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Highly enantioselective hydrogenation of α,β-unsaturated phosphonates with iridium–phosphinooxazoline complex: synthesis of a phosphorus analogue of naproxen

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Abstract—A number of pharmaceutically interesting optically active 1-arylethylphosphonates, including a phosphorus analogue of naproxen, has been synthesized with ee 92–95% via asymmetric hydrogenation under mild conditions using [Ir(cod)(phosphine oxazoline)]$^+$ [BAr_F]$^-$ catalysts. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

Phosphonic acid analogues of α-arylpropionic acids (a well-known class of non-steroidal anti-inflammatory and analgesic drugs such as naproxen and ibuprofen) deserve attention since many of these derivatives exhibit interesting biological activity profiles. 1-Arylethylphosphonates were reported to possess negative inotropic and Ca^{2+}-antagonistic activity,[1] as well as cyclooxygenase inhibitor properties.[2] They were successfully used as haptens for reactive immunisation as a strategy for the generation of catalytic antibodies for enantioselective hydrolysis.[3,4] Recently it was shown[5] that some 1-arylethylphosphonic acids reveal antidopaminergic and neuroprotective functions. Therefore, 1-arylethylphosphonates may be considered as a promising class of compounds in the search of new potent antipsychotic drugs.

Synthetic approaches to racemic 1-arylethylphosphonic acids and esters are well elaborated.[6] Since, in general, the biological activity of chiral compounds is highly dependent on the absolute configuration, the preparation of enantiopure 1-arylethylphosphonates is necessary for correct evaluation of their structure–activity relationships. Optically active 1-phenylethylphosphonates have been obtained via enantioselective methylation of benzylphosphonic acid derivatives (phosphonamides or 1,3,2-oxazaphosphorinanes) bearing chiral auxiliaries[7–9] and by photo-Arbuzov rearrangement of optically active 2-(1-phenylethoxy)-1,3,2-dioxaphosphorinanes.[10–12] Recently a series of optically active 1-aryl substituted ethylphosphonic acids was prepared with high enantioselectivity by homogeneous catalytic hydrogenation of corresponding α,β-unsaturated precursors, using chiral ruthenium complexes.[13] However, Ru-catalyzed hydrogenation of diethyl 1-arylethenylphosphonates using chiral Ru(II)-catalysts required vigorous conditions and gave only moderate enantioselectivities. Herein we report our results on iridium(I)-catalyzed hydrogenation of prochiral diethyl 1-arylethenylphosphonates **1** to corresponding diethyl 1-arylethylphosphonates **2** under mild conditions with good catalytic activity and enantioselectivity (Scheme 1).

2. Results and discussion

The starting prochiral diethyl 1-arylethenylphosphonates **1** were easily prepared by palladium-catalysed hydrophosphorylation of terminal arylacetylenes[14,15] or

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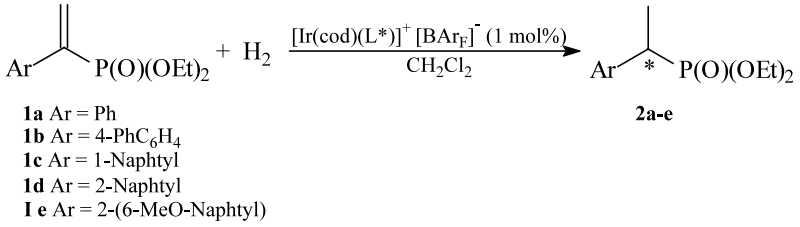

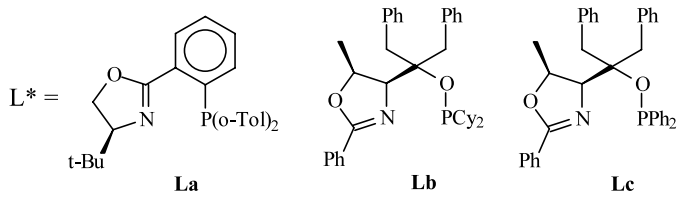

Scheme 1.

by esterification of 1-arylethenylphosphonic acids, which are readily available by a Conant reaction.[6] As catalysts, air-stable cationic iridium(I) complexes bearing either the phosphinooxazoline ligand **La** or oxazoline–phosphinite ligands **Lb** or **Lc** were tested.[16,17] Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ($[BAr_F]^-$) was used as the counterion because this anion is known to reduce the sensitivity of the Ir complexes against moisture and to prevent deactivation of the catalyst during the reaction.[16,17]

Initial optimisation of reaction conditions was performed using the iridium–phosphinooxazoline complex $[Ir(cod)(\mathbf{La})]^+[BAr_F]^-$ (1 mol%) and diethyl 1-phenylethenylphosphonate **1a** as a model substrate. The reactions were carried out in CH_2Cl_2 and monitored using ^{31}P NMR spectroscopy. Disappearance of the peak of starting **1a** at δ ($CDCl_3$) 16.8 ppm with increase of the peak of final product **2a** at 29.5 ppm[13] indicated a clean reaction with no detectable side products.

The catalyst $[Ir(cod)(\mathbf{La})]^+[BAr_F]^-$ was highly effective and quantitative conversions were observed in all reactions (Table 1, entries 1–7).

The rate and enantioselectivity of this reaction were found to increase significantly with the decrease of hydrogen pressure from 60 to 5 bar (Table 1, entries 1–5). A similar pressure dependence of the ee has been previously observed in the hydrogenation of terminal olefins with Ir catalysts.[17] Variation of the temperature between 20 and 60°C had a small effect on enantioselectivity (entries 5–7). The highest ee (94%, entry 6) was observed at 40°C and a hydrogen pressure of 5 bar. Under these conditions complexes $[Ir(cod)(\mathbf{Lb})]^+[BAr_F]^-$ and $[Ir(cod)(\mathbf{Lc})]^+[BAr_F]^-$ bearing oxazoline–phosphinite ligands showed very low activity (entries 8 and 9).

The absolute configuration (*R*) of **2a** was assigned based on the specific rotation of the corresponding

Table 1. Optimisation of enantioselective hydrogenation of **1a** in CH_2Cl_2 with use of $[Ir(cod)(\mathbf{L}^*)]^+$ $[BAr_F]^-$ catalysts

Entry	L*	Pressure (bar)	Temperature (°C)	Time (h)	Conversion (%) (^{31}P NMR)	Ee (%)
1	**La**	60	20	6	82	
				24	100	70
2	**La**	50	20	24	100	72
3	**La**	30	20	3	88	
				6	100	90
4	**La**	10	20	3	89	
				6	100	91
5	**La**	5	20	3	95	
				6	100	91
6	**La**	5	40	3	94	
				6	100	94
7	**La**	5	60	3	93	
				6	100	91
8	**Lb**	5	40	3	7	
				28	7	
9	**Lc**	5	40	3	8	
				216	8	

1-phenylethylphosphonic acid ($[\alpha]_D$ +4.6 (*c* 0.9, MeOH)), obtained by McKenna procedure,[18] in comparison with literature data $[\alpha]_D$ +4.8 (*c* 0.9, MeOH) for the (*R*)-enantiomer.[7]

Under optimum conditions a range of substrates **1** was investigated and high enantioselectivities and good conversions were achieved in most cases (Table 2). Only a small steric effect of the aromatic substituent was observed and reaction rates and enantioselectivities were practically the same when aryl was phenyl, 4-diphenyl, 1- or 2-naphthyl (entries 1–4). Substrate **1e** showed very low reactivity and deactivation of the catalyst was observed in the course of the reaction. Such a dramatic effect of the MeO-group is difficult to explain since several 4-methoxyphenyl substituted olefins have been previously used as test substrates for hydrogenation with iridium-phosphinooxazoline catalysts without any problems with conversion. However, as a possible cause of the low reactivity, traces of impurities in the substrate cannot be ruled out. We could improve the yield of **2e** (phosphorus analogue of naproxen) up to 78% after 115 h when the catalyst (total amount 2 mol%) was added in two portions; the second portion after 27 h of the reaction. Diethyl 1-(3-pyridyl)ethenylphosphonate proved to be totally unreactive under the reaction conditions, which is not surprising, because coordinating species are known to deactivate Ir catalysts of this type.[17]

Table 2. Enantioselective hydrogenation of diethyl 1-arylethenylphosphonates **1** catalyzed by $[Ir(cod)(\mathbf{La})]^+$ $[BAr_F]^-$ (1 mol%) (CH_2Cl_2, 5 bar, 40°C)

Entry	Substrate	Time (h)	Conversion (%) (^{31}P NMR)	ee (%)
1	**1a**	6	100	(+)94
2	**1b**	6	95	94
3	**1c**	5	90	
		24	93	92
4	**1d**	6	96	93
5	**1e**	6	<10	
		115	78[a]	95

[a] An additional portion of $[Ir(cod)(\mathbf{La})]^+$ $[BAr_F]^-$ (1 mol%) was added after 27 h of the reaction.

3. Experimental

3.1. Physical measurements

^{1}H, ^{13}C and ^{31}P NMR spectra were recorded in $CDCl_3$ with a Varian VXR-400 (^{1}H at 400, ^{13}C at 100 and ^{31}P at 162 MHz) spectrometer. Chemical shifts of ^{1}H spectra are referenced to tetramethylsilane internal standard ($\delta = 0$), ^{13}C spectra are referenced to $CDCl_3$ ($\delta = 77.00$), ^{31}P spectra are referenced to H_3PO_4 (85%) external standard ($\delta = 0$). IR spectra were obtained on a IKAR FT spectrophotometer (Microtek, Russia). HPLC analyses were performed with a Bischoff (Germany) liquid chromatograph. Optical rotation was recorded using a Perkin–Elmer 241 polarimeter.

3.2. Synthesis of starting materials

3.2.1. Diethyl 1-phenylethenylphosphonate 1a. A mixture of 1-phenylethenylphosphonic acid (3.26 g, 17.7 mmol) and triethyl orthoformate (13.0 mL, 78.2 mmol) was slowly heated in a gentle stream of argon, ethyl formate and ethanol being allowed to distil out. As volatile materials were removed the reaction mixture was heated to 140–145°C and maintained at reflux for 1–2 h until the completion of the reaction (TLC control). The excess $HC(OEt)_3$ was removed under reduced pressure and the residue was distilled in vacuo to afford **1a** (4.09 g, 96%) as a colourless viscous liquid, $Bp_{2\ mmHg}$ 132°C,[15] R_f 0.6 (Silufol UV 254, $CHCl_3$/EtOH, 10:1).

3.2.2. Diethyl 1-(4-diphenyl)ethenylphosphonate 1b. Diethyl 1-(4-diphenyl)ethenylphosphonate **1b** was prepared in 80% yield analogously to **1a** from 1-(4-diphenyl)ethenylphosphonic acid[6] (0.94 g, 3.6 mmol) and $HC(OEt)_3$ (4.4 mL, 26.5 mmol). Yellowish thick oil, $Bp_{0.1\ mmHg}$ 185°C, R_f 0.75 (Silufol UV 254, $CHCl_3$/EtOH, 10:1). ^{31}P NMR ($CDCl_3$): δ (ppm) 16.8. ^{1}H NMR ($CDCl_3$): δ (ppm) 1.29 (t, $^3J_{HH}$ 7.1 Hz, 6H, CH_3), 4.12 (m, 4H, OCH_2), 6.19 (dd, $^2J_{HH}$ 1.5 Hz, $^3J_{HP}$ 45.7 Hz, 1H, *trans*-PC=CH), 6.34 (dd, $^2J_{HH}$ 1.5 Hz, $^3J_{HP}$ 21.9 Hz, 1H, *cis*-PC=CH), 7.33 (m, $^3J_{HH}$ 7.3 Hz, 1H, (C-4″)H), 7.42 (m, 2H, H_{ar}), 7.55–7.62 (m, 6H, H_{ar}). ^{13}C NMR ($CDCl_3$): δ (ppm) 16.0 (d, $^3J_{CP}$ 4.8 Hz, CH_3), 62.0 (d, $^2J_{CP}$ 5.3 Hz, OCH_2), 126.7 (CH_{ar}), 126.8 (CH_{ar}), 127.2 (C-4″), 127.6 (d, $^3J_{CP}$ 4.7 Hz, C-3′ and C-5′), 128.6 (CH_{ar}), 131.2 (d, $^2J_{CP}$ 6.7 Hz, C-2), 135.3 (d, $^2J_{CP}$ 11.2 Hz, C-4′), 139.0 (d, $^1J_{CP}$ 174.9 Hz, C-1), 140.1 (C_{ar}), 140.7 (C_{ar}).

3.2.3. Diethyl 1-(1-naphthyl)ethenylphosphonate 1c. Diethyl 1-(1-naphthyl)ethenylphosphonate **1c** was prepared in 91% yield analogously to **1a** from 1-(1-naphthyl)ethenylphosphonic acid[6] (1.70 g, 7.3 mmol) and $HC(OEt)_3$ (6.0 mL, 36.1 mmol). Yellowish viscous liquid, $Bp_{0.1\ mmHg}$ 135°C, R_f 0.6 (Silufol UV 254, $CHCl_3$/EtOH 10/1). ^{31}P NMR ($CDCl_3$): δ (ppm) 15.4. ^{1}H NMR ($CDCl_3$): δ (ppm) 1.17 (t, $^3J_{HH}$ 7.0 Hz, 6H, CH_3), 4.03 (m, 4H, OCH_2), 6.00 (dd, $^2J_{HH}$ 2.0 Hz, $^3J_{HP}$ 46.8 Hz, 1H, *trans*-PC=CH), 6.66 (dd, $^2J_{HH}$ 2.0 Hz, $^3J_{HP}$ 22.4 Hz, 1H, *cis*-PC=CH), 7.42–7.48 (m, 4H, H_{ar}), 7.77–7.84 (m, 2H, H_{ar}), 7.99–8.03 (m, 1H, H_{ar}). ^{13}C NMR ($CDCl_3$): δ (ppm) 16.0 (d, $^3J_{CP}$ 7.0 Hz, CH_3), 62.2 (d, $^2J_{CP}$ 6.2 Hz, OCH_2), 124.7 (CH_{ar}), 125.5 (CH_{ar}), 125.7 (CH_{ar}), 125.8 (CH_{ar}), 126.2 (d, $^3J_{CP}$ 4.7 Hz, C-2′), 128.0 (CH_{ar}), 128.1 (CH_{ar}), 131.4 (d, $^3J_{CP}$ 4.2 Hz, C-9′), 133.5 (C-10′), 134.3 (d, $^2J_{CP}$ 6.1 Hz, C-2), 134.4 (d, $^2J_{CP}$ 9.7 Hz, C-1′); 138.7 (d, $^1J_{CP}$ 177.1 Hz, C-1); IR (film): 2983, 1251, 1234, 1051, 1024, 968, 808, 779.

3.2.4. Diethyl 1-(2-naphthyl)ethenylphosphonate 1d. Diethyl 1-(2-naphthyl)ethenylphosphonate **1d** was prepared in 85% yield analogously to **1a** from 1-(2-naphthyl)ethenylphosphonic acid[6] (2.34 g, 10.0 mmol) and $HC(OEt)_3$ (6.7 mL, 40.3 mmol). Yellowish viscous liquid, $Bp_{0.1\ mmHg}$ 167°C, R_f 0.8 (Silufol UV 254, $CHCl_3$/EtOH, 10:1). ^{31}P NMR ($CDCl_3$): δ (ppm) 16.7. ^{1}H NMR ($CDCl_3$): δ (ppm) 1.27 (t, $^3J_{HH}$ 7.1 Hz, 6H, CH_3),

4.12 (m, 4H, OCH_2), 6.25 (dd, $^2J_{HH}$ 1.5 Hz, $^3J_{HP}$ 45.4 Hz, *trans*-PC=CH), 6.40 (dd, $^2J_{HH}$ 1.5 Hz, $^3J_{HP}$ 22.0 Hz, *cis*-PC=CH), 7.46 (m, 2H, (C-6′)H and (C-7′)H), 7.62 (m, $^3J_{HH}$ 8.5 Hz, 1H, (C-3′)H), 7.78–7.85 (m, 3H, H_{ar}), 8.02 (brs, 1H, (C-1′)H). ^{13}C NMR ($CDCl_3$): δ (ppm) 16.0 (d, $^3J_{CP}$ 6.7 Hz, CH_3), 62.0 (d, $^2J_{CP}$ 6.5 Hz, OCH_2), 124.9 (d, $^3J_{CP}$ 5.1 Hz, C-3′), 126.0 and 126.1 (C-6′ and C-7′), 126.5 (d, $^3J_{CP}$ 6.7 Hz, C-1′), 127.3 (CH_{ar}), 127.8 (CH_{ar}), 128.1 (CH_{ar}), 131.7 (d, $^2J_{CP}$ 8.7 Hz, C-2), 132.7 (C_{ar}), 132.9 (C_{ar}), 133.7 (d, $^2J_{CP}$ 12.3 Hz, C-2′), 139.4 (d, $^1J_{CP}$ 173.3 Hz, C-1).

3.2.5. Diethyl 1-(6-methoxy-2-naphthyl)ethenylphosphonate 1e. Diethyl 1-(6-methoxy-2-naphthyl)ethenylphosphonate **1e** was prepared according to the literature procedure.[15]

3.3. General procedure for the enantioselective hydrogenation

The autoclave was deaerated with argon and filled with hydrogen. A Schlenk flask was charged with **1** (0.4 mmol), $[Ir(cod)(L^*)]^+$ $[BAr_F]^-$ (4 μmol) and deaerated CH_2Cl_2 (20 mL, freshly distilled over CaH_2) under argon and the mixture was stirred at room temperature for 15 min. The resulting orange solution was transferred by syringe to autoclave under hydrogen stream. The autoclave was sealed and pressurised with H_2, and the mixture was stirred under the conditions (temperature and time). The samples of reaction mixture (ca. 0.8 ml) were taken at times and analysed by ^{31}P NMR to assess the conversion. After completing of the reaction CH_2Cl_2 was removed and replaced with Et_2O (2–2.5 mL). The solution was passed through a short column (Silpearl 10×1 cm, Et_2O) to afford **2** in essentially quantitative yield. The identity of products **2** was confirm by ^{1}H NMR. The enantiomeric excesses of samples obtained were determined by HPLC (Chiralpak AD-H 25×0.46 cm column, hexane/*i*-PrOH 9/1, 1.0 mL min^{-1}, 254 nm). Retention times of two enantiomers: **2a**, 7.1 and 5.2 min (ratio 33/1); **2b**, 8.9 and 8.2 min (ratio 30/1); **2c**, 10.4 and 6.6 min (ratio 23/1); **2d**, 25.5 and 11.6 min (ratio 26.5/1); **2e**, 19.8 and 13.3 min (ratio 38/1).

3.4. Synthesis of racemic diethyl 1-arylethylphosphonates (±)-2

Synthesis of racemic (±)-**2a** and (±)-**2e** has been described previously.[6,13] In the same manner racemic (±)-**2b–d** were prepared in 77–86% yield by hydrogen transfer reduction of **1b–d** with ammonium formate (6 equiv.) in the presence of 10% Pd/C (2.9 mol%) in absolute MeOH; reaction time 4–9 h. Spectroscopic data for these compounds are given below.

3.4.1. Diethyl (±)-1-(4-diphenyl)ethylphosphonate (±)-2b. Yellowish viscous liquid, R_f 0.3 (Silufol UV 254, Et_2O). ^{31}P NMR ($CDCl_3$): δ (ppm) 29.3. ^{1}H NMR ($CDCl_3$): δ (ppm) 1.17 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_2CH_3), 1.29 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_2CH_3), 1.61 (dd, $^3J_{HH}$ 7.2 Hz, $^3J_{HP}$ 18.6 Hz, 3H, $CHCH_3$), 3.22 (dq, $^3J_{HH}$ 7.2 Hz, $^2J_{HP}$ 22.4 Hz, 1H, CH), 3.86 (m, 1H, OCH_2), 3.96 (m, 1H, OCH_2), 4.05 (m, 2H, OCH_2), 7.32 (m, $^3J_{HH}$ 7.4 Hz, 1H, (C-4″)H), 7.42 (m, 4H, H_{ar}), 7.57 (m, 4H, H_{ar}). ^{13}C NMR ($CDCl_3$): δ (ppm) 15.5 (d, $^2J_{CP}$ 5.4 Hz, $CHCH_3$), 16.2 (d, $^3J_{CP}$ 6.8 Hz, CH_2CH_3), 16.4 (d, $^3J_{CP}$ 6.4 Hz, CH_2CH_3), 38.0 (d, $^1J_{CP}$ 137.2 Hz, $CHCH_3$), 61.9 (d, $^2J_{CP}$ 5.9 Hz, OCH_2), 62.4 (d, $^2J_{CP}$ 8.6 Hz, OCH_2), 126.9 (CH_{ar}), 127.0 (d, $^4J_{CP}$ 2.2 Hz, C-2′ and C-6′), 127.2 (C-4″), 128.7 (CH_{ar}), 129.0 (d, $^3J_{CP}$ 6.8 Hz, C-3′ and C-5′), 136.9 (d, $^2J_{CP}$ 6.1 Hz, C-4′), 139.8 (C_{ar}), 140.6 (C_{ar}).

3.4.2. Diethyl (±)-1-(1-naphthyl)ethylphosphonate (±)-2c. Yellowish liquid, R_f 0.3 (Silufol UV 254, Et_2O). ^{31}P NMR ($CDCl_3$): δ (ppm) 29.8. ^{1}H NMR ($CDCl_3$): δ (ppm) 0.92 (t, $^3J_{HH}$ 7.2 Hz, 3H, CH_2CH_3), 1.26 (t, $^3J_{HH}$ 7.2 Hz, 3H, CH_2CH_3), 1.72 (dd, $^3J_{HH}$ 7.4 Hz, $^3J_{HP}$ 18.2 Hz, 3H, $CHCH_3$), 3.57 (m, 1H, OCH_2), 3.82 (m, 1H, OCH_2), 4.00–4.16 (m, 3H, OCH_2 and CH), 7.48 (m, 2H, H_{ar}), 7.54 (m, 1H, H_{ar}), 7.72 (m, 1H, H_{ar}), 7.76 (m, $^3J_{HH}$ 8.0 Hz, 1H, H_{ar}), 7.85 (m, $^3J_{HH}$ 8.0 Hz, 1H, H_{ar}), 8.12 (m, $^3J_{HH}$ 8.4 Hz, 1H, H_{ar}). ^{13}C NMR ($CDCl_3$): δ (ppm) 16.0 (d, $^2J_{CP}$ 4.3 Hz, $CHCH_3$), 16.2 (d, $^3J_{CP}$ 4.5 Hz, CH_2CH_3), 16.4 (d, $^3J_{CP}$ 6.3 Hz, CH_2CH_3), 32.2 (d, $^1J_{CP}$ 139.8 Hz, $CHCH_3$), 61.8 (d, $^2J_{CP}$ 7.5 Hz, OCH_2), 62.4 (d, $^2J_{CP}$ 7.6 Hz, OCH_2), 123.1 (CH_{ar}), 125.3 (d, $^4J_{CP}$ 5.4 Hz, C-3′), 125.4 (CH_{ar}), 125.9 (d, $^3J_{CP}$ 6.5 Hz, C-2′), 126.0 (CH_{ar}), 127.4 (d, $^2J_{CP}$ 3.1 Hz, C-8′), 128.8 (CH_{ar}), 131.6 (d, J_{CP} 7.1 Hz, C_{ar}), 133.7 (C_{ar}), 134.2 (d, J_{CP} 5.7 Hz, C_{ar}).

3.4.3. Diethyl (±)-1-(2-naphthyl)ethylphosphonate (±)-2d. Colourless viscous liquid, $Bp_{0.1\ mmHg}$ 171°C, R_f 0.4 (Silufol UV 254, Et_2O). ^{31}P NMR ($CDCl_3$): δ (ppm) 29.3. ^{1}H NMR ($CDCl_3$): δ (ppm) 1.09 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_2CH_3), 1.25 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_2CH_3), 1.66 (dd, $^3J_{HH}$ 7.4 Hz, $^3J_{HP}$ 18.4 Hz, 3H, $CHCH_3$), 3.33 (dq, $^3J_{HH}$ 7.4 Hz, $^2J_{HP}$ 22.4 Hz, 1H, CH), 3.77 (m, 1H, OCH_2), 3.91 (m, 1H, OCH_2), 4.03 (m, 2H, OCH_2), 7.42 (m, 2H, H_{ar}), 7.50 (d, $^3J_{HH}$ 8.4 Hz, 1H, H_{ar}), 7.75–7.81 (m, 4H, H_{ar}). ^{13}C NMR ($CDCl_3$): δ (ppm) 15.4 (d, $^2J_{CP}$ 6.2 Hz, $CHCH_3$), 16.0 (d, $^3J_{CP}$ 5.7 Hz, CH_2CH_3), 16.2 (d, $^3J_{CP}$ 5.4 Hz, CH_2CH_3), 38.3 (d, $^1J_{CP}$ 138.0 Hz, $CHCH_3$), 61.6 (d, $^2J_{CP}$ 6.3 Hz, OCH_2), 62.1 (d, $^2J_{CP}$ 7.2 Hz, OCH_2), 125.4 (CH_{ar}), 125.8 (CH_{ar}), 126.6 (d, $^3J_{CP}$ 4.5 Hz, CH_{ar}), 127.0 (d, $^3J_{CP}$ 7.9 Hz, CH_{ar}), 127.3 (CH_{ar}), 127.5 (CH_{ar}), 127.7 (CH_{ar}), 135.3 (d, $^2J_{CP}$ 4.8 Hz, C-2′), 132.2 (C_{ar}), 133.1 (C_{ar}).

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