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Catalyst structure and the enantioselective cyclopropanation of alkenes by copper complexes of biaryldiimines: the importance of ligand acceleration

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Abstract—The use of chiral non-racemic biaryl copper(I) complexes in the enantioselective cyclopropanation of a number of olefins with either ethyl or *tert*-butyl diazoacetate is described. Lack of ligand acceleration and the presence of equilibrium amounts of catalytically active uncomplexed Cu(I) ions account for lowered enantioselectivity when using certain ligands.

1. Introduction

Nozaki's catalytic cyclopropanation of alkenes in 1966 represented the first catalytic reaction involving the synthesis of optically active compounds.[1] Although the enantiomeric excess (e.e.) was modest, the basic protocol involving the decomposition of a diazo-compound by a metal catalyst in the presence of an alkene has remained largely unchanged. Aratani was able to improve on Nozaki's results with the use of a large number of Schiff-base ligands, achieving e.e.s of up to 94%.[2] Pfaltz used semicorrin ligands with copper(II) in the enantioselective reaction; reduction via diazoacetate or phenylhydrazine is believed to be essential in the formation of catalytically active species.[3] The use of neutral 5-aza-semicorrin ligands was subsequently reported.[4] In 1990, Masamune reported the use of bis-oxazoline ligands with copper(II) ions.[5] As with the Pfaltz systems, these complexes required reductive activation. At almost the same time Evans reported the use of copper(I)-bis-oxazoline complexes, and used them to achieve e.e.s of up to 99% in the cyclopropanation of styrene with ethyl diazoacetate.[6]

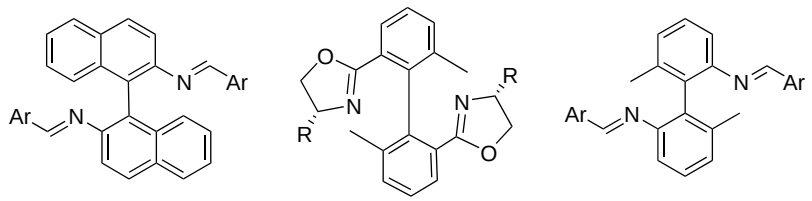

Figure 1. Ligands used in enantioselective cyclopropanation.

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Metals other than copper have been used in enantioselective cyclopropanation reactions: the groups of Doyle[7] and Müller[8] have used rhodium complexes, Aggarwal's group has also used a rhodium system with the intermediacy of a chiral non-racemic sulphonium ylid,[9] cobalt catalysis has been reported by Nakamura et al.,[10] and Kobayashi's group developed the Simmons–Smith reaction using an Et_2Zn–CH_2I_2–disulphonamide system.[11] Nishiyama et al. reported ruthenium(II)-(pybox) [pybox = pyridine-2,6-bis(oxazoline)] catalysed cyclopropanation,[12] with more recent examples from Katsuki[13] and other research groups.[14]

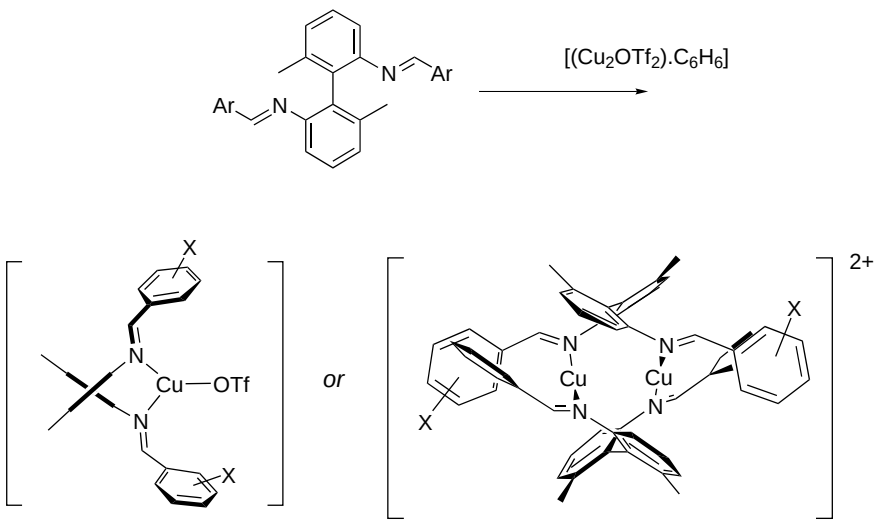
There have been a number of reports on the use of biaryl ligands in catalytic enantioselective cyclopropanation reactions (Fig. 1). Corey used a biphenyl bearing chiral oxazoline substituents in the synthesis of the natural form of sirenin.[15] Hayashi et al. synthesised an analogue of this ligand bearing a binaphthyl core[16] and Suga et al. synthesised an axially chiral ligand with a binaphthyl core lacking other chiral substituents.[17]

Our group has been involved in the synthesis of complexes containing chiral biaryl Schiff bases[18] and, recently, we described the structural origins of a dramatic variation in catalyst efficiency in the copper-catalysed enantioselective aziridination of alkenes.[19] Diimine derivatives **L**^{1}–**L**^{6} of 2,2′-diamino-6,6′-dimethylbiphenyl form complexes with Cu(I) with either the monometallic structure **I** (Scheme 1) or the L_2Cu_2 double-helix structure **II**, depending on the substitution pattern at the *N*-aryl group. *ortho*-Disubstitution favours the former and this leads to catalysts with rapid turnover and high enantioselectivity in alkene aziridination.[19] Herein, we describe related research in the cyclopropanation of alkenes that highlights the importance of 'ligand acceleration' in catalytic metal systems formed through complex equilibria.

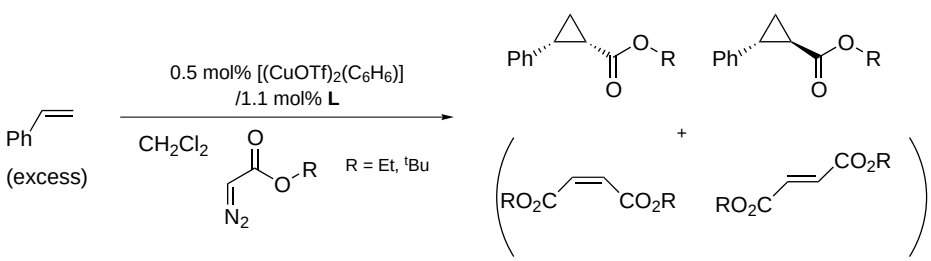
2. Results and discussion

The yield and chemical selectivity of the cyclopropanation reaction (Scheme 2) was optimised for ligand **L**^{1} such that a four-fold excess of styrene to ethyl or *tert*-butyl diazoacetate was used in the presence of 1 mol% of copper(I) triflate and 1.1 mol% ligand. The diazoacetate was added slowly over 1 h using a syringe pump. Use of lower concentrations of alkene or more rapid addition rates led to increased formation of diethyl malonate and fumarate. These conditions compare favourably with related systems in terms of convenience.

The diimine ligands were screened for their effectiveness in the cyclopropanation of styrene and the results are shown in Table 1. Good yields were obtained in all cases but it is significant that only the *ortho*-disubstituted ligands **L**^{1} and **L**^{2} led to products with measurable e.e. In reactions using the ligands **L**^{3}–**L**^{6} the *trans*/*cis* ratios of the products were almost identical.



Scheme 1. The reaction of ligands **L** with sources of Cu(I).



Scheme 2. The cyclopropanation of styrene using copper catalysts based on ligand **L**.

Table 1. The effect of ligand substitution on stereoselectivity in the cyclopropanation of styrene with ethyl diazoacetate

Ligand	Yield (%)	*trans*/*cis*	% e.e.$_{trans}$	% e.e$_{cis}$
L^{1}	94	82:18	46	57
L^{2}	81	70:30	40	34
L^{3}	75	66:34	0	0
L^{4}	80	63:37	0	0
L^{5}	88	62:38	0	0
L^{6}	90	63:37	0	0
None	75	64:36	0	0

Given that the catalytic species in copper-catalysed cyclopropanation is almost certainly a metal–carbene complex,[3] it seems unlikely that a complex of the type **II**, which has no readily accessible coordination sites, could be involved in the catalytic reaction without at least partial disassembly of the structure. Since similar complexes give modest enantioselection in alkene aziridination reactions, catalysis by a species **I** should presumably lead to some enantioselectivity but this is not observed in practice. However, the similarity in yield and *trans*/*cis* ratios obtained in these systems and the lack of measurable enantioselectivity strongly suggest that the catalyst precursor species in these reactions is an achiral copper complex such as $[Cu(solv)_n]^+$. Indeed the use of CuOTf as pre-catalyst gave a similar yield and diastereoselectivity.

Most interestingly, the complex of structural type **I** (Scheme 1) formed from ligand **L**^{3} also appears to be an ineffective catalyst. This seemingly anomalous behaviour can be traced to the fact that the copper centre is highly sterically shielded by the 10-anthryl substituents. It can be seen from the space-filling model

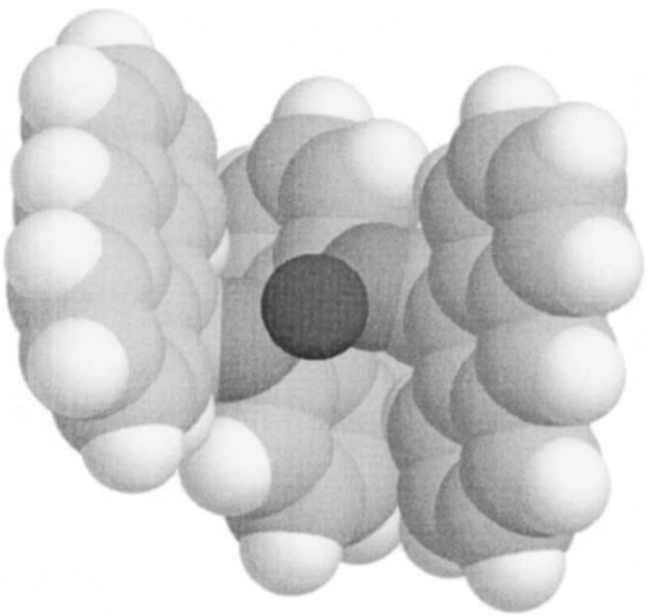


Figure 2. Space-filling model of the structure of [Cu**L**^{3}] based on the molecular structure of [Cu**L**^{1}][19] (OTf ligand omitted for clarity).

in Fig. 2 that approach of EDA or subsequently the alkene to the copper centre would be impeded; the copper atom is at the centre of a long and deep channel formed by the anthryl groups, which are necessarily coplanar. Notably, this ligand complex gives modest enantioselection even in the ligand accelerated aziridination reaction.[19]

The copper(I) triflate-catalysed aziridination of alkenes is dramatically accelerated by the addition of ligands **L**^{1}–**L**^{3}.[19] However, copper(I) triflate itself is an extremely efficient pre-catalyst for the cyclopropanation, and rates and yields appear to be essentially independent of the added ligand **L**. This lack of significant *ligand acceleration* in the reaction is presumably responsible for the modest d.e. and e.e. figures obtained. The results however compare, as expected, with those obtained by Suga et al. using binaphthyl analogues of **L**^{1}–**L**^{6} where the *ortho*-dichloro substituted system was the most selective.[17]

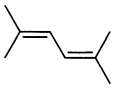
In order to determine if lower catalyst loading would alter the selectivity, the reaction was carried out with styrene using 0.1 mol% of complex. This resulted in a 76% yield of cyclopropane and 5% of fumarate. The *trans*/*cis* ratio was slightly lower at 21:79 and the e.e.s were 41% for the *trans*-isomer and 44% for the *cis*-isomer. Thus, the catalyst appears to be long-lived. The prevalence of an achiral copper complex at these lower concentrations may be responsible for the lowering of selectivity.

Further investigation using the ligand **L**^{1} was undertaken using various alkenes and both ethyl and *tert*-butyl diazoacetate. The results are shown in Table 2. The cyclopropanes were obtained in good to excellent yields. The *trans*/*cis* ratios vary considerably, although the *trans*-diastereomer always predominated. Surprisingly the isomer ratio for the *tert*-butyl ester was marginally lower in most cases than those for the ethyl ester. The e.e.s of cyclopropanes were moderate to good, with the *cis*-isomer of a given cyclopropane generally having greater e.e. than its *trans*-isomer. This phenomenon has also been reported by Katsuki,[20] using a copper(I) chiral non-racemic bipyridine ligand complex, and Ahn,[21] using a copper(I) bis(oxazolinyl)biferrocene catalyst.

3. Conclusions

Atropisomeric biaryl ligands have a distinguished history in catalytic enantioselective transformations, including hydrogenation,[22] Diels–Alder cycloadditions,[23] aldol condensations[24] and, recently, Zr-catalysed formation of chiral non-racemic Mannich bases.[25] The success of these ligands can be attributed to the fact that the axial chirality of the ligand is well expressed in the steric environment of the active site and that the biaryl backbone provides structural rigidity.

Table 2. Cyclopropanation of olefins with alkyl diazoacetate using [Cu**L**^{1}(OTf)] as catalyst

Substrate	Entry	Diazoacetate	Yield%	*Trans-/Cis-*	%e.e.$_{trans-}$	%e.e.$_{cis-}$
	1	Ethyl	94	82:18	46	57
	2	*tert*-Butyl	81	83:17	42	74
	4	Ethyl	99	65:35	42	70
	5	*tert*-Butyl	84	60:40	n/d[a]	76
	7	Ethyl	63	69:31	35	64
	8	*tert*-Butyl	96	61:39	86	68
	10	Ethyl	95	76:24	<63	76
	11	*tert*-Butyl	98	75:25	72	n/d
	12	Ethyl	89	-	68	
	13	*tert*-Butyl	80	-	n/d	

[a] n/d = not determined

The relatively inconspicuous performance of the **L**^{1}–**L**^{6} system can be attributed to a combination of the equilibrium presence of 'uncomplexed' metal ions and the absence of ligand acceleration in the catalytic reaction. Our future contribution to the design of catalysts for the cyclopropanation of alkenes, which give both high enantio- and diastereocontrol, will thus focus on systems with more stable chiral ligand–metal binding.

4. Experimental

4.1. General experimental methods

Catalytic procedures were carried out under an argon atmosphere using a dual manifold vacuum/argon line and standard Schlenk techniques. Dichloromethane was dried by refluxing for 3 days over calcium hydride under nitrogen. All glassware, cannulae and Celite were stored in an oven (>100°C) and flame dried immediately prior to use. Deuterated chloroform was dried in the bottle over 4 Å molecular sieves.

NMR spectra were recorded on Bruker ACF-250, DPX-300, DPX-400 and ACP-400 spectrometers and the spectra were referenced internally using residual protio solvent resonances relative to tetramethylsilane ($\delta = 0$ ppm). EI/CI and FAB mass spectra were measured on a Micromass Autospec mass spectrometer. IR spectra were obtained either as Nujol mulls or by evaporation of dichloromethane solutions onto IR plates, using a Perkin–Elmer FTIR spectrometer. Chiral GC–MS experiments were carried out on a GC-17A Shimadzu QP-5000 analyser using a Chrompak CP-Chirasil-Dex CB column (25 m×0.25 mm, 0.25 μm i.d.). The conditions were as follows: injection temp. 250°C, interface temp. 250°C, column pressure 50 kPa, column flow 1.2 mL/min, linear velocity 36.8 mL/min, split ratio 45, total flow 57 mL/min. Column chromatography was performed using a selection of column widths and Merck silica gel 60. Thin-layer chromatography was performed using Merck 0.25 mm silica layer foil-backed plates.

The ligands **L**^{1}–**L**^{6} were synthesised as previously reported.[19]

4.2. General cyclopropanation procedure

A round-bottomed flask, incorporating a side-arm with a PTFE stopcock, was charged with $(CuOTf)_2C_6H_6$ (0.5 mol%) and the required ligand (1.1 mol%) under an atmosphere of argon. The solids were dissolved in dichloromethane (6 mL) with stirring. Alkene (4 equiv.) was added to the flask. A syringe was charged with a solution of the diazoacetate (1 equiv.) in dichloromethane (4 mL). The contents of the syringe were added to the reaction mixture over 1 h using a

syringe pump. The reaction mixture was stirred for an additional 15 min, filtered through a silica plug, washed with dichloromethane (2×15 mL) and concentrated. The excess alkene was either removed in vacuo or by column chromatography (hexane/ethyl acetate). The product was identified by comparison of the NMR spectra with those reported in the literature; *cis*/*trans* ratios were calculated from NMR and from GC–MS, and e.e.s were calculated from chiral GC–MS as described.

4.3. Data for cyclopropane products

4.3.1. Ethyl 2-phenylcyclopropane-1-carboxylate.[3b] Obtained as a colourless oil from the reaction of styrene with EDA. Yield: 94%. ^{1}H NMR ($CDCl_3$) *trans* isomer: δ 7.08–7.31 (m, 5H, Ar-H), 4.17 (q, $J=7$, 2H, CH_2CH_3), 2.46–2.55 (m, 1H, **H**-C1), 1.86–1.93 (m, 1H, **H**-C2), 1.54–1.62 (m, 1H, **H**-C3), 1.28 (t, $J=7$, 4H, CH_2CH_3/**H**-C3); ^{1}H NMR ($CDCl_3$) *cis* isomer: δ 7.08–7.31 (m, 5H, Ph), 3.87 (q, $J=7.2$, 1H, CH_3CH_2), 2.46–2.55 (m, 1H, **H**-C1), 2.03–2.11 (m, 1H, **H**-C2), 1.68–1.75 (m, 1H, **H**-C3), 1.54–1.62 (m, 1H, **H**-C3), 0.97 (t, $J=7.2$, 1H, CH_2CH_3). IR (thin film) ν cm^{-1}: 3063, 3030, 2982, 2936, 2906, 2873, 1725, 1605, 1498, 1460, 1439, 1408, 1386, 1366, 1337, 1325, 1306, 1266, 1221, 1186, 1078, 1042, 1018, 936, 850, 755, 723, 698. MS (EI$^+$) m/z: 190 (M^+), 162 ($PhCH(CH_2)CHCO_2^+$), 145 ($PhCH(CH_2)CHCO^+$), 117 ($PhCH(CH_2)CH^+$). Chiral GC–MS (80°C, 4°C/min): t_{Rcis} 18.0 (minor), 18.3 (major) min; t_{Rtrans} 18.9 (major), 19.1 (minor) min.

4.3.2. *tert*-Butyl 2-phenylcyclopropane-1-carboxylate.[26] Obtained as a colourless oil from the reaction of styrene with ^{t}BDA. Yield: 81%. ^{1}H NMR ($CDCl_3$) *trans* isomer: δ 7.28–7.07 (m, 5.0H, Ph), 2.40–2.45 (m, 1H, **H**-C1), 1.80–1.85 (m, 1H, **H**-C2), 1.49–1.54 (m, 1H, **H**-C3), 1.46 (s, 9H, $C(CH_3)_3$), 1.19–1.25 (m, 1H, **H**-C3); ^{1}H NMR ($CDCl_3$) *cis* isomer: δ 7.28–7.07 (m, 5H, Ph), 2.49–2.55 (m, 1H, **H**-C1), 1.94–2.00 (m, 1H, **H**-C2), 1.61–1.66 (m, 1H, **H**-C3), 1.26–1.31 (m, 0.27H, **H**-C3), 1.13 (s, 9H, $C(CH_3)_3$). IR (thin film) ν cm^{-1}: 3005, 2978, 2933, 1721 (s), 1606, 1498, 1457, 1438, 1402, 1367, 1342, 1327, 1287, 1256, 1231, 1208, 1152 (s), 1077, 1031, 969, 937, 844, 782, 757, 744, 723, 697.

2-Phenylcyclopropanecarboxylic acid *tert*-butyl ester was hydrolysed by TFA/C_6H_6 to give the free acid, which was then analysed by chiral GC–MS. Chiral GC–MS (80°C, 4°C/min): t_{Rtrans} 26.40 (major), 26.74 (minor) min; t_{Rcis} 27.48 (major), 28.10 (minor) min.

4.3.3. Ethyl 2-methyl-2-phenylcyclopropane-1-carboxylate.[10a] Obtained as a colourless oil from the reaction of α-methylstyrene with EDA. Yield: 99%. ^{1}H NMR ($CDCl_3$) *trans* isomer: δ 7.36–7.20 (m, 5H, Ph), 4.19 (qd, $J=2$, 7, 2H, CH_2CH_3), 1.88–1.99 (m, 1H, **H**-C1), 1.75–1.79 (m, 1H, **H**-C3), 1.52 (s, 3H, CCH_3), 1.39–1.45 (m, 1H, **H**-C3), 1.30 (t, $J=7$, 3H, CH_2CH_3); ^{1}H NMR ($CDCl_3$) *cis* isomer: δ 7.36–7.20 (m, 5H, Ph), 3.83 (qd, $J=4$, 8, 2H, CH_2CH_3), 1.88–1.99 (m, 1H, **H**-C1), 1.75–1.79 (m, 1H, **H**-C3), 1.46 (s, 3H, CCH_3), 1.12–1.16 (m, 1H, **H**-C3), 0.94 (t, $J=8$, 3H, CH_2CH_3); IR (CH_2Cl_2) ν cm^{-1}: 3058, 3025, 2979, 2929, 2904, 1725, 1602, 1496, 1445, 1400, 1382, 1296, 1267, 1238, 1178, 1117, 1086, 1067, 1023, 968, 900, 849, 763, 737. Chiral GC–MS (80°C, 4°/min): t_{Rcis} 16.48 (minor), 16.74 (major) min; t_{Rtrans} 17.78 (major), 17.96 (minor) min.

4.3.4. *tert*-Butyl 2-methyl-2-phenylcyclopropane-1-carboxylate. Obtained as a colourless oil from the reaction of α-methylstyrene with ^{t}BDA. Yield: 84%. ^{1}H NMR ($CDCl_3$) *trans* isomer: δ 7.31–7.18 (m, 5H, Ph), 1.90 (m, 1H, **H**-C1), 1.49 (s, 9H, $C(CH_3)_3$), 1.35 (m, 2H, H_2-C3), 1.13 (s, 3H, CCH_3); ^{1}H NMR ($CDCl_3$) *cis* isomer: δ 7.31–7.18 (m, 5H, Ph), 1.80 (m, 1H, **H**-C1), 1.70 (m, 1H, **H**-C3), 1.51 (s, 9H, $C(CH_3)_3$), 1.44 (s, 3H, CCH_3), 1.07 (m, 1H, **H**-C3); IR (thin film) ν cm^{-1}: 3059, 3004, 2978, 2929, 1721 (s), 1602, 1497, 1478, 1446, 1391, 1367, 1295, 1245, 1208, 1151 (s), 1118, 1086, 1068, 1029, 847, 763, 739, 700. Chiral GC–MS (80°C, 4°C/min): t_{Rcis} 17.95 (minor), 18.13 (major) min; t_{Rtrans} 19.62 min.

4.3.5. Ethyl 2-methyl-3-phenylcyclopropane-1-carboxylate.[27] A colourless oil obtained from the reaction of β-methylstyrene with EDA. Yield: 63%. ^{1}H NMR ($CDCl_3$) *trans* isomer: δ 7.35–7.06 (m, 5H, Ph), 4.16 (q, 2H, $J=7$, CH_2CH_3), 2.69–1.64 (m, 3H, **H**-C1/**H**-C2/**H**-C3), 1.35 (d, 3H, $J=8$, CH-CH_3), 1.28 (t, 3H, $J=7$, CH_2CH_3); ^{1}H NMR ($CDCl_3$) *cis* isomer: δ 7.35–7.06 (m, 5H, Ph), 3.87 (q, 1H, $J=7$, CH_2CH_3), 2.69–1.64 (m, 3H, **H**-C1/**H**-C2/**H**-C3), 1.32 (d, 3H, $J=8$, CH-CH_3), (t, 3H, $J=8$, CH_2CH_3); IR (thin film) ν cm^{-1}: 3060, 3025, 2959, 2931, 2872, 1726 (s), 1603, 1496, 1443, 1371, 1349, 1266, 1179 (s), 1135, 1101, 1050, 1034, 963, 850, 736 (s), 696 (s), 588, 520, 499. Chiral GC–MS (80–120°C, 0.5°C/min, 120–200°C, 10°C/min): t_{Rcis} 61.85 (minor), 62.84 (major) min; t_{Rtrans} 73.10 (minor), 73.62 (major) min.

4.3.6. *tert*-Butyl 2-methyl-3-phenylcyclopropane-1-carboxylate. Obtained as a colourless oil from the reaction of β-methylstyrene with ^{t}BDA. Yield: 96%. ^{1}H NMR ($CDCl_3$) *trans* isomer: δ 7.26–7.05 (m, 5H, Ph), 2.35–1.47 (m, 3H, **H**-C1/**H**-C2/**H**-C3), 1.47 (s, 9H, $C(CH_3)_3$), 1.32 (d, 3H, $J=8$, CH-CH_3); ^{1}H NMR ($CDCl_3$) *cis* isomer: δ 7.26–7.05 (m, 5H, Ph), 2.35–1.47 (m, 3H, **H**-C1/**H**-C2/**H**-C3), 1.24 (d, 3H, $J=8$, CH-CH_3), 1.14 (s, 9H, $C(CH_3)_3$); IR (thin film) ν cm^{-1}: 3062, 3027, 3005, 2977, 2931, 2872, 1720 (s), 1605, 1497, 1457, 1437, 1391, 1366, 1290, 1256, 1209, 1154 (s), 1102, 1078, 1045, 963, 845, 738, 697. Chiral GC–MS (80°C, 4°C/min): t_{Rcis} 18.99 (minor), 20.81 (major) min; t_{Rtrans} 19.14 (minor), 21.35 (major) min.

4.3.7. Ethyl 2,2-diphenylcyclopropane-1-carboxylate.[5] Obtained as a colourless oil from the reaction of 1,1′-diphenylethylene with EDA. Yield: 89%. ^{1}H NMR ($CDCl_3$): δ 7.35–7.13 (m 10H, Ph), 3.83–3.99 (m, 2H, CH_2CH_3), 2.55 (dd, $J=6$, 8, 1H, **H**-C1), 2.17 (dd, $J=5$, 6, 1H, **H**-C3), 1.59 (dd, $J=5$, 8, 1H, **H**-C3), 1.00 (t, $J=8$, 3H, CH_2CH_3); IR (CH_2Cl_2) ν cm^{-1}: 3058, 3025, 2980, 2251, 1729, 1660, 1600, 1494, 1446, 1397, 1381, 1268, 1180, 1096, 1026, 748, 732, 702. Chiral HPLC analysis (hexane, 0.5 mL/min): $t_R=21.1$, (major), 23.2 (minor).

4.3.8. *tert*-Butyl 2,2-diphenylcyclopropane-1-carboxylate.[5] Obtained as a colourless oil from the reaction of 1,1′-diphenylethylene with ᵗBDA. Yield: 80%. ^{1}H NMR ($CDCl_3$): δ 7.29–7.04 (m, 10H, Ph), 2.38–2.34 (m, 1H, **H**-C1), 2.02–1.99 (m 1H, **H**-C3), 1.42–1.36 (m, 1H, **H**-C3), 1.11 (s, 9H, C($C\mathbf{H}_3$)$_3$); IR (thin film) ν cm^{-1}: 3082, 3058, 3026, 3003, 2975 (s), 2930, 1725 (s), 1660, 1600, 1494, 1446, 1389, 1366, 1291, 1256, 1206, 1150 (s), 1095, 972, 910, 846, 745, 701 (s), 594, 548; MS (EI$^+$) m/z: 238 ([M−ᵗBu]$^+$), 221 ([M−OᵗBu]$^+$), 193 ([M−CO_2ᵗBu]$^+$); MS (CI$^+$) m/z: 256 ([M−ᵗBuNH$_4$]$^+$).

4.3.9. Ethyl 2,2-dimethyl-3-(2-methylpropenyl)cyclopropane-1-carboxylate.[28] Obtained as a colourless oil from the reaction of 3,5-dimethyl-2,4-hexadiene with EDA. Yield: 95%. ^{1}H NMR ($CDCl_3$) *trans* isomer: δ 4.89 (m, 1H, C=C**H**), 4.11 (m, 2H, C$\mathbf{H}_2$CH$_3$), 2.05 (m, 1H, **H**-C2), 1.71 (s, 6H, ($C\mathbf{H}_3$)$_2$C=CH), 1.37 (d, 1H, $J=5$, **H**-C1), 1.26 (m, 6H, C($C\mathbf{H}_3$)$_2$/CH$_2$C$\mathbf{H}_3$), 1.13 (s, 3H, C($C\mathbf{H}_3$)); ^{1}H NMR ($CDCl_3$) *cis* isomer: δ 5.39 (m, 1H, C=C**H**), 4.11 (m, 2H, C$\mathbf{H}_2$CH$_3$), 1.87 (m, 1H, **H**-C2), 1.68 (s, 6H, ($C\mathbf{H}_3$)$_2$C=CH$_{cis}$), 1.63 (d, 1H, $J=9$, **H**-C1), 1.24 (m, 6H, C($C\mathbf{H}_3$)$_2$/CH$_2$C$\mathbf{H}_3$), 1.19 (s, 3H, C($C\mathbf{H}_3$)); IR (thin film) ν cm^{-1}: 2975 (s), 2925 (s), 2872 (s), 2735, 1724 (s), 1446, 1417, 1377, 1351, 1318, 1282, 1234, 1194 (s), 1161 (s), 1115, 1064, 1031, 964, 910, 851, 779, 738. Chiral GC–MS (80°C, 0.5°C/min): t_{Rcis} 23.06 (minor), 23.20 (major) min; t_{Rtrans} 23.71 (minor), 23.81 (major) min.

4.3.10. *tert*-Butyl-2,2-dimethyl-3-(2-methylpropenyl)-cyclopropane-1-carboxylate. A colourless oil obtained from the reaction of 3,5-dimethyl-2,4-hexadiene with ᵗBDA. Yield: 80%. ^{1}H NMR ($CDCl_3$) *trans* isomer: δ 4.87 (m, 1H, $J=8$, C=C**H**), 1.96 (m, 1H, **H**-C2), 1.71 (s, 6H, ($C\mathbf{H}_3$)$_2$C=CH), 1.45 (s, 9H, C($C\mathbf{H}_3$)$_3$), 1.31 (d, 1H, $J=3$, **H**-C1), 1.24 (s, 3H, C($C\mathbf{H}_3$)$_2$), 1.11 (s, 3H, C($C\mathbf{H}_3$)$_2$); ^{1}H NMR ($CDCl_3$) *cis* isomer: δ 5.35 (d, 1H, $J=10$, C=C**H**), 1.99–1.11 (m, H, CH, Me), 1.68 (s, 6H, ($C\mathbf{H}_3$)$_2$C=CH), 1.43 (s, 9H, C($C\mathbf{H}_3$)$_3$), 1.22 (s, 3H, C($C\mathbf{H}_3$)$_2$), 1.17 (s, 3H, C($C\mathbf{H}_3$)$_2$), **H**-C-(1) and **H**-C-(2) not resolved; IR (thin film) ν cm^{-1}: 2977, 2928, 1720 (s), 1455, 1417, 1378, 1366, 1320, 1285, 1237, 1208, 1151 (s), 1115, 1080, 848. The ester was then hydrolysed by NaOH/MeOH to give the free acid and then analysed by chiral GC–MS. The free acid was identical to that derived from ethyl ester and corresponded to literature values.[29] Chiral GC–MS (90°C, 2°C/min): t_{Rcis} 24.18 (major), 25.89 (minor) min; t_{Rtrans} 24.39 (major), 25.37 (minor) min.

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