Results in Chemistry 4 (2022) 100525

Contents lists available at ScienceDirect

Results in Chemistry

journal homepage: www.sciencedirect.com/journal/results-in-chemistry

A synthetic methodology for the preparation of a water-soluble quaternized amino phosphine oxide ligand

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ARTICLE INFO

Keywords:
PN Ligand
Phosphine oxide
Water-soluble ligand
Quaternization

ABSTRACT

After several unsuccessful attempts to synthesize quaternized aniline-derived phosphanes, we succeeded to develop a synthetic methodology for the preparation of a water-soluble amino phosphine oxide ligand containing a quaternary ammonium ion by insertion of a second amino moiety on the aniline derivative before the insertion of the phosphino group. The methodology involves insertion of an amino moiety on the alkyl chain of the aniline derivative *via* its mesylate, subsequent insertion of the phosphino group *via ortho*-lithiation of the aromatic ring, oxidation to the corresponding phosphine oxide and finally quaternization of the alkyl chain amino moiety.

1. Introduction

The development of synthetic methodologies for the preparation of novel and efficient ligands towards transition metal homogeneous catalysis remains an important goal in chemistry. Hemilabile hybrid ligands with soft and hard donor atoms such as P, N, O, S, and in particular *P,N*-ligands, have received much attention in this field [1,2]. The presence of an amino moiety in a phosphane ligand can be used not only as a metal donor, but also for increasing the hydrophilicity *via* its quaternization or protonation with an aim of developing water-soluble ligands for aqueous catalysis as an important environmentally friendly process [3].

As a part of our efforts in this area [4], we have previously reported the synthesis of the methoxy-amino phosphine **2** and the hydroxy analogue **3** (Scheme 1) from [*N*-(2-Hydroxyethyl)-*N*-methyl]aniline (**1**) [4a]. Both of them were found to be efficient ligands for the Rh-catalyzed hydroformylation of styrene [4a], while ligand **2** was also successfully evaluated towards the Pt-catalyzed hydrogenation of *trans*-cinnamaldehyde [4i]. The aim of the present work is the development of analogous hydrophilic phosphanes bearing quaternary ammonium ions. Despite several unsuccessful attempts, finally we succeeded to develop a synthetic protocol for the preparation of a water-soluble *P(O),N*-ligand containing a positively charged quaternary ammonium ion.

2. Results and discussion

Initially, we tried the quaternization of the amino group in ligand **2** in order to achieve its hydrophilicity. Since quaternization of the amino group with alkylating agents *versus* alkylation of the phosphorus atom is not selective, ligand **2** was oxidized to the corresponding phosphine oxide **4** with aqueous H_2O_2 at room temperature (Scheme 1).

Quaternization of **4** was attempted by a variety of methods regarding the alkylating agent (BuBr, BnBr, MeI, $Me_3O^+BF_4^-$), the solvent (CH_2Cl_2, CH_3CN, propylene carbonate [5] or solvent-free conditions) and the reaction conditions (room temperature, conventional heating, microwave irradiation or ultrasounds in short or in prolonged reaction times in the absence or in the presence of a base such as KOH or basic alumina) as shown in Table 1. Unfortunately, no quaternization was achieved, while in some cases the reaction was not a clean one as shown in the ^1H NMR spectra of the reaction products, in accordance to which, the starting compound or part of this, was converted to a mixture of products, which were not further identified. Quaternization was not possible even with MeI after 20 days of reflux (entry 13) in contrast to the previously reported conversion of 4-(dimethylamino)phenyldiphenylphosphine oxide to the corresponding methylated anilinium salt under identical conditions [6]. The reason for the unsuccessful quaternization of **4** is obviously the very low nucleophilicity of the aniline nitrogen atom. Reaction of **4** with the Meerwein reagent

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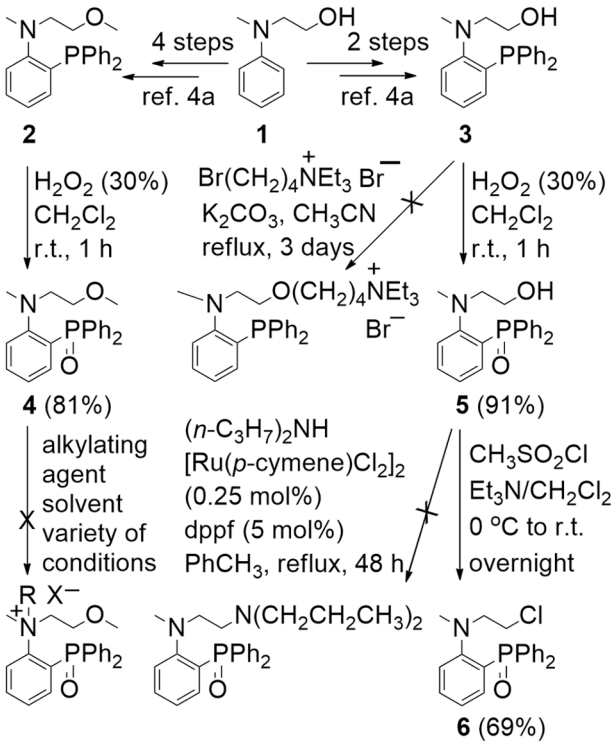
https://doi.org/10.1016/j.rechem.2022.100525
Received 19 July 2022; Accepted 12 September 2022
Available online 16 September 2022



Scheme 1. Unsuccessful attempts for the synthesis of ligands bearing quaternary ammonium ions.

Table 1
Unsuccessful attempts for quaternization of ligand **4**.

Entry	Alkylating agent	Solvent	Conditions	Results[1]
1	BuBr	CH_2Cl_2	r.t., 18 h; reflux, 2 h	(a)
2	BnBr	CH_2Cl_2	r.t., 20 h	(a)
3	BnBr	CH_3CN	r.t., 1 h; 70 °C, 19 h	(a)
4	BnBr	CH_2Cl_2	KOH, r.t., 20 h	(a)
5	BnBr	PC[2]	KOH, r.t., 23 h; 70 °C, 6 h	(b)
6	BnBr	PC[2]	r.t., 3 days; 70 °C, 5 h	(b)
7	BnBr	CH_3CN	MW, 100 W, 70 °C, 0.5 h	(a)
8	BnBr	CH_3CN	MW, 150 W, 110 °C, 1 h	(b)
9	BnBr	–	MW, 110 or 150 W, 110 °C, 1 h	(b)
10	BnBr	PC[2]	MW, basic alumina, 180 W, 100 °C, 10 min	(a)
11	BnBr	–	MW, 180 W, basic alumina, 90 °C, 10 min	(a)
12	BnBr	CH_3CN	ultrasound, r.t., 1 h	(a)
13	MeI	CH_2Cl_2	reflux, 20 days	(a)
14	MeI	PC[2]	basic alumina, r.t., 3 days; 100 °C, 2 days	(b)
15	MeI	acetone	MW, 100 W, 70 °C, 1 h	(a)
16	MeI	PC[2]	MW, 180 W, basic alumina, 100 °C, 10 min	(b)
17	MeI	–	MW, 180 W, basic alumina, 100 °C, 10 min	(b)
18	$Me_3O^+BF_4^-$	CH_2Cl_2	0 °C to r.t., 20 h	(b), (c)

[1] (a) Starting material with no quaternization; (b) crude reaction mixture with several non-identified products; (c) *N*- and *O*-methylation and/or protonation probably occurred.
[2] Propylene carbonate.

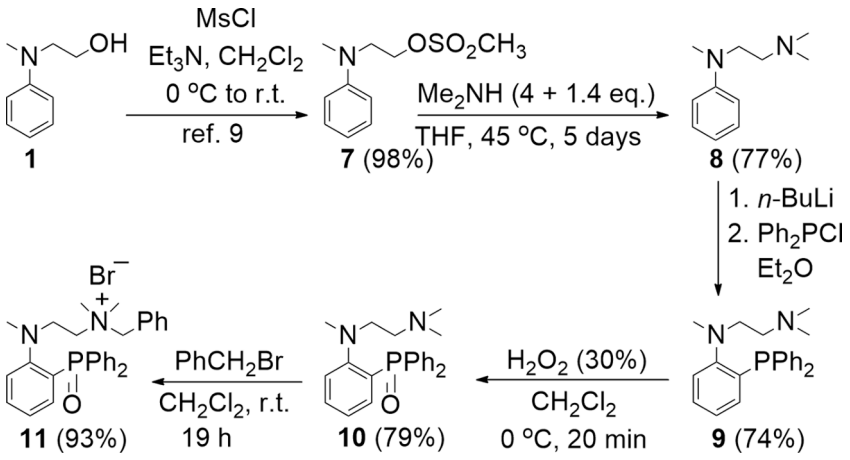
($Me_3O^+BF_4^-$) as a strong methylating agent yielded a mixture of products, in which in addition to a possible *N*-methylation, *O*-methylation and/or protonation also probably occurred. However, these products were not further isolated to be identified (entry 18).

Then, our attention turned to the phosphino amino alcohol **3** (Scheme 1). Unfortunately, treatment of **3** with (4-bromobutyl) trimethylammonium bromide for the formation of the corresponding hydrophilic ether bearing a quaternary ammonium ion, using the conditions previously described for the formation of the quaternized analogue of 2,2′-dihydroxy-1,1′-binaphthyl [7], was not a clean reaction and led to a mixture of several products as shown in the ^{1}H NMR spectrum, which were not further identified. In other efforts, the aim was the replacement of the hydroxyl by an amino group, which should subsequently be quaternized, and thus, ligand **3** was firstly oxidized to the corresponding phosphine oxide **5** by aqueous H_2O_2. Treatment of **5** with di(*n*-propyl)amine catalyzed by [Ru(*p*-cymene)Cl_2]$_2$/dppf under reflux in accordance with a known method for the formation of tertiary amines by ruthenium-catalyzed *N*-alkylation of amines with alcohols [8], unfortunately led to several by-products without the formation of the desired tertiary amine as shown by the ^{1}H NMR spectra of the fractions isolated after a column chromatography of the crude reaction mixture. After that, we thought that the replacement of the hydroxyl by an amino group in **5** should be achieved *via* its mesylate, but unfortunately the synthesis and isolation of the corresponding mesylate was not successful. Treatment of **5** with mesylchloride in CH_2Cl_2/Et_3N at 0 °C and then stirring at room temperature overnight, led to the replacement of the hydroxyl group by a chlorine atom and the formation of **6** in 69 % yield after column chromatography. The same product was also isolated by the reaction of **5** with tosylchloride under identical conditions. In other experiments, the reaction was performed in a shorter reaction time, and TLC showed that the conversion of **5** is complete even after 15 min at 0 °C, while the ^{1}H NMR spectrum of the crude reaction mixture indicated that the formation of the mesylate is possible, but however several other by-products were present, and isolation of the mesylate was not successful due to its instability as an oil or in solution as indicated by the ^{1}H NMR spectrum of the crude reaction mixture, which showed more compounds over the time. Since the replacement of the mesyl by the amino group requires a prolonged reaction time as shown below, synthesis of the mesylate without being isolated and subsequent treatment with a secondary amine is not the appropriate process due to the instability of this mesylate.

The above-mentioned unsuccessful attempts led to the conclusion that insertion of a second amino moiety on the alkyl chain of **1** is necessary for further quaternization, and this insertion must be performed before the insertion of the phosphino group. The synthetic strategy towards the formation of a quaternized *P,N*-ligand is shown in Scheme 2.

Mesylate **7** was easily prepared from **1** in accordance with a known procedure [9]. Despite the absence of a phosphino group, compound **7** is not stable for a long period even when kept at 4 °C as indicated by its ^{1}H NMR spectrum after three weeks. Mesylate **7** was then converted into amine **8** by its reaction with dimethylamine using similar conditions previously reported for the synthesis of 2-(4-bromophenyl)-*N*,*N*-dimethylethylamine from its mesylate [10]. We found that a prolonged reaction time is necessary for a relatively good yield. Insertion of the phosphino group towards the formation of ligand **9** was performed *via ortho*-lithiation of **8** with *n*-BuLi and subsequent reaction of the resulting organolithium with chlorodiphenylphosphine.

In the next step, protection of the trivalent phosphorus atom from quaternization was achieved by its conversion to phosphine oxide moiety and the formation of ligand **10**. The oxidation was initially attempted by the reaction of **9** with aqueous H_2O_2 at room temperature as described for the synthesis of phosphine oxides **4** and **5**. Unfortunately, the ^{1}H and ^{31}P NMR data of the reaction product provided evidence that the reaction is not a clean one, and this is probably due to both *P*- and dimethylamine *N*-oxidation. This nitrogen oxidation is in contrast to ligands **2** and **3** in which the aniline nitrogen is not so reactive towards hydrogen peroxide oxidation, at least under the conditions used. The stability of the aniline nitrogen atom towards oxidation is probably due to steric hindrance around this atom, in accordance to previously reported kinetics of hydrogen peroxide oxidation of alkyl dimethyl amines, in which the branched analogues create substantial



Scheme 2. Synthesis of a water-soluble quaternized amino phosphine oxide ligand.

steric hindrance around the nitrogen atom and retards the rate of oxidation [11]. An electronic influence could also be in place, since aniline nitrogen atom has a very low nucleophilicity. In order to dramatically decrease the rate of the alkyl dimethylamine *N*-oxidation, treatment of **9** with aqueous H_2O_2 was performed at 0 °C for a shorter reaction time, leading to the pure phosphine oxide **10**. The resonance at –13.51 ppm in the ^{31}P NMR spectrum of **9** is shifted to 26.98 ppm upon *P*-oxidation as shown in the ^{31}P NMR spectrum of **10**.

Finally, quaternization of **10** was performed by its reaction with benzyl bromide in dichloromethane at room temperature. Upon quaternization of the dimethylamine nitrogen, $N(CH_3)_2$ proton and carbon resonances in the ^1H and ^{13}C NMR spectra of **11** are shifted downfield by 1.16 and 4.31 ppm, respectively, compared to those of **10**. On the other hand, the aniline NCH_3 resonance has the same chemical shift in the ^1H NMR spectrum while it is shifted upfield by 2.80 ppm in the ^{13}C NMR spectrum of **11** compared to **10**. Compound **11** is a very hygroscopic white solid, which is turned to a sticky material upon standing on air for a while, and for that reason, it is preferably kept in a Schlenk flask under argon. It is soluble in dichloromethane, chloroform, acetonitrile, water, very slightly soluble in methanol or toluene, while it is insoluble in ether. It has previously reported that removal of oxygen from a quaternized amino phosphine oxide ligand by the usual procedure (trichlorosilane at high temperature in the presence of an amine additive) has two major problems [6]. The first problem is the formation of the amine accelerator hydrochloride salt, which would be difficult to get rid of in the presence of ionic product. On the other hand, a reaction in refluxing acetonitrile without an additional amine affords an undesired phosphonium salt as a second problem, and thus the reaction must be performed at ambient temperature for a prolonged reaction time [6]. In our experiments concerning the reduction of the phosphine oxide moiety in **11** to the phosphine analogue, compound **11** was treated with trichlorosilane in refluxing acetonitrile for two days and led to a mixture of products, which were not further identified, while a reaction at room temperature for ten days displayed only 30 % conversion to the trivalent phosphorus compound as estimated by the ^{31}P NMR spectrum of the crude reaction mixture. Since mixed amino phosphine oxide ligands are often more active and selective compared with the phosphine analogues for some catalytic reactions [12–14], at this stage, we did not proceed to a further investigation for a successful reduction of the phosphine oxide moiety.

3. Conclusion

In our preliminary efforts to synthesize water-soluble amino phosphanes bearing a quaternary ammonium ion starting from aniline derivatives, we found that quaternization of the aniline amino group was unsuccessful, probably due to its very low nucleophilicity. So, another alkyl amino group for further quaternization should be inserted in the molecule. Several unsuccessful attempts led to the conclusion that this insertion must be performed before the insertion of the phosphino group, and thus, we developed a synthetic methodology for the preparation of an interesting water-soluble amino phosphine oxide ligand containing a quaternary ammonium ion. The presented methodology is considered to be useful for the development of analogous quaternized *P*, *N*-ligands including chiral analogues with an aim of preparing new water-soluble ligands for aqueous transition metal homogeneous catalysis, a cutting edge area of research with environmental benefits.

4. Experimental

4.1. General experimental part

Compounds **1**, **2** and **3** [4a], **7** [9] and (4-bromobutyl)triethylammonium bromide [15] were prepared by known procedures. All other chemicals were commercially available. All syntheses were carried out under argon with dry and degassed reagents and solvents. Diethyl ether, toluene and hexane were distilled over Na, dichloromethane over CaH_2, and acetone over drierite. NMR spectra were recorded on a Varian 300 (300.13 MHz, 75.47 MHz and 121.50 MHz for ^1H, $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$, respectively) or a Varian 600 (599.827 MHz and 150.842 for ^1H and $^{13}C\{^1H\}$, respectively). The assignment of protons and carbons in the ^1H and ^{13}C NMR spectra was performed by HSQC NMR spectra. Chemical shift values in ^1H and ^{13}C NMR spectra were referenced internally to the residual solvent resonances, and the ^{31}P NMR spectra were referenced to external 85 % H_3PO_4 in H_2O. Electron impact gas chromatography – mass spectrometry was carried out using a Varian Saturn 2000 with a 30 m × 0.25 mm DB5-MS column; experimental details: initial column temperature 60 °C, initial column hold time 3 min, rate of increasing temperature 10 °C / min, final column temperature 260 °C, column hold time 37 min. HRMS was determined by a Thermo Scientific LTQ Orbitrap Velos (ESI). Melting points were measured on a Büchi melting point apparatus.

4.2. 2-(Diphenylphosphinyl)-[N-(2-methoxyethyl)-N-methyl]aniline (4)

Aqueous H_2O_2 (30 % w/w, 0.32 mL, 3.13 mmol) was added dropwise to a solution of **2** (1.00 g, 2.86 mmol) in dichloromethane (15 mL) and the mixture was stirred at room temperature for 1 h. Aqueous $Na_2S_2O_3$ (10 % w/v, 5 mL) was added and the product was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated to dryness. The residue was washed with cold ether and dried by vacuum at 60 °C, yielding **4** (0.85 g, 2.33 mmol, 81 %) as a white solid, m.p. 84–85 °C. ^1H NMR ($CDCl_3$): δ 7.72–7.65 (m, 4H, Ar), 7.54–7.38 (m, 7H,

Ar), 7.32–7.28 (m, 1H, Ar), 7.19–7.05 (m, 2H, Ar), 3.15 (s, 3H, OCH_3), 3.00 (m, 4H, OCH_2CH_2N), 2.44 (s, 3H, NCH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 159.00–124.11 (Ar), 71.00 (CH_2O), 58.45 (OCH_3), 56.84 (CH_2N), 43.67 (NCH_3). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 26.62 (s). GC–MS (EI): *m/z* (relative intensity) 366 ($[M+H]^+$, 100), 334 (26), 318 (33), 242 (54), 91 (28), 45 (13). HRMS (ESI): calcd for $C_{22}H_{25}NO_2P$ ($[M+H]^+$ 366.1617, found 366.1611.

4.3. 2-(Diphenylphosphinyl)-[N-(2-hydroxyethyl)-N-methyl]aniline (5) [16]

It was prepared as described for **4** from **3** (1.80 g, 5.37 mmol) and a 30 % w/w aqueous H_2O_2 (0.60 mL, 5.87 mmol) in dichloromethane (25 mL) to form **5** (1.72 g, 4.89 mmol, 91 %) as a white solid. ^1H NMR ($CDCl_3$): δ 7.71–7.68 (m, 4H, Ar), 7.56 (t, J = 7.5 Hz, 1H, arom), 7.52–7.50 (m), 7.47–7.46 (m) and 7.40 (m) (7H, arom), 7.16–7.14 (m, 1H, arom), 7.02– 6.99 (m, 1H, arom), 6.22 (brs, 1H, OH, exchangeable with D_2O), 3.57 (m, 2H, CH_2O), 3.06 (m, 2H, CH_2N), 2.00 (s, 3H, NCH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 158.94–125.42 (Ar), 62.00 (CH_2N), 59.19 (CH_2O), 41.81 (NCH_3). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 29.63 (s).

4.4. 2-(Diphenylphosphinyl)-[N-(2-chloroethyl)-N-methyl]aniline (6) [16]

To the solution of **5** (726.1 mg, 2.07 mmol) and triethylamine (430 μL, 3.09 mmol) in dichloromethane (4 mL), mesyl chloride (200 μL, 2.58 mmol) was added dropwise with an ice-water cooling bath and stirred at room temperature for 22 h. Ice-water was added to the reaction mixture, followed by addition of aqueous saturated sodium bicarbonate. The product was extracted with dichloromethane (3 × 20 mL), the organic extracts were washed with brine, dried over Na_2SO_4, filtered and evaporated to dryness. Purification was carried out by column chromatography using ethyl acetate as eluent, affording **6** (525.2 mg, 1.42 mmol, 69 %) as a white solid, R_f = 0.69 (AcOEt). ^1H NMR ($CDCl_3$): δ 7.69–7.66 (m, 4H, Ar), 7.56–7.53 (m, 1H, Ar), 7.51–7.49 (m, 2H, Ar), 7.45–7.42 (m, 4H, Ar), 7.38 (m, 1H, Ar), 7.14–7.10 (m, 2H, Ar), 3.19 (m, 2H, CH_2), 3.07 (m, 2H, CH_2), 2.50 (m, 3H, NCH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 157.55–124.37 (Ar), 59.62 (CH_2), 43.31 (NCH_3), 40.59 (CH_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 27.30 (s). HRMS (APCI): calcd for $C_{21}H_{22}ClNOP$ $[M+H]^+$ 370.1122, found 370.1117.

4.5. 2-(N-Methyl-N-phenylamino)ethyl methanesulfonate (7) [9]

Synthesis was achieved as previously described [9] from **1** (5.78 g, 38.28 mmol) and methanesulfonyl chloride (3.30 mL, 42.64 mmol) in dichloromethane (80 mL) and triethylamine (8.00 mL, 57.40 mmol) to form **7** (8.56 g, 37.33 mmol, 98 %) as a yellow–brown oil, which was used in the next step without purification. Herein, we report its analytical data, being absent in the previous paper [9]. ^1H NMR ($CDCl_3$): δ 7.26–7.23 (m, 2H, Ar), 6.76–6.73 (m, 3H, Ar), 4.36 (t, J = 5.9 Hz, 2H, CH_2N), 3.69 (t, J = 5.9 Hz, 2H, CH_2O), 3.00 (s, 3H, SO_2CH_3), 2.90 (s, 3H, NCH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 148.40, 129.28, 117.21 and 112.33 (Ar), 66.69 (CH_2N), 51.60 (CH_2O), 38.85 (SO_2CH_3), 37.28 (NCH_3). HRMS (APCI): calcd for $C_{10}H_{16}NO_3S$ $[M+H]^+$ 230.0845, found 230.0839.

4.6. [N-(2-Dimethylamino-ethyl)-N-methyl]aniline (8) [8]

A 2 M solution of dimethylamine in THF (73 mL, 146 mmol) was added to a solution of the mesylate **7** (8.38 g, 36.55 mmol) in THF (50 mL) and the mixture was stirred at 45 °C for 3 days. It was then cooled down to room temperature, dimethylamine (25 mL, 2 M in THF, 50 mmol) was once again added and the resulting solution was stirred for additional 2 days at 45 °C. After cooling to room temperature, the precipitate was filtered off, the filtrate was concentrated and alkalized with aqueous NaOH 10 % w/v (10 mL). The product was extracted with dichloromethane (3 × 30 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated to dryness. The resulting residue was subjected to column chromatography (CH_2Cl_2/MeOH, 9:1) to give **8** (5.02 g, 28.16 mmol, 77 %) as a yellow–brown oil, R_f = 0.35 (CH_2Cl_2/MeOH, 9:1). ^1H NMR ($CDCl_3$): δ 7.25–7.22 (m, 2H, Ar), 6.73–6.69 (m, 3H, Ar), 3.51 (t, J = 7.5 Hz, 2H, CH_2), 2.96 (s, 3H, NCH_3), 2.56 (t, J = 7.5 Hz, 2H, CH_2), 2.36 (s, 6H, N$(CH_3)_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 149.08, 129.20, 116.27 and 112.11 (Ar), 55.82 (CH_2), 50.95 (CH_2), 45.75 ($N(CH_3)_2$), 38.56 (NCH_3).

4.7. 2-Diphenylphosphino-[N-(2-dimethylamino-ethyl)-N-methyl]aniline (9)

n-Butyllithium (1.74 M in methylcylcohexane, 6.8 mL, 11.83 mmol) was added to a solution of **8** (1.93 g, 10.811 mmol) in ether (10 mL) and the reaction mixture was stirred at room temperature for 21 h. A solution of chlorodiphenylphosphine (2 mL, 11.14 mmol) in ether (6 mL) was then added dropwise with an ice-water cooling bath and the mixture was stirred at room temperature overnight. The solvents were removed by evaporation, water was added, the product was extracted with toluene (3 × 25 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated to dryness to form a viscous oil which was crystallized by addition of ether, yielding **9** as a white solid (2.92 g, 8.05 mmol, 74 %), m.p. 72–74 °C. ^1H NMR ($CDCl_3$): δ 7.33–7.30 (m, 7H, Ar), 7.26–7.24 (m, 4H, Ar), 7.21–7.19 (m, 1H, Ar), 7.01 (t, J = 7.4 Hz, 1H, Ar), 6.77–6.75 (m, 1H, Ar), 2.93–2.90 (m, 2H, CH_2), 2.61 (s, 3H, NCH_3), 2.09–2.06 (m, 2H, CH_2), 2.06 (s, 6H, N$(CH_3)_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 157.41–122.01 (Ar), 57.01 (s, CH_2), 55.29 (d, $^4J_{C,P}$ = 1.5 Hz, CH_2), 45.53 (s, $N(CH_3)_2$), 43.60 (d, $^4J_{C,P}$ = 3.0 Hz, NCH_3). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ – 13.51 (s). HRMS (APCI): calcd for $C_{23}H_{28}N_2P$ $[M+H]^+$ 363.1985, found 363.1985.

4.8. 2-Diphenylphosphinyl-[N-(2-dimethylamino-ethyl)-N-methyl]aniline (10)

Aqueous H_2O_2 (30 % w/w, 0.78 mL, 7.64 mmol) was added dropwise to a solution of **9** (2.52 g, 6.95 mmol) in dichloromethane (35 mL) with an ice-water cooling bath and the mixture was stirred for 20 min. Aqueous $Na_2S_2O_3$ (10 % w/v, 5 mL) was added and the product was extracted with dichloromethane (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated to dryness. The residue was washed with cold ether and dried by vacuum at 70 °C, yielding **10** (2.08 g, 5.50 mmol, 79 %) as a white solid, m.p. 103–105 °C. ^1H NMR ($CDCl_3$): δ 7.69–7.66 (m, 4H, Ar), 7.52 (t, J = 7.6 Hz, 1H, Ar), 7.49–7.46 (m, 2H, Ar), 7.43–7.40 (m, 4H, Ar), 7.31–7.28 (m, 1H, Ar), 7.17–7.14 (m, 1H, Ar), 7.11–7.08 (m, 1H, Ar), 2.88–2.85 (m, 2H, CH_2), 2.44 (s, 3H, NCH_3), 2.10 (s, 6H, $N(CH_3)_2$), 1.87 (m, 2H, CH_2). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 159.18–123.95 (Ar), 56.50 (CH_2), 55.40 (CH_2), 45.54 ($N(CH_3)_2$), 44.13 (NCH_3). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 26.98 (s). HRMS (APCI): calcd for $C_{23}H_{28}N_2OP$ $[M+H]^+$ 379.1934, found 379.1928.

4.9. [2-Diphenylphosphinyl-[N-(2-dimethylbenzylammonium-ethyl)-N-methyl]aniline]bromide (11)

Benzyl bromide (0.80 mL, 6.73 mmol) was added to a solution of **10** (2.04 g, 5.40 mmol) in dichloromethane (30 mL) and the mixture was stirred at room temperature for 19 h, after which the volatile materials were removed by evaporation. The resulting solid was precipitated twice from dichloromethane (10 mL) using ether (80 mL). Finally, it was washed with ether (4 × 30 mL) and dried by vacuum at 70 °C, yielding **11** (2.76 g, 5.02 mmol, 93 %) as a white solid, m.p. 137–142 °C. ^1H NMR ($CDCl_3$): δ 7.68 (d, J = 7.0 Hz, 2H, Ar), 7.61 (t, J = 7.0 Hz, 1H, Ar), 7.54–7.47 (m, 8H, Ar), 7.45–7.42 (m, 6H, Ar), 7.18–7.16 (m, 1H, Ar), 6.98–6.95 (m, 1H, Ar), 5.00 (s, 2H, CH_2Ph), 3.98 (m, 2H, CH_2), 3.53 (m, 2H, CH_2), 3.26 (s, 6H, $N(CH_3)_2$), 2.45 (s, 3H, NCH_3). $^{13}C\{^1H\}$ NMR

($CDCl_3$): δ 157.75–124.76 (Ar), 68.26 (CH_2Ph), 61.40 (CH_2), 53.05 (CH_2), 49.85 ($N(CH_3)_2$), 41.33 (NCH_3). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 29.65 (s). HRMS (APCI): calcd for $C_{29}H_{32}N_2OP$ $[M-Br^--CH_3+H]^+$ 455.2247, found 455.2240.

CRediT authorship contribution statement

Ioannis D. Kostas: Conceptualization, Methodology, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **Georgia Antonopoulou:** Methodology, Investigation. **Polydoros-Chrysovalantis Ioannou:** Methodology, Investigation, Writing – review & editing. **Eleftherios Ferentinos:** Methodology, Investigation, Writing – review & editing. **Panayotis Kyritsis:** Data curation, Writing – review & editing, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

Acknowledgments

This research is co-financed by Greece and the European Union (European Social Fund- ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning 2014-2020» in the context of the project "Aqueous Asymmetric Homogeneous Catalysis –YDAK" (MIS 5048211).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rechem.2022.100525.

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