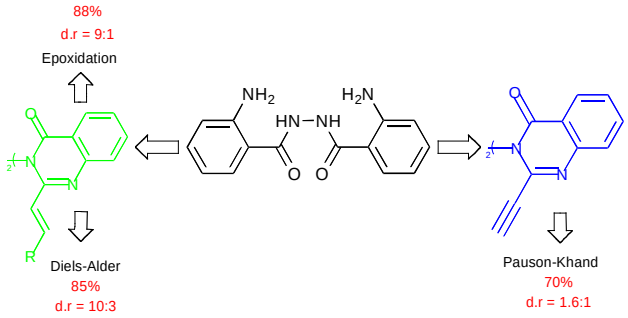


Synthesis and Substrate-Controlled Reactions of 2,2'-Unsaturated Biquinazolinones.

Fabrizio Pertusati, [a*] **Eva Nutz** [c]**, Benson M. Kariuki** [c] **and Michael P. Coogan**[b]

[a] School of Pharmacy and Pharmaceutical sciences, Cardiff University, King Edwards VII Avenue, Cardiff, CF10 3AT, Wales, UK; [b] Department of Chemistry, Lancaster University, Lancaster, LA1 4YB, UK; [c] School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff, CF10 3AT, Wales, UK

ABSTRACT: A series of BiQuinazolinones bearing either double or triple bonds in their lateral chains have been synthesized. These compounds were then subjected to substrate-controlled reactions such as Diels-Alder, epoxidation and Pauson-Khand reactions. The stereoselective outcome observed in these transformations is very promising for the future application of BiQuinazolinones as chiral auxiliaries.

Keywords: BiQuinazolinone, Atropisomers, Diastereoselectivity, Chiral induction.

1. Introduction

Chiral auxiliaries and templates are effective tools for the asymmetric synthesis of homochiral molecules.[1] Most chiral auxiliaries are small heterocyclic compounds, which rely on sterically demanding functional groups to control the conformation of their ring systems. Under ideal circumstances, the conformation of an auxiliary should be constrained to ensure that its prochiral centre reacts with a reagent via diastereoisomeric transition states, which are sufficiently different in energy to ensure that only a single diastereoisomer is formed as product. As remarkable auxiliaries and scaffolds, chiral biaryls are widely used in a large number of efficient stereo-differentiating reactions.[2]

Atropisomers, which arise from restricted rotation in bonds to aromatic rings, can be seen as chiral modifications of the aromatic rings themselves. The famous and powerful atropisomeric phosphine ligands such as BINAP are in essence modifications to triphenylphosphine.

Enantiomerically pure non-biaryl atropisomers have found uses in different asymmetric syntheses, and the most well studied class to date are anilides (Figure 1).

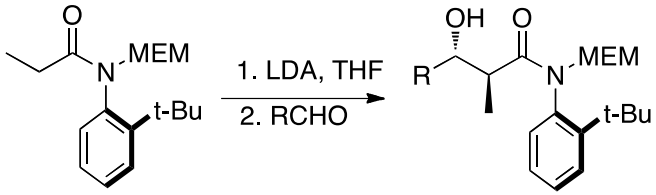


Figure 1 Stereoselective aldol reaction of atropisomeric benzamide.

These atropisomeric amides were obtained in pure enantiomeric form by the Simpkins[3,4] group and employed by others as chiral auxiliaries to different asymmetric transformations such as iodolactonization,[5] and cycloadditions.[6] Clayden and co-workers have demonstrated that the aldehydic group on atropisomeric naphthimides stereoselectively undergo nucleophilic addition from a variety of lithiated substrates (Fig. 2).[7]

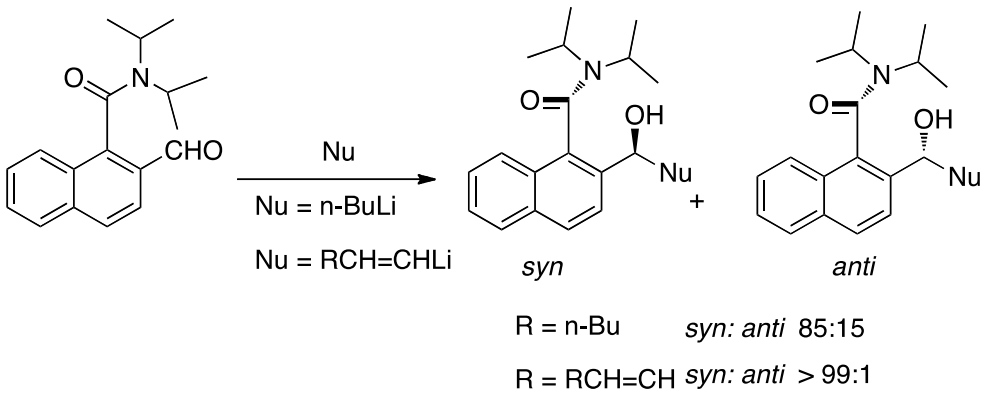


Figure 2 Nucleophilic addition of lithiated compounds to aldehydic groups on atropoisomeric naphthimides

In continuation of previously conducted studies with symmetrical 3,3′-biquinazoline-

4,4′-diones[8-10] and unsymmetrical 2,2′-disubstituted-3,3′-biquinazoline-4,4′-diones,[11] we have recently reported a facile route for the synthesis of 2-substituted bisquinazolinones incorporating a chiral center into one or both of their lateral chains.[12] In all these studies we have unambiguously proved that the BiQs can have high barriers to rotation around the N–N bond and thus are able to form stable atropisomers. In particular 2,2'-H,H'-3,3'-biquinazoline-4,4'–dione was found to have a minimum rotational barrier of 96 kJ mol^{-1}, whereas the 2-chirally substituted BiQs were generated as mixtures of diastereoisomers. Both results confirm the atropoisomeric nature of the BiQ scaffold.

The synthesis of these axially chiral bis-heterocycles, was accomplished either via condensation of 2-substituted-3-aminoquinazolinones and 4H-3,1-benzoxazin-4-one or by an acylation-dehydration sequence of bisanthraniloyl hydrazine.[8-10]

Given our interest in the preparation and application of this class of molecule to substrate controlled asymmetric reactions, in this paper we report the synthesis of symmetrical and unsymmetrical biquinazolinones bearing prochiral unsaturation, and the preliminary results on their application in selected asymmetric reactions.

In this scenario, double and triple bond containing moieties appeared immediately to us to be very appealing functionalities, due to the fact that they can be asymmetrically transformed into a variety of other functional groups like e.g. epoxides, Diels-Alder and Pauson-Khand adducts (Figure 3).

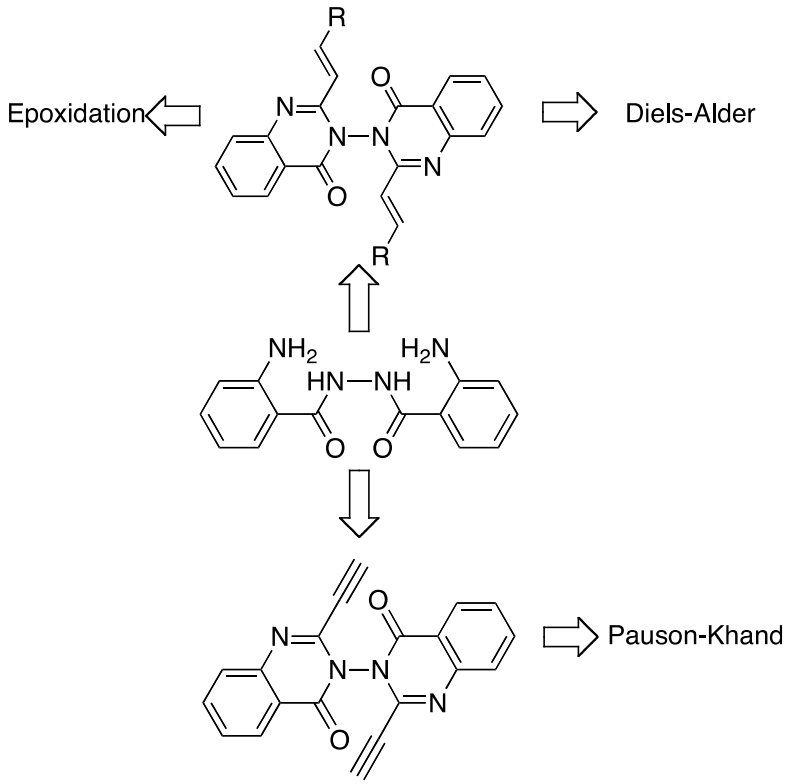
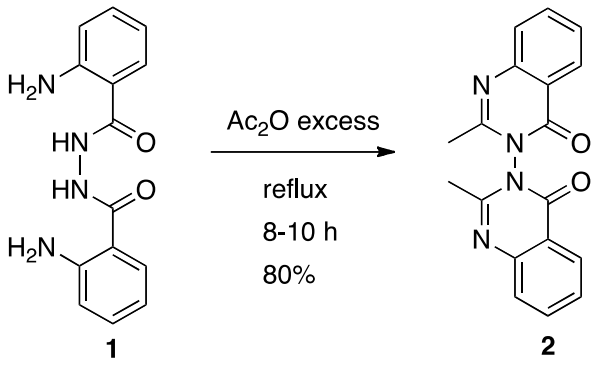


Figure 3 Strategies for the synthesis and substrate-controlled reactions of 2,2'-unsaturated biquinazolinones.

2. Results And Discussion

2.1 Synthesis of 2,2'-unsaturated BiQs. In our experience, condensation of 2-substituted-3-aminoquinazolinones with 4H-3,1-benzoxazin-4-one is a synthetic methodology quite sensitive to the steric hindrance of the functional group present in the lateral chains of the aminoquinazolinone. Therefore, we envisaged that modification of an alkyl group of the bisquinazolinone could be a suitable approach to access a variety of new structures.

Symmetrical 2,2-dimethylbiquinazolinone **2** was easily synthesized on a multigram scale, from bisanthraniloyl hydrazine **1** and acetic anhydride (Scheme 1).[13,14] The desired product **2**, was collected in 80% yield by simple filtration and purified by recrystallization from toluene.

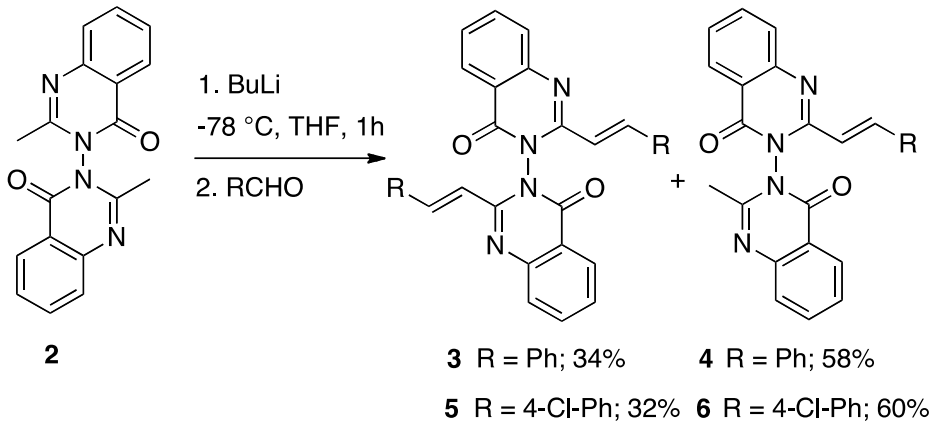


Scheme 1 Synthesis of 2,2'-dimethyl BiQs 2

With **2** in hand, we started to investigate the preparation of the 2,2'-bis-styrylbiquinazolinone. Initially, we envisioned that acid catalysed condensation of carbonyl compounds with 2,2'-dimethyl-3,3'-biquinazoline-4,4'-dione (**2**) would be a feasible way to introduce an alcohol group, which could be dehydrated to the corresponding styryl derivative. All attempts to prepare styryl BiQs via acid catalysed condensation of benzadehyde with **2** gave the desired product in only very low yield. Formation of an intractable and insoluble material during this reaction could be interpreted as a catalysed formation of benzaldehyde polymers (or copolymer with styryl derivative) or oligomers.[15]

The poor results obtained forced us to abandon this route and to turn our attention toward alternative strategies. From an extensive literature screening, it arose that "monomeric" methyl or ethyl substituted quinazolinone and 3-aminoquinazolinones are easily functionalized by metalation with organometallic bases and further reaction with electrophiles.[16-18] We therefore envisioned the possibility to apply this strategy to our advantage. Addition of a 2.5 M butyl lithium solution to a -78 °C solution of 2,2'-dimethyl-3,3'-biquinazolin-4,4'-one (**2**) in THF provided the lithiated species as indicated from the resulting bright red solution, followed by formation of a bright red precipitate. When benzaldehyde was added an almost immediate reaction occurred. Workup of the resulting solution afforded a bright yellow crystalline solid. ^{1}H-NMR

spectroscopic analysis (two sets of doublets at 6.42 and 8.05 ppm and an extra singlet at 2.3 ppm), and APCI mass analysis (two peaks, at m/z 495 [M+1] and at m/z 407 [M+1]) of the crude reaction mixture suggested the presence of structures **3** and **4**, which were indeed isolated by column chromatography on silica gel (ethyl acetate/ hexane 1:3) in 34% and 58% yield respectively. By the same procedure we were also able to synthesize the p-chlorostyryl derivatives **5** (32% yield) and **6** (60% yield) (Scheme 2). When the reaction was carried out under the same conditions but in the presence of different bases such as LDA, LiHMDS and KHMDS, the corresponding styryl derivatives were obtained but in lower yield when compared with those carried out with nBuLi.



Scheme 2 Synthesis of 2,2'-styryl 3-4, and *p*-chlorostyryl BiQs 5-6

In contrast with literature results, which for LDA metalation of monomeric 2-methyl-3-substituted quinazolinones[19] and further reaction with benzaldehyde, always report the formation of the corresponding alcohol derivative as major product (and only small amount of styryl derivative detected), reaction between the lithiated biquinazolinone **2** and benzaldehyde lacks of the isolation of the hydroxyl derivative. In our case, spontaneous dehydration occurred because the increase in the conjugation of the double bond with the quinazolinone rings. The formation of the mono-styryl derivatives **4** can instead be tentatively explained invoking steric reasons which may operate after the first double bond is formed, hampering to some extent the attack of a second molecule of

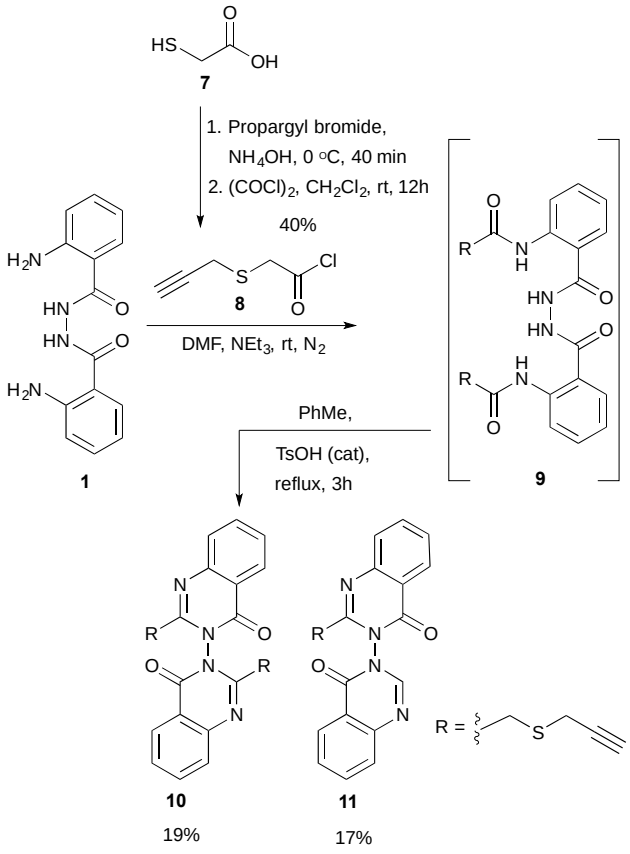
benzaldehyde to the lithiated species on the second ring, although the operation of a retro-aldol mechanism cannot be excluded.[18] Crystals of **3**, suitable for X-ray diffraction studies, were easily obtained by slow evaporation of an acetonitrile/methanol solution. The structure of this compound clearly showed the chirality around the N-N bond. One of the two quinazolinone rings is planar with the side chain parallel to the ring plane, meanwhile the other ring is in an almost perpendicular position relative to the other half of the molecule (see SI, Fig. S1).

To further confirm the atropoisomeric nature of the BiQ scaffold, compound **3** was treated with 2 equivalents of (+)-CSA in refluxing toluene for 16 hours. After this period, ^{1}H-NMR spectroscopic analysis of this mixture revealed two sets of signals for the double bond, thus confirming the presence of two diastereisomeric salts (see SI, Fig. S2). To investigate a possible asymmetric transformation, deracemization experiments on **3** were attempted. Unfortunately, heating the two diastereisomeric salts either at 80°C (in toluene) or at 110°C (in p-Xylene) for 48 hours, returned the two diastereoisomeric salts unmodified. Heating **3** at 140 °C was also unsuccessful, and alongside the two diastereoisomeric salts (in a 1:1 ratio), decomposition was observed.

With unsaturated BiQs in hand we attempted to introduce a triple bond on the quinazolinone scaffold by the addition-elimination of a halogen to the double bond. Bromination of **3** proceeded smoothly affording the tetra-bromo derivative as confirmed by APCI mass analysis (peak at *m/z* 824 [M+1]). However, this compound proved to be quite unstable, due to rapid loss of bromine. It decomposes to an inseparable mixture of side products, and thus could not be isolated with adequate purity sufficient for a proper characterization.

Introduction of an alkyne moiety was instead successfully accomplished via treatment of hydrazine **1** with propargylic thioether **8** under the conditions outlined in Scheme 3. Compound **8** was prepared in two steps starting from commercially available

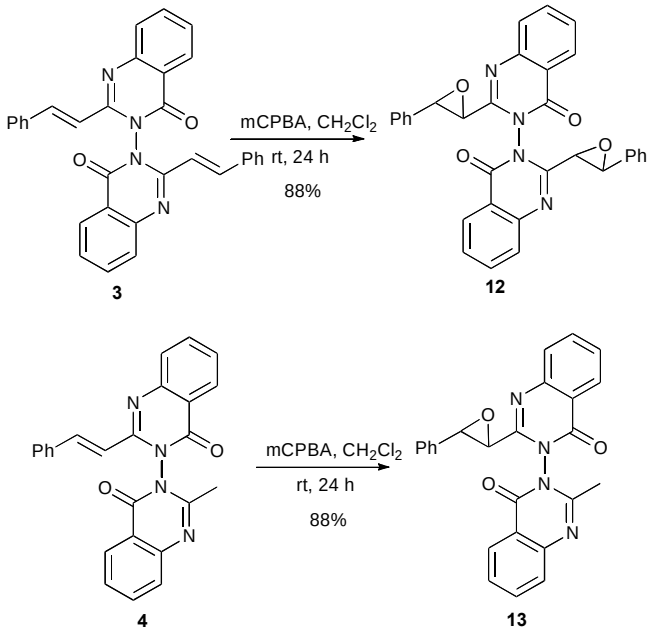
mercaptoacetic acid **7** according to a literature procedure.[20] The desired alkynyl BiQ **10** was isolated in 19 % yield after column chromatography, along with the monosubstituted BiQ **11**, recovered in 17% yield.



Scheme 3 Synthesis of 2,2'-bis-thio-alkynyl BiQs 10 and 11.

The formation of **11** can be explained by the formation of the Vilsmeier reagent from DMF and the acid chloride **8**, which undergoes the attack of the nitrogen of the hydrazine **1** generating after dehydration the corresponding BiQ **11**, as we have previously observed.[9] The crystal structure of compound **10** confirmed its atropisomeric nature (see SI, Fig. S2).

2.2 Stereoselective reactions of unsaturated BiQs. With different examples of unsaturated Biqs in hand, we then explored the diastereoselective modification of these structures. In pursuing our goal of using the BiQ scaffold in substrate-controlled stereoselective reactions, the investigation of the diastereoselective epoxidation of compounds **3** and **4** was performed (Scheme 4).

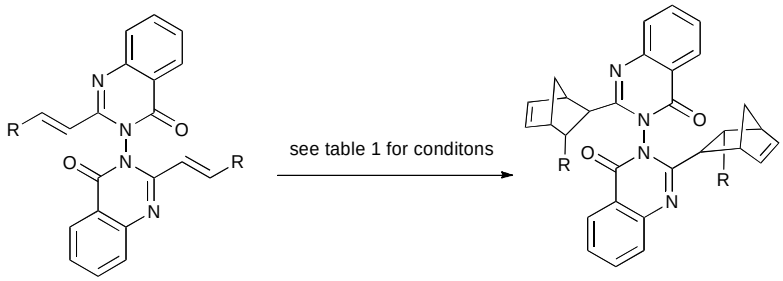


Scheme 4 Epoxidation reactions of BiQs 3 and 4.

From a choice of oxidizing agents commonly employed in epoxidation reactions, 3-chloroperbenzoic acid (*m*-CPBA) was selected. In a typical procedure, the bis-styryl derivative **3** was dissolved in dichloromethane and *m*-CPBA added portion-wise over a period of 30 minutes. The resulting mixture was then stirred at room temperature for 24 hours. In the absence of stereocontrol, three diastereoisomers in a 1:2:1 ratio are expected owing to the formation of four new chiral centres. From the ^{1}H-NMR spectrum of the crude reaction mixture, two major isomers were detected in a 9:1 ratio, confirming that this reaction proceed with high diastereoselectivity. Traces of a third diastereoisomer were barely detectable in the ^{1}H-NMR spectrum of the crude sample. The major diastereoisomer **12** was obtained in 88% yield after crystallization from ethanol. A possible explanation of the high diastereoselectivity observed is that the oxidant might coordinate to the carbonyl group of the quinazolinone ring by hydrogen bonding in such a way that the oxygen can be delivered preferentialy on one face of the double bond depending on the nature of the chiral axis. In addition the rotation around the single bond between the alkene and the quinazolinone ring (-CH=CH-CH=N) seems

to be hindered by the second styryl moiety and thus one of the alkenes remains on the more "exposed face" to the peroxy acid and hence undergoes epoxidation more easily. It is then probable that *m*-CPBA approaches the double bond from that face, which appears to be virtually free from any steric interaction. It is noteworthy that the epoxidation of the mono-styryl derivative **4** in CH_2Cl_2 at room temperature with *m*-CPBA gave a mixture of two diastereoisomers with a poor diastereoselectivity (4:1 ratio). In this case it is highly probable that the methyl group is not bulky enough to allow differentiation between the two faces of the double bond. Any attempts to improve the diastereoselectivity outcome of the epoxidation of **3** and **4** varying the temperature or replacing the solvent were unsuccessful.

Delighted by the positive asymmetric induction in the diastereoselective epoxidation of the prochiral double bond, a study of the stereochemical outcome of the Diels-Alder reaction between the prochiral double bond in compound **5** and cyclopentadiene was carried out (Scheme 5).



Scheme 5 Diels-Alder reaction with BiQ 5.

The first experiments were conducted reacting the bis-styryl derivative **3** with a large excess (20 equivalents) of freshly prepared cyclopentadiene in toluene in the absence of catalyst, either at room temperature or at reflux. All these attempts were unsuccessful (Table 1, Entries 1 and 2). No sign of the desired products was observed by ^{1}H-NMR spectroscopic analysis of the crude material, and only unreacted **3** and cyclopentadiene

dimer were recovered. Moreover, when the reaction was carried out at reflux, partial polymerization of **3** occurred. Since the cycloaddition reaction was reluctant to proceed without catalyst we repeated the experiment in the presence of either 10% $AlCl_3$ or 10% $Cu(OTf)_2$ at room temperature. However, toluene proved an inappropriate solvent for this reaction (Table 1, Entries 3 and 4), and only when it was replaced with CH_2Cl_2 was the formation of Diels-Alder adducts observed. In particular, with 10% $Cu(OTf)_2$ as catalyst, two main adducts (**14a** and **14b**), were obtained in 80% overall yield (Table 1, Entry 5) with a diastereoisomeric ratio of 10:3 along with only traces of two other adducts (**14c** and **14d**) as estimated from ^{1}H NMR spectroscopy of crude mixture (Figure 4)

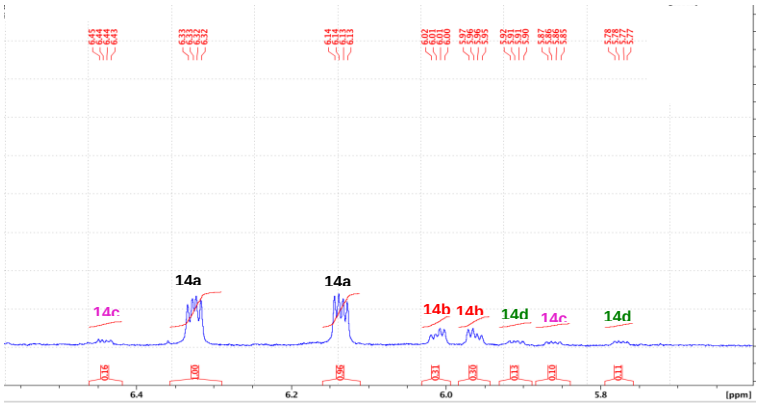


Figure 4 Expansion of the ^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of the crude reaction mixture between compound 3 and cyclopentadiene.

A slightly increased yield (85%) was obtained under the same set of conditions, with 10% copper triflate, but no improvement in the diastereoselectivity ratio was observed (Table 1, Entry 6). Major diastereoisomer **14a** was isolated in 58% yield by repetitive crystallization from acetonitrile/methanol mixture. Attempts to reduce the amount of Lewis acid failed to give the products in good yield and with any significant change in the diasteroisomeric ratio. (Table 1, Entry 7). Moreover, attempts to increase the stereoselectivity by lowering the temperature were unproductive. When the Diels-Alder reaction was carried out at 0 °C in CH_2Cl_2 in the presence of either 10% $AlCl_3$ or 10% $Cu(OTf)_2$, no formation of the cycloadducts was observed. When the Diels-Alder

reaction was performed on the bis-*p*-Cl-styryl derivative **5** identical stereochemical results were obtained. In this case the major diastereoisomer **15a** was isolated by silica gel column chromatography in 45% yield.

Table 1. Optimization of Diels-Alder Reaction from 3

Entry	Diene (eq)	Cat. (%)	Solvent	Temp (°C)	Yield (%)[a]	Ratio 14a/14b
1	20	-	Toluene	rt	-	-
2	20	-	Toluene	reflux	-	-
3	20	$AlCl_3$ (10)	Toluene	rt	-	-
4	20	$Cu(OTf)_2$ (10)	Toluene	rt	-	-
5	20	$AlCl_3$ (10)	CH_2Cl_2	rt	80	10/3
6	20	$Cu(OTf)_2$ (10)	CH_2Cl_2	rt	85 (58)[b]	10/3
7	20	$AlCl_3$ (1)	CH_2Cl_2	rt	10	10/3
8	20	$AlCl_3$ (10)	CH_2Cl_2	0	-	-
9	20	$Cu(OTf)_2$ (10)	CH_2Cl_2	0	-	-

[a] Crude yield; [b] Isolated yield

With the formation of the Diels-Alder adducts on both the two lateral chains of the bisquinazolinones, eight new chiral centers are introduced. *Endo* and *Exo* attacks on the *Re-Si* and *Si-Re* faces of the two olefins in addition to the chiral axis, offer the potential formation of a high number of Diels-Alder adducts, out of which mainly two were generated as shown by the ^{1}H-NMR spectrum of the crude reaction mixture. In principle,

analysis of the coupling constant pattern of the bridgehead protons in the ^{1}H-NMR spectra of isolated **14a** should be useful for the determination of the *Exo/Endo* stereochemistry. Unfortunately, in our case the signals belonging to the bridgehead protons appeared as two broad singlets making impossible to use them as a stereochemical probe. Nevertheless, we were able to obtain crystals of **14a**, suitable for X-Ray (Figure 5). From the crystal structure it is clear that the major adduct has both the two-phenyl groups with an *exo* orientation, whereas the two BiQ rings have *endo* orientations with assigned stereochemistry *M,1S, 2S, 3R, 4 S, 1'S,2'S,3'R,4'S.*

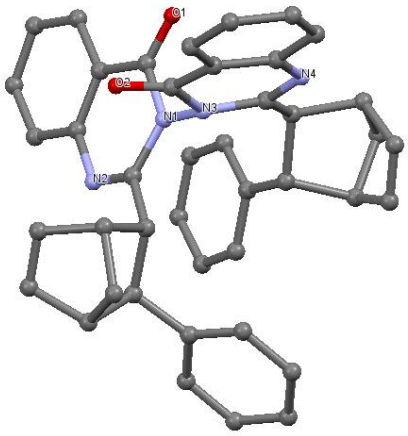


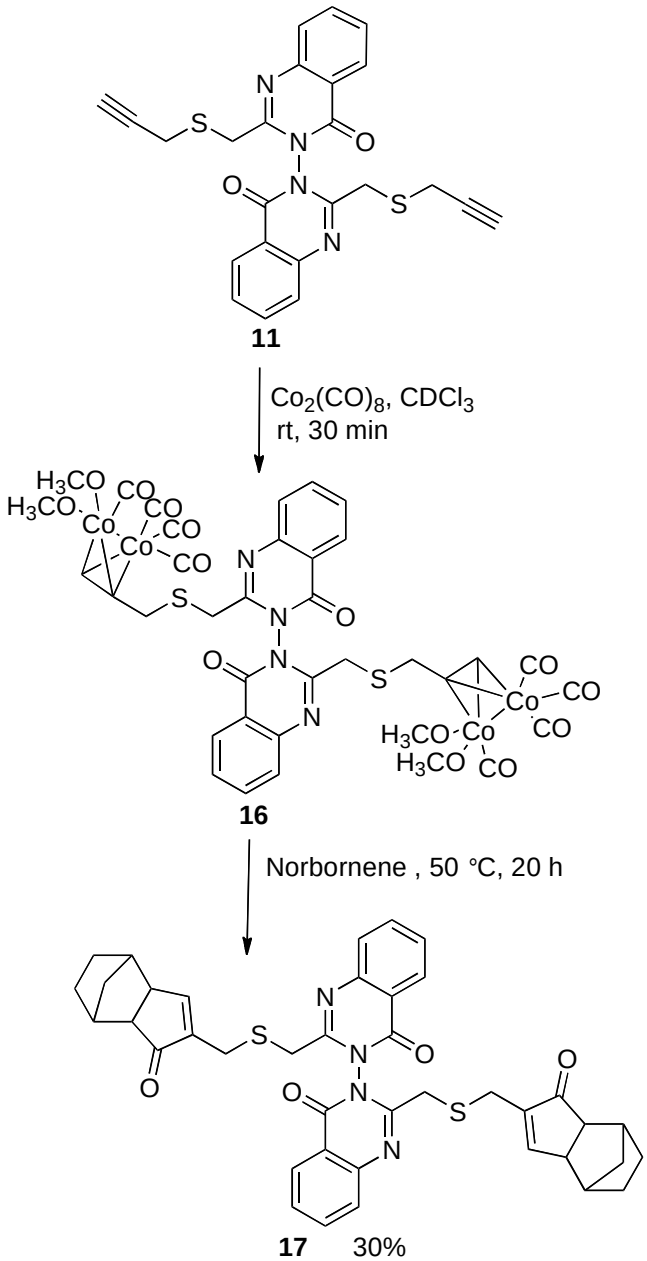
Figure 5 X-ray structure of Diels-Alder adduct 14a. ORTEP displayed at 50% probability ellipsoids. Hydrogen atoms omitted for clarity.

Results from this investigation showed that the chiral axis of the biquinazolinone is able to influence the stereochemical outcome of the Diels-Alder cycloaddition.

Delighted by these results we decided to examine the possibility of achieving auxiliary-driven asymmetric Pauson–Khand (PK) cycloadditions on the biquinazolinone scaffold. The PK reaction is the [2 + 2 + 1] cyclo-addition reaction of an alkyne, alkene, and CO (from $Co_2(CO)_8$), providing an efficient route to structurally diverse cyclopentenones. Interestingly, Moyano and co-workers found that chiral alkynyl sulfides are excellent at controlling diastereoselectivity of these reactions, as sulfides chelate one of the

diastereotopic cobalt atoms in the dicobalt acetylene complex and control their reactivity.[21,22] In this scenario, we envisaged BiQ **10** as an ideal substrate for this reaction. To explore the feasibility, BiQ **10** was treated with 2 equiv. of $Co_2(CO)_8$ at rt in $CDCl_3$ and the reaction was then monitored by ^{1}H-NMR spectroscopy (Scheme 6). Although formation of the cobalt complex **16** was almost instantaneous, after addition of norbornene, formation of the P-K product was not detected by ^{1}H-NMR spectroscopy even after 24 hours at room temperature. Subsequent heating of the mixture at 50 ºC for 20 hours afforded the desired compound **17** as a mixture of two diastereoisomers 1:1 ratio as detected by ^{1}H-NMR spectroscopy of the crude mixture. Compound **17** was then isolated in 30% yield as brown solid after silica gel column chromatography. The Pauson-Khand reaction has been shown to have a high degree of both regio- and stereoselectivity. In particular, it has been demonstrated that when norbornene is used, the products had exclusively the exo-configuration and that the reaction yields almost exclusively the 2- substituted ketone when the alkyne is terminal.[23-25] These observations rule out several of the theoretical stereoisomers that can be generated by the formation of four new chiral centers. Among three possible diastereoisomers (in a 1:2:1 ratio) only a mixture of two in a 1:1 ratio, was observed in the ^{1}H-NMR spectrum of the crude product. In the case of a total lack of stereocontrol, we should have observed the presence of three diastereoisomers with a 1:2:1 ratio. Thus, we concluded that a certain grade of stereocontrol has been obtained. Considering the low yield achieved, the possibility to use a promoter, that allows the reaction to take place either at lower temperatures and with shorter times, was explored. More specifically, we used *N*-methylmorpholine-*N*-oxide (NMO), which was reported to readily promote intramolecular Pauson-Khand cyclizations at room temperature, under an inert atmosphere of argon. Addition of NMO to the cobalt complex **16** followed by addition of norbornene, afforded the title compound **17** in 70% yield as a mixture of two diastereoisomers in a 1.6:1 ratio.

Cyclization reactions run under thermal or N-oxide-promoted activation provided a different stereoisomer ratio. This shows that the activation method does significantly affect the yield and the stereochemical outcome of the reaction. These observations are particularly interesting considering that, although the chiral centers are formed relatively remotely from the axis, high levels of induction are achieved.



Scheme 6 Pauson-Khand reaction with BiQ 11.

2.3 Attempts to cleave the newly formed chiral centers.

Once demonstrated that BiQ scaffolds are able to induce the formation of stereoisomerically enriched molecules, the next step in our research program was to find a way to release these molecules from the BiQ scaffold.

In order to study the release of the newly formed chiral scaffold from the BiQ unit, we decided to use the DA adduct **14** as substrate. Initially, we envisaged that acidic and basic hydrolysis would be a reasonable approach. Unfortunately, compound **14a** was recovered totally unchanged after reflux with 6N HCl in ethanol for 48 hours. Under the same conditions, but with more concentrated acid (12 N HCl), a slight decomposition of **14** was observed along with intact starting material. Treatment with a Lewis acid such as copper triflate in THF/water at 40 ˚C was also unsuccessful. Basic conditions (1M LiOH in THF/H_2O, both at room temperature and at 50 °C), were also not successful and unreacted starting material was always recovered. Interestingly, when **14a** was treated with the $(C_5H_5)_2ZrHCl$, (zirconocene chloride hydride, Schwartz reagent), we could detect by ^{1}H-NMR spectroscopy of the crude mixture, some degree of cleavage, however we were not able to identify the nature of the product, which may be derived by the cleavage of the amide-like bond (N3-CO)[26,27] in the Biquinazolinone. Further studies are now in progress to understand in full the outcome of this reaction.

3. Conclusions

In conclusion, we have successfully reported the synthesis of a range of biQs bearing either a prochiral double or triple bonds in the lateral chains, and their application to substrate controlled asymmetric induction. Epoxidaton, Diels-Alder and Pauson-Khand reactions, all proceeded with high level of diastereoselectivity.

We are currently investigating on the application of BiQs to other asymmetric reactions like aziridination, cyclopropanation and 1,3 dipolar cycloaddition, focusing our studies on establishing the absolute configuration of the all the BiQs prepared. Methods of

cleaving the newly formed chiral centers from the scaffold under the mildest conditions still represent a challenge at the moment. Although basic and acidic hydrolysis failed to release the norbornene unit from the Biquinazolinone, reducing agents may be the answer to this problem, especially when the results from the use of the Schwartz reagent are considered. Clearly, there are a great many additional prospects for the application of these systems, especially in asymmetric catalysis and other areas of stereoselective synthesis.

4. EXPERIMENTAL SECTION

4.1 General Methods. All starting materials and reagents were purchased from commercial suppliers and used as received unless otherwise stated. All PK work was done under dry nitrogen and with degassed solvent using standard Schlenk techniques. NMR spectra were recorded on a 400 MHz at 400 MHz (proton) and 160 MHz (carbon). FTIR spectra were recorded as thin films or nujol. Mass spectra were recorded with electrospray ionization technique and quadrupole mass analizer. Elemental analyses, were performed by Warwick Analytical Services (University of Warwick).

2,2'-Dimethyl-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (2).

2-Amino-N'-(2-aminobenzoyl)benzohydrazide **1** (10 g, 34 mmol) was refluxed in acetyl anhydride (100 mL) for 24 hours. The reaction mixture was cooled at 0 °C with an ice bath and the resulted precipitate filtered off and crystallised from ethanol. The filtrate was reduced to half volume and the solid obtained filtered off and crystallised from ethanol. The two crops were re-crystallised from ethanol to obtain pure **2** (8.65g, 80% yield). m.p. 176 °C, (Lit.[17] 175 °C); ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.20 (2H, dd *J* = 7.9 and 1.5 Hz, 5-H, 5'-H), 7.77 (2H, ddd *J* = 8.3, 7.9 and 1.5 Hz, 7-H, 7'-H), 7.70 (2H, dd *J* = 7.9 and 1.2 Hz, 8-H, 8'-H), 7.46 (2H, ddd *J* = 8.3, 7.9 and 1.2 Hz, 6-H, 6'H), 2.34

(6H, s, 2 x CH_3).

2,2'-Di((E)-styryl)-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (3). To a cooled (-78 °C, dry ice/acetone), stirred solution of 2,2'-dimethyl-3,3'- biquinazoline-4,4'-dione **2** (0.20 g, 0.60 mmol) in dry THF (6 mL), 2.5 M butyl lithium solution in hexane (0.57 mL, 1.44 mmol) was added under N_2. Formation of the dianion was observed as a deep red solution along with a red precipitate. The resulting mixture was stirred at -78 °C for an additional 15 min, after which a solution of benzaldehyde (0.140 g, 1.32 mmol) in THF (2 mL) was added. The mixture was stirred for further 30 min at -78 °C, then allowed to reach room temperature and then stirred for further 60 min., diluted with CH_2Cl_2 (30 mL), and quenched with aqueous saturated solution of NH_4Cl (10 mL). The organic layer was then washed with water (2 x 10 mL), dried over Na_2SO_4 and evaporated to dryness. Chromatography on silica gel using hexane/ethyl acetate 3:1 afforded **3** as yellow crystals (0.11 g, 34 % yield); R_f = 0.29 (hexane/ethyl acetate, 3:1); m.p. 210 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.25 (2H, dd, *J* = 7.9 and 0.7 Hz, 5-H, 5'-H), 8.14 (2H, d *J* = 15.3 Hz, 2 x CH=CHPh), 7.88-7.78 (4H, m, 7-H, 8-H, 7'-H, 8'-H), 7.49-7.38 (2H, m, Ar), 7.28 (4H, dd *J* = 8.5 and 1.8 Hz, Ar), 7.20 (6H, dd *J* = 8.5 and 1.8 Hz, Ar), 6.45 (2H, d *J* = 15.4 Hz, 2x CH=CHPh); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 159.4, 151.7, 147.6, 143.9, 136.1, 135.0, 130.7, 129.2, 128.6, 128.4, 128.2, 127.6, 121.2, 115.3; ν_{max} (nujol)/cm^{-1} 1697, 1548, 1469, 1334; *m*/*z* APCI (%) 495.17 (100) $[M+H]^+$; HRMS for $C_{32}H_{22}N_4O_2$ requires: 495.1743 $[M+H]^+$, found: 495.1749 $[M+H]^+$; Anal. Calcd for: $C_{32}H_{22}N_4O_2$ requires: C, 77.72; H, 4.48; N, 11.33. Found: C, 77.66; H, 4.42; N, 11.78; Further elution with the same solvents afforded: **(E)-2-methyl-2'-styryl-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (4),** obtained as yellow crystals, (0.15 g, 58% yield); R_f = 0.22 (hexane/ethyl acetate, 3:1); m.p. 207°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.20 (2H, d *J* = 7.9 Hz, 5- H, 5'-H), 8.15 (1H, d *J* = 15.4 Hz, CH=CHPh), 7.99-7.80 (3H, m, Ar), 7.52-7.54 (1H, m, Ar), 7.55-7.40 (2H, m, Ar), 7.35-7.28 (2H, m, Ar), 7.23-7.17 (3H, m,

Ar), 6.45 (1H, d, *J* = 15.4 Hz, CH=CHPh), 2.40 (3H, s, -CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 157.9, 152.7, 149.7, 146.2, 145.8, 142.6, 134.6, 133.5, 129.4, 127.8, 127.1, 126.9, 126.7, 126.6, 126.5, 126.4, 126.2, 119.8, 119.7, 113.5, 20.3; IR ν_{max} (nujol)/cm^{-1} 1694, 1551, 1465; *m*/*z* (APCI) (%) 407.1 (40) $[M+H]^+$; HRMS for $C_{25}H_{18}N_4O_2$ requires: 407.1430 $[M+H]^+$, found: 407.1424 $[M+H]^+$; Anal. Calcd for $C_{25}H_{18}N_4O_2$: C, 73.88; H, 4.46; N, 13.78 (%). Found. C, 73.61; H, 4.46; N, 13.70 (%).

2,2'-Bis-((E)-4-chlorostyryl)-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (5). To a cooled (-78 °C, dry ice/acetone), stirred solution of 2,2'-dimethyl-3,3'- biquinazoline-4,4'-dione **2** (0.20 g, 0.60 mmol) in dry THF (6 mL) 2.5 M butyl lithium solution in hexane (0.57 mL of, 1.44 mmol) was added under N_2. The resulting mixture was stirred at -78 °C for an additional 15 min after which *p*-chloro-benzaldehyde (0.19 g, 1.35 mmol) was added as a solid. The mixture was stirred for 30 min at -78 °C, allowed to reach room temperature and stirred for a further 60 min., diluted with CH_2Cl_2 (30 mL), and quenched with aqueous saturated solution of NH_4Cl (10 mL). The organic layer was then washed with water (2 x 10 mL), dried over Na_2SO_4 and evaporated to dryness. Chromatography on silica gel using like eluents hexane/ethyl acetate 3:1 afforded **5** as yellow crystals (0.11 g, 32% yield). R_f = 0.3 (hexane: ethyl acetate, 3:1); m.p. 270 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.22 (2H, d, *J* = 8.4 Hz, 5-H, 5'-H), 8.11 (2H, d, *J* = 15.4 Hz, 2x CH=CHPh), 7.91-7.88 (4H, m, Ar), 7.61-7.50 (2H, m, Ar), 7.24 (4H, d, *J* = 8.5 Hz, Ar), 7.18 (4H, d, *J* = 8.4 Hz, Ar), 6.48 (2H, d, *J* = 15.4 Hz, 2x -CH=CHPh); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 158.0, 150.0, 146.1, 141.0, 135.2, 134.7, 132.0, 128.3, 128.1, 127.0, 126.8, 126.4, 119.7, 114.3; IR ν_{max} (nujol)/cm^{-1} 1701, 1550, 1467; *m*/*z* (APCI) (%) 563.1 (5) $[M+H^+]$ 281.1 (50), 90 (100); HRMS for $C_{32}H_{20}Cl_2N_4O_2$ requires: 563.0963 $[M+H]^+$, found: 563.0950 $[M+H]^+$; Anal. Calcd for $C_{32}H_{20}Cl_2N_4O_2$: C, 68.21; H, 3.58; N, 9.94. Found: C, 68.04; H, 3.65; N, 9.80. Further elution with the same solvents afforded: **(E)-2-(4-chlorostyryl)-2'-methyl-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (6)**, obtained as

yellow crystals (0.32 g, 60% yield). m.p. 216 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.23 (2H, d, *J* = 7.9 Hz, 5H, 5'-H), 8.13 (1H, d, *J* = 15.3 Hz, -CH=CHPh), 7.83-7.76 (3H, m, Ar), 7.70 (1H, d, *J* = 7.9 Hz, Ar), 7.55-7.48 (2H, m, Ar), 7.46 (2H, d, *J* = 8.4 Hz, Ar), 7.30-7.22 (2H, m, Ar), 6.45 (1H, d, *J* = 15.3 Hz, -CH=CHPh), 2.36 (3H, s, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 159.3, 159.2, 154.2, 150.9, 147.5, 147.1, 142.6, 136.7, 136.2, 136.1, 133.4, 129.7, 129.6, 128.4, 128.1, 128.0, 127.9, 127.8, 121.2, 121.1, 115.4, 21.6; IR ν_{max} (thin film)/cm^{-1} 1702, 1626, 1573, 1467, 1404, 1399, 1221, 1091, 769, 692; *m*/*z* 197 (APCI)(%) 441.1 (100) [M+H$^+$]; HRMS $C_{25}H_{17}ClN_4O_2$ requires: 441.1040 [M+H]$^+$, found: 441.1030 [M+H]$^+$; Anal. Calcd for $C_{25}H_{17}ClN_4O_2$: C, 68.11; H, 3.89; N, 12.71. Found: C, 67.98; H, 4.01; N, 12.69.

(Prop-2-ynylthio) acetyl chloride (8).[19] To a stirred solution of mercaptoacetic acid **7** (6.78 mL, 99 mmol) in aqueous ammonia (35 % solution, 135 ml) was added propargyl bromide (21.36 mL, 147 mmol) at 0 °C. The reaction mixture was stirred under these conditions for 40 minutes. $NaHCO_3$ was added and the solution was washed with CH_2Cl_2. The aqueous layer was acidified with conc. HCl and extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and the solvent was removed in vacuum. Re-crystallisation from cyclohexane gave (prop-2-ynylthio) acetic acid (**8**) as white needles (5.18 g, 40% yield) mp: 53.7°C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 9.53 (1H, bs, COO*H*), 3.53 (2H, s, C*H*$_2$CO$_2$H), 3.48 (2H, d *J* = 2.6 Hz, C*H*$_2$*C*≡), 2.35 (1H, t *J* = 2.6 Hz, 1H, *H*C≡); IR ν_{max} (nujol)/cm^{-1} 3269.9, 2667.9, 1666.5. To a solution of **8** (2.6 g, 20 mmol) in CH_2Cl_2 (20 ml) under N_2 oxalyl chloride (1.87 ml, 21 mmol) was added dropwise at room temperature and the resulting mixture was stirred overnight. The obtained yellow solution was used without any purification or concentration for the next step.

2,2'-Bis-((ethynylthio)methyl)-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (10). To an ice-cold stirred solution of bisanthranoyl hydrazine **1** (2.16 g, 8 mmol) and triethyl amine

(5.84 mL, 42 mmol) in DMF (25 mL) was added dropwise under N_2 the solution of acid chloride **8** (20 mmol) in CH_2Cl_2 (25 mL). The reaction was stirred at room temperature and under N_2 atmosphere overnight, diluted with CH_2Cl_2 and washed with water and a saturated solution of $NaHCO_3$. The organic layer was dried with $MgSO_4$ and the solvent was removed under vacuum to give the **9** as a brown solid. To a suspension of **9** in toluene (200 mL) was added *p*-toluenesulfonic acid (0.152 g, 0.8 mmol) and the resulting mixture was heated at reflux for 3 hours. The toluene was removed under vacuum and the residue was taken up in CH_2Cl_2, washed with water and a saturated solution of $NaHCO_3$. The organic layer was dried with $MgSO_4$ and concentrated in vacuum. The crude mixture was purified by column chromatography using CH_2Cl_2 as eluent to give **10** as a light brown solid (0.68 g, 19% yield). R_f = 0.73 (Et_2O); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 8.20 (2H, dd, *J* = 0.8, 7.9, 5-H, 5'H), 7.87-7.80 (4H, m, 7-H, 7'-H, 8-H, 8'-H), 7.60-7.51 (2H, m, 6-H, 6'-H), 3.89 (1H, d, *J* = 15.4 Hz, 2 x CH_{2a}S)], 3.83 (1H, d, *J* = 15.4 Hz, 2 x CH_{2b}S)], 3.48, 3.40 (2 x 2H, 2dd, *J* = 16.9 and 2.5 Hz, 2 x C*H*$_2$C≡), 2.05 (2H, t, *J* = 2.6 Hz, *H*C≡); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 158.3, 151.4, 145.4, 134.7, 127.2, 126.8, 126.5, 120.0, 78.3, 70.9, 32.5, 19.0; IR ν_{max} (nujol)/cm^{-1} 2305.4, 1700.8, 1603.8; *m*/*z* (APCI) 459 (100) $[M+H]^+$; HRMS for $C_{24}H_{18}N_4O_2S_2$ requires: 459.0951 $[M+H]^+$, observed 459.0901$[M+H]^+$; Further elution with the same solvent afforded: **2-((ethynylthio)methyl)-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (11)** as light yellow solid (0.49 g, 17% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H 8.31-8.22 (2H, m, 5-H, 5'-H), 8.23 (s, 1H, 2'-H), 7.84-7.78 (m, 4H, 7-H, 7'-H, 8-H, 8'-H), 7.48-7.39 (2H, m, 6-H, 6'-H), 3.88 (1H, d, *J*= 14.3 Hz, 2 x C*H*$_{2a}$S)], 3.55 (1H, d, *J*= 14.3 Hz, 2 x C*H*$_{2b}$S)], 3.39, 3.30 (2H, dd, *J* = 2.5 and 17.0 Hz, C*H*$_2$*C*≡)], 2,00 (1H t, *J* =2.5 Hz, *H*C≡); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 158.3, 157.6, 150.6, 145.4, 145.6, 145.2, 134.6, 127.3, 127.2, 127.7, 126.9, 126.4, 126.4, 121.3, 120.2, 78.1, 75.2, 70.5, 33.10, 18.6; IR ν*m*ax (nujol)/cm^{-1} 2360.9, 1700.1, 1605.3; m/z 375.5 $[M+H]^+$; $C_{20}H_{14}N_4O_2S$ requires

375.0917 $[M+H]^+$, observed 375.0899 $[M+H]^+$. Anal. Calcd for $C_{20}H_{14}N_4O_2S$: C, 64.16; H, 3.77; N, 14.96. Found: C, 64.01; H, 3.88; N, 14.80.

2,2'-Bis-(3-phenyloxiran-2-yl)-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (12). To a solution of **3** (0.20 g, 0.40 mmol) in CH_2Cl_2 (10 mL) was added MCPA (0.280 g, 1.62 mmol) and the resulting mixture stirred at room temperature for 24 hours. After this period the mixture was washed with aqueous saturated sodium thiosulfate (2 x 10 mL), water (2 x 10 mL), dried over magnesium sulfate and evaporated. The epoxide **12** was obtained after crystallization from ethanol as a mixture of two diastereoisomers (9:1 ratio referred to as A and B, many signals overlap) (0.18 g, 88% yield). m.p. 260 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.24 (2H, d, *J* = 8.4 Hz, 5-H, 5'-H), 7.82-7.74 (4H, m, 7-H, 8-H, 7'-H, 8'-H), 7.57-7.42 (2H, m, 6-H, 6'-H), 7.18-7.09 (10H, m, Ar), 4.32 (1H, d, *J* = 1.72 Hz, 10-HB), 4.27 (1H, d, *J* = 1.75 Hz, 10-H-A), 3.68 (1H, d, *J* = 1.75 Hz, 9-H-A), 3.61 (1H, d, *J* = 1.75 Hz, 9-H-B); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 157.9, 157.8, 149.4, 149.3, 145.3, 145.2, 134.8, 133.2, 132.6, 129.2, 128.7, 127.8, 127.6, 127.5, 127.4, 127.2, 127.1, 126.5, 124.7, 124.6, 58.8, 58.8, 56.5, 56.3; IR ν_{max} (nujol)/cm^{-1} 2922, 1713, 1600, 1458; *m/z* (APCI) 527.1 (100) $[M+H]^+$, 409 (20); HRMS for $C_{32}H_{22}N_4O_4$ requires: 527.1641, found: 527.1608; Anal. Calcd for $C_{32}H_{22}N_4O_4$ requires: C 72.99; H 4.21; N 10.64. Found C 72.80; H 4.23; N 10.63.

2-Methyl-2'-(3-phenyloxiran-2-yl)-4H,4'H-[3,3'-biquinazoline]-4,4'-dione (13). To a solution of **4** (0.19 g, 0.46 mmol) in CH_2Cl_2 (10 mL) was added MCPBA (0.44 g, 1.83 mmol) and the resulting mixture stirred at room temperature for 24 hours. After this period the mixture was washed with aqueous saturated sodium thiosulfate (2 x 10 ml), water (2 x 10 ml), dried over magnesium sulfate and evaporated. The epoxide **13** was obtained after crystallization from ethanol as a mixture of two diastereoisomers (5:1 ratio referred to as A and B, many signals overlap) (0.17 g, 88% yield); ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.26 (1H, d, *J* = 7.9 Hz, 5-H), 8.26 (1H, d, *J* = 7.9 Hz, 5-H), 8.25 (1H, d, *J* =

7.7 Hz, 5'-H-A), 8.24 (1H, d, *J* = 7.7 Hz, 5'-H-B), 7.82-7.25 (6H, m, 7-H, 8-H, 7'-H, 8'-H, 6-H, 6'-H), 7.18-7.08 (5H, m, Ar), 4.30 (1H, d, *J* = 1.66 Hz, 10-H-B), 4.26 (1H, d, *J* = 1.87 Hz, 10-H-B), 2.42 (3H, s, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 158.1, 157.7, 152.3, 149.2, 145.7, 145.5, 134.8, 134.6, 133.1, 127.8, 127.5, 127.4, 127.2, 127.3, 126.6, 126.5, 126.4, 126.2, 124.6, 58.5, 56.2, 20.2.

2,2'-Bis-[3-phenyl-bicyclo[2.2.1]hept-5-en-2-yl]-[3,3']biquinazolinyl-4,4'-dione (14a).

To a stirred solution of **3** (0.10 g, 0.20 mmol), in CH_2Cl_2 (2 mL) was added cyclopentadiene (0.26 g, 3.91 mmol, 0.31 mL) and copper (II) triflate (0.0026 g, 10% mol) at room temperature, under N_2. The mixture was stirred for an additional 24 hours then the solvent was evaporated, and the waxy solid obtained was triturated with light petroleum ether. Further purification by silica gel column chromatography using hexane/ethyl acetate 4:1 affording crude compound **14** containing a major (**14a**) and minor isomer (**14b**) along with traces of two other isomers. The residue was purified repeatedly by crystallization from MeCN/MeOH affording **14a** as white powder (58%). m.p. 290 ˚C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H 8.21 (2H, dd, *J* = 8.0 and 1.6 Hz, 5-H, 5'-H), 7.78 (2H, ddd, *J* = 8.0, 7.2 and 1.2 Hz, 7-H, 7'-H), 7.69 (2H, d, *J* = 8.0 Hz, 8-H, 8'-H), 7.43 (2H, ddd *J* = 8.0, 7.2, 1.2 Hz, 6-H, 6'-H), 7.02-6.99 (4H, m, Ar), 6.95-6.91 (6H, m, Ar), 6.33 (2H, dd, *J* = 5.8 and 3.2 Hz, 12-H, 12'-H), 6.13 (2H, dd, *J* = 5.6 and 2.9 Hz, 11-H, 11'-H), 3.67 (2H, d, *J* = 4.8 Hz, 14-H, 14'-H), 3.32 (2H, dd, *J* = 5.1 and 3.4 Hz, 9-H, 9'-H), 3.08 (2H, s br, 13-H, 13'-H), 2.68 (2H, s br, 10-H, 10'-H), 1.62 (2H, d, *J* = 8.9 Hz, 15-Ha, 15'-Ha), 1.37 (2H, d, *J* = 8.9 Hz, 15-Hb, 15'-Hb); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 160.7, 156.85, 146.3, 143.3, 137.5, 134.9, 134.6, 128.3, 128.2, 127.3, 127.0, 126.1, 70.1, 49.7, 48.5, 48.50, 46.4; IR ν_{max}(nujol)/cm^{-1} 2980, 1681, 1506, 1413; HRMS for $C_{42}H_{34}N_4O_2$ requires: 627.2682 $[M+H]^+$, found: 626.2910 $[M+H]^+$.

2,2'-Bis-[3-(*p*-chloro-phenyl)-bicyclo[2.2.1]hept-5-en-2-yl]-[3,3']biquinazolinyl-4,4'-dione (15a). To a stirred solution at room temperature of **5** (0.10 g, 0.19 mmol), in CH_2Cl_2 (2 mL) was added cyclopentadiene (0.25 g, 3.72 mmol, 0.3 mL) and aluminum chloride (0.0025 g, 10% mol) under N_2. The mixture was stirred for additional 24 hours at room temperature then the solvent was evaporated, and the waxy solid obtained was washed with light petroleum ether and further purified by silica gel column chromatography using hexane/ethyl acetate 4:1 affording compound **15a** as white powder (59 mg, 45% yield); m.p. 270 °C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.18 (2H, dd, *J* = 8.0 and 1.2 Hz, 5-H, 5'-H), 7.78 (2H, dd, *J* = 8.0 and 1.2 Hz, 7-H, 7'-H), 7.62 (2H, d, *J* = 8.0 Hz, 8-H, 8'-H), 7.48-7.40 (2H, m, 6-H, 6'-H), 6.92 (4H, d, *J* = 8.4 Hz, Ar), 6.78 (4H, d, *J* = 8.4 Hz, Ar), 6.22 (2H, dd, *J* = 5.4 and 3.1 Hz, 12-H, 12'-H), 6.03 (2H, dd, *J* = 5.5 and 2.7 Hz, 11-H, 11'-H), 3.59 (2H, d, *J* = 4.4 Hz, 14-H, 14'-H), 3.05 (2H, dd, *J* = 4.9 and 3.4 Hz, 9-H, 9'-H), 2.96 (2H, s br, 13-H, 13'-H), 2.66 (2H, s br, 10-H, 10'-H), 1.47 (2H, d, *J* = 8.6 Hz, 15-Ha, 15'-Ha), 1.21 (2H, d, *J* = 8.8 Hz, 15-Hb, 15'-Hb); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 159.5, 155.4, 145.1, 140.9, 136.5, 134.1, 133.5, 130.7, 127.3, 127.2, 127.0, 126.3, 126.2, 119.7, 49.5, 47.9, 47.3, 46.5, 45.7; IR ν_{max}(nujol)/cm^{-1} 2960, 1691, 1596, 1463; *m*/*z* (APCI) 695.2 (100) $[M+H]^+$; HRMS for $C_{42}H_{32}Cl_2N_4O_2$ requires: 695.1902 $[M+H]^+$, found: 695.1900 $[M+H]^+$.

2,2'-Bis-(1-oxo-3a,4,5,6,7,7a-hexahydro-1H-4,7-methano-inden-2-ylmethylsulfanylmethyl)-[3,3']biquinazolinyl-4,4'-dione (17). To a solution of **10** (0.150 g, 0.33 mmol) in $CDCl_3$ (10 mL) was added cobalt carbonyl (0.22 g, 0.66 mmol). This mixture was stirred for 15 minutes before norbornene (0.31 g, 3.3 mmol) was added. The reaction was stirred for 20 hours at 50 °C. ^{1}H-NMR spectroscopy indicated disappearance of the starting material and the formation of [2,2'-bis-(prop-2-

ynylthiomethyl)-3,3'-bisquinazoline-4,4'-dione]-hexacarbonyldicobalt (**16**). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.21 (2H, d, *J* = 5.97 Hz, 5-H, 5'-H), 7.73 (4H, m, 7-H, 7'-H, 8-H, 8'-H), 7.54-7.42 (2H, m, 6-H, 6'-H), 6.16 (2H, s, 2 x Co-complex-C*H*), 4.22, 4.09 (2 x 2H , 2d, *J*=14.4 Hz, 2 x C*H*$_2$-S), 3.87, 3.74 (2 x 2H, 2d, *J* = 14.9 Hz, C*H*$_2$-C-Co-complex); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 201 (br), 198 (br), 158.4, 151.2, 145.3, 134.7, 127.1, 126.9, 126.6, 120.0, 90.2, 72.5, 34.7, 32.6; IR ν_{max} (nujol)/cm^{-1} 2361.5, 2338.1, 2095.0, 2056.6, 2030.9; 1862.4, 1698.1, 1602.0. *m/z* (ACPI) 1052.8 (100) $[M+Na]^+$. The solvent was then removed under vacuum and the residue taken up in diethyl ether and filtered through Celite. The ether fraction was concentrated under vacuum and purified by silica gel column chromatography using CH_2Cl_2 and then Et_2O as eluent. The ether fraction gave **17a** as a brown solid as a mixture of two diastereoisomers (1:1 ratio referred to as A and B, many signals overlap (0.066 g, 30 % yield). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.22 (2H, m, 5-H, 5'-H), 7.82-7.73 (4H, m, 7-H, 7'-H, 8-H, 8'-H), 7.54-7.48 (2H, m, 6-H, 6'-H), 7.40 (1H, d, J = 3.0 Hz, =C*H*-A), 7.42 (1H, d, J = 3.0 Hz, =C*H*-B), 3.62 (4H, d, *J* =15.4 Hz, 2 x QCH_2S), 3.45-3.39 (4H, m, 2 x SCH_2), 2.50-2.44 (2H, m, 2 x 3a"-H), 2.36-2.30 (2H, m, 2 x 7a"-H), 2.15-2.09 (2H, m, 2 x 8"-Ha), 1.96-1.44 (4H, m, 2 x 8"-Hb, 2 x 4"-H), 1.39-1.26 (2H, m, 2 x 7"-H), 1.20-1.08 (4H, m, 5"-H), 0.95-0.72 (4H, m, 6"-H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ_C 208.3, 208.2, 160.7, 160.6, 138.3, 151.4, 151.3, 145.3, 143.1, 143.1, 134.7, 127.1, 126.7, 126.4, 119.9, 52.8, 52.7, 50.2, 47.2, 43.8, 39.1, 38.7, 38.1, 38.1, 37.1, 37.1, 34.8, 34.4, 32.6, 32.5, 30.2, 29.3, 28.1, 27.3, 26.7, 24.1, 24.0; ν_{max}(nujol)/cm^{-1} 3056.4, 2985.0, 1710.7, 1602.7 cm^{-1}; $C_{40}H_{38}N_4O_4S_2$ requires 703.2412 $[M+H]^+$, observed 703.2399 $[M+H]^+$; Anal. Calcd for $C_{40}H_{38}N_4O_4S_2$: C, 68.35; H, 5.45; N, 7.97. Found: C, 68.26; H, 5.50; N, 7.78.

2,2'-Bis-(1-oxo-3a,4,5,6,7,7a-hexahydro-1H-4,7-methano-inden-2-yl-

methylsulfanylmethyl)-biQ 17 (NMO promoted Pauson-Khand reaction). To a solution of 10 (0.15 g, 0.33 mmol) in $CDCl_3$ (10 ml) was added cobalt carbonyl (0.22 g, 0.66 mmol). This mixture was stirred for 15 minutes before norbornene (308.32 mg, 3.3 mmol) was added and another minute later the addition of NMO (446 mg, 3.3 mmol) was done. The reaction was stirred at room temperature overnight. The solvent was removed in vacuum and the residue was filtered through silica and celite. First CH_2Cl_2 was used and then Et_2O. Evaporating the Et_2O fraction under vacuum gave **17** as brown solid as a mixture of two diastereoisomers (1.6:1 ratio referred to as A and B, many signals overlap (0.21 g, 70 % yield). ^{1}H-NMR (400 MHz, $CDCl_3$): δ_H 8.24-8.18 (2H, m, 5-H, 5'-H), 7.77-7.71 (4H, m, 7-H, 7'-H, 8-H, 8'-H), 7.50-7.41 (2H, m, 6-H, 6'-H), 7.40 (1H, d *J* = 3.0 Hz, 2 x =C*H*-A), 7.40 (1H, d *J* = 3.0 Hz, 2 x =C*H*-B), 3.75 (4H, d, *J* =15.4 Hz, 2 x CH_2S), 3.44-3.39 (4H, m, 2 x SCH_2), 2.43 (2H, m, 2 x 3a"-H), 2.31 (2H, m, 2 x 7a"-H), 2.1 (2H, m, 2 x 8"-Ha), 1.88-1.40 (4H, m, 2 x 8"-Hb, 2 x 4"-H), 1.38-1.31 (2H, m, 2 x 7"-H), 1.17-1.06 (4H, m, 5"-H), 0.97-0.70 (4H, m, 6"-H).

Supplementary Data

Copies of ^{1}H-NMR and ^{13}C-NMR spectra for target compounds. Crystallographic data (CCDC-1441830, -1441831 and -920660, excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk).

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Corresponding Author

Dr. Fabrizio Pertusati

E-mail: pertusatif1@cf.ac.uk; Fax: +44 (0)29 208 74149; Tel: +44 (0)29 20874551 .