

Reductive metalation of 1,2-diaryl-substituted ethenes: synthetic applications

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Abstract—Reduction of 1,2-diaryl-substituted ethenes with Na metal in dry THF allowed easy access to a variety of 1,2-diaryl-1,2-disodiummethanes. These diorganometallic intermediates were elaborated into the corresponding 1,2-diarylethanes (aqueous work up), or cycloalkylated with 1,3-dichloropropanes. The last reaction led to a highly diastereoselective synthesis of *trans*-1,2-diaryl-substituted cyclopentanes.

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1. Introduction

Reduction of stilbene with alkali metals in aprotic solvents is a well known reaction, allowing easy access to the corresponding dianions.¹ Despite the relatively high stabilities of the resulting diorganometals, this reaction was investigated mainly from a mechanistic point of view.^{2–5} Indeed, reaction of these intermediates with alkyl halides, phosphonates and sulfates, is of limited synthetic usefulness, due to the formation of diastereoisomeric mixtures of alkylated products,^{2–5} whilst reaction with carbonyl compounds, under Barbier-type conditions, afforded 1,2-diphenylethane.⁶

At odds with these results, the reaction of 1,2-disodium-1,2-diphenylethane (1,2-disodiumstilbene) with 1,3-dichloropropane or 1,4-dichlorobutane in 1,2-dimethoxyethane (DME), afforded good yields of the corresponding *trans*-1,2-diphenyl cyclopentane or -cyclohexane, respectively, with very high diastereoselectivity.³ Surprisingly, the latter reaction was not synthetically exploited, despite the potential usefulness of *trans*-1,2-diaryl-substituted cyclopentanes as *C*₂-symmetric ligands, for employment in catalysis.^{7–11}

Furthermore, it is worth noting that only few reports concern the reductive metalation of functionalized stilbenes.^{12,13}

Following on from our interest in the application of

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reductive metalation reactions to the regioselective preparation of substituted aromatic derivatives, we have previously reported that reduction of several 3,4,5-trimethoxystilbenes, with Na metal in THF, results in regioselective cleavage of the methoxy group at the 4-position and, depending upon reaction conditions, to reduction of the olefinic bond.^{14,15}

As a further useful application to this approach, we investigated the reductive metalation of several 1,2-diarylethenes in THF, currently the most commonly used solvent for this kind of reaction,^{16,17} with the purpose to apply this procedure to a general synthesis of *trans*-1,2-diarylcyclopentanes.

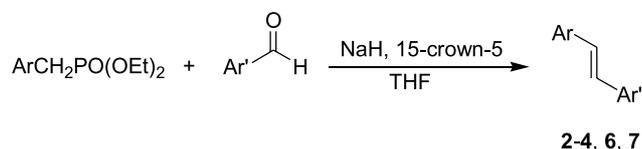
2. Results and discussion

2.1. Synthesis of starting materials

Compounds (*E*)-**1** and (*Z*)-**1**, as well as (*E*)-**5**, are commercially available. Other starting materials were synthesized according to reported procedures,^{18,19} by the deprotonation of either diethyl benzylphosphonate, or diethyl 2-methoxybenzylphosphonate, with NaH in THF, in the presence of the appropriate aldehyde and a catalytic amount of 15-crown-5. The corresponding (*E*)-stilbenes **2–4**, **6** and **7** were recovered in good to satisfactory yields (Scheme 1).

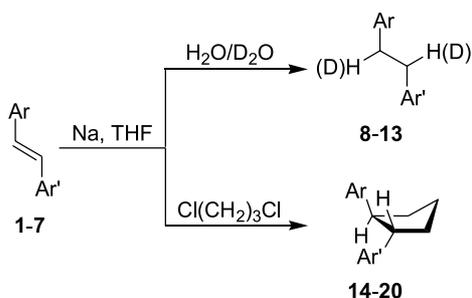
2.2. Reductive metalation reactions

Reductive metalations of stilbenes **1–7** were run in the



Scheme 1. Synthesis of 1,2-diarylethenes: **2**: Ar=Ph, Ar'=1-naphthyl, 85%; **3**: Ar=Ph, Ar'=4-pyridyl, 57%; **4**: Ar=Ph, Ar'=2-pyridyl, 61%; **6**: Ar=Ar'=2-(CH₃O)C₆H₄, 92%; **7**: Ar=Ph, Ar'=3,4,5-(CH₃O)₃C₆H₂, 90%.

presence of an excess of the freshly cut metal, in dry THF, under argon gas. Reaction mixtures were quenched either with H₂O, or with D₂O to provide evidence for the intermediate formation of dicarbanions. Cl(CH₂)₃Cl quenching was performed by adding 2 equiv of the electrophile to the reduction mixtures at –80 °C, and stirring the resulting mixtures for 12 h whilst allowing it to reach 0 °C, before aqueous work up (**Scheme 2**).



Scheme 2. Reductive metalation of stilbenes: **1, 8, 14**: Ar=Ar'=Ph; **2, 9, 15**: Ar=Ph, Ar'=1-naphthyl, **3, 10, 16**: Ar=Ph, Ar'=4-C₅H₄N; **4, 11, 17**: Ar=Ph, Ar'=2-C₅H₄N; **5, 12, 18**: Ar=Ar'=2-C₅H₄N; **6, 13, 19**: Ar=Ar'=2-(CH₃O)C₆H₄; **7**: Ar=C₆H₅, Ar'=3,4,5-(CH₃O)₃C₆H₂; **20**: Ar=Ph, Ar'=3,5-(CH₃O)₂C₆H₃.

We initially investigated the reduction of (*E*)- and (*Z*)-stilbene **1** under the above reaction conditions.²⁰ Indeed, literature data do not agree on the relative reactivities of diastereoisomeric stilbenes towards alkali metals.^{1,2} It was also necessary to check the stereochemical outcome of the reaction of the resulting diorganometals with Cl(CH₂)₃Cl in THF; several authors reported a solvent effect on the diastereoselectivities of several alkylation reactions of these intermediates.^{2,3} Selected results are reported in **Table 1**.

Reduction of (*E*)-**1** with 3 equiv of Na metal during 5 h, followed by aqueous work up, afforded bibenzyl, **8**, as the only detectable reaction product (**Table 1**, entry 1).

Table 1. Reductive metalation of (*E*)-**1** and (*Z*)-**1**^a

Entry	Substrate	Metal	<i>t</i> (h)	Quencher	Product	Yield (%) ^b
1	(<i>E</i>)- 1	Na	5	H ₂ O	8 (H)	>95
2	(<i>E</i>)- 1	Na	5	D ₂ O	8-d₂ (D)	>95
3	(<i>E</i>)- 1	Na	5	Cl(CH ₂) ₃ Cl	14	72 ^c
4	(<i>E</i>)- 1	Li	5	H ₂ O	8 (H)	>95
5	(<i>E</i>)- 1	Li	5	D ₂ O	8-d₂ (D)	>95
6	(<i>E</i>)- 1	Li	5	Cl(CH ₂) ₃ Cl	14	76 ^c
7	(<i>Z</i>)- 1	Na	7	H ₂ O	8 (H)	>95
8	(<i>Z</i>)- 1	Na	1	H ₂ O	8 (H)	41 ^d

^a All reductions were run at rt in the presence of 3 equiv of the metal.

^b Yields calculated by ¹H NMR spectroscopy, unless otherwise indicated.

^c Yields calculated on isolated products.

^d (*E*)-**1** (59%) was also recovered.

Intermediate, quantitative formation of 1,2-diphenyl-1,2-disodiummethane resulted by quenching the reduction mixture with D₂O (**Table 1**, entry 2). Under these conditions, quenching the reduction mixture with Cl(CH₂)₃Cl, at –80 °C, allowed the recovery of 1,2-diphenylcyclopentane, **14**, as a single diastereoisomer, in 72% yield (**Table 1**, entry 3). According to the literature, we assigned a relative trans-configuration to cyclopentane **14**.²¹

The same results were obtained using Li in reductive metalations of (*E*)-**1** quenched with H₂O or D₂O (**Table 1**, entries 4 and 5), whilst quenching the reduction mixture with Cl(CH₂)₃Cl led to recover cyclopentane **14** with a slightly improved yield (**Table 1**, entry 6).

Reduction of (*Z*)-**1** with Na metal, followed by aqueous work up, led to the recovery of 1,2-diphenylethane, although, a relatively longer reaction time (7 h) was required (**Table 1**, entry 7). Furthermore, a similar reaction, quenched after 1 h reaction time, led to recover bibenzyl **8** and (*E*)-stilbene **1** in 41 and 59% yield, respectively (**Table 1**, entry 8), thus, confirming fast isomerization of the starting material, in agreement with original observations of Schlenk and Bergmann.^{1,2}

We next, extended our investigation to the reductive metalation of differently substituted 1,2-diarylethenes **2–7**, to check the applicability of this reaction to the synthesis of an eclectic array of trans-1,2-diarylcyclopentanes. Attention was focused on the employment of Na metal as a reducing agent as it is, by far, the most economical of the alkali metals. The results are reported in **Table 2** (**Scheme 2**).

Reduction of naphthyl derivative **2** with an excess of Na metal in THF at 25 °C, afforded a complex reaction mixture (not reported in **Table 2**). A much better result was obtained performing this reduction at –20 °C, in the presence of 6 equiv of the metal: under these conditions, aqueous work up afforded 1-(1-naphthyl)-2-phenylethane, **9**, in almost quantitative yield, via quantitative intermediate formation of the corresponding dianion (**Table 2**, entries 1 and 2).

Quenching with Cl(CH₂)₃Cl afforded a single diastereoisomer of the corresponding 1-(1-naphthyl)-2-phenylcyclopentane, **15**, in good yield (**Table 2**, entry 3).

Reductive metalation of pyridyl-substituted derivatives **3–5** were run at 0 °C, in the presence of variable amounts

Table 2. Reductive metalation of 1,2-diarylethenes **2–7**

Entry	Substrate	Na (equiv)	T (°C)	t (h)	Quencher	Product	Yield (%) ^a
1	2	6	−20	7	H ₂ O	9 (H)	81
2	2	6	−20	7	D ₂ O	9-<i>d</i>₂ (D)	>95 ^b
3	2	6	−20	7	Cl(CH ₂) ₃ Cl	15	87
4	3	6	0	12	H ₂ O	10 (H)	73
5	3	6	0	12	D ₂ O	10-<i>d</i>₂ (D)	88 ^b
6	3	6	0	12	Cl(CH ₂) ₃ Cl	16	64
7	4	8	0	12	H ₂ O	11 (H)	78
8	4	8	0	12	D ₂ O	11-<i>d</i>₂ (D)	82 ^b
9	4	8	0	12	Cl(CH ₂) ₃ Cl	17	81
10	5	8	0	12	H ₂ O	12 (H)	83
11	5	8	0	12	D ₂ O	12-<i>d</i>₂ (D)	90 ^b
12	5	8	0	12	Cl(CH ₂) ₃ Cl	18	78
13	6	3	0	7	H ₂ O	13 (H)	70
14	6	3	0	7	D ₂ O	13-<i>d</i>₂ (D)	80 ^b
15	6	3	0	7	Cl(CH ₂) ₃ Cl	19	62
16	7	6	20	7	Cl(CH ₂) ₃ Cl	20	59

^a Yields calculated on isolated products, unless otherwise indicated.

^b Yields calculated by ¹H NMR spectroscopy.

(6–8 equiv) of Na metal. Under these conditions, the corresponding heteroaryl-substituted ethanes, **10–12**, were recovered, and intermediate formations of 1,2-disodium derivatives was evidenced by quenching the reduction mixtures with D₂O (Table 2, entries 4 and 5, 7 and 8, 10 and 11).

Cycloalkylation reactions, performed as described above, afforded the desired pyridyl-substituted cyclopentanes, **16–18**, as single diastereoisomers, in good to satisfactory yields (Table 1, entries 6, 9 and 12).

Good results were obtained in the reduction of dimethoxy-substituted stilbene **6** with 3 equiv of Na metal at 0 °C during 7 h. Under these conditions, aqueous work up afforded the dihydrostilbene **13** in good yield, with no evidence of cleavage of carbon–oxygen bonds¹⁴ (Table 2, entry 13). Intermediate formation of a diorganometallic derivative was evidenced, as quenching the reduction mixture with D₂O (Table 2, entry 14), whilst cycloalkylation afforded 1,2-di-(2-methoxy-phenyl)cyclopentane, **19**, as a single diastereoisomer, in 62% yield (Table 2, entry 15). The relative trans-configuration of this compound was confirmed by a comparison of its ¹H and ¹³C NMR spectra with literature data.⁸

Reductive metalation of 3,4,5-trimethoxystilbene, **7**, was performed under previously optimized reaction conditions (6 equiv of Na metal, 20 °C, 7 h);¹⁴ quenching with Cl(CH₂)₃Cl afforded, after aqueous work up and flash chromatography, 1-(3,5-dimethoxyphenyl)-2-phenylcyclopentane, **20**, as a single diastereoisomer, in 59% yield (Table 1, entry 16).

To extend the scope of this reductive cycloalkylation, as well as to confirm the trans stereochemistry of this reaction, we investigated the reactivity of symmetrically-substituted 1,2-disodium intermediates towards a functionalized 1,3-dichloropropane, namely 1,3-dichloro-2-ethoxy-methoxypropane.²²

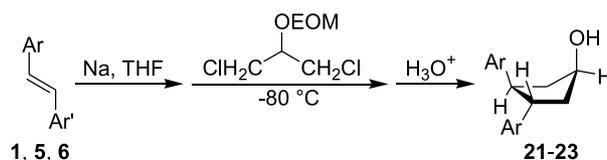
Reductive metalations were performed as described above, and reduction mixtures were chilled to −80 °C and

quenched with 2 equiv of the electrophile, as described above. Aqueous work up, followed by acidic hydrolyses, afforded the corresponding 3,4-diaryl-1-cyclopentanol (Table 3, Scheme 3).

Table 3. Synthesis of *trans*-3,4-diaryl-1-hydroxycyclopentanes

Entry	Substrate [Ar=]	Product	Yield (%) ^a
1	1 [Ph]	21	60
2	5 [2-C ₅ H ₄ N]	22	35
3	6 [2-(CH ₃ O)C ₆ H ₄]	23	32

^a Yields calculated on isolated products.



Scheme 3. Synthesis of *trans*-3,4-diaryl-1-hydroxycyclopentanes: **1**, **21**: Ar=Ph; **5**, **22**: Ar=2-C₅H₄N; **6**, **23**: Ar=2-(CH₃O)C₆H₄; EOM=CH₂OCH₂CH₃.

Results obtained with stilbenes **1**, **5** and **6** are reported in Table 3: cyclopentanol **21–23** were recovered in 60, 35 and 32% isolated yield, respectively, as single diastereoisomers (Table 3, entries 1–3). Besides showing the possibility to synthesize *vic*-diarylcyclopentanes functionalized on the alicyclic moiety, these results support the relative trans orientation of aryl substituents at C3 and C4; indeed, a relative cis orientation of these substituents would result in the presence of a stereocenter at C1, with formation of a couple of diastereoisomers.

3. Conclusions

The reported synthetic procedure allows for the generation of several 1,2-disodium-1,2-diarylethenes, bearing an array of different aromatic rings. Interestingly, this procedure was successfully applied to ethenes substituted either with electron-rich or with electron-poor aromatic rings. In both cases, the corresponding diorganometal derivatives were generated under particularly mild reaction conditions.

Reaction of intermediate diorganometals with 1,3-dichloropropanes allowed a simple and highly diastereoselective approach to the synthesis of several trans-1,2-diaryl-substituted cyclopentanes. The employment of some of these derivatives (possessing C_2 -symmetry and/or suitable functional groups) as ligands for transition metals, is under investigation in our laboratories.²³

4. Experimental

4.1. General

Boiling and melting points are uncorrected; the air bath temperature on bulb-to-bulb distillation are given as boiling points. Starting materials were of the highest commercial quality and were purified by distillation immediately prior to use. Na metal (stick) was 99% purity, and Li metal (wire, diameter 3.2 mm) was 99.9% purity. D_2O was 99.8% isotopic purity. THF was distilled from Na/K alloy under N_2 immediately prior to use. 1H NMR spectra were recorded at 300 MHz and ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$ with $SiMe_4$ as internal standard. Deuterium incorporation was calculated by monitoring the 1H NMR spectra of crude reaction mixtures, and by comparing the integration of the signal corresponding to protons in the arylmethyl position with that of known signals. Flash chromatography were performed on Merck silica gel 60 (40–63 μm), and TLC analyses on Macherey-Nagel silica gel pre-coated plastic sheets (0.20 mm). Elemental analyses were performed by the microanalytical laboratory of the Dipartimento di Chimica, Università di Sassari.

4.2. Starting materials

Compounds **1** and **5** are commercially available. Compounds **2**,²⁴ **3**,²⁵ **4**,²⁶ and **7**¹⁴ were synthesized according to a general procedure,¹⁶ by the reaction of commercially available diethyl benzylphosphonate with the appropriate arylaldehyde in the presence of 15-crown-5 in dry THF, and characterized according to the literature. Compound **6**²⁷ was similarly obtained by the reaction of diethyl 2-methoxybenzylphosphonate²⁸ with 2-methoxybenzaldehyde. Isolated yields are reported in Scheme 1.

4.3. Reductive metalation of 1,2-diarylethenes 1–8, and reaction with electrophiles. General procedure

Two to three pieces of freshly cut metal (3–9 equiv) were placed under Ar in a 50 mL two-necked flask equipped with reflux condenser and magnetic stirrer, and suspended in THF (10 mL) at the reported temperature (Tables). The appropriate 1,2-diarylethene (5 mmol), dissolved in dry THF (2 mL), was added dropwise, and each metal piece was cut into 2–3 smaller pieces with a spatula, and the mixture was vigorously stirred for the reported time at the reported temperature (Tables).

Aqueous work-up was performed by slow dropwise addition of 10 mL of H_2O (caution!) the cold bath removed, and the resulting mixture extracted with Et_2O (3×10 mL). The

organic phase was washed with brine (10 mL), dried (K_2CO_3) and the solvent evaporated.

D_2O quenching was performed by slow dropwise addition of 0.75 mL of the electrophile dissolved in dry THF (2 mL), followed by aqueous work-up as described above.

Quenching with $Cl(CH_2)_3Cl$ was performed by adding the appropriate electrophile (2 equiv) to the reduction mixture chilled to $-80^\circ C$. The reaction mixture was allowed to warm to $0^\circ C$ during 12 h, before aqueous work-up as described above.

Quenching with 1,3-dichloro-2-ethoxymethoxypropane was performed by adding the appropriate electrophile (2 equiv) to the reduction mixture chilled to $-80^\circ C$. The reaction mixture was allowed to warm to $0^\circ C$ during 12 h, before aqueous work-up as described above. Crude products were added under Ar to a stirred 0.6 M solution of HCl in MeOH [obtained by adding AcCl (0.5 mL) to MeOH (10 mL)] chilled to $0^\circ C$. The mixture was stirred at rt for 3 h, until complete disappearance of starting material, as determined by TLC. The mixture was diluted with H_2O (10 mL), and the MeOH evaporated under reduced pressure. The resulting mixture was basified (1N NaOH), extracted with Et_2O (4×10 mL), and the organic phase dried (K_2CO_3) and evaporated.

1,2-Diphenylethane, **8**, was purified by flash chromatography (petroleum ether), and characterized by comparison with a commercial sample. Compounds **9**,²⁹ **10**,³⁰ **11**,³¹ **12**,³² **13**,³³ **14**,²¹ and **19**⁸ were purified by flash chromatography (petroleum ether/AcOEt or petroleum ether/AcOEt/ Et_3N), and characterized by comparison with literature data. Deuterated compounds were characterised by 1H and ^{13}C NMR spectroscopy: the resonances of arylmethyl CHD protons appear as unresolved broad triplets shifted 0.02–0.05 ppm (δ) upfield relatively to the corresponding CH_2 protons; the resonances of arylmethyl CHD carbons appear as triplets ($J=18$ –21 Hz) shifted 0.3–0.5 ppm (δ) upfield relatively to the corresponding CH_2 carbons.

Other products were purified and characterized as follows.

4.3.1. trans-1-(1-Naphthyl)-2-phenylcyclopentane (15).

Purified by flash chromatography (petroleum ether/AcOEt=9.5:0.5), white solid; mp 74 – $75^\circ C$ (EtOH); $R_f=0.50$ (petroleum ether/AcOEt=9.5:0.5). Anal. Found: C, 92.30; H, 7.56; $C_{21}H_{20}$ requires: C, 92.58; H, 7.42%. 1H NMR: δ 1.71–1.9 (1H, m, CH), 1.91–2.11 (3H, m, CH), 2.30–2.44 (1H, m, CH), 2.44–2.61 (1H, m, CH), 3.46–3.60 (1H, m, CH), 3.98 (1H, q, $J=8.4$ Hz, CH), 6.42–7.11 (1H, m, ArH), 7.11–7.24 (4H, m, $4 \times$ ArH), 7.32–7.50 (4H, m, $4 \times$ ArH), 7.64 (1H, d, $J=8.1$ Hz, ArH), 7.74–7.83 (1H, m, ArH), 7.98–8.06 (1H, m, ArH). ^{13}C NMR: δ 24.3, 35.5, 35.6, 47.8, 51.3, 122.7, 123.7, 125.1, 125.4, 125.6, 125.9, 126.3, 127.4, 128.2, 128.7, 132.4, 133.9, 140.6, 144.3.

4.3.2. trans-1-(4-Pyridyl)-2-phenylcyclopentane (16).

Purified by flash chromatography (petroleum ether/AcOEt=1:4), yellow oil; $R_f=0.53$ (petroleum ether/AcOEt=3:7). Anal. Found: C, 85.76; H, 7.94; N, 6.26 $C_{16}H_{17}N$ requires: C, 86.04; H, 7.69; N, 6.27%. 1H NMR: δ

1.81–2.04 (4H, m, 2×CH₂), 2.19–2.34 (2H, m, CH₂), 2.90–3.15 (2H, m, CH₂), 7.00 (2H, dd, *J*=4.5, 1.8 Hz, 2×ArH), 7.07–7.25 (5H, m, 5×ArH), 8.39 (2H, dd, *J*=4.5, 1.8 Hz, 2×ArH). ¹³C NMR: δ 24.5, 34.4, 35.3, 53.2, 53.8, 122.7, 126.2, 127.2, 128.3, 143.3, 149.5, 153.4.

4.3.3. *trans*-1-(2-Pyridyl)-2-phenylcyclopentane (17).

Purified by flash chromatography (petroleum ether/AcOEt=3:2), white solid; mp 41–43 °C (Et₂O); *R*_f=0.67 (petroleum ether/AcOEt=3:2). Anal. Found: C, 85.81; H, 7.96; N, 6.20 C₁₆H₁₇N requires: C, 86.04; H, 7.69; N, 6.27%. ¹H NMR: δ 1.81–2.19 (4H, m, 2×CH₂), 2.20–2.36 (2H, m, CH₂), 3.18–3.31 (1H, m, CH), 3.32–3.45 (1H, m, CH), 6.91 (1H, dt, *J*=7.8, 0.9 Hz, ArH), 7.03 (1H, ddd, *J*=7.2, 4.8, 0.9 Hz, ArH), 7.07–7.16 (3H, m, 3×ArH), 7.16–7.24 (2H, m, 2×ArH), 7.44 (1H, td, *J*=7.8, 1.8 Hz, ArH), 8.53–8.56 (1H, m, ArH). ¹³C NMR: δ 24.7, 34.0, 35.3, 52.8, 55.9, 121.0, 122.8, 125.8, 127.3, 128.2, 135.9, 144.4, 149.4, 163.6.

4.3.4. *trans*-1,2-Di-(2-pyridyl)cyclopentane (18).

Purified by flash chromatography (petroleum ether/AcOEt/Et₃N=3:7:1), white solid; mp 76–78 °C; *R*_f=0.60 (petroleum ether/AcOEt/Et₃N=3:7:1). Anal. Found: C, 80.11; H, 7.41; N, 12.23 C₁₅H₁₆N₂ requires: C, 80.31; H, 7.20; N, 12.49%. ¹H NMR: δ 1.94–2.19 (4H, m, 2×CH₂), 2.21–2.36 (2H, m, CH₂), 3.52–3.66 (2H, m, CH), 6.97 (2H, dt, *J*=7.8, 0.9 Hz, ArH), 7.02–7.08 (2H, m, ArH), 7.46 (2H, td, *J*=7.8, 2.1 Hz, ArH), 8.54 (2H, dq, *J*=4.8, 0.9 Hz, ArH). ¹³C NMR: δ 24.9, 34.1, 54.4, 121.0, 122.9, 136.0, 149.2, 163.5.

4.3.5. *trans*-1-(3,5-Dimethoxyphenyl)-2-phenylcyclopentane (20).

Purified by flash chromatography (petroleum ether/AcOEt=9:1), colourless oil; *R*_f=0.4 (petroleum ether/AcOEt=9:1). Anal. Found: C, 80.63; H, 8.03; C₁₉H₂₂O₂ requires: C, 80.80; H, 7.87%. ¹H NMR: δ 1.77–1.98 (4H, m, 2×CH₂), 2.18–2.31 (2H, m, CH), 2.96–3.14 (2H, m, CH), 3.69 (6H, s, 2×CH₃), 6.24 (1H, t, *J*=2.1 Hz, ArH), 6.27 (2H, d, *J*=2.1 Hz, 2×ArH), 7.09–7.17 (3H, m, 3×ArH), 7.18–7.26 (2H, m, 2×ArH). ¹³C NMR: δ 24.3, 34.9, 35.2, 53.5, 54.0, 54.9, 97.5, 105.4, 125.8, 127.3, 128.1, 144.4, 146.9, 160.4.

4.3.6. *trans*-3,4-Diphenylcyclopentane-1-ol (21).

Purified by flash chromatography (gradient elution, from petroleum ether/AcOEt=9:1 to petroleum ether/AcOEt=1:1), white solid; mp 70–72 °C (petroleum ether); *R*_f=0.63 (petroleum ether/AcOEt=3:7). IR (neat) 3186 cm⁻¹. Anal. Found: C, 85.38; H, 7.83; C₁₇H₁₈O requires: C, 85.66; H, 7.61%. ¹H NMR: δ 1.65 (1H, br s, OH), 1.85–1.95 (1H, m, CH), 2.09–2.28 (2H, m, 2×CH), 2.70 (1H, ddd, *J*=14.1, 9.0, 6.0 Hz, CH), 3.40–3.66 (1H, dd, *J*=20.1, 9.8 Hz, CH), 3.48 (1H, td, *J*=10.8, 7.8 Hz, CH), 4.58–4.63 (1H, m, CHO), 7.08–7.25 (10H, m, 10×ArH). ¹³C NMR: δ 44.9, 44.9, 51.5, 52.6, 72.1, 126.1, 126.1, 127.3, 127.5, 128.2, 128.2, 143.0, 143.7.

4.3.7. *trans*-3,4-Di-(2-pyridyl)cyclopentane-1-ol (22).

Purified by flash chromatography (gradient elution, from petroleum ether/AcOEt/Et₃N=5:5:1 to petroleum ether/AcOEt/Et₃N=3:2:1), yellow oil; *R*_f=0.24 (petroleum ether/AcOEt/Et₃N=3:2:1). IR (neat) 3300 cm⁻¹. Anal. Found: C, 74.69; H, 6.91; N, 11.45; C₁₅H₁₆N₂O requires: C, 74.96; H, 6.72; N, 11.66%. ¹H NMR: δ 2.02–2.12 (1H, m,

CH), 2.14–2.20 (1H, m, CH), 2.17 (1H, br s, OH), 2.30–2.39 (1H, m, CH), 2.50–2.61 (1H, m, CH), 3.60 (1H, dt, *J*=11.7, 6.9 Hz, CH), 3.79 (1H, dd, *J*=9.6, 6.3, 1.8 Hz, CH), 4.51 (1H, t, *J*=3.6 Hz, CHO), 6.97 (1H, dt, *J*=7.8, 0.9 Hz, ArH), 7.02 (1H, dt, *J*=7.8, 0.9 Hz, ArH), 7.10 (1H, ddd, *J*=5.1, 2.4, 0.9 Hz, ArH), 7.13 (1H, ddd, *J*=5.1, 2.4, 0.9 Hz, ArH), 7.54 (1H, ddd, *J*=7.8, 4.2, 1.8 Hz, ArH), 7.52 (1H, ddd, *J*=7.8, 4.2, 1.8 Hz, ArH), 8.57 (1H, ddd, *J*=5.1, 1.8, 0.9 Hz, ArH), 8.60 (1H, ddd, *J*=5.1, 1.8, 0.9 Hz, ArH). ¹³C NMR: δ 41.7, 46.0, 51.8, 54.7, 74.2, 121.1, 121.3, 122.5, 122.9, 136.2, 136.8, 149.3, 149.6, 163.4, 165.5.

4.3.8. *trans*-3,4-Di-(2-methoxyphenyl)cyclopentane-1-ol (23).

Purified by flash chromatography (petroleum ether/AcOEt=2:3), colourless oil; *R*_f=0.69 (petroleum ether/AcOEt=2:3). IR (neat) 3230 cm⁻¹. Anal. Found: C, 76.21; H, 7.73; C₁₉H₂₂O₃ requires: C, 76.47; H, 7.45%. ¹H NMR: δ 1.75 (1H, dddd, *J*=13.5, 9.6, 4.2, 1.5 Hz, CH), 1.99 (1H, ddd, *J*=13.5, 11.7, 6.6 Hz, CH), 2.05 (1H, br s, OH), 2.24 (1H, ddt, *J*=13.5, 7.2, 1.5 Hz, CH), 2.73 (1H, ddd, *J*=13.5, 9.0, 6.6 Hz, CH), 3.55–3.75 (1H, m, CH), 3.68 (3H, s, OCH₃), 3.77 (3H, s, OCH₃), 4.00–4.10 (1H, m, CH), 4.50–4.56 (1H, m, CHO), 6.74–6.85 (4H, m, 4×ArH), 7.06–7.13 (2H, m, 2×ArH), 7.16–7.22 (2H, m, 2×ArH). ¹³C NMR: δ 41.6, 43.5, 43.5, 55.1, 55.3, 72.3, 110.4, 110.5, 120.3, 120.6, 126.7, 126.7, 127.2, 128.0, 131.5, 131.8, 157.2, 157.6.

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