash chromatography (SiO_2, 1:1 *V/V* petroleum ether–diethyl ether) afforded the product as a white amorphous solid (m.p. 86–87 °C) in 97 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 210 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 9.48 min, t_r (major) = 11.28 min), *e.e.* 53 %.

(R)-2-[2,2-Bis(phenylsulphonyl)ethyl]hexanal[7] (***7***). Flash chromatography (SiO_2, 1:1 *V/V* petroleum ether–diethyl ether) afforded the product as a white amorphous solid (m.p. 60–62 °C) in 99 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK

IA column at 230 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 9.23 min, t_r (major) = 10.55 min), *e.e.* 28 %.

*(*R*)-2-[2,2-Bis(phenylsulphonyl)ethyl]dodecanal* ***(8)***. Flash chromatography (SiO_2, 1:1 *V/V* petroleum ether–diethyl ether) afforded the product as a colourless oil in 70 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 230 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate =1.0 mL min^{-1}, t_r (minor) = 7.43 min, t_r (major) = 8.68 min), *e.e.* 20 %.

*(*R*)-2-Benzyl-4,4-bis(phenylsulphonyl)butanal*[7] ***(9)***. Flash chromatography (SiO_2, 1:1 *V/V* petroleum ether–diethyl ether) afforded the product as a white amorphous solid (m.p. 80––81 °C) in 99 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 230 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 14.07 min, t_r (major) = 15.87 min), *e.e.* 22 %.

*(*R*)-2-(4-Methoxybenzyl)-4,4-bis(phenylsulphonyl)butanal* ***(10)***. Flash chromatography (SiO_2, 4:6 *V/V* petroleum ether–diethyl ether) afforded the product as a white amorphous solid (m.p. 95–96 °C) in 98 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 230 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 15.08 min, t_r (major) = 17.85 min), *e.e.* 24 %.

*(*R*)-2-[(Naphthalen-1-yl)methyl]-4,4-bis(phenylsulphonyl)butanal* ***(11)***. Flash chromatography (SiO_2, 4:6 *V/V* petroleum ether–diethyl ether) afforded the product as a yellow amorphous solid (m.p. 120–121 °C) in 99 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 230 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 15.95 min, t_r (major) = 20.21 min), *e.e.* 12 %.

*(*R*)-2-(3,4-Dichlorobenzyl)-4,4-bis(phenylsulphonyl)butanal (12)*. Flash chromatography (SiO_2, 4:6 *V/V* petroleum ether–diethyl ether) afforded the product as a colourless oil in 98 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 210 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 16.99 min, t_r (major) = 22.095 min), *e.e.* 18 %.

*(*R*)-2-(4-Fluorobenzyl)-4,4-bis(phenylsulphonyl)butanal (13)*. Flash chromatography (SiO_2, 4:6 *V/V* petroleum ether–diethyl ether) afforded the product as a colourless oil in 77 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 210 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate =1.0 mL min^{-1}, t_r (minor) = 16.10 min, t_r (major) = 17.93 min), *e.e.* 32 %.

The spectral data for the addition products **6**–**13** of aldehydes to 1,1-bis(phenylsulphonyl)ethylene are given in the Supplementary material to this paper.

General procedure for the catalytic conjugate addition of ketones to 1,1-bis(phenylsulphonyl)ethylene

To a mixture of catalyst (4 mg, 0.01 mmol) and 1,1-bis(phenylsulphonyl)ethylene (15 mg, 0.05 mmol) in 1.0 mL of CH_2Cl_2 (saturated with H_2O) was added the corresponding ketone (0.15 mmol) and the mixture was stirred for 18 h at room temperature. After solvent evaporation, the residue was purified by flash column chromatography (SiO_2).

*(*S*)-2-[2,2-Bis(phenylsulphonyl)ethyl]cyclohexanone*[12] ***(14)***. Flash chromatography (SiO_2, 1:1 *V/V* petroleum ether–diethyl ether) afforded the product as a white amorphous solid (m.p. 149–151 °C) in 42 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 210 nm (heptane/EtOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 24.15 min, t_r (major) = 25.13 min), *e.e.* 11 %.

*(*S*)-2-[2,2-Bis(phenylsulphonyl)ethyl]cyclopentanone* ***(15)***. Flash chromatography (SiO_2, 1:1 *V/V* petroleum ether–diethyl ether) afforded the product as a white amorphous solid (m.p.

110–112 °C) in 56 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 210 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 13.76 min, t_r (major) = 16.29 min), *e.e.* 33 %.

*(*S*)-4-Methyl-6,6-bis(phenylsulphonyl)hexan-3-one (**16**)*. Flash chromatography (SiO_2, 1:1 *V/V* petroleum ether–diethyl ether) afforded the product as a colourless oil in 51 % yield. The enantiomeric excess was determined by HPLC with a CHIRALPAK IA column at 230 nm (heptane/*i*-PrOH in the ratio of 70/30, flow rate = 1.0 mL min^{-1}, t_r (minor) = 8.78 min, t_r (major) = 9.36 min), *e.e*. 44%.

CONCLUSIONS

This initial study of substituted proline derivatives suggested that these compounds might have potential as organocatalysts but additional investigation is necessary to optimise their catalytic properties. As they are easily accessible *via* highly stereoselective cycloaddition reactions of azomethine ylides and potentially may be used in various organocatalytic transformations requiring secondary amines, they might be attractive molecules for additional investigation.

SUPPLEMENTARY MATERIAL

Spectroscopic data for the cycloaddition products **18**–**31**are available electronically from http://www.shd.org.rs/JSCS/, or from the corresponding author on request.

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ИЗВОД

СУПСТИТУИСАНИ ПРОЛИНСКИ ДЕРИВАТИ КАО ОРГАНОКАТАЛИЗАТОРИ У МАЈКЛОВОЈ РЕАКЦИЈИ

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Хирални, полисупституисани естри пролина, добијени циклоадиционим реакцијама азометинских илида, проучавани су као органокатализатори у Мајкловој реакцији алдехида/кетона и винил-сулфона. Под оптималним реакционим условима, у којима се користило 10 mol % катализатора у влажном метилен-хлориду приноси реакција су генерално били добри док је енантиоселективност варирала достижући 52 %.

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