Bulgarian Chemical Communications, Volume 49, Special Issue D (pp. 106 – 112) 2017

Atropisomeric phopshorus-decorated 1-phenyl-3,4-dihydroquinazolin-1-ium NHC precursors

R. H. Lyapchev[1], M. G. Dangalov[2], G. G. Gencheva[1], N. G. Vassilev[2], P. Y. Petrov[1]*

[1] *Department of Organic Chemistry and Pharmacognosy, Faculty of Chemistry and Pharmacy, Sofia University St. Kliment Ohridsky, James Bourchier 1, 1164 Sofia, Bulgaria*

[2] *Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, Acad. G. Bonchev street, bl. 9, 1113 Sofia, Bulgaria*

Received May 03, 2017; Revised May 22, 2017

Dedicated to Acad. Ivan Juchnovski on the occasion of his 80th birthday

Bidentate atropisomeric 3-(2-(diphenylphosphorothioyl)phenyl)-1-phenyl 3,4-dihydroquinazolinium salts as N-heterocyclic carbene (NHC) precursors were prepared using *N*-(2-(diphenylphosphorothioyl)phenyl)-2-(N-phenylformamido)benzamide as starting material.

Key words: organophosphorous compounds; N-heterocyclic carbenes; homogeneous catalysis; atropisomerism; ligand

INTRODUCTION

N-heterocyclic carbenes (NHCs) in their σ-donor abilities towards transition metals as ligands surpass phosphanes and form more stable complexes which are not prone to ligand dissociation and are excellent catalysts for hydrogenation and cross-coupling reactions [1]. One area in which NHCs still lack (due to the intristic distance between the metal center and the substituents on the N-atoms) is asymmetric catalytic transformations, where phosphanes are still indispensable. Only scarce examples of successful asymmetric induction by NHC ligands can be found in the literature [2–6]. Hereign we present our first efforts towards an atropisomeric 3,4-dihydroquinazolin concept in which dessymetrization of the quinazoline plane is achieved by an angular 3-2-(diphenylphosphoro-thioyl)phenyl or 3-2-(diphenylphosphanyl)phenyl substituent at N3 - these bidentate ligand precursors contain two (protected) donor centers - a phosphorus atom and a carbene at C2.

EXPERIMENTAL

Synthesis

All solvents and chemicals were purchased from commercial suppliers. Petroleum ether and methanol were used as received. Raney Ni was obtained immediately before use by treating 0.603 g of nickel-aluminum alloy ($NiAl_2$) with a twofold excess of degassed 15% aqueous solution of NaOH for 40 min at room temperature and subsequent washing with degassed methanol.

Dichloromethane was dried over anhydrous $CaCl_2$ and distilled. THF was distilled from sodium/benzophenone. Silica gel 0.035-0.070 mm, 60 A was used for flash chromatography. TLC on silica gel 60 F_{254} on aluminum sheets was used for monitoring of the reactions.

The NMR spectra were recorded on a Bruker Avance II+ 600 (600.13 for ^{1}H NMR, 150.92 MHz for ^{13}C NMR and 242.92 MHz for ^{31}P NMR) spectrometer with a reference TMS (85% H_3PO_4 for ^{31}P) as internal standard or chemical shifts of residue solvent peaks (δ, ppm). ^{1}H and ^{13}C NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants J (Hz), integration and identification.

*N-(2-(diphenylphosphorothioyl)phenyl)-2-(N-phenylformamido)benzamide (**2**):* 0.400 g (7.93 x 10^{-4} mol) of compound **1** were suspended in 9.5 ml THF. The reaction mixture was cooled in an ice bath, and dropwise for about 10 min were added 16 ml of mixture of equal volumes of formic acid and acetic anhydride, which had been stirred at room temperature for 2 hours. After 24 hours, another 5 ml of Ac_2O/HCOOH mixture were added. 3 hours later the acidic solution was neutralized with K_2CO_3, extracted with ethyl acetate, dried (Na_2CO_3) and purified by column chromatography on silica gel. Yield: 0.330 g (**2**) (78%) of slowly solidifying colorless oil.

* To whom all correspondence should be sent:
E-mail: *ppetrov@chem.uni-sofia.bg*

^{1}H NMR (600 MHz, $CDCl_3$, two conformers in ratio 1:0.7 at 293K) Major δ = 10.03 (s, 1H, ***NH***), 8.64 (s, 1H, ***CHO***), 7.92 (dd, *J* = 4.8, 8.0 Hz, 1H, ***H6'***), 7.74 (ddd, *J* = 1.2, 8.4, 13.8 Hz, 4H, ***o-Ar-P***), 7.58-7.53 (m, 2H, ***p-Ar-P***), 7.51-7.47 (m, 5H, ***m-Ar-P, H5'***), 7.41 (dt, *J* = 1.5, 7.7 Hz, 1H, ***H6***), 7.34 (dd, *J* = 7.5, 8.3 Hz, 1H, ***p-Ar-N***), 7.24-7.21 (m, 2H, ***m-Ar-N***), 7.20-7.19 (m, 3H, ***H8*** and ***o-Ar-N***), 7.16-7.13 (m, 1H, ***H7***), 7.07-7.04 (m, 1H, ***H4'***), 6.98 (dd, *J* = 1.3, 7.7 Hz, 1H, ***H5***), 6.77-6.72 (m, 1H, ***H3'***); Minor δ = 10.29 (s, 1H, N***H***), 8.36 (s, 1H, ***CHO***), 7.78 (dd, *J* = 4.8, 8.0 Hz, 1H, ***H6'***), 7.69 (ddd, *J* = 1.2, 8.4, 13.8 Hz, 4H, ***o-Ar-P***), 7.58-7.53 (m, 2H, ***p-Ar-P***), 7.51-7.47 (m, 6H, ***m-Ar-P, H5'*** and ***H6***), 7.34 (dd, *J* = 7.5, 8.3 Hz, 1H, ***p-Ar-N***), 7.27-7.25 (m, 1H, ***H8***), 7.24-7.21 (m, 2H, ***m-Ar-N***), 7.22-7.21 (m, 1H, ***H7***), 7.20-7.19 (m, 2H, ***o-Ar-N***), 7.07-7.04 (m, 1H, ***H4'***), 6.91 (dd, *J* = 1.3, 7.7 Hz, 1H, ***H5***), 6.77-6.72 (m, 1H, ***H3'***); ^{13}C NMR (151 MHz, $CDCl_3$, two conformers in ratio 1:0.7 at 293K) Major δ = 165.00 (***^{4}C$_{carbonyl}$***), 162.09 (***CHO***), 141.94 (***^{4}C-Ar***), 140.97 (d, *J* = 4.4 Hz, ***C1'***), 133.46 (***^{4}C-Ar***), 132.95 (d, *J* = 2.3 Hz, ***C5'***), 132.48-132.29 (***o-Ar-P***, ***p-Ar-P***, ***C3'***), 131.57 (***C6***), 130.98 (d, *J* = 86.1 Hz, ***ipso-Ar-P***), 129.54 (***p-Ar-N***), 129.13-128.88 (***m-Ar-P***, ***C7***), 127.89 (***C8***), 127.71 (***C5***), 126.27 (d, J=8.0 Hz, ***C6'***), 125.59 (***m-Ar-N***), 124.64 (d, J=12.1 Hz, ***C4'***), 124.53 (***o-Ar-N***), 123.14 (d, *J* = 85.2 Hz, ***ipso-Ar-P***); Minor δ = 164.58 (***^{4}C$_{carbonyl}$***), 161.71 (***CHO***), 140.64 (d, *J* = 4.4 Hz, ***C1'***), 139.88 (***^{4}C-Ar***), 139.39 (***^{4}C-Ar***), 137.56 (***^{4}C-Ar***), 133.73 (***^{4}C-Ar***), 133.08 (d, *J* = 2.2 Hz, ***C5'***), 132.48-132.29 (***o-Ar-P***, ***p-Ar-P***, ***C3'***), 131.78 (***C6***), 130.68 (d, *J* = 86.1 Hz, ***ipso-Ar-P***), 129.54 (***p-Ar-N***), 128.88 (***m-Ar-P***, ***C7***), 128.71 (***C5***), 128.03 (***C8***), 125.62 (d, J=8.0 Hz, ***C6'***), 125.59 (***m-Ar-N***), 124.67 (d, J=12.1 Hz, ***C4'***), 124.53 (***o-Ar-N***), 122.35 (d, *J* = 85.2 Hz, ***ipso-Ar-P***); ^{31}P{^{1}H} NMR (243 MHz, $CDCl_3$, two conformers in ratio 1:0.7 at 293K) Major δ = 40.20 (bs); Minor δ = 40.19 (bs). $C_{32}H_{25}N_2O_2PS$: calcd. C, 72.17; H, 4.73; N, 5.26; S, 6.02; found: C, 72.34; H, 4.60; N, 5.38; S, 5.89.

*3-(2-(diphenylphosphorothioyl)phenyl)-4-oxo-1-phenyl-3,4-dihydroquinazolin-1-ium perchlorate (**3**):* 0.089 g (1.67 x 10^{-4} mol) of the formamide (**2**) were dissolved in 1 ml of methanol. The resulting solution was heated to reflux and 14,3 μl of 70% perchloric acid were added. Heating was continued for 3 hours. The reaction mixture was filtered. The white precipitate was washed with methanol and DCM, and then recrystallized from methanol. Crystal suitable for X-ray analysis was obtained from methanol solution by slow evaporation of the solvent. Yield - 24 mg (**3**) (23%).

^{1}H NMR (600 MHz, DMSO-d_6) δ = 10.48 (s, 1H, ***H2***), 8.01 (t, *J* = 7.9 Hz, 1H, ***H6***), 7.96 (t, *J* = 7.7 Hz, 1H, ***H5'***), 7.90 (d, *J* = 7.7 Hz, 1H, ***H5***), 7.88-7.75 (m, 9H, ***H6'(7.84)***, ***H4'(7.77)***, ***H7(7.76)***, ***o-Ar-N***, ***m-Ar-N***, ***m-Ar-P***), 7.69 (m, *J* = 5.7 Hz, 3H, ***m-Ar-P*** and ***p-Ar-P***), 7.64-7.59 (m, 3H, ***o-Ar-P*** and ***p-Ar-N***), 7.46 (t, *J* = 7.1 Hz, 1H, ***p-Ar-P***), 7.34 (dt, *J* = 2.7, 7.6 Hz, 2H, ***o-Ar-P***), 7.27 (dd, *J* = 7.9, 13.8 Hz, 1H, ***H3'***), 7.15 (d, *J* = 8.5 Hz, 1H, ***H8***); ^{13}C NMR (151 MHz, DMSO-d_6) δ = 157.26 (***^{4}C4***), 156.05 (***C2***), 138.80 (***^{4}C-Ar***), 137.84 (***C6***), 137.67 (d, *J* = 4.1 Hz, ***^{4}C-Ar-N***), 136.01 (***^{4}C-Ar***), 134.40 (***C5'***), 133.93 (d, *J* = 8.8 Hz, ***C3'***), 133.25 (d, *J* = 13.2 Hz, ***m-Ar-P***), 133.23 (d, *J* = 13.3 Hz, ***p-Ar-P***), 132.64 (d, *J* = 11.2 Hz, ***m-Ar-P***), 132.56 (d, *J* = 12.2 Hz, ***p-Ar-P***), 132.25 (***C7***), 131.82 (d, *J* = 10.7 Hz, ***C4'***), 131.21 (d, *J* = 24.8 Hz, ***C6'***), 130.58 (***m-Ar-N***), 130.23 (d, *J* = 81.7 Hz, ***^{4}C-Ar-P***), 130.09 (d, *J* = 86.7, ***^{4}C-Ar-P***), 129.70 (d, *J* = 12.5 Hz, ***o-Ar-P***), 128.94 (, *J* = 84.7 Hz, ***^{4}C-Ar-P***), 129.13 (d, *J* = 12.0 Hz, ***o-Ar-P***), 128.70 (***C5***), 127.77 (***o-Ar-N***), 127.25 (***p-Ar-N***), 120.04 (***^{4}C-Ar***), 119.53 (***C8***); ^{31}P{^{1}H} NMR (243 MHz, DMSO-d_6) δ = 38.54 (s). $C_{32}H_{24}ClN_2O_5PS$: calcd. C, 62.49; H, 3.93; N, 4.55; S, 5.21; found: C, 62.62; H, 3.83; N, 4.59; S, 5.01.

*3-(2-(diphenylphosphorothioyl)phenyl)-4-oxo-1-phenyl-3,4-dihydroquinazolin-1-ium tetrafluoroborate (**4**):* 0.500 g (9.9 x 10^{-4} mol) of **1** and 12 ml trimethylorthoformate were heated to 80°C under argon. 0.114 g (1.09 x 10^{-3} mol) NH_4BF_4 were added in four portions for 9 hours. Heating was continued for 52 hours, then another 0.030 g (2.86x10^{-4} mol) of NH_4BF_4 were added and the heating was continued for 17 hours. The volatiles were evaporated under reduced pressure. The residue was dissolved in a minimal amount of DCM, filtered and equal volume of Et_2O was added to the solution. One half of the volume of the solution was evaporated and the resulting white crystalline precipitate was filtered, washed with ether and dried. Yield - 0.575 g (96%) white powder which can be recrystallized from acetonitrile or methanol.

^{1}H NMR (600 MHz, DMSO-d_6) δ = 10.48 (s, 1H, ***H2***), 8.01 (tddd, J=1.4, 7.3, 8.6 Hz, ***H6***), 7.96 (t, *J* = 7.7 Hz, 1H, ***H5'***), 7.90 (d, *J* = 7.7 Hz, 1H, ***H5***), 7.88-7.75 (m, 9H, ***H6'(7.84)***, ***H4'(7.77)***, ***H7(7.76)***, ***o-Ar-N***, ***m-Ar-N***, ***m-Ar-P***), 7.69 (m, *J* = 5.7 Hz, 3H, ***m-Ar-P*** and ***p-Ar-P***), 7.64-7.59 (m, 3H, ***o-Ar-P*** and ***p-Ar-N***), 7.46 (t, *J* = 7.1 Hz, 1H, ***p-Ar-P***), 7.34 (dt, *J* = 2.7, 7.6 Hz, 2H, ***o-Ar-P***), 7.27 (dd, *J* = 7.9, 13.8 Hz, 1H, ***H3'***), 7.15 (d, *J* = 8.5 Hz, 1H, ***H8***); ^{13}C NMR (151 MHz, DMSO-d_6) δ = 157.26 (***^{4}C4***), 156.05 (***C2***), 138.80 (***^{4}C-Ar***), 137.84 (***C6***),

137.67 (d, *J* = 4.1 Hz, ***^{4}C-Ar-N***), 136.01 (***^{4}C-Ar***), 134.40 (***C5'***), 133.93 (d, *J* = 8.8 Hz, ***C3'***), 133.25 (d, *J* = 13.2 Hz, ***m-Ar-P***), 133.23 (d, *J* = 13.3 Hz, ***p-Ar-P***), 132.64 (d, *J* = 11.2 Hz, ***m-Ar-P***), 132.56 (d, *J* = 12.2 Hz, ***p-Ar-P***), 132.25 (***C7***), 131.82 (d, *J* = 10.7 Hz, ***C4'***), 131.21 (d, *J* = 24.8 Hz, ***C6'***), 130.58 (***m-Ar-N***), 130.23 (d, *J* = 81.7 Hz, ***^{4}C-Ar-P***), 130.09 (d, *J* = 86.7, ***^{4}C-Ar-P***), 129.70 (d, *J* = 12.5 Hz, ***o-Ar-P***), 128.94 (, *J* = 84.7 Hz, ***^{4}C-Ar-P***), 129.13 (d, *J* = 12.0 Hz, ***o-Ar-P***), 128.70 (***C5***), 127.77 (***o-Ar-N***), 127.25 (***p-Ar-N***), 120.04 (***^{4}C-Ar***), 119.53 (***C8***); $^{31}P\{^1H\}$ NMR (243 MHz, DMSO-d_6) δ = 38.54 (s). The spectra completely match with the reported spectra of **3**. $C_{32}H_{24}BF_4N_2OPS$: calcd. C, 63.80; H, 4.02; N, 4.65; S, 5.32; found: C, 63.67; H, 4.16; N, 4.56; S, 5.46.

*2-(diphenylphosphanyl)-N-(2-(phenylamino) benzyl)aniline (**5**):* 0.650 g (1.29 x 10^{-3} mol) of **1** and 0.147 g (3.86 x 10^{-3} mol) $LiAlH_4$ were flushed with argon in a flask and 19.5 ml dry THF were added. The suspension was stirred at room temperature until hydrogen evolution ceases (about 40 minutes), then was heated for 1 hour at 83°C. 0.65 ml H_2O were added and the aqueous layer was extracted with Et_2O. The combined ether extracts were dried (Na_2SO_4) and the solvent was evaporated under reduced pressure, leaving white crystals (quantitative yield).

^1H NMR (600 MHz, $CDCl_3$) δ 7.49 (bs, 1H, NH), 7.40-7.27 (m, 13H), 7.21-7.19 (m, *2*H), 7.13 (dd, *J* = 7.4, 8.4 Hz, 2H), 6.96 (bs, 1H, NH), 6.87 (dt, *J* = 1.1, 7.4 Hz, 1H), 6.86-6.83 (m, 2H), 6.81 (t, *J* = 7.3 Hz, 1H), 6.59 (d, *J* = 8.0 Hz, 2H), 4.29 (s, 2H, CH_2); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.18 (d, *J* = 32.5 Hz), 135.26 (d, *J* = 6.9 Hz), 134.67 (s), 133.82 (d, *J* = 19.0 Hz), 132.23 (d, *J* = 10.2 Hz), 130.95 (s), 130.73 (s), 129.20 (s), 129.13 (s), 128.89 (d, *J* = 7.0 Hz), 126.23 (s), 120.73 (d, *J* = 13.7 Hz), 118.27 (s), 117.20 (s), 53.58 (s);$^{31}P\{^1H\}$ NMR (243 MHz, $CDCl_3$) δ (-23.32). $C_{31}H_{27}N_2P$: calcd. C, 81.20; H, 5.94; N, 6.11; found: C, 80.99; H, 5.77; N, 6.20.

*Diphenyl(2-((2-(phenylamino)benzyl)amino) phenyl)phosphine sulfide (**7**):* 0.591 g (1.29 x 10^{-3} mol) of **5** were dissolved in 20 ml DCM and 0.050 g (1.55 x 10^{-3} mol) of finely powdered sulfur were added. The suspension was stirred for 24 hours at room temperature, then the solvent was removed under reduced pressure and the crude product was purified by flash chromatography (hexanes:DCM= 2:1). Yield 0.583 g (92%) of white powder.

^1H NMR (600 MHz, DMSO-d_6) δ 7.70-7.64 (m, 6H), 7.60-7.58 (m, 4H), 7.42 (bs, 1H, NH), 7.32-7.29 (m, 1H), 7.18 (dd, *J* = 7.5, 8.4 Hz, 2H), 7.15 (bs, 1H), 7.11 (ddd, *J* = 2.0, 6.3, 8.2 Hz, 1H), 6.84-6.80 (m, 3H), 6.78-6.75 (m, 3H), 6.62-6.59 (m, 2H), 6.57 (dt, *J* = 1.8, 7.5 Hz, 1H), 4.25 (d, *J* = 5.5 Hz, 2H, CH_2); ^{13}C NMR (151 MHz, DMSO-d_6) δ 150.45 (d, *J* = 5.6 Hz), 144.88 (s), 140.69 (s), 133.59 (s), 132.52 (d, *J* = 9.4 Hz), 132.19 (d, *J* = 2.2 Hz), 131.90 (d, *J* = 10.7 Hz), 130.97 (d, *J* = 85.1 Hz), 129.84 (s), 129.12 (s), 128.97 (d, *J* = 12.4 Hz), 127.44 (s), 127.16 (s), 122.04 (s), 120.14 (s), 119.13 (s), 116.20 (s), 116.01 (d, *J* = 12.5 Hz), 112.04 (d, *J* = 7.4 Hz), 42.50 (s); $^{31}P\{^1H\}$ NMR (243 MHz, DMSO-d_6) δ (38.61). $C_{31}H_{27}N_2PS$: calcd. C, 75.89; H, 5.55; N, 5.71; S, 6.53; found: C, 75.97; H, 5.38; N, 5.62; S, 6.71.

*3-(2-(diphenylphosphorothioyl)phenyl)-1-phenyl-3,4-dihydroquinazolin-1-ium tetrafluoroborate (**8**):* 0.100 g (2.04 x 10^{-4} mol) of **7**, 0.024 g (2.24 x 10^{-4} mol) NH_4BF_4 and 4 ml trimethylorthoformate were heated under argon for 5 hours at 80°C. The volatile components were removed under reduced pressure. The residue was dissolved in a minimal amount of DCM, filtered and precipitated with Et_2O as described for **4**. Yield - 0.113 g (94%) of white powder.

^1H NMR (600 MHz, DMSO-d_6) δ 8.93 (s, 1H), 8.01 (ddd, *J* = 1.1, 4.9, 7.9 Hz, 1H), 87.93 (tt, *J* = 1.4, 7.7 Hz, 1H), 7.87-7.84 (m, 4H), 7.70-7.64 (m, 5H), 7.57 (bs, 1H), 7.50-7.48 (m, 3H), 7.46 (bs, 1H), 7.28-7.24 (m, 2H), 7.19 (ddd, *J* = 1.4, 7.9, 14.3 Hz, 1H), 6.93-6.91 (m, 1H), 6.49-6.46 (m, 1H), 5.30 (d, *J* = 14.5 Hz, 1H), 4.56 (d, *J* = 14.5 Hz, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 155.68 (s), 142.22 (d, *J* = 3.6 Hz), 136.18 (s), 134.43 (s), 133.87 (d, *J* = 9.3 Hz), 132.77 (d, *J* = 35.1 Hz), 131.95 (s), 131.83 (d, *J* = 77.1 Hz), 130.78 (d, *J* = 11.0 Hz), 130.56 (s), 130.46 (s), 130.19 (d, *J* = 6.3 Hz), 129.65 (s), 129.23 (s), 128.24 (s), 127.18 (d, *J* = 11.6 Hz), 118.64 (s), 116.32 (s), 51.11 (s); $^{31}P\{^1H\}$ NMR (243 MHz, DMSO-d_6) δ (38.36). $C_{32}H_{26}BF_4N_2PS$: calcd. C, 65.32; H, 4.45; N, 4.76; S, 5.45; found: C, 65.55; H, 4.26; N, 4.67; S, 5.59.

*3-(2-(diphenylphosphanyl)phenyl)-1-phenyl-3,4-dihydroquinazolin-1-ium tetrafluoroborate (**6**):* 0.200 g (4.36 x 10^{-4} mol) of **5**, 0.055 g (5.23 x 10^{-4} mol) NH_4BF_4 and 4 ml trimethylorthoformate were heated at 85°C for 15 hours under argon. The volatile components of the mixture were removed under reduced pressure. The residue was dissolved in 5 ml of DCM, 35 ml of Et_2O were added and after 20 minutes of stirring the resulting white precipitate was filtered and washed with ether. Yield: 0.192 g (79%) white powder.

^1H NMR (600 MHz, DMSO-d_6) δ 9.03 (d, *J* = 2.3 Hz, 1H), 7.84 (ddd, *J* = 0.8, 4.2, 8.0 Hz, 1H),

7.69 (dt, *J* = 1.3, 7.7 Hz, 1H), 7.67-7.64 (m, *J* = 2.8 Hz, 3H), 7.57 (dt, *J* = 0.8, 7.6 Hz, 1H), 7.46-7.27(m, *J* = 7.9 Hz, 14H), 7.17 (dd, *J* = 0.9, 7.5 Hz, 1H), 6.96 (ddd, *J* = 1.2, 3.7, 7.7 Hz, 1H), 6.51 (dd, *J* = 0.7, 8.1 Hz, 1H), 5.30-4.93 (bs, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 154.56 (s), 143.00 (d, *J* = 19.9 Hz), 136.01 (s), 134.66 (d, *J* = 16.8 Hz), 133.87 (d, *J* = 20.8 Hz), 133.67 (s), 133.46 (d, *J* = 8.7 Hz), 132.20 (s), 131.17 (s), 130.69 (d, *J* = 26.4 Hz), 130.55 (s), 130.02 (s), 129.37 (s), 129.24 (d, *J* = 7.5 Hz), 128.45 (s), 127.35 (s), 127.26 (s), 50.70 (d, *J* = 5.6 Hz). ^{31}P{^{1}H} NMR (243 MHz, DMSO-d_6) δ (-16.52).$C_{32}H_{26}BF_4N_2P$: calcd. C, 69.08; H, 4.71; N, 5.04; found: C, 68.97; H, 4.81; N, 5.11.

*Synthesis of **6** from **8**:* 0.070 g (1.19x10^{-4} mol) of **8**, freshly prepared Raney nickel and 3 ml of methanol were stirred for 24 hours at room temperature. The reaction mixture was diluted with DCM, filtered through celite and the solvents were removed under reduced pressure. The residue is washed with Et_2O and dried. Yield 0.023 g (35%) of white powder.

X-ray crystallography

A colorless plate crystal of **3** with the size 0.07 x 0.22 x 0.45 was selected for geometry and intensity data collection with a Bruker SMART X2S diffractometer using a monochromatic Mo-Kα (κ=0.71073 Å) microfocus source with a Bruker APEX-II CCD detector at 300.15 K. A Bruker SMART APEX II system was applied for data collection, cell refinement and data reduction [7]. The intensities were measured by ω scan mode for θ ranges 2.30 to 22.44°. 2480 reflections were treated as observed (I> 2σ(I)). Data were corrected for Lorentz, polarisation and absorption factors. The structure was solved by direct method using SHELXS97 [8, 9]. All non-hydrogen atoms of the molecule were located in the best electron-density map. To refine the structure the program SHELXL97, version 2014/7 implemented in program OLEX2 was used [9, 10]. Full-matrix least-squares refinement was carried out until the final refinement cycles converged to an R = 0.0564 and wR(F^2) = 0.0933 for the observed data. Residual electron densities ranged from $-0.334<\Delta\rho<0.439$ eA^{-3}. The OLEX software was applied to prepare the materials for publication. The crystallographic data are summarized in Table S1, and the respective bond lengths and angles are shown in Table S2 and S3. ORTEP diagram and crystal packing for compound **3** are shown in Fig. 1 and Fig. 2. CCDC-1403455 contains the supplementary crystallographic data for the compound **3** [11]. The diagrams were prepared using Mercury version 3.3 [12].

RESULTS AND DISCUSSION

It is known that for asymmetric induction in a reaction to occur, there must be an intermediate or a transition state in which a possible creation of a bond (be it on a face, a side or on/in a conformation) must be favored. Most transition metal catalyzed reactions proceed through cis-arranged reactive ligands/species, therefore bidentate cis-binding spectactor ligands that are chiral, are desirable in the field of asymmetric homogeneous catalysis. Guided by these fundamental principles we designed a concept bidentate ligand structure that have the potential for atropisomerism, combined with the beneficial properties of both an NHC and a phosphane donors.

Hereign we present the synthesis and structures of 3-(2-(diphenylphosphorothioyl)phenyl)-1-phenyl 3,4-dihydroquinazolinium and 3-(2-(diphenylphosphanyl)phenyl)-1-phenyl 3,4-dihydroquinazolinium salts (Fig. 1).

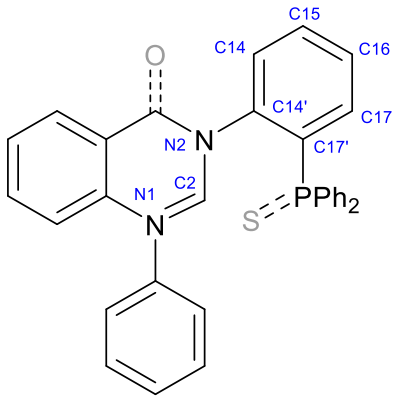


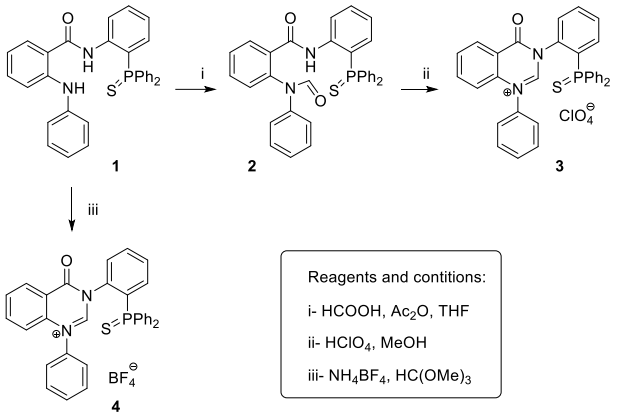
Fig. 1. General structure of target compounds.

These NHC precursors possess atropisomerism due to the chiral N2-C14' axis that connects the quinazoline plane with the C_6H_4 (C14'-C17') one. The 4-oxo substituent on the quinazoline combined with the bulky PPh_2 provide steric hindrance to prevent easy rotation around the chiral axis and therefore - interconversion of the rotamers.

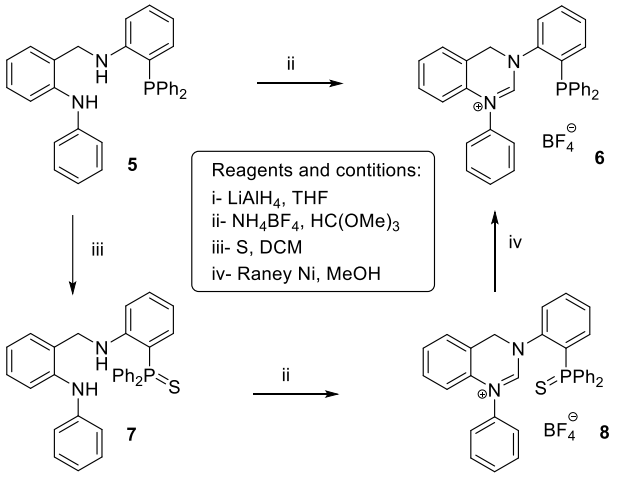
Synthesis

Starting from *N*-(2-(diphenylphosphorothioyl) phenyl)-2-(phenylamino)benzamide **1**, which we have reported in a previous communication [13], two types of 1-phenyl-3,4-dihydroquinazolinium

salts - 4-oxo (**3** and **4** on Scheme 1) and 4-H (**6** and **8** on Scheme 2) were synthesized.



Scheme 1. Synthesis of **3** and **4**.



Scheme 2. Synthesis of **5** - **8**.

Compound **1** was cleanly converted to the respective formamide **2** using HCOOH/Ac_2O mixture[14]. This product was cyclized in boiling methanol in the presence of excess $HClO_4$ [15] to the desired 3-(2-(diphenylphosphorothioyl)phenyl)-4-oxo-1-phenyl-3,4-dihydroquinazolinium perchlorate (**3**). An alternative simpler approach to 3,4-dihydroquinazolinium salts was also tested, by reacting **1** with trimethyl orthoformate and ammonium tetrafluoroborate [16] in one step, thus eliminating the steps of synthesis and purification of the formamide **2**. This reaction, although time consuming, proved to be more straightforward and high yielding and was adopted as a standard method in the following synthetic steps.

The amido group in **1** opens opportunities for the synthesis of 1-phenyl-3,4-dihydroquinazolinium salts that have different than in **3** and **4** rotation barriers. To remove the oxo-group, **1** was reacted with LAH to the diamine **5**. This reaction also led to deprotection of the phosphorus atom. The resulting **5** was either directly cyclized to **6** or the phosphorus atom in it was protected, then the resulting phosphorothioate **7** was converted to **8**. Alternatively, **6** could be prepared from **8** by deprotecting the phosphane moiety with the aid of Raney Ni.

X-ray crystallography

Crystal data collection and refinement parameters are presented in Table S1. The crystal structure of the compound **3** consists of a 3-(2-diphenylphosphorothioyl)-4-dihydro-quinazolin-1-ium) cation neutralized with a perchlorate anion. An ORTEP view of the compound with atomic labeling is shown in Fig. 2. The overall molecular geometry of the compound, including bond distances and angles has a normal range [17]. The deviation from the least-squares aromatic plane of the fused rings in the 4-quinazolinone moiety is ~2,3°. The bond lengths C4-N2 (1.433(4) Å), C2-N1 (1.319(4)Å) and N1-C8' (1.425(4)Å) prove the electronic density delocalization in the dihydroquinazolin-1-ium ring and the C-O distance of 1.205(5) Å are consistent with a double bond. In the tertiary phosphine oxide residue, the phosphorus atoms possess distorted tetrahedral arrangement with bond angles range between 105.80(1) – 113.21 (1)° and relatively delocalized P=S double bonds (1.955(1)Å. The aromatic rings of this part of the molecule are inclined towards each other with 107.49° and 100.28°.

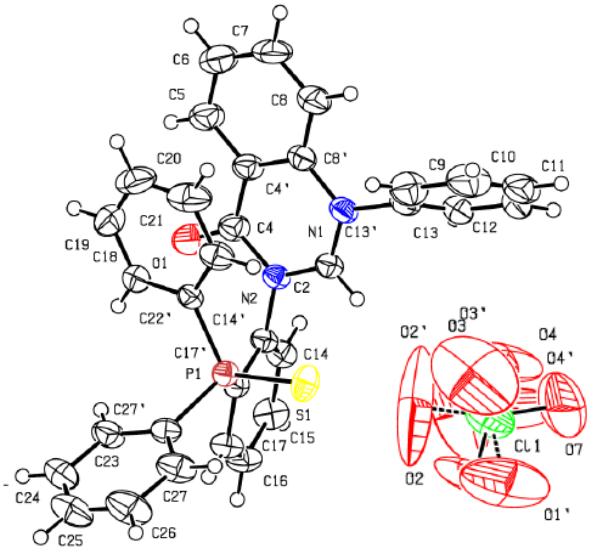


Fig. 2. ORTEP drawing of molecular structure of the compound **3**. The thermal displacement ellipsoids are drawn at the 50% probability.

Some groups in chemical compounds exhibit disorder problems very often and the perchlorate anions are amongst them. In this structure, the all four oxygen atoms in the perchlorate anion are found disordered over two set of sites with occupancy ratio 0.545:0.455.

Packing view of the molecule in the unit cell viewed down the b-axis is shown in Fig. 3. The unit cell consists of two enantiomeric molecules located opposite with parallel 4-quinazolinone moieties.

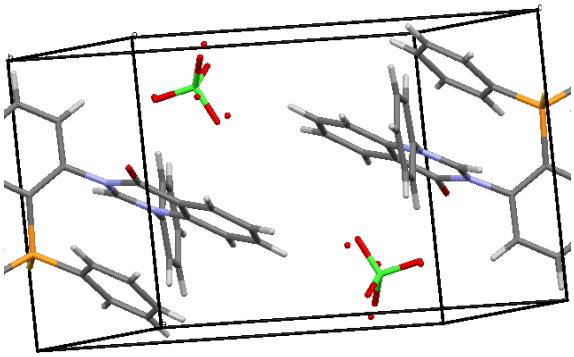


Fig. 3. View of the compound **3** cell packing.

Compound **3** crystallizes in the centrosymmetric triclinic *P-1* space group. The bond lengths and angles are shown in Tables S2 and S3.

CONCLUSION

Atropisomeric 3-(2-(diphenylphosphorothioyl) phenyl)-1-phenyl 3,4-dihydroquinazolinium (**3**, **4** and **8**) and 3-(2-(diphenylphosphanyl)phenyl)-1-phenyl 3,4-dihydroquinazolinium (**6**) salts were designed and successfully synthesized by means of straightforward synthetic procedures. Structure studies of **3** reveals the existence of two well defined expected axial enantiomers. Fine tuning of the rotational barriers is possible by modifying the fourth position of the dihydroquinazolinium ring system. The synthesized compounds are precursors to chiral NHC and P-NHC ligands. Undergoing studies will reveal the exact interconversion barriers of the newly synthesized compounds and test their properties as ligands for transition metals.

Acknowledgements: *The authors acknowledge the support by the Horizon 2020 program of the European Commission (project Materials Networking, ref. no. 692146) and the Research Fund of Sofia University (project 093/08.05.2014).*

Electronic Supplementary Data available here.

REFERENCES

1. M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature*, **510**, 485 (2014).
2. L. G. Bonnet, R. E. Douthwaite, *Organometallics*, **22**, 4187 (2003).
3. F. Wang, L.-J. Liu, W. Wang, S. Li, M. Shi, *Coord. Chem. Rev.*, **256**, 804 (2012).
4. M. T. Powell, D.-R. Hou, M. C. Perry, X. Cui, K. Burgess, *J. Am. Chem. Soc.*, **123**, 8878 (2001).
5. A. Schumacher, M. Bernasconi, A. Pfaltz, *Angew. Chem. Int. Ed.*, **52**, 7422 (2013).
6. N. Ortega, S. Urban, B. Beiring, F. Glorius, *Angew. Chem. Int. Ed.* **51**, 1710 (2012).
7. Bruker (2012). SADABS. Bruker AXS Inc., Madison, Wisconsin, USA; Bruker (2013). APEX2 and SAINT. Bruker AXS Inc., Madison, Wisconsin, USA.
8. G. M. Sheldrick, *Acta Cryst. A*, **64**, 112 (2008).
9. G. M. Sheldrick, *Acta Cryst.C*, **71**, 3 (2015).
10. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. Howard, H. Puschmann, *J. Appl. Cryst.*, **42**, 339 (2009).
11. The crystallographic data for **3** were deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 1403455. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; tel: +441223762910; fax: +441223336033; e-mail: deposit@ccdc.cam.ac.uk; http://www.ccdc.cam.ac.uk/deposit.
12. C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidock, L. Rodriguez-Monge, R. Taylor, J. Van de Streek, P. A. Wood, *J. Appl. Crystallogr.*, **41**, 466 (2008).
13. R. H. Lyapchev, M. G. Dangalov, N. G. Vassilev, P. Y. Petrov, *Bulg. Chem. Commun.*, **49**, Special Edition B, 50 (2017).
14. A. Furstner, M. Alcarazo, V. Cesar, C. W. Lehmann, *Chem. Commun.*, 2176 (2006).
15. N. I. Chernobrovin, Y. V. Kozhevnikov, G. E. Morozova, *Pharm. Chem. J.*, **26**, 245 (1992).
16. J. Zhang, X. Qin, J. Fu, X. Wang, X. Su, F. Hu, J. Jiao, M. Shi; *Organometallics*, **31**, 8275 (2012).
17. P. W. Coddind, K. A. Kerr, *Acta Cryst. B*, **34**, 3785 (1978).

АТРОПИЗОМЕРНИ ФОСФОР ЗАМЕСТЕНИ 1-ФЕНИЛ-3,4-ДИХИДРОХИНАЗОЛИН-1-ИЕВИ NHC ПРЕКУРСОРИ

Р. Хр. Ляпчев[1], М. Г. Дангалов[2], Г. Г. Генчева[1], Н. Г. Василев[2], П. Й. Петров[1]*

[1] *Катедра "Органична химия и фармакогнозия", Факултет по химия и фармация, Софийски университет „Св. Климент Охридски", бул. „Джеймс Баучер" 1, София 1164, България*
[2] *Институт по органична химия с Център по фитохимия, Българска академия на науките, ул. Акад. Г. Бончев, бл. 9, 1113 София, България*

Постъпила на 03 май 2017 г.; Коригирана на 22 май 2017 г.

(Резюме)

Бидентатни атропизомерни 3-(2-(дифенилфосфоротиоил)фенил)-1-фенил 3,4-дихидрохиназолиниеви соли като прекурсори на N-хетероциклени карбени са синтезирани с използване на *N*-(2-(дифенил-фосфоротиоил)фенил)-2-(фениламино)бензамид.