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O-Protecting groups as long-range stereocontrolling elements in the addition of acetylides to 4-substituted quinolines

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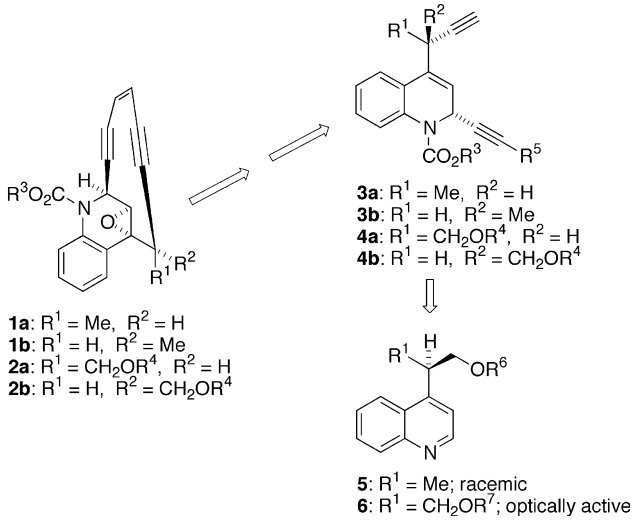
Abstract—Addition of magnesium acetylides in the presence of chloroformate esters to racemic differently *O*-protected 2-(4-quinolyl)propanols and to enantiopure 2-(4-quinolyl)-1,3-dialkoxypropanes, prepared by a chemoenzymatic route, gives almost exclusive regioselective attack at C-2, with stereoselectivities from moderate to good, depending mainly on the bulkiness of the *O*-protecting group present.

1. Introduction

The quinoline nucleus, and also its hydrogenated form are fragments frequently found in many natural products.[1–3] Moreover, many quinoline derivatives are known for their interesting biological properties, such as antimalarial activity,[4,5] antagonist activity with respect to neurokinin-3,[6] glucagon[7] or cannabinoid[5] receptors, antiprotozoal[8] and antitumor[9,10] activity. Dynemicin A, a recently discovered[11] enediyne, containing a quinoline derivative, has attracted the attention of many research groups for its notable cytotoxicity and novel mode of action. Some syntheses of this compound have also been reported.[12–14] However, its complex structure and low stability has prompted many research groups to design simplified analogues, which still have their biological activity promoted by the presence of the enediyne moiety.[15] In the last years our group has been involved in the preparation of new artificial enediynes.[16] Among them, we aimed to synthesize a new family of analogues of natural Dynemicin A, namely compounds **1a**,**b**, and the corresponding hydroxymethyl derivatives **2a**,**b**.

In our strategy we planned to assemble the 10-membered enediyne ring, starting from highly functionalized quinoline-derived intermediates **3** and **4**, provided with both triple bonds. Because we envisaged the employment of the appropriate 4-substituted quinolines as the first stage of the synthesis, we had to study the regio- and diastereoselective functionalization of the parent heterocycle, starting from compounds of general formula **5** and **6**, as summarized in Scheme 1. Preliminary results in this field have already been reported on racemic compounds **5**.[17] Herein, we report more details on diastereoselective additions to **5** and extend our study to optically active **6**.



1a: R^1 = Me, R^2 = H
1b: R^1 = H, R^2 = Me
2a: R^1 = CH_2OR^4, R^2 = H
2b: R^1 = H, R^2 = CH_2OR^4

3a: R^1 = Me, R^2 = H
3b: R^1 = H, R^2 = Me
4a: R^1 = CH_2OR^4, R^2 = H
4b: R^1 = H, R^2 = CH_2OR^4

5: R^1 = Me; racemic
6: R^1 = CH_2OR^7; optically active

Scheme 1.

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2. Results and discussion

2.1. Preparation of quinolines (±)-5 and 6 and addition of acetylides to the heterocyclic ring

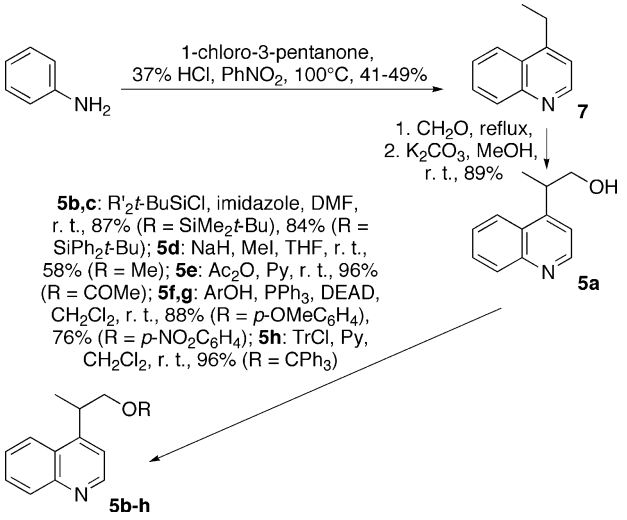
For the preparation of (±)-**5a**, 4-ethylquinoline, obtained through a Skraup-like reaction (Scheme 2),[18,19] was heated under reflux in aqueous formaldehyde, following the same procedure employed for the preparation of 1,3-propanediols with 2- or 4-pyridyl[20] or quinolyl[21] substituents at C-2. In this case, however, a complex mixture of hemiacetal compounds of formaldehyde was formed. The mixture is best hydrolyzed under basic conditions, which afford the desired (±)-**5a** in high yield.

Several *O*-protected derivatives of (±)-**5a**, with different properties, have been prepared in satisfactory to excellent yields, following standard procedures, as reported in Scheme 2.[22] We also tried to introduce other protecting groups into (±)-**5a**, with the groups differing not only in their steric hindrance properties, but also in their ability to give chelation in reactions involving organometallic intermediates. Actually, in some cases this is a great opportunity for controlling diastereoselectivity.[23] However, all attempts to transform (±)-**5a** into a series of common ethers characterized by chelating properties, like benzyl, 4-methoxybenzyl, methoxymethyl (MOM), methoxyethoxyethyl (MEM) or 2,4-dinitrophenyl ether, employing different conditions,[22] failed. We observed unexpectedly low reactivity of (±)-**5a** and, in every case, the desired products could not be isolated since the starting alcohol usually did not react, while forcing reaction conditions only led to decomposition of the substrate.

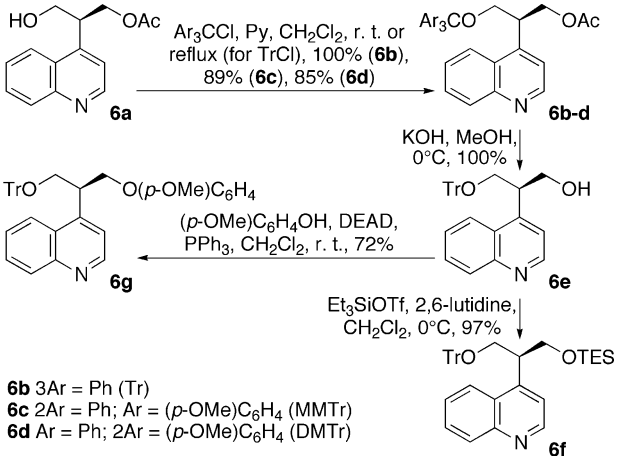
The optically active quinolines **6b–g** were synthesized starting from monoacetate **6a**, which could be prepared in very high chemical yield, with enantiomeric excess up to 97.5% by asymmetrization of the corresponding diol catalyzed by lipase from *Candida antarctica*, as previously reported.[21] This compound was then protected varying the groups at the two oxygenated functionalities. For this purpose we planned to introduce two *O*-protecting groups with orthogonal properties, having in mind to manipulate them at different times after the addition reaction. As previously experienced with (±)-**5a**, we succeeded with the introduction of only a limited number of protecting groups: triphenylmethyl ether and their analogues, silyl ethers, anisyl ether, esters (Scheme 3). Protecting groups requiring the formation of the alcoholate of **6a** could not be introduced. Acetal protecting groups were the most troublesome: while the methoxymethyl ether could be prepared in moderate yield (40%) but with poorly reproducible results; we did not succeed, for example, in the introduction of the very versatile tetrahydropyranyl ether.

This was quite puzzling, since it prevented the study of the addition reaction on a system bearing at the same time a chelating and a 'non-chelating' group,[23] a condition that should influence the diastereoselectivity during the nucleophilic attack.

Having in hand a certain number of *O*-protected quinolines **5** and **6**, we started our studies on the regio- and diastereoselective addition of *C*-nucleophiles. The propensity of quinolines, pyridines and isoquinolines to undergo nucleophilic addition at C-2 and/or C-4 is well known, and has received increased attention after the discovery of Dynemicin A. For the synthesis of simplified analogues of Dynemicin A, the functionalization of the quinoline nucleus by means of *C*-nucleophiles is a milestone either when performed on achiral derivatives[24–28] or partially rigid quinolines fused with other rings and bearing at least two stereocenters.[29–31] The asymmetric synthesis of 1,2- and 1,4-dihydroquinolines by nucleophilic addition to a chiral aminal (with C_2-symmetry) of quinoline-3-carbaldehyde is also known.[32] To the best of our knowledge only one example is known in which the reaction is performed on a quinoline with just one stereocenter.[33] In order to prepare the precursors of **1a**,**b** and **2a**,**b** it is important to fully understand the regio- and stereochemical course of the addition on such a conformationally flexible



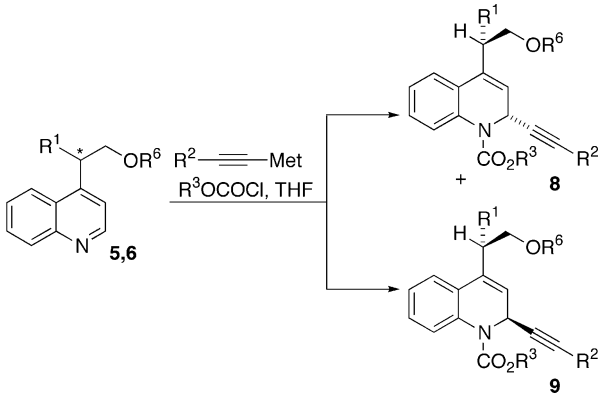
Scheme 2.



Scheme 3.

quinolyl derivative with a pre-existing stereogenic center remote from the one generated during the reaction. Thus, every factor that can affect the regio- and diastereoselectivity as well as the yield, leading to compounds **8** and **9** (Scheme 4), was carefully investigated.[17]

Compound (±)-**5b** was first chosen as the starting substrate and some meaningful data are presented in Table 1.† The low electrophilicity of the heterocycle was enhanced by performing the addition of the nucleophile in the presence of a suitable alkyl or aryl chloroformate.[34] In this case, the best results were obtained using phenyl chloroformate, which allowed the addition to be complete in most cases at −78°C. In contrast, the reaction was very slow when benzyl or methyl chloroformate were used (entries 1 and 2) and, with the first reagent, we observed a decrease in the diastereomeric ratio. The reaction was always very regioselective, with nucleophilic attack occurring only on C-2 (with the exception of entry 6 in which cerous acetylide also gave a small additional amount of attack on C-4). Changing the order of addition of the reagents, the reaction temperature, or the counterion of the acetylide affected only the yields, while the observed d.r. were not influenced in an appreciable manner. One exception was seen with lithium acetylide, which gave a complex reaction mixture, the addition products being present only in negligible amounts. The screening was performed on 100 mg of (±)-**5b** using 3 molar equiv. of a 0.5 M solution of acetylide in THF and 3 molar equiv. of chloroformate. When the reaction was scaled up to 10–14 mmol, the amount of reagents was reduced to not more than 1.5–2 molar equiv., without observing appreciable changes. In all cases, however, the d.r. was moderate, with **8** always predominating. This fact prompted us to study the influence of the protecting group of the primary alcohol function on the diastereoselectivity.



Scheme 4.

The same reaction was performed on the complete series of racemic quinolines **5**, reproducing the conditions of entry 3 (Table 1). The results are shown in Table 2.

Apart from acetyl as a protecting group, for which a diminished d.r. with respect to $SiMe_2t$-Bu was observed (entry 5), in all other cases (entries 1–4, 6–11) higher d.r. was noticed. In particular, the best results were obtained using the triphenylmethyl group; in this case d.r. up to 87:13 was observed (entry 8). This ratio can be viewed as excellent considering the distance between the newly formed and pre-existing stereogenic centers. Moreover, simple fractional crystallization allowed us to increase the d.r. up to 99:1 in a very simple manner.

Table 1. Addition of acetylides to (±)-**5b** using different experimental conditions ($R^6 = SiMe_2t$-Bu; $R^1 = Me$; $R^2 = SiMe_3$)

Entry	R^3	Nucleophile	Temperature (°C)	Isolated yield (%)[a]	(±)-**8a–c**:(±)-**9a–c**[b]
1	Bn	$SiMe_3C{\equiv}CMgBr$	−78 to −2[c]	72 (69)	59:41[d] (**a**)
2	Me	$SiMe_3C{\equiv}CMgBr$	0[c]	78 (76)	66:34 (**b**)
3	Ph	$SiMe_3C{\equiv}CMgBr$	−78 to −2[c]	77 (64)	68:32[d] (**c**)
4	Ph	$SiMe_3C{\equiv}CMgBr$	−78 to 0[c]	87 (84)	68:32 (**c**)
5	Ph	$SiMe_3C{\equiv}CMgBr$	−78[c]	66 (63)[e]	67:33 (**c**)
6	Ph	$SiMe_3C{\equiv}CCeCl_2$	0[c]	30 (24)[f]	68:32 (**c**)
7	Ph	$SiMe_3C{\equiv}CMgCl$	−78 to 0[c]	35 (34)	68:32 (**c**)

[a] Since by-products derived from chloroformate are always present and not easy to separate from **8**/**9**, the yield after purity determination by GLC analysis is reported in brackets.

[b] Determined by GLC, if not otherwise specified.

[c] Reaction conditions: [for each entry order of addition of reagents was reported (quinoline = a, nucleophile = b, chloroformate = c, temperature and reaction times were reported only if necessary); reactions were performed on 100 mg of (±)-**5b**, using 3 molar equiv. of nucleophile (0.5 M sol. in THF) and 3 molar equiv. of chloroformate]. *E1*, *E3*, *E7*: a+b+c, *E2*: b+a+c (after 10 min), *E4*: b+c (−78→0°C, 1.5 h)+a (−78°C), *E5*: b+a (3 h)+c, *E6*: b+a+c.

[d] Determined by GC–MS (HP-1 column).

[e] This reaction was performed on a preparative scale (10 mmol) under these conditions, but using 2–3 molar equiv. of nucleophile and 1.5 molar equiv. of chloroformate to give, after 15 h, the mixture (±)-**8**,**9** in 96% yield.

[f] Together with 4–5% products derived from addition of nucleophile on C-4.

† Complete data have already been reported (Ref. 17).

Table 2. Addition of acetylides to quinolines (±)-**5** and **6** (R^3 = Ph; Met = MgBr)

Entry	Compound	R^6	R^1	R^2	Temperature (°C)	Isolated yield (%)[a]	**8d–o**:**9d–o**[b]
1	(±)-**5a**	H	Me	$SiMe_3$	−78→−45[c]	61 (41)	73:27[d] (**d**)
2	(±)-**5c**	$SiPh_2t$-Bu	Me	$SiMe_3$	−78→0[c]	56 (41)	70:30[d] (**e**)
3	(±)-**5c**	$SiPh_2t$-Bu	Me	$SiMe_3$	−78→−21[c]	95 (86)	69:31[d] (**e**)
4	(±)-**5d**	Me	Me	$SiMe_3$	−78→−14[c]	76 (73)	67:33[e] (**f**)
5	(±)-**5e**	Ac	Me	$SiMe_3$	−78[c]	80 (69)	61:39[d] (**g**)
6	(±)-**5f**	p-OMe-C_6H_4	Me	$SiMe_3$	−78→−30[c]	75 (73)	70:30[e] (**h**)
7	(±)-**5g**	p-NO_2-C_6H_4	Me	$SiMe_3$	−78→−35[c]	88 (82)	75:25[d] (**i**)
8	(±)-**5h**	Tr	Me	$SiMe_3$	−78[c]	77 (76)	87:13[d,f] (**j**)
9	(±)-**5h**	Tr[g]	Me	$SiMe_3$	−78[c]	98 (85)	84:16[d,f] (**j**)
10	(±)-**5h**	Tr	Me	CH_2OCH_2Ph	−78[c]	77[h]	84:16[i] (**k**)
11	(±)-**5h**	Tr	Me	CH_2OCH_2(p-OMe)C_6H_4	−78[c]	75[h]	84:16[j] (**l**)
12	**6b**	Tr	CH_2OAc	$SiMe_3$	−78[c]	94	70:30[i] (**m**)
13	**6c**	MMTr[k]	CH_2OAc	$SiMe_3$	−78[c]	44	70:30[i] (**n**)
14	**6d**	DMTr[l]	CH_2OAc	$SiMe_3$	−78[c]	See text	–
15	**6e**	Tr	CH_2OH	$SiMe_3$	−78[c]	See text	–
16	**6f**	Tr	CH_2OSiEt_3	$SiMe_3$	−78[c]	87	60:40[i] (**o**)
17	**6g**	Tr	CH_2O(p-OMe)C_6H_4	$SiMe_3$	−78[c]	See text	–

[a] See note (a), Table 1 (in this case GLC or HPLC).
[b] In all cases **8** prevailed.
[c] see note (c), Table 1: *E1*, *E3–E17*: a+b+c, *E2*: a+c (0°C, 30 min)+b (−78°C).
[d] Determined by HPLC.
[e] Determined by GLC.
[f] D.r. determined more precisely after Tr removal to give the corresponding alcohols (±)-**8**,**9d**.
[g] This reaction was performed on a preparative scale (14 mmol) under these conditions, but using 2–3 molar equiv. of nucleophile and 1.5 molar equiv. of chloroformate to give, after 18 h, the mixture (±)-**8**,**9j** in 99% yield.
[h] After removal of Tr.
[i] Determined by ^1H NMR.
[j] Determined by ^{13}C NMR after Tr removal.
[k] p-Methoxyphenyldiphenylmethyl.
[l] Di(p-methoxyphenyl)phenylmethyl.

Using different acetylides—compounds having an alkoxymethyl group instead of $SiMe_3$—we did not observe appreciable effects on the results (entries 10 and 11), since these groups are probably too far away from the zone responsible for asymmetric induction. In this case, the addition products could not be separated from the excess of alkyne employed, which meant that accurate characterization and precise determination of the d.r. could not be performed until after removal of the trityl group. For analytical purposes, the mixture of products could always be separated into pure (±)-**8** and (±)-**9**, with the exception of compounds (±)-**8**–**9h**,**k**,**l**. Anyway, the best separation in view of further synthetic elaborations was obtained after *O*-protecting group removal.

The additions to **6b**–**g** were performed using trimethylsilylmagnesium acetylide (entries 12–17, Table 2). With **6b** the chemical yield was excellent (entry 12), while the d.r. was considerably lower than with compound (±)-**5h**. Planning the forthcoming elaboration of **8**,**9**, we also tested the addition reaction with substituted trityl derivatives, that can, in principle, be removed under milder conditions.[22] For this reason we employed both *p*-methoxyphenyldiphenylmethyl (MMTr) and di(*p*-methoxyphenyl)phenylmethyl (DMTr) ethers: with the first protecting group we obtained **8**,**9** with the same d.r. as the trityl protected derivative, but the yield was only moderate (entry 13), while the DMTr group in **6c** proved to be unstable under the conditions utilized and, the disappearance of starting material was accompanied by the formation of many other products. Unexpected behavior was also observed with **6e**: the presence of a free hydroxyl function was actually responsible for extensive decomposition, which is in contrast with the results obtained with alcohol (±)-**5a** (entry 1). Triethylsilyl protected **6f** was a good substrate for the addition reaction (entry 16), giving indeed an inseparable mixture of diastereoisomers but in excellent overall yield, albeit with a diminished diastereoisomeric ratio. Curious behavior was seen with **6g**, since the reaction evolved in the usual manner, with the complete disappearance of the quinoline and the formation of the expected adducts. However, during purification of the crude mixture by chromatography, only the starting material **6g** was recovered in near-quantitative yield, demonstrating that in some cases this reaction can be reversible.

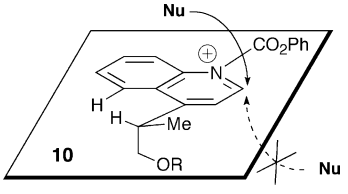
A rational interpretation of the factors affecting the stereoselectivity in the racemic series is not easy. It is clear from the experimental data that the attack of the nucleophile always takes place on the same face of the

heterocycle, since diastereoisomer **8** always prevailed. Use of force field calculations performed with CSC Chem 3D Plus for the simple trimethylsilyl ether derived from (±)-**5a** suggested that the C-4-substituent should preferentially adopt the conformation shown in Scheme 5. In it the benzylic hydrogen—the smaller substituent on the carbon bonded to the heterocycle—is directed toward the *peri* hydrogen, slightly tilted away from the aromatic plane.

Of the other two substituents, one is therefore nearly perpendicular to the aromatic ring. In this hypothesis it is reasonable that the bulkier $-CH_2OR$ group prefers to occupy this perpendicular position, and that the nucleophile will attack preferentially from the opposite side, as shown in transition state **10**. However, the extent of the d.r. cannot depend on steric effects alone. Actually, while the highest induction observed with bulky groups ($SiPh_2t$-Bu and the best of all, triphenylmethyl) can be reasonably explained on steric grounds, it is not easy to understand the behavior of (±)-**5a** and (±)-**5g**. In the first case (entry 1) the reaction must occur on the alcoholate of (±)-**5a**, and this fact should be responsible for a different electronic environment in the transition state. On the other hand, either anisyl or *p*-nitrophenyl groups (entries 6 and 7) induced higher diastereoselectivities and this can probably not be attributed to steric factors, but only to stereoelectronic effects, that have not been clearly understood.

The diminished stereoselectivity observed in the additions to derivatives **6** is most likely a consequence of the fact that the two differently protected hydroxymethyl groups are more similar than the methyl and the $-CH_2OR$ of quinolines (±)-**5**, thus making the differentiation between the two faces of the heterocycle, based on steric hindrance, less pronounced. Also in this case stereoisomer **8** prevailed, with the bulkier $-CH_2OCAr_3$ group lying nearly perpendicular to the aromatic ring.

Generally, although the stereoselectivity of these reactions is not impressive, it should be noted that they involve the formation of a new stereocenter that has a 1,4-relationship with the pre-existing one. Moreover, the first point of difference in the two oxygenated substituents of the stereogenic centers, that is the *O*-protecting group, has a 1,7-relationship with the newly created center. This reaction therefore represents an example of long-range stereocontrol.[35]



Scheme 5.

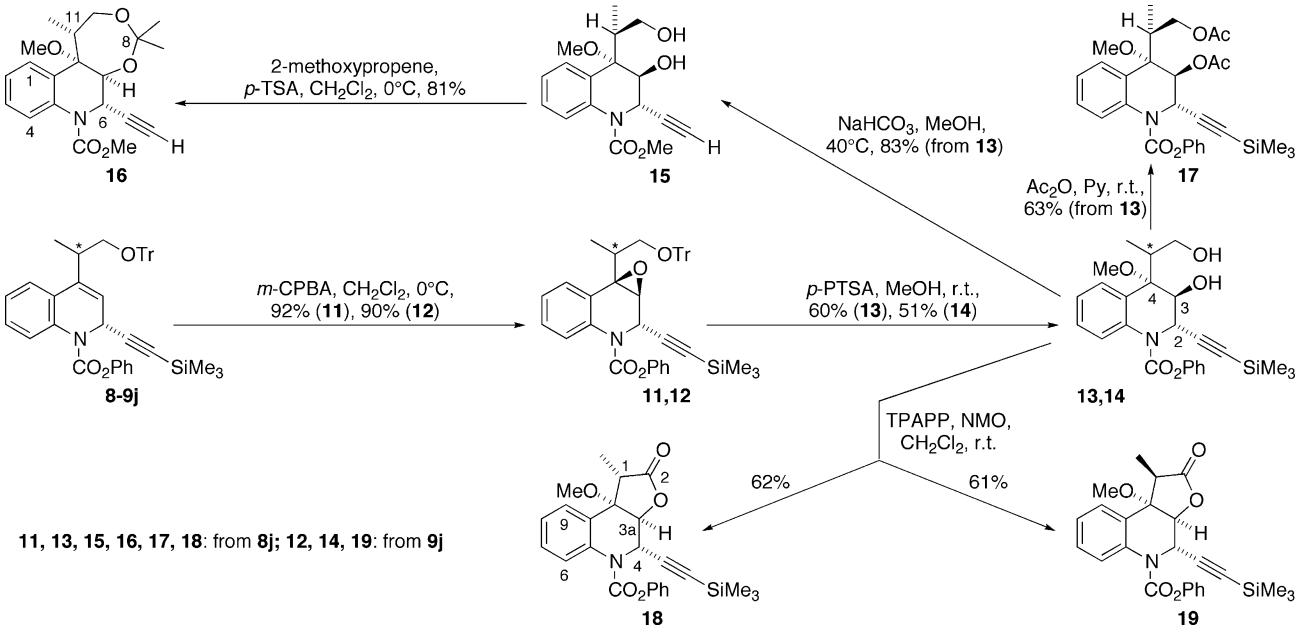
The influence of the protecting groups on the stereoselectivity of nucleophilic additions to heterocycles is well known. Isobe's group observed good diastereoselectivity (up to 93:7) during the addition of acetylides to 4-substituted quinolines bearing an *O*-protecting group in a 1,6-relationship with the newly created stereocenter.[36] Moreover, we obtained excellent results performing the same reaction on 3-substituted isoquinolines (with d.r. up to 95:5), bearing an *O*-protecting group in the same relationship with the newly formed stereogenic carbon at C-2.[37]

2.2. Relative configuration of compounds 8 and 9

After our screening was complete we had to establish the relative configuration of compounds **8**,**9** and to correlate the addition products to demonstrate which epimer prevails during the addition of the acetylide.

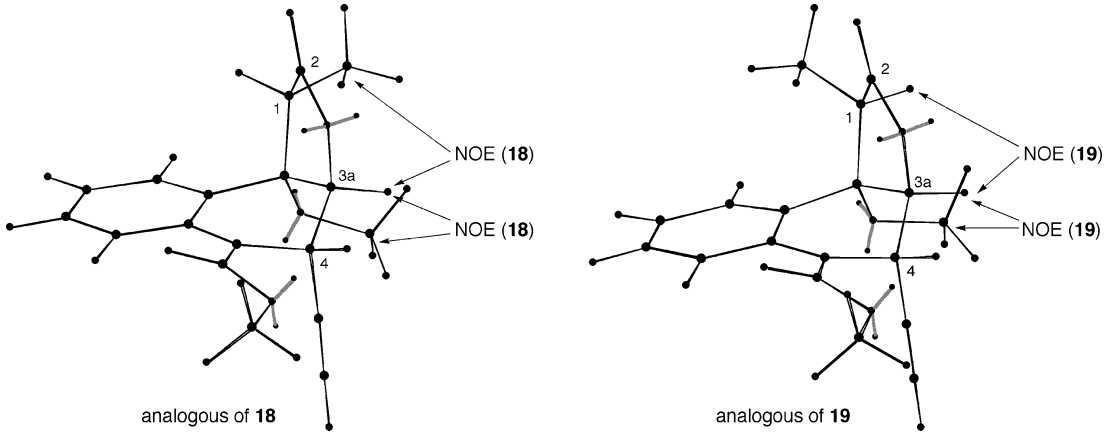
To solve the first problem, we decided to transform both (±)-**8j** and (±)-**9j** into tricyclic derivatives, hopefully suitable for NOE studies. As a first goal we planned to synthesize a cyclic acetonide. For this purpose we exploited the epoxidation of (±)-**8**,**9j**, a reaction that is known to be highly stereoselective on this family of compounds, with the epoxide forming on the opposite side of the triple bond on C-2.[38] Both compounds (±)-**11**,**12** were obtained as a single diastereoisomer when (±)-**8j** and (±)-**9j** were separately treated with *m*-chloroperbenzoic acid (Scheme 6). Both derivatives were then reacted with *p*-toluenesulfonic acid in dry methanol. Under these conditions, the trityl group was removed and the oxirane underwent an acid catalyzed ring opening, with methanol acting as nucleophile. The structure of compounds (±)-**13**,**14** was established on the basis of the following considerations: (1) the methoxy group must be bonded on benzylic carbon; actually, acetylating (±)-**13**, diacetate (±)-**17** was isolated in which H_3 was shifted downfield as expected, passing from an alcoholic function to an acetoxy group (from 4.02 ppm as broad doublet to 5.30 ppm as doublet); (2) the *trans* relationship between OMe and OH was supposed on the basis of the opening mechanism of epoxides and confirmed later on acetonide (±)-**16** and on lactones (±)-**18**,**19**; (3) the *trans* relationship between H_2 and H_3 was established by the coupling constants in the proton spectrum.

For the transformation of (±)-**8j** into a cyclic acetonide we first treated (±)-**13** with $NaHCO_3$ in methanol to cleave the C–$SiMe_3$ bond. We were surprised to isolate as the major product, methyl carbamate (±)-**15**, which was transformed into acetonide (±)-**16** under standard conditions. Since we demonstrated that the transformation of phenyl carbamate into methyl carbamate does not occur during the treatment with acid, the only step responsible for the observed reaction must be the second, although this reaction is peculiar just for this



Scheme 6.

substrate.‡ However, (±)-**16** was found to be unsuitable for the determination of the relative configuration of all the four stereocenters using spectroscopic methods and this is most likely due to the fact that several conformations with comparable energy are present. NOEDIFF experiments on (±)-**16** confirmed only that the junction between the two saturated rings must be *cis*. Finally, more useful information on the relative configuration of the stereocenters could be obtained from lactones (±)-**18**,**19**, obtained by selective oxidation of the primary alcoholic function of (±)-**13** and (±)-**14** with tetrapropylammonium perruthenate (TPAPP), to give a one-pot conversion into the tricyclic derivatives (±)-**18** and (±)-**19**.[39] Force field calculations on slightly simplified analogues, with H instead of $SiMe_3$ and OMe instead of OPh (Scheme 7), helped us make some hypotheses on the three-dimensional structure of (±)-**18**,**19**, which were confirmed by ^1H NMR spectra (both chemical shift and coupling constants data) and NOEDIFF experiments. In particular, the information collected for both lactones, allowed us to make certain conclusions: (1) the C_{3a}–O bond is axial with respect to the nitrogen containing ring. A dihedral angle (C_{3a}–H_{3a}–C_4–H_4) of 54–56° was predicted by calculations for both stereoisomers, which is in good agreement with the spectroscopic data obtained. Actually, H_4 and H_{3a} gave two singlets at 5.10 and 5.73 ppm, respectively, in **18** and two doublets at 5.12 and 5.73 ppm, respectively, in **19** with a constant of 1.5 Hz; (2) the lactone ring is nearly planar; (3) one of the two substituents (H for **18** and Me for **19**) is directed toward the aromatic ring, causing a strong upfield shift



Scheme 7.

‡ The same reaction performed on an advanced intermediate in the synthesis of **1a**,**b** gave indeed the expected product (Ref. 45).

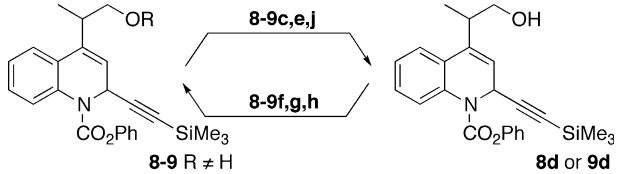
in proton spectrum with respect to the opposite situation [H (**18**): 2.52 ppm; H (**19**): 3.15 ppm; Me (**18**): 1.21 ppm; H (**19**): 0.77 ppm]; (4) a strong NOE is observed between H_{3a} and OMe as a consequence of the *cis* junction between the five- and the six-membered ring; (5) a moderate NOE effect is present between H_{3a} and Me α to C=O in **18** and between H_{3a} and H α to C=O in **19**.

In conclusion, all the data obtained agree with the attribution of structure (±)-**18** to the lactone derived from (±)-**8j** and (±)-**19** to the lactone obtained from (±)-**9j**. The most striking evidence for the assignment of the relative stereochemistry to the carbon α to C=O with respect to the other stereogenic centers is shown by the chemical shifts of the substituents attached to it. Since, during the transformation of (±)-**8j** and (±)-**9j** into (±)-**18**,**19**, the initial present stereogenic centers were not subjected to manipulations, the determination of the relative configuration of the two lactones allows us to attribute structure (±)-**8j** to the prevailing stereoisomer obtained by the addition of acetylides to (±)-**5h** and (±)-**9j** to the minor stereoisomer.

At this point we had only to correlate all major obtained diastereoisomers reported in Table 2 with (±)-**8j** and the minor diastereoisomers with (±)-**9j**. The correlation between (±)-**8**,**9c**,**d**,**e** and (±)-**8**,**9j** was quite simple and was based on the interconversion of protecting groups (Scheme 8). We established that (±)-**8d** can be obtained after trityl removal from (±)-**8j**, and (±)-**8c**,**e** were transformed into (±)-**8d**, by simple removal of the silyl protecting group.

Since a methyl ether requires drastic conditions for its removal, we preferred the methylation of (±)-**8d**, a reaction that was found to be unexpectedly troublesome. Many methods were tested (NaH, MeI; MeOTf, 2,6-lutidine; CH_2N_2, SiO_2;[40] MeI, Ag_2O[41]) but (±)-**8f** was isolated in negligible amounts or did not form at all and, in the last case, only decomposition of the starting material was observed. Finally, using methyl triflate and 2,6-di-*t*-butyl-4-methylpyridine instead of 2,6-lutidine and working at 60°C, allowed the desired (±)-**8f** to be obtained in reasonable yield.[42]

Hydrolysis of the acetyl group in (±)-**8g** was not trivial, since basic conditions also cleaved the C–Si bond. The alternative hydrolysis in the presence of a lipase (from *Candida antarctica* or porcine pancreas) was unsuccessful: while the latter enzyme did not accept this substrate at all, the former required the reaction to be carried out at 60°C or above[§] before a very sluggish reaction began. For this reason we preferred to acetylate (±)-**8d** under standard conditions, thus obtaining (±)-**8g**.



8-9c,e: HF, MeCN, -20°C, 91% (**c**) and 75% (**e**)
8,9j: *p*-TSA, MeOH, 0°C, 99%

8,9f: MeOTf, 2,6-di*t*-Bu-4-methylpyridine, $CHCl_3$, 60°C, 73%
8,9g: Ac_2O, Py, r.t., 87%
8,9h: *p*-$OMeC_6H_4$, PPh_3, CH_2Cl_2, r.t., 67-68%

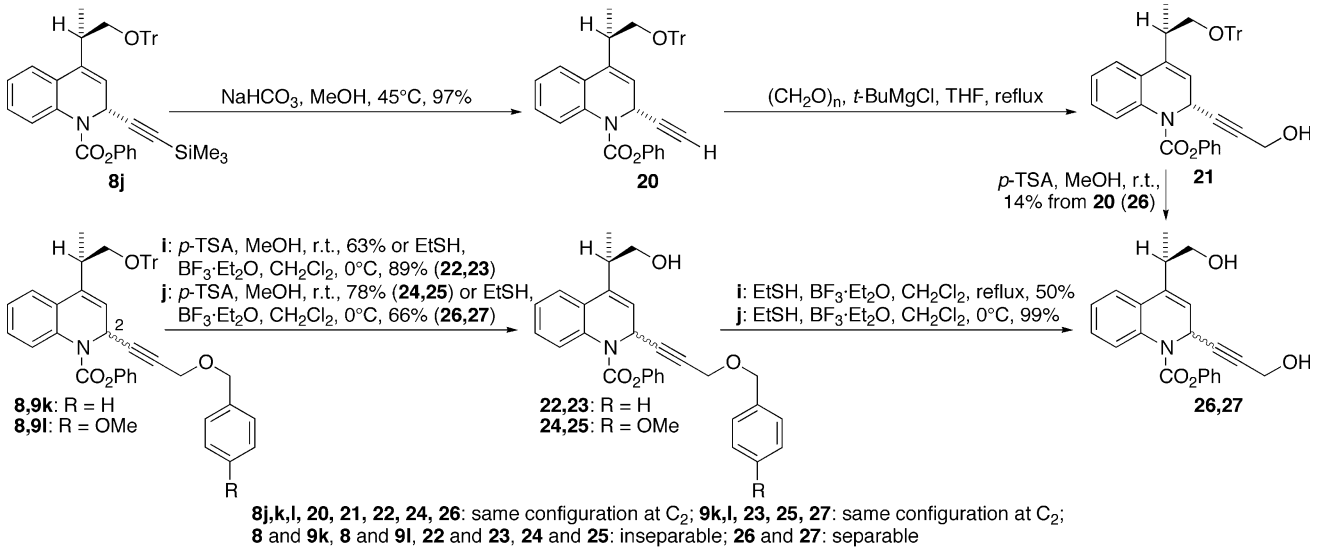
Scheme 8.

Removal of the *p*-anisyl group under oxidative conditions (cerium ammonium nitrate) gave a faster competitive 1,2-oxidation, with the formation of a quinoline bearing the acetylenic moiety at C-2, followed by slower protecting group cleavage. In this case we correlated (±)-**8h** by transforming (±)-**8d** into the *O*-protected derivative under Mitsunobu conditions. However, the same reaction performed in order to prepare (±)-**8i** did not succeed and so the relative stereochemistry of that compound is assumed just by analogy with the very similar *p*-anisyl derivative. For compounds (±)-**8**–**9a**,**b** we did not demonstrate the relative configuration, although, on the basis of spectroscopic and chromatographic analogies, also in this case the relative stereochemistry of the prevailing diastereoisomer is most likely the same as the very similar (±)-**8c** derivative.

We chose to transform compounds (±)-**8**–**9k**,**l** into a common intermediate that can also be obtained from (±)-**8**,**9j** after homologation at the acetylenic carbon. Diastereomerically pure (±)-**8j** was transformed into alkyne (±)-**20**, which was treated with *t*-butylmagnesium chloride and paraformaldehyde (Scheme 9). The reaction was sluggish and very slow, affording, after trityl removal, diol (±)-**26** in modest yield. On the other hand we tried to transform both diastereoisomeric mixtures (±)-**8**–**9k**,**l** into chromatographically separable diols (±)-**26**,**27**. Both epimeric mixtures were separately treated with boron trifluoride etherate in the presence of ethanethiol, a method known to give cleavage of benzyl-, *p*-methoxybenzyl- and trityl ethers.[43] While the mixture composed by (±)-**8**,**9l** was transformed, albeit in moderate yield into (±)-**26**,**27**, under the same conditions (±)-**8**,**9k** underwent only trityl cleavage in excellent yield. The benzyl group could be removed only forcing the conditions, that is working at reflux, but in this case the reaction was not clean. For (±)-**8**,**9l** a two-step sequence as summarized in Scheme 9 gave better results. Since (±)-**26** and (±)-**27** are readily separated, we ascertained that also in this series (±)-**26**, which has been also obtained from (±)-**8j**, prevailed.

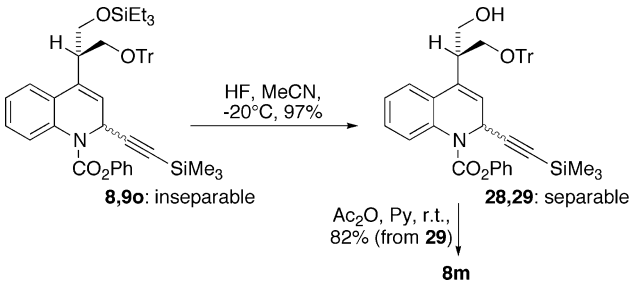
As the final step we had to correlate compounds obtained by nucleophilic addition to **6b**,**c**,**f** with **8**,**9**. We easily demonstrated that the same diastereoisomer predominated, by cleaving the triethylsilyl ether of the mixture **8**,**9o** and acetylating the prevailing diastereoiso-

[§] This enzyme can usually work at this temperature without losing its activity (Ref. 37).



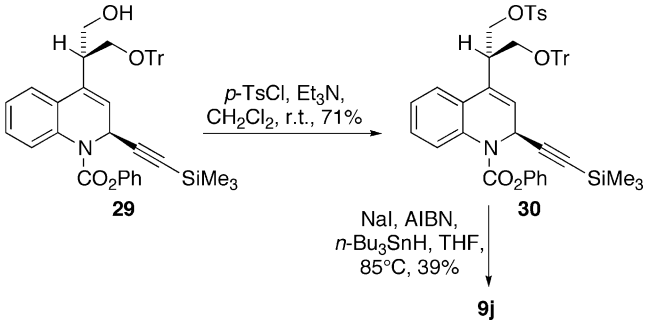
Scheme 9.

mer of the free alcohol, that is **28** to give **8m** (Scheme 10).¶



Scheme 10.

On the other hand, the reductive cleavage of one of the two C–O bonds permitted conversion of **29** into (–)-**9j** (Scheme 11). This reaction was quite difficult and many usually employed conditions ($NaBH_4$/DMSO, Red-Al®, Super-Hydride®) failed. Finally, the reaction succeeded under radical conditions with tri-*n*-butyltin hydride in the presence of sodium iodide. The choice of solvent was crucial: when commonly employed 1,2-dimethoxyethane was used[44] **9j** was not obtained, while using THF and working in a sealed tube at 85°C, compound **9j** could be isolated, albeit in moderate yield.



Scheme 11.

3. Conclusions

In this paper we have reported a new example of diastereoselective functionalization of quinoline derivatives, in which the d.r. is mostly influenced by the nature of a *O*-protecting group. The reaction has been performed on racemic substrates like **5** and enantiomerically pure compounds like **6** to give polyfunctionalized derivatives, useful intermediates for more complex molecules of potential biological activity. Part of this project has already been realized in our group,[45] while other studies are currently under investigation and will be presented in due course.

4. Experimental

4.1. General

NMR spectra were taken in $CDCl_3$, at 200 MHz (^1H), and 50 MHz (^{13}C), using TMS as internal standard. Chemical shifts are reported in ppm (δ scale), coupling constants are reported in hertz. Peak assignment in ^1H

¶ The spectroscopic analogies between **8**,**9m** and **8**,**9n** allowed us to suggest **8n** as the most likely structure for the prevailing diastereoisomer obtained by acetylide addition to **6c**.

NMR spectra was also made with the aid of double resonance experiments. In ABX systems, the proton A is considered downfield and B upfield. Peak assignment in ^{13}C spectra was made with the aid of DEPT experiments. GC–MS were carried out on a HP-5971A instrument, using an HP-1 column (12 m long, 0.2 mm wide), electron impact at 70 eV, and a mass temperature of about 170°C. Unless otherwise indicated analyses were performed with a constant He flow of 0.9 ml/min, init. temp. 100°C, init. time 2 min, rate 20°C/min, final temp. 260°C, final time 4 min, inj. temp. 250°C, det. temp. 280°C. Diastereomeric ratios were determined by GLC using a Carlo Erba FRACTOVAP gas chromatograph equipped with a RSL-150 or SE-54 (both 25 m long, 0.25 mm wide) column or by HPLC using a Waters mod. 6000 instrument with an absorbance detector mod. 440 (at 245 nm) and equipped with an Erbasil column (10 μm, 250 mm×4.6 mm). R_t are in min. IR spectra were measured with a Perkin–Elmer 881 instrument as $CHCl_3$ solutions. Values of $[\alpha]_D$ were determined on a Jasco DIP 181 polarimeter, in $CHCl_3$ (containing 0.75–1% EtOH) solution. Melting points were measured on a Büchi 535 apparatus and are uncorrected. TLC analyses were carried out on silica gel plates, which were developed by these detection methods: (**A**) UV; (**B**) dipping into a solution of $(NH_4)_4MoO_4{\cdot}4H_2O$ (21 g) and $Ce(SO_4)_2{\cdot}4H_2O$ (1 g) in H_2SO_4 (31 ml) and H_2O (469 ml) and warming. R_f were measured after an elution of 7–9 cm. Chromatographies were carried out on 220–400 mesh silica gel (if not otherwise specified) using the 'flash' methodology. Petroleum ether (40–60°C) is abbreviated as PE. In extractive work-up, aqueous solutions were always re-extracted thrice with the appropriate organic solvent. Organic extracts were washed with brine, dried over Na_2SO_4 and filtered, before evaporation of the solvent under reduced pressure. All reactions employing dry solvents were carried out under a nitrogen atmosphere. The purity of all compounds was established by TLC, ^1H NMR, GC–MS. Lipase from recombinant *C. antarctica* was a kind gift from Novo Nordisk, while PLE was purchased from Fluka.

4.2. 4-Ethylquinoline, 7

A solution of 1-chloro-3-pentanone (5.00 g, 85%, 35.25 mmol) in nitrobenzene (10 ml) was treated with freshly distilled aniline (6.42 ml, 70.50 mmol) and concentrated hydrochloric acid (2.94 ml, 35.25 mmol) and then stirred at 100°C for 18 h. The solution was diluted with Et_2O and extracted trice with 1N HCl. The aqueous extract was treated with 6N NaOH until pH 10 was reached. After filtration over a Celite pad, an usual extraction with Et_2O was performed. A rapid filtration over silica gel with PE→PE/Et_2O, 8:2, then Et_2O, followed by distillation under reduced pressure, gave compound **7** in 41–49% overall yield as a colorless oil. Bp: 83°C, 0.9 mbar. R_f 0.31 (PE/Et_2O 1:1, **A**). GC–MS (usual conditions, but with init. temp. 70°C): R_t 6.75; m/z 158 (12), 157 (M^+, 100), 154 (11), 143 (5.5), 142 (52), 130 (5.9), 129 (7.3), 128 (8.4), 116 (5.5), 115 (22), 89 (5.1), 77 (7.8), 51 (5.4), 40 (6.3). ^1H NMR: 1.40 [3H, t, >CHCH_3, J=7.6]; 3.13 [2H, q, –CH_2CH$_3$, J=7.6]; 7.26 [1H, d, H_3, J=4.7]; 7.56 [1H, ddd, H_6, J=1.4, 6.8, 8.3]; 7.70 [1H, ddd, H_7, J=1.5, 6.9, 8.3]; 8.05 [1H, dd, H_5, J=1.1, 8.4]; 8.12 [1H, dd, H_8, J=1.1, 8.4]; 8.82 [1H, d, H_2, J=4.5].

4.3. 2-Quinolin-4-yl-propan-1-ol, 5a

Ethylquinoline **7** (10.0 g, 63.61 mmol) was refluxed with aqueous formaldehyde (37%, 19 ml, 254.4 mmol) for 15.5 h. Excess formaldehyde was removed under reduced pressure and the residue was taken up with methanol and concentrated again. The residue was dissolved in MeOH and stirred under nitrogen at rt in the presence of anhydrous K_2CO_3 (2.5 g) for 20 h. After filtration of the carbonate, the solution was concentrated under reduced pressure, diluted with water and extracted as usual with Et_2O. After solvent removal, crude product was chromatographed with PE/AcOEt, 2:8→AcOEt and then AcOEt/EtOH, 97:3, to give pure **5a** as a pale yellow oil (10.59 g, 89%). R_f 0.16 (Et_2O, **A**). IR: ν_{max} 3612, 2964, 1591, 1255, 1021. GC–MS (usual conditions, but with init. temp. 80°C): R_t 8.21; m/z 188 (5.6), 187 (M^+, 42), 157 (42), 156 (100), 155 (11), 154 (30), 130 (7.5), 129 (8.6), 128 (14), 127 (7.8), 101 (5.2), 77 (6.4). ^1H NMR: 1.45 [3H, d, >CHCH_3, J=6.5]; 3.82–4.04 [3H, m, >CHCH_2OH]; 7.32 [1H, d, H_3, J=4.5]; 7.57 [1H, ddd, H_6, J=1.1, 6.9, 8.2]; 7.70 [1H, ddd, H_7, J=1.4, 6.9, 8.5]; 8.11 [1H, dd, H_5, J=1.1, 7.9]; 8.13 [1H, dd, H_8, J=1.1, 8.1]; 8.84 [1H, d, H_2, J=4.6]. ^{13}C NMR: 17.33 [>CHCH$_3$]; 36.44 [>CHCH$_3$]; 67.20 [–CH$_2$O–]; 118.12 [C_3]; 123.06 [C_5]; 126.30 [C_6]; 127.40 [C_{4a}]; 128.92 and 129.53 [2C, C_7 and C_8]; 147.67 [C_4]; 149.44 [C_2]; 150.9 [C_{8a}].

4.4. Silylation of 5a

A solution of **5a** (1.00 g, 5.34 mmol) in dry DMF (12 ml) was treated with imidazole (618 mg, 9.08 mmol) and R$_2$*t*BuSiCl and stirred at rt for 1.5–2.5 h. The solution was diluted with water/$NaHCO_3$ sat. solution (1:1) and extracted with Et_2O. The crude product was purified by chromatography using PE/AcOEt 7:3→1:1 to give the corresponding products **5b** (87% yield) and **5c** (84% yield) as colorless oils.

4.4.1. 4-{[2-(*tert*-Butyldimethylsilyloxy)-1-methyl]ethyl}-quinoline, 5b. R_f 0.45 (PE/Et_2O 1:1, **A**). IR: ν_{max} 2829, 2883, 1244, 1092. GC–MS: R_t 8.57; m/z 301 (M^+, 0.12), 246 (5.6), 245 (21), 244 (100), 214 (6.6), 170 (6.8), 154 (7.3), 89 (5.4), 75 (16), 73 (19), 59 (5.6). ^1H NMR: –0.07 and –0.08 [6H, 2 s, >Si(CH_3)$_2$]; 0.81 [9H, s, –C(CH)$_3$]; 1.43 [3H, d, >CHCH_3, J=6.6]; 3.72–3.94 [3H, m, >CHCH_2O–]; 7.31 [1H, d, H_3, J=4.7]; 7.56 [1H, ddd, H_6, J=1.4, 6.8, 8.4]; 7.70 [1H, ddd, H_7, J=1.4, 6.9, 8.2]; 8.12 [1H, dd, H_5 or H_8, J=1.1, 8.1]; 8.14 [1H, dd, H_5 or H_8, J=1.1, 8.1]; 8.85 [1H, d, H_2, J=4.6]. ^{13}C NMR: –5.51 and –5.48 [2C, >Si(CH$_3$)$_2$]; 17.24 [>CHCH$_3$]; 18.24 [–C(CH$_3$)$_3$]; 25.82 [3C, –C(CH$_3$)$_3$]; 36.25 [>CHCH$_3$]; 68.04 [–CH$_2$O–]; 118.36 [C_3]; 123.20 [C_5]; 126.18 [C_6]; 127.48 [C_{4a}]; 128.80 and 130.23 [2C, C_7 and C_8]; 148.25 [C_4]; 150.00 [C_2]; 150.58 [C_{8a}].

4.4.2. 4-{[2-(*tert*-Butyldiphenylsilyloxy)-1-methyl]ethyl}-quinoline, 5c. R_f 0.54 (PE/Et_2O 2:8, **A**). IR: ν_{max} 2930, 2859, 1729, 1590, 1462, 1374, 1240, 1105. GC–MS: R_t 12.67; m/z 425 (M^+, 0.059), 370 (8.1), 369 (31), 368 (100), 290 (19), 199 (20), 184 (6.4), 181 (8.6), 154 (5.6), 135 (5.0). ^{1}H NMR: 0.95 [9H, s, –C(C*H*)$_3$], 1.47 [3H, d, >CHC*H*$_3$, J=6.4]; 3.75–3.91 [3H, m, >C*H*C*H*$_2$O–]; 7.20–7.57 [12H, m, H_3, H_6, aromatics of TBDPS], 7.67 [1H, ddd, H_7, J=1.3, 6.9, 8.3]; 7.85 [1H, d, H_5, J=8.4]; 8.10 [1H, d, H_8, J=8.0]; 8.82 [1H, d, H_2, J=4.6]. ^{13}C NMR: 17.08 [>CH*C*H$_3$]; 19.18 [–*C*(CH$_3$)$_3$]; 26.75 [3C, –C(*C*H$_3$)$_3$]; 36.17 [>*C*HCH$_3$]; 68.60 [–*C*H$_2$O–]; 118.54 [C_3]; 123.17 [C_5]; 126.23 [C_6]; 127.50 [C_{4a}]; 127.61 and 127.67 [4C, *C meta* of TBDPS]; 128.80 and 130.24 [2C, C_7 and C_8]; 129.61 and 129.71 [2C, *C para* of TBDPS]; 133.31 and 133.44 [2C, *C ipso* of TBDPS]; 135.50 and 135.61 [4C, *C ortho* of TBDPS]; 148.31 [C_4]; 150.03 [C_2]; 150.27 [C_{8a}].

4.5. 4-[(2-Methoxy-1-methyl)ethyl]quinoline, 5d

A solution of **5a** (520 mg, 2.78 mmol) in dry THF was cooled to 0°C and treated with methyl iodide (346 μl, 5.55 mmol) and NaH (60% in mineral oil, 167 mg, 4.17 mmol). After 10 min the reaction was allowed to stir at rt for 24 h (after 3 h an equivalent amount of both reagents was added). The mixture was partitioned between NH_4Cl sat. sol. and AcOEt and extracted as usual. Chromatography with PE/Et_2O, 8:2→Et_2O gave **5d** as a pale yellow oil (324 mg, 58%). R_f 0.48 (Et_2O, **A**). IR: ν_{max} 2928, 2876, 1590, 1570, 1450, 1214, 1108. GC–MS: R_t 6.68; m/z 202 (6.5), 201 (M^+, 46), 200 (27), 170 (18), 157 (8.0), 156 (25), 155 (5.4), 154 (15), 128 (8.1), 127 (5.2), 45 (100). ^{1}H NMR: 1.44 [3H, d, >CHC*H*$_3$, J=6.8]; 3.36 [3H, s, –OC*H*$_3$]; 3.57 and 3.72 [2H, AB part of ABX system, >CHC*H*$_2$O–, J_{AB}=9.2, J_{AX} and J_{BX}=5.8, 7.2]; 3.91 [1H, sextuplet, >C*H*CH$_2$O–, J=6.7]; 7.31 [1H, d, H_3, J=4.7]; 7.58 [1H, ddd, H_6, J=1.5, 6.9, 8.3]; 7.71 [1H, ddd, H_7, J=1.3, 6.9, 8.5]; 8.13 [2H, dd, H_5 and H_8, J=1.1, 8.4]; 8.87 [1H, d, H_2, J=4.7]. ^{13}C NMR: 18.01 [>CH*C*H$_3$]; 34.04 [>*C*HCH$_3$]; 59.00 [–O*C*H$_3$]; 77.28 [–*C*H$_2$O–]; 118.08 [C_3]; 122.93 [C_5]; 126.40 [C_6]; 127.26 [C_{4a}]; 128.94 and 130.40 [2C, C_7 and C_8]; 148.43 [C_4]; 150.19 [C_2]; 150.25 [C_{8a}].

4.6. Acetic acid 2-quinolin-4-yl-propyl ester, 5e

A solution of **5a** (537 mg, 2.87 mmol) in dry pyridine (3 ml) was stirred at rt in the presence of acetic anhydride (541 μl, 5.74 mmol) for 2.5 h. The solution was partitioned between water/Et_2O and extracted as usual. After solvent removal, residue pyridine was azeotropically removed with heptane. Chromatography with PE/AcOEt 1:1→4:6 gave **5e** as a pale yellow oil (631 mg, 96%). R_f 0.55 (PE/AcOEt 1:1, **A**). IR: ν_{max} 3005, 3962, 1728, 1591, 1374, 1191. GC–MS: R_t 7.44; m/z 229 (M^+, 14), 170 (11), 169 (66), 168 (15), 157 (35), 156 (91), 155 (15), 154 (79), 130 (6.6), 129 (7.7), 128 (11), 127 (8.8), 101 (6.5), 77 (7.3), 51 (5.6), 43 (100). ^{1}H NMR: 1.46 [3H, d, >CHC*H*$_3$, J=6.9]; 2.00 [3H, s, –COC*H*$_3$]; 4.02 [1H, sextuplet, >C*H*CH$_2$O–, J=6.9]; 4.25 and 4.43 [2H, AB part of ABX system, >CHC*H*$_2$O–, J_{AB}=10.9, J_{AX} and J_{BX}=6.6, 7.1]; 7.32 [1H, d, H_3, J=4.7]; 7.60 [1H, ddd, H_6, J=1.3, 6.9, 8.5]; 7.73 [1H, ddd, H_7, J=1.4, 6.8, 8.1]; 8.15 [2H, dd, H_5 and H_8, J=1.6, 8.5]; 8.89 [1H, d, H_2, J=4.6]. ^{13}C NMR: 17.52 [>CH*C*H$_3$]; 20.77 [–CO*C*H$_3$]; 32.90 [>*C*HCH$_3$]; 68.18 [–*C*H$_2$O–]; 117.95 [C_3]; 122.62 [C_5]; 126.59 [C_6]; 127.14 [C_{4a}]; 129.08 and 130.41 [2C, C_7 and C_8]; 148.41 and 148.95 [2C, C_4 and C_{8a}]; 150.12 [C_2]; 170.90 [*C*O].

4.7. Preparation of O-Ar derivatives of 5a under Mitsunobu's conditions

A solution of **5a** (350 mg, 1.87 mmol) in dry CH_2Cl_2 (15 ml) was treated at rt with PPh_3 (637 mg, 2.43 mmol), the appropriate phenol (*p*-methoxyphenol for **5f** and *p*-nitrophenol for **5g**, 5.60 mmol) and diethyl azodicarboxylate (382 μl, 2.43 mmol). The solution was stirred for 1 h (**5f**) and 24 h (**5g**) with the addition of an equivalent amount of the reagents after 7 h. After quenching with NH_4Cl sat. sol. the mixture was extracted with AcOEt. The organic layers were rapidly washed with 1N aqueous NaOH and brine until pH≈8 was reached. After solvent removal, chromatography with the appropriate PE/Et_2O mixture gave **5f** (77% yield, colorless oil) and **5g** (76% yield, pale yellow oil).

4.7.1. 4-{[2-(*p*-Methoxyphenoxy)-1-methyl]ethyl}quinoline, 5f. R_f 0.49 (PE/AcOEt 1:1, **A**). IR: ν_{max} 2960, 1733, 1590, 1496, 1464, 1191, 1028. GC–MS: R_t 10.52; m/z 294 (12), 293 (M^+, 60), 171 (14), 170 (100), 168 (5.8), 155 (15), 154 (25), 124 (61), 123 (5.4, 109 (18). ^{1}H NMR: 1.55 [3H, d, >CHC*H*$_3$, J=6.6]; 3.75 [3H, s, –OC*H*$_3$]; 4.08 [1H, center of m, >C*H*CH$_2$O–]; 4.17 and 4.23 [2H, AB part of ABX system, >CHC*H*$_2$O–, J_{AB}=6.8, J_{AX} and J_{BX}=2.0, 4.1]; 6.80 [4H, s, *p*-anisyl]; 7.36 [1H, d, H_3, J=4.4]; 7.58 [1H, ddd, H_6, J=1.6, 7.0, 8.4]; 7.72 [1H, ddd, H_7, J=1.2, 6.6, 8.4]; 8.15 [2H, d, H_5 and H_8, J=8.8]; 8.88 [1H, d, H_2, J=4.8]. ^{13}C NMR: 17.75 [>CH*C*H$_3$]; 33.75 [>*C*HCH$_3$]; 55.60 [–O*C*H$_3$]; 72.62 [–*C*H$_2$O–]; 114.58 [2C, *C ortho* to –OMe]; 115.50 [2C, *C meta* to –OMe]; 118.13 [C_3]; 122.87 [C_5]; 126.44 [C_6]; 127.12 [C_{4a}]; 128.95 and 130.33 [2C, C_7 and C_8]; 148.35 and 149.55 [2C, C_4 and C_{8a}]; 150.10 [C_2]; 152.77 and 153.95 [2C, *C* quat. of *p*-anisyl].

4.7.2. 4-[1-Methyl-2-(*p*-nitrophenoxy)ethyl]quinoline, 5g. R_f 0.67 (AcOEt 1:1, A). IR: ν_{max} 2966, 1592, 1497, 1342, 1193, 1111, 1016. GC–MS: R_t 12.37; m/z 309 (6.1), 308 (M^+, 30), 171 (13), 170 (100), 169 (6.7), 168 (7.5), 156 (19), 155 (25), 154 (35), 143 (7.4), 142 (6.5), 128 (8.4), 127 (5.0). ^{1}H NMR: 1.60 [3H, d, >CHC*H*$_3$, J=6.5]; 4.07–4.41 [3H, m, >C*H*C*H*$_2$O–]; 6.91 [2H, dt, *H meta* to NO_2, J=2.8, 9.3]; 7.37 [1H, d, H_3, J=4.5]; 7.62 [1H, ddd, H_6, J=1.4, 6.9, 8.3]; 7.75 [1H, ddd, H_7, J=1.3, 6.8, 8.3]; 8.14 [2H, dd, H_5 and H_8, J=1.1, 8.2]; 8.18 [2H, dt, *H ortho* to NO_2, J=2.8, 9.2]; 8.90 [1H, d, H_2, J=4.6]. ^{13}C NMR: 17.66 [>CH*C*H$_3$]; 33.54 [>*C*HCH$_3$]; 72.77 [–*C*H$_2$O–]; 114.44 [2C, *C meta* to –NO_2]; 118.15 [C_3]; 122.63 [C_5]; 125.89 [2C, *C ortho* to –NO_2]; 126.77 [C_6]; 128.91 [C_{4a}]; 129.24 and 130.60 [2C, C_7 and C_8]; 141.75 [CNO_2]; 148.49 and 148.61 [2C, C_4 and C_{8a}]; 150.18 [C_2]; 163.58 [*C para* to –NO_2].

4.8. 4-[1-Methyl-2-(trityloxy)ethyl]quinoline, 5h

A solution of **5a** (493 mg, 2.63 mmol) in dry CH_2Cl_2 (20 ml) was treated with dry pyridine (317 μl, 3.94 mmol) and trityl chloride (807 mg, 2.89 mmol) and stirred at rt for 22 h. The reaction was partitioned between NH_4Cl sat. sol. and AcOEt and then extracted. Residue pyridine was removed azeotropically with heptane and the crude mixture was purified by chromatography with PE/AcOEt 7:3→6:4 to give a white foam (1.131 g, 96%), which crystallized from Et_2O to give a white solid. Mp 124.3–125.9°C (Et_2O). R_f 0.68 (PE/AcOEt 1:1, **A**, **B**). IR: ν_{max} 2969, 1591, 1487, 1449, 1189, 1070. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 14.21; m/z 429 (M^+, 0.20), 244 (22), 243 (100), 170 (8.1), 165 (24), 154 (6.2), 105 (7.9), 77 (5.1). ^{1}H NMR: 1.45 [3H, d, >CHCH_3, J=6.9]; 3.34 and 3.41 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.1, J_{AX} and J_{BX}=6.2, 7.2]; 3.91 [1H, sextuplet, >CHCH$_2$O–, J=6.7]; 7.17–7.34 [16H, m, H_3 and aromatics of Tr]; 7.52 [1H, ddd, H_6, J=1.2, 6.9, 8.3]; 7.70 [1H, ddd, H_7, J=1.4, 6.7, 8.3]; 8.02 [1H, d, H_5 or H_8, J=8.4]; 8.12 [1H, d, H_5 or H_8, J=8.0]; 8.80 [1H, d, H_2, J=4.7]. ^{13}C NMR: 17.81 [>CHCH$_3$]; 34.36 [>CHCH$_3$]; 68.21 [–CH$_2$O–]; 86.59 [–CPh$_3$]; 118.32 [C_3]; 123.26 [C_5]; 126.16 [C_6]; 126.90 [3C, *C para* of Tr]; 127.42 [C_{4a}]; 127.66 and 128.59 [12C, *C ortho* and *meta* of Tr]; 128.81 and 130.26 [2C, C_7 and C_8]; 143.90 [3C, *C ipso* of Tr]; 148.32 [C_4]; 150.06 [C_2]; 150.58 [C_{8a}].

4.9. Triarylmethyl derivatives of 6a

The same procedure described above for the preparation of **5h** was followed, starting from **6a** and using TrCl at reflux, to give **6b** (100% yield) as a white foam and MMTrCl at rt to give **6c** (95% yield) as a white foam or DMTrCl at rt to give **6d** (85% yield) as a yellow foam.

4.9.1. (*S*)-Acetic acid 2-(quinolin-4-yl)-3-(trityloxy)-propyl ester, 6b

R_f 0.35 (PE/Et_2O 2:8, A, B). $[\alpha]_D$=+31.4 (*c* 2.06, $CHCl_3$). IR: ν_{max} 2961, 1736, 1449, 1194, 1070, 1033. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 16.52; m/z 410 (M^+–77, 0.095), 244 (24), 243 (100), 228 (9.5), 186 (5.2), 168 (9.9), 167 (5.0), 166 (5.6), 165 (32), 154 (9.2), 105 (14), 77 (7.9), 43 (27). ^{1}H NMR: 1.91 [3H, s, –COCH_3]; 3.52 [2H, d, –CH_2OTr, J=5.8]; 4.16 [1H, quintuplet, –CH(CH$_2$O–)$_2$, J=6.2]; 4.58 [2H, d, –CH_2OAc, J=6.8]; 7.16–7.35 [16H, m, H_3 and aromatics of Tr]; 7.54 [1H, ddd, H_6, J=1.3, 6.3, 8.3]; 7.72 [1H, ddd, H_7, J=1.3, 6.9, 8.3]; 7.98 [1H, broad d, H_5, J=8.4]; 8.13 [1H, broad d, H_8, J=8.4]; 8.82 [1H, d, H_2, J=4.6]. ^{13}C NMR: 20.73 [–COCH$_3$]; 39.18 [–CH(CH$_2$O–)$_2$]; 63.53 and 64.27 [2C, –CH(CH$_2$O–)$_2$]; 86.92 [–CPh$_3$]; 119.16 [C_3]; 122.88 [C_5]; 126.59 [C_6]; 127.04 [3C, *C para* of Tr]; 127.36 [C_{4a}]; 127.76 and 128.51 [12C, *C ortho* and *meta* of Tr]; 129.07 and 130.39 [2C, C_7 and C_8]; 143.53 [3C, *C ipso* of Tr]; 145.43 [C_4]; 148.40 [C_{8a}]; 149.82 [C_2]; 170.81 [CO].

4.9.2. (*S*)-Acetic acid 3-{[(*p*-methoxyphenyl)-diphenyl]methoxy}-2-(quinolin-4-yl)propyl ester, 6c

R_f 0.30 (PE/Et_2O 2:8, **A**, **B**). $[\alpha]_D$=+30.4 (*c* 1.08, $CHCl_3$). IR: ν_{max} 2953, 1732, 1591, 1075, 1030. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 18.73; m/z 517 (M^+, 2.9), 273 (100), 228 (11), 195 (5.2), 186 (5.3), 168 (10), 165 (8.9), 154 (6.2), 105 (12), 77 (5.4), 43 (18). ^{1}H NMR: 1.92 [3H, s, –COCH_3]; 3.52 [2H, d, –CH_2OMMTr, J=5.8]; 3.77 [3H, s, –OCH_3]; 4.11 [1H, quintuplet, –CH(CH$_2$O–)$_2$, J=6.2]; 4.59 [2H, d, –CH_2OAc, J=6.6]; 6.76 [2H, dt, *H ortho* to –OMe, J=3.0, 9.2]; 7.14–7.36 [13H, m, H_3 and aromatics of MMTr]; 7.55 [1H, ddd, H_6, J=1.6, 7.0, 8.4]; 7.72 [1H, ddd, H_7, J=1.4, 7.0, 8.4]; 7.98 [1H, broad d, H_5, J=8.0]; 8.13 [1H, dd, H_8, J=1.2, 8.6]; 8.82 [1H, d, H_2, J=4.8]. ^{13}C NMR: 20.73 [–COCH$_3$]; 39.17 [–CH(CH$_2$O–)$_2$]; 55.11 [–OCH$_3$]; 63.42 and 64.29 [2C, –CH(CH$_2$O–)$_2$]; 86.60 [–CPh$_2$Ar]; 112.99 [2C, *C ortho* to OMe]; 119.16 [C_3]; 122.88 [C_5]; 126.56 [C_6]; 126.86 [2C, *C para* of Ph]; 127.35 [C_{4a}]; 127.73 and 128.19 [8C, *C ortho* and *meta* of Ph]; 129.05 and 130.33 [2C, C_7 and C_8]; 130.24 [2C, *C meta* to OMe]; 135.11 [*C para* to OMe]; 144.04 [2C, *C ipso* of Ph]; 145.49 [C_4]; 148.36 [C_{8a}]; 149.80 [C_2]; 158.49 [COMe of MMTra]; 170.82 [CO].

4.9.3. (*S*)-Acetic acid 3-{[bis-(*p*-methoxyphenyl)phenyl]-methoxy}-2-(quinolin-4-yl)propyl ester, 6d

R_f 0.42 (PE/Et_2O 2:8, **A**, **B**). $[\alpha]_D$=+33.0 (*c* 1.31, $CHCl_3$). IR: ν_{max} 2953, 1730, 1604, 1299, 1196, 1029. GC–MS: (usual conditions, but with final temp. 290°C) R_t 23.16; m/z 547 (M^+, 0.79), 303 (100), 228 (9.2), 186 (5.6), 168 (10), 155 (7.3), 154 (9.6), 135 (12), 105 (13), 77 (6.2), 43 (24). ^{1}H NMR: 1.92 [3H, s, –COCH_3]; 3.51 [2H, d, –CH_2ODMTr, J=5.4]; 3.77 [6H, s, –OCH_3]; 4.10 [1H, quintuplet, –CH(CH$_2$O–)$_2$, J=6.2]; 4.58 [2H, d, –CH_2OAc, J=6.6]; 6.75 [4H, apparent dd, *H ortho* to –OMe, J=1.4, 8.8]; 7.12–7.34 [10H, m, H_3 and aromatics of DMTr]; 7.54 [1H, ddd, H_6, J=1.4, 7.0, 8.4]; 7.72 [1H, ddd, H_7, J=1.4, 7.0, 8.0]; 7.98 [1H, broad d, H_5, J=8.4]; 8.13 [1H, dd, H_8, J=1.2, 8.4]; 8.82 [1H, d, H_2, J=4.4]. ^{13}C NMR: 20.74 [–COCH$_3$]; 39.20 [–CH(CH$_2$O–)$_2$]; 55.12 [2C, –OCH$_3$]; 63.36 and 64.34 [2C, –CH(CH$_2$O–)$_2$]; 86.33 [–CPhAr$_2$]; 113.00 [4C, *C ortho* to OMe]; 119.18 [C_3]; 122.92 [C_5]; 126.55 [C_6]; 126.73 [*C para* of Ph]; 127.37 [C_{4a}]; 127.73 and 127.95 [4C, *C ortho* and *meta* of Ph]; 129.05 and 130.35 [2C, C_7 and C_8]; 129.91 [4C, *C meta* to OMe]; 135.67 [2C, *C para* to OMe]; 144.56 [*C ipso* of Ph]; 145.55 [C_4]; 148.38 [C_{8a}]; 149.82 [C_2]; 158.40 [2C, COMe of DMTr]; 170.84 [CO].

4.10. (*R*)-2-(Quinolin-4-yl)-3-(trityloxy)propan-1-ol, 6e

A solution of **6b** (1.90 g, mmol) was dissolved in dry methanol (13 ml) and cooled to 0°C. A solution of 1 M solution of KOH in MeOH (5 ml) was added and the resulting mixture was stirred at the same temperature for about 2 h. The resulting solution was treated with NH_4Cl sat. sol. (10 ml) and concentrated under reduced pressure. The residue was diluted with water and extracted with AcOEt. Chromatography with PE/Et_2O 3:7→Et_2O then AcOEt gave pure **6e** (1.72 g, 99%) as a

white foam. R_f 0.26 (PE/Et_2O 1:9, **A**, **B**). $[\alpha]_D = +59.7$ (*c* 2.18, $CHCl_3$). IR: ν_{max} 3518, 3000, 2958, 1729, 1589, 1447, 1065. GC–MS: **6e** decomposed in the column. ^1H NMR: 2.50 [1H, broad s, –O*H*]; 3.62 [2H, d, –CH_2O–, $J = 6.2$]; 3.98 [1H, quintuplet, –C*H*(CH_2O–)$_2$, $J = 5.9$]; 4.02–4.18 [2H, m, –CH_2O–]; 7.13–7.41 [16H, m, H_3 and aromatics of Tr]; 7.53 [1H, ddd, H_6, $J =$ 1.2, 7.0, 8.4]; 7.68 [1H, ddd, H_7, $J = 1.4$, 7.0, 8.4]; 7.95 [1H, dd, H_5, $J = 0.8$, 8.4]; 8.08 [1H, dd, H_8, $J = 1.2$, 8.4]; 8.74 [1H, d, H_2, $J = 4.6$]. ^{13}C NMR: 42.30 [–*C*H(CH_2O–)$_2$]; 64.45 and 65.20 [2C, –CH(*C*H_2O–)$_2$]; 87.26 [–*C*Ph_3]; 119.07 [C_3]; 123.00 [C_5]; 126.50 [C_6]; 127.11 [3C, *C para* of Tr]; 127.37 [C_{4a}]; 127.85 and 128.50 [12C, *C ortho* and *meta* of Tr]; 129.05 and 130.05 [2C, C_7 and C_8]; 143.56 [3C, *C ipso* of Tr]; 146.40 [C_4]; 148.07 [C_{8a}]; 149.67 [C_2].

4.11. (*S*)-4-{1-[(Triethylsilyl)oxymethyl]-2-(trityloxy)-ethyl}quinoline, 6f

A solution of **6e** (523 mg, 1.17 mmol) in dry CH_2Cl_2 (10 ml) was cooled to 0°C and treated with 2,6-lutidine (232 μl, 2.00 mmol) and triethylsilyl triflate (319 μl, 1.41 mmol). After about 2 h at the same temperature, the solution was partitioned between water and Et_2O. After the addition of aqueous $NaHCO_3$ until pH 8 of the aqueous layer, an usual extraction was performed. After solvent evaporation, 2,6-lutidine was azeotropically removed with *n*-octane. Chromatography with PE/Et_2O 6:4→4:6 gave **6f** as a yellow oil. R_f 0.77 (PE/Et_2O 1:9, **A**, **B**). $[\alpha]_D = +15.6$ (*c* 2.06, $CHCl_3$). IR: ν_{max} 2948, 2872, 1590, 1447, 1193, 1094, 1002. GC–MS: **6f** decomposed in the column. ^1H NMR: 0.46 [6H, dq, –Si(C$H_2$$CH_3$)$_3$, $J = 1.2$, 7.8]; 0.82 [9H, t, –Si(CH_2CH_3)$_3$, $J = 7.4$]; 3.48 and 3.65 [2H, AB part of ABX system, –CH_2O–, $J_{AB} = 8.8$, J_{AX} and $J_{BX} = 5.6$, 5.8]; 3.50 [1H, quintuplet, –C*H*(CH_2O–)$_2$, $J = 5.7$]; 3.98–4.04 [2H, m, –CH_2O–]; 7.13–7.34 [16H, m, H_3 and aromatics of Tr]; 7.54 [1H, ddd, H_6, $J =$ 1.0, 7.0, 8.4]; 7.70 [1H, ddd, H_7, $J = 1.0$, 6.6, 8.0]; 8.08 [1H, d, H_5 or H_8, $J = 8.8$]; 8.12 [1H, d, H_5 or H_8, $J = 8.4$]; 8.78 [1H, d, H_2, $J = 4.8$]. ^{13}C NMR: 4.26 [3C, –Si(*C*$H_2$$CH_3$)$_3$]; 6.66 [3C, –Si($CH_2$*C*$H_3$)$_3$]; 42.58 [–*C*H($CH_2O$–)$_2$]; 63.33 and 63.81 [2C, –CH(*C*H_2O–)$_2$]; 86.67 [–*C*Ph_3]; 119.46 [C_3]; 123.33 [C_5]; 126.21 [C_6]; 126.89 [3C, *C para* of Tr]; 127.66 and 128.60 [12C, *C ortho* and *meta* of Tr]; 127.82 [C_{4a}]; 128.81 and 130.25 [2C, C_7 and C_8]; 143.86 [3C, *C ipso* of Tr]; 147.28 [C_4]; 148.35 [C_{8a}]; 149.76 [C_2].

4.12. (*S*)-4-[1-(*p*-Methoxyphenoxymethyl)-2-(trityloxy)-ethyl]quinoline, 6g

The same procedure employed for the preparation of **5f**,**g** from **5a** was followed, starting from **6e** to give **6g** in 72% yield as a white foam. R_f 0.56 (PE/Et_2O 1:9, **A**, **B**). $[\alpha]_D = -13.0$ (*c* 2.00, $CHCl_3$). IR: ν_{max} 2955, 1730, 1590, 1464, 1444, 1250, 1067. GC–MS: **6g** decomposed in the column. ^1H NMR: 3.60 and 3.69 [2H, AB part of ABX system, –CH_2O–, $J_{AB} = 9.0$, J_{AX} and $J_{BX} = 5.8$, 5.9]; 3.79 [3H, s, –OCH_3]; 4.20 [1H, center of m, >C*H*CH_2O–]; 4.34–4.46 [2H, m, –CH_2O–]; 6.75–6.86 [4H, m, *p*-anisyl]; 7.17–7.36 [16H, m, H_3 and aromatics of Tr]; 7.53 [1H, ddd, H_6, $J = 1.4$, 7.0, 8.4]; 7.71 [1H, ddd, H_7, $J = 1.3$, 7.0, 8.4]; 7.99 [1H, d, H_5, $J =$ 8.8]; 8.13 [1H, dd, H_8, $J = 1.0$, 8.4]; 8.81 [1H, d, H_2, $J = 4.4$]. ^{13}C NMR: 40.05 [–*C*H(CH_2O–)$_2$]; 55.63 [–O*C*H_3]; 62.07 and 68.44 [2C, –CH(*C*H_2O–)$_2$]; 86.84 [–*C*Ph_3]; 114.57 [2C, *C ortho* to –OMe]; 115.56 [2C, *C meta* to –OMe]; 119.48 [C_3]; 122.97 [C_5]; 126.45 [C_6]; 126.96 [3C, *C para* of Tr]; 127.42 [C_{4a}]; 127.71 and 128.52 [12C, *C ortho* and *meta* of Tr]; 128.94 and 130.26 [2C, C_7 and C_8]; 143.65 [3C, *C ipso* of Tr]; 146.18 [C_4]; 148.28 [C_{8a}]; 149.80 [C_2]; 152.62 and 153.98 [2C, *C* quat. of *p*-anisyl].

4.13. Preparation of commercially unavailable alkynes

4.13.1. Prop-2-ynyloxymethylbenzene (used for the preparation of 8,9k). A suspension of NaH (60% in mineral oil, 672 mg, 1.68 mmol) in dry DMF (10 ml) was cooled to 0°C; then benzyl alcohol (1.65 g, 15.28 mmol) was added through an addition funnel during a period of 10 min. The funnel was washed with additional DMF (3 ml) and the mixture was vigorously stirred for 25 min at 0°C. Propargyl bromide (80%, 1.87 ml, 1.68 mmol) was added dropwise via the addition funnel during 5 min. The mixture was allowed to react at 0°C for 2.5 h and 30 min at rt. Additional 122 mg of NaH and overnight stirring at rt were necessary in order to complete the reaction. After cooling again at 0°C, the reaction was quenched with NH_4Cl sat. sol. and extracted with Et_2O (1:1). Chromatography with PE/Et_2O 95:5→9:1 gave pure alkyne as a yellow oil (2.03 g, 91%). R_f 0.76 (PE/Et_2O 8:2, **A**, **B**). GC–MS: R_t 2.77; *m*/*z* 146 (M^+, 2.8), 145 (8.4), 118 (5.7), 117 (17), 116 (47), 115 (24), 107 (29), 106 (5.0), 105 (4.1), 92 (65), 91 (100), 89 (10), 79 (56), 78 (14), 77 (58), 65 (28), 63 (9.7), 52 (6.4), 51 (30), 50 (12), 40 (8.7), 39 (53), 38 (8.7). ^1H NMR: 2.48 [1H, t, –C≡C*H*, $J = 2.4$]; 4.18 [2H, d, –CH_2C≡CH, $J = 2.2$]; 4.62 [2H, s, –CH_2Ph]; 7.26–7.38 [5H, m, aromatics].

4.13.2. 1-Methoxy-4-prop-2-ynyloxymethylbenzene (used for the preparation of 8,9l). The same procedure described above was followed, performing the reaction on 80.2 mmol of 4-methoxybenzyl alcohol. The reaction was completed over 2.5 h at 0°C and 30 min at rt. After cooling again at 0°C, quenching with 50 ml of a 0.65 M aqueous solution of K_2CO_3 was performed. After extraction with Et_2O, chromatography with PE/Et_2O 95:1→9:1 gave pure alkyne as a yellow oil (10.75 g, 76%). R_f 0.62 (PE/Et_2O 7:3, **A**, **B**). GC–MS: R_t 4.75; *m*/*z* 176 (M^+, 24), 175 (8.4), 146 (9.2), 145 (5.7), 137 (7.1), 136 (50), 135 (61), 131 (5.2), 122 (17), 121 (100), 109 (14), 108 (6.5), 107 (8.2), 94 (12), 92 (9.5), 91 (14), 89 (7.7), 78 (20), 77 (46), 65 (11), 64 (7.7), 63 (9.4), 53 (5.5), 52 (8.3), 51 (16), 50 (7.6), 40 (6.4), 39 (40), 37 (6.6). ^1H NMR: 2.46 [1H, t, –C≡C*H*, $J = 2.4$]; 3.80 [3H, s, –OCH_3]; 4.14 [2H, d, –CH_2C≡CH, $J = 2.5$]; 4.54 [2H, s, –CH_2Ar]; 6.85–6.89 [2H, m, *H ortho* to OMe]; 7.26–7.32 [2H, m, *H meta* to OMe]. ^{13}C NMR: 55.27 [–O*C*H_3]; 56.68 [–*C*H_2C≡CH]; 71.14 [–*C*H_2OAr]; 74.44 [–C≡*C*H]; 79.81 [–*C*≡CH]; 113.81 [2C, *C ortho* to OMe]; 129.31 [*C para* to OMe]; 129.68 [2C, *C meta* to OMe]; 159.34 [*C*OMe].

4.14. General procedure for the addition of acetylides to 5a–h and 6a–g

Preparation of magnesium acetylide: a solution of the desired alkyne (4.44 mmol) in dry THF (6.03 ml, when EtMgBr was used, 5.36 ml when *i*-PrMgCl was used) was cooled to −15°C, before EtMgBr (1.33 ml of a 3 M solution in Et_2O, 4.0 mmol) or *i*-PrMgCl (2 ml of a 2 M solution in Et_2O) was added. The resulting red–brown solution was stirred at rt for 1 h to give a 0.5 M solution of acetylide.

Preparation and employment of cerous acetylide: a suspension of anhydrous $CeCl_3$, [previously dried by known procedure[46] from $CeCl_3{\cdot}6H_2O$ (494.6 mg 1.40 mmol)] in dry THF (1 ml) was cooled to −30°C and treated with an equimolecular amount of lithium trimethylsilyl acetylide [0.5 M solution in THF, obtained by treatment of ethynyl trimethyl silane at −30°C with a 1 M solution in THF of $LiN(SiMe_3)_2$]. The temperature was then allowed to raise to rt, before quinoline **5b** (105 mg, 350 μmol) and phenyl chloroformate (176 μl, 1.40 mmol) are added. Work-up followed the same protocol described later in the general procedure.

Addition reaction (conditions of Table 2): a solution of quinoline (the screening was performed on about 100 mg of derivative) in dry THF (5 ml) was cooled to −78°C. The acetylide solution was added (3 molar equiv.), followed by phenyl chloroformate (3 molar equiv.). The resulting solution was allowed to react at the reported temperature until complete (3–15 h). After quenching with NH_4Cl sat. sol., the mixture was extracted as usual with Et_2O. Chromatography was performed with the appropriate PE/Et_2O mixture. With the exception of **8,9d**, the mixture of purified diastereoisomers was obtained. They were further separated, with the exceptions reported below, by preparative thin layer chromatography, as reported for every addition mixture. The yields are reported in Tables 1 and 2. For preparative purposes the same procedure was followed, reducing THF quantities (about 2 ml/mmol of substrate) and acetylide or chloroformate, as reported in the Tables 1 and 2.

4.14.1. Determination of d.r. by chromatographic methods (compounds 8,9a–j). **8,9a**: GC–MS (usual conditions but with final temperature 290°C); R_t 12.25 (**8a**) and 12.60 (**9a**). **8,9b**: GLC [SE-54 column, inj. temp. 300°C, det. temp. 300°C, oven temp. 250°C, carrier (He) press. 1.60 kg/cm^2]; R_t 3.42 (**8b**) and 3.87 (**9b**). **8,9c**: GLC [RSL-150 column, inj. temp. 300°C, det. temp. 250°C, oven temp. 250°C, carrier (He) press. 1.60 kg/cm^2]; R_t 8.90 (**8c**) and 10.70 (**9c**) or GC–MS (usual conditions but with final temperature 290°C) R_t 11.89 (**8c**) and 12.21 (**9c**). **8,9d**: HPLC (hexane/Et_2O 4:6, flow 1.5 ml/min); R_t 21.55 (**8d**) and 11.90 (**9d**). **8,9e**: HPLC (hexane/CH_2Cl_2/Et_2O 95:3:2, flow 1.5 ml/min); R_t 13.20 (**8e**) and 16.40 (**9e**). **8,9f**: GLC [SE-54 column, inj. temp. 300°C, det. temp. 300°C, oven temp. 250°C, carrier (He) press. 1.60 kg/cm^2]; R_t 5.77 (**8f**) and 6.06 (**9f**). **8,9g**: HPLC (hexane/Et_2O 8:2, flow 1.2 ml/min); R_t 5.54 (**8g**) and 4.50 (**9g**). **8,9h**: GLC [RSL-150 column, inj. temp. 300°C, det. temp. 250°C, oven temp. 280°C, carrier (He) press. 1.60 kg/cm^2]; R_t 10.43 (**8h**) and 11.51 (**9h**). **8,9i**: HPLC (hexane/Et_2O 8:2, flow 1.2 ml/min); R_t 7.30 (**8i**) and 10.17 (**9i**). **8,9j**: HPLC (hexane/Et_2O 95:5, flow 1.5 ml/min); R_t 12.02 (**8j**) and 14.28 (**9j**).

4.14.2. 4-{(*S)-[2-(*tert*-Butyldimethylsilyloxy)-1-methyl]-ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid benzyl ester 8a and its epimer, 9a**. Preparative thin layer chromatography was performed with PE/Et_2O (9:1) to give **8a** and **9a** as pale yellow oils. R_f 0.55 (**8a**) and 0.44 (**9a**) (PE/Et_2O 9:1, **A**, **B**). **Characterization of 8a**: IR: ν_{max} 2929, 2858, 2168, 2091, 1696, 1391, 1288, 1247. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 12.25; *m*/*z* 398 (M^+−135, 9.6), 316 (6.4), 266 (14), 245 (55), 244 (26), 238 (5.6), 92 (7.1), 91 (100), 75 (7.3), 73 (47). ^{1}H NMR: −0.09 and −0.07 [6H, 2 s, >Si(CH_3)$_2$]; 0.02 [9H, s, –Si(CH_3)$_3$]; 0.82 [9H, s, –C(CH)$_3$]; 1.26 [3H, d, >CHCH_3, J=6.6]; 3.04 [1H, center of m, >CHCH$_3$]; 3.30 and 3.64 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.6, J_{AX} and J_{BX}=4.1, 7.8]; 5.22 and 5.30 [2H, AB system, –CH$_2$Ph, J_{AB}= 12.4]; 5.83 and 5.83 [2H, AB system, H_2 and H_3, J_{AB}=6.9]; 7.14 [1H, dt, H_6 or H_7, J=1.5, 7.4]; 7.24 [1H, dt, H_6 or H_7, J=1.5, 7.8]; 7.31–7.44 [6H, m, H_5 and Ph]; 7.64 [1H, broad d, H_8, J=8.2]. ^{13}C NMR: −5.45 and −5.37 [2C, >Si(*C*H$_3$)$_2$]; −0.13 [3C, –Si(*C*H$_3$)$_3$]; 15.88 [>CH*C*H$_3$]; 18.28 [–*C*(CH$_3$)$_3$]; 25.90 [3C, –C(*C*H$_3$)$_3$]; 36.11 [>*C*HCH$_3$]; 44.81 [C_2]; 67.32 and 67.89 [2C, –*C*H$_2$O–]; 88.08 and 101.99 [2C, –*C*≡*C*–TMS]; 121.22 [C_8]; 122.99, 124.36, 124.85 and 127.25 [4C, C_3, C_5, C_6, C_7]; 127.94 and 128.49 [4C, *C ortho* and *meta* of Ph]; 128.10 [*C para* of Ph]; 127.78 [C_{4a}]; 134.52 [C_4]; 136.05 [*C ipso* of Ph]; 137.09 [C_{8a}], 153.20 [*C*O]. **Characterization of 9a**: IR: ν_{max} 2956, 2928, 2169, 1696, 1391, 1247, 1095, 1025. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 12.60; *m*/*z* 398 (M^+−135, 12), 316 (5.0), 266 (13), 244 (10), 238 (6.1), 155 (8.2), 92 (8.7), 91 (100), 89 (7.3), 75 (6.6), 73 (46). ^{1}H NMR: 0.02 [9H, s, –Si(CH_3)$_3$]; 0.04 and 0.06 [6H, 2 s, >Si(CH_3)$_2$]; 0.90 [9H, s, –C(CH)$_3$]; 1.09 [3H, d, >CHCH_3, J=6.9]; 2.98 [1H, sextuplet, >CHCH$_3$, J=6.7]; 3.63 and 3.81 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.8, J_{AX} and J_{BX}=5.9, 6.8]; 5.24 and 5.30 [2H, AB system, –CH$_2$Ph, J_{AB}=12.5]; 5.83 and 5.83 [2H, AB system, H_2 and H_3, J_{AB}=7.2]; 7.14 [1H, dt, H_6 or H_7, J=1.4, 7.5]; 7.24 [1H, dt, H_6 or H_7, J=1.5, 7.7]; 7.32–7.44 [6H, m, H_5 and Ph]; 7.64 [1H, broad d, H_8, J=7.5]. ^{13}C NMR: −5.24 [2C, >Si(*C*H$_3$)$_2$]; −0.12 [3C, –Si(*C*H$_3$)$_3$]; 17.47 [>CH*C*H$_3$]; 18.35 [–*C*(CH$_3$)$_3$]; 26.00 [3C, –C(*C*H$_3$)$_3$]; 36.11 [>*C*HCH$_3$]; 44.62 [C_2]; 67.43 and 67.89 [2C, –*C*H$_2$O–]; 87.92 and 102.02 [2C, –*C*≡*C*–TMS]; 120.22 [C_8]; 123.17, 124.34, 124.66 and 127.16 [4C, C_3, C_5, C_6, C_7]; 127.86 and 128.48 [4C, *C ortho* and *meta* of Ph]; 128.08 [*C para* of Ph]; 128.55 [C_{4a}]; 134.41 [C_4]; 136.05 [*C ipso* of Ph]; 137.95 [C_{8a}], 153.29 [*C*O].

4.14.3. 4-{(*S)-[2-(*tert*-Butyldimethylsilyloxy)-1-methyl]-ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid methyl ester 8b and its epimer, 9b**. Preparative thin layer chromatography was performed with PE/Et_2O (9:2) to give **8b** and **9b** as pale yellow oils.

R_f 0.62 (**8b**) and 0.53 (**9b**) (PE/Et_2O 8:2, **A**, **B**). **Characterization of 8b**: IR: ν_{max} 2954, 2927, 2169, 2089, 1702, 1381, 1332, 1096, 1035. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 10.21; m/z 457 (M^+, 0.39), 400 (7.1), 284 (17), 180 (6.3), 155 (11), 89 (35), 75 (17), 74 (8.8), 73 (100), 59 (22), 45 (6.6). ^{1}H NMR: −0.07 and −0.05 [6H, 2 s, >Si(CH_3)$_2$]; 0.01 [9H, s, –Si(CH_3)$_3$]; 0.84 [9H, s, –C(CH)$_3$]; 1.26 [3H, d, >CHCH_3, J=6.6]; 3.04 [1H, center of m, >CHCH$_3$]; 3.28 and 3.64 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.7, J_{AX} and J_{BX}=4.1, 7.9]; 3.80 [3H, s, –OCH_3]; 5.80 and 5.86 [2H, AB system, H_2 and H_3, J_{AB}=6.8]; 7.15 [1H, dt, H_6 or H_7, J=1.4, 7.5]; 7.26 [1H, dt, H_6 or H_7, J=1.6, 7.6]; 7.40 [1H, dd, H_5, J=1.6, 7.6]; 7.58 [1H, broad d, H_8, J=7.0]. ^{13}C NMR: −5.56 and −5.44 [2C, >Si(CH_3)$_2$]; −0.20 [3C, –Si(CH_3)$_3$]; 15.81 [>CHCH_3]; 18.22 [–C(CH$_3$)$_3$]; 25.84 [3C, –C(CH_3)$_3$]; 36.08 [>CHCH$_3$]; 44.64 [C_2]; 53.18 [–OCH_3]; 67.28 [–CH_2O–]; 87.99 and 101.93 [2C, –C≡C–TMS]; 121.45 [C_8]; 123.00, 124.43, 124.96 and 127.25 [4C, C_3, C_5, C_6, C_7]; 127.87 [C_{4a}]; 134.56 [C_4]; 137.08 [C_{8a}], 153.90 [CO]. **Characterization of 9b**: IR: ν_{max} 2927, 2855, 1697, 1440, 1380, 1094, 1036. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 10.01; m/z 457 (M^+, 2.9), 443 (11), 442 (30), 402 (12), 401 (32), 400 (100), 370 (5.9), 339 (6.3), 338 (21), 310 (8.4), 285 (14), 284 (60), 180 (6.0), 278 (6.5), 268 (5.3), 266 (18), 252 (7.5), 194 (5.5), 192 (6.2), 180 (8.7), 89 (24), 75 (9.5), 73 (50), 59 (9.7). ^{1}H NMR: −0.005 [9H, s, –Si(CH_3)$_3$]; 0.04 and 0.07 [6H, 2 s, >Si(CH_3)$_2$]; 0.89 [9H, s, –C(CH)$_3$]; 1.09 [3H, d, >CHCH_3, J=6.9]; 2.97 [1H, sextuplet, >CHCH$_3$, J=6.6]; 3.62 and 3.81 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.8, J_{AX} and J_{BX}=6.0, 6.8]; 3.81 [3H, s, –OCH_3]; 5.81 and 5.83 [2H, AB system, H_2 and H_3, J_{AB}=7.0]; 7.14 [1H, dt, H_6 or H_7, J=1.4, 7.4]; 7.25 [1H, dt, H_6 or H_7, J=1.7, 8.1]; 7.42 [1H, dd, H_5, J=1.8, 7.8]; 7.58 [1H, broad d, H_8, J=8.2]. ^{13}C NMR: −5.34 and −5.29 [2C, >Si(CH_3)$_2$]; −0.19 [3C, –Si(CH_3)$_3$]; 17.44 [>CHCH_3]; 18.30 [–C(CH$_3$)$_3$]; 25.96 [3C, –C(CH_3)$_3$]; 36.12 [>CHCH$_3$]; 44.46 [C_2]; 53.25 [–OCH_3]; 67.50 [–CH_2O–]; 87.88 and 102.00 [2C, –C≡C–TMS]; 120.45 [C_8]; 123.22, 124.43, 124.78 and 127.18 [4C, C_3, C_5, C_6, C_7]; 128.21 [C_{4a}]; 134.48 [C_4]; 138.05 [C_{8a}], 154.02 [CO].

4.14.4. 4-{(*S)-[2-(*tert*-Butyldimethylsilyloxy)-1-methyl]-ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8c and its epimer, 9c**. Preparative thin layer chromatography was performed with PE/Et_2O (9:1) to give **8c** and **9c** as pale yellow oils. R_f 0.77 (**8c**) and 0.72 (**9c**) (PE/Et_2O 8:2, **A**, **B**). **Characterization of 8c**: IR: ν_{max} 2955, 2171, 1715, 1382, 1328, 1289, 1243. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 12.06; m/z 398 (M^+−121, 2.8), 347 (8.7), 346 (28), 338 (8.3), 278 (6.0), 266 (12), 252 (5.5), 222 (5.3), 180 (8.6), 151 (25), 115 (6.0), 89 (30), 77 (12), 75 (15), 74 (9.0), 73 (100), 59 (7.6). ^{1}H NMR: −0.038 and −0.028 [6H, 2 s, >Si(CH_3)$_2$]; 0.04 [9H, s, –Si(CH_3)$_3$]; 0.86 [9H, s, –C(CH)$_3$]; 1.30 [3H, d, >CHCH_3, J=6.7]; 3.09 [1H, center of m, >CHCH$_3$]; 3.37 and 3.69 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.7, J_{AX} and J_{BX}=4.2, 7.5]; 5.91 [2H, apparent s, H_2 and H_3]; 7.14–7.46 [8H, m, H_5, H_6, H_7, Ph]; 7.73 [1H, broad d, H_8, J=8.0]. ^{13}C NMR: −5.38 [2C, >Si(CH_3)$_2$]; −0.13 [3C, –Si(CH_3)$_3$]; 15.90 [>CHCH_3]; 18.31 [–C(CH$_3$)$_3$]; 25.93 [3C, –C(CH_3)$_3$]; 36.14 [>CHCH$_3$]; 45.17 [C_2]; 67.31 [–CH_2O–]; 88.49 and 101.54 [2C, –C≡C–TMS]; 121.61 [2C, *C ortho* of Ph]; 121.33 [C_8]; 123.14, 124.79, 125.62 and 127.40 [4C, C_3, C_5, C_6, C_7]; 125.66 [*C para* of Ph]; 128.05 [C_{4a}]; 129.30 [2C, *C meta* of Ph]; 134.24 [C_4]; 137.28 [C_{8a}]; 151.00 [*C ipso* of Ph]; 151.77 [CO]. **Characterization of 9c**: IR: ν_{max} 2954, 2927, 2169, 1714, 1381, 1327, 1304, 1246, 1190. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 12.40; m/z 398 (M^+−121, 2.4), 347 (6.5), 346 (22), 338 (6.1), 266 (8.1), 180 (7.5), 156 (5.4), 155 (13), 151 (20), 115 (5.3), 89 (34), 77 (14), 75 (14), 74 (7.5), 73 (100), 59 (8.0). ^{1}H NMR: 0.04 [9H, s, –Si(CH_3)$_3$]; 0.08 and 0.06 [6H, 2 s, >Si(CH_3)$_2$]; 0.91 [9H, s, –C(CH)$_3$]; 1.14 [3H, d, >CHCH_3, J=6.9]; 3.02 [1H, sextuplet, >CHCH$_3$, J=6.6]; 3.67 and 3.85 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.5, J_{AX} and J_{BX}=5.7, 6.7]; 5.92 [2H, apparent s, H_2 and H_3]; 7.14–7.49 [8H, m, H_5, H_6, H_7, Ph]; 7.72 [1H, broad d, H_8, J=7.0]. ^{13}C NMR: −5.25 and −5.21 [2C, >Si(CH_3)$_2$]; −0.13 [3C, –Si(CH_3)$_3$]; 17.52 [>CHCH_3]; 18.36 [–C(CH$_3$)$_3$]; 26.02 [3C, –C(CH_3)$_3$]; 36.22 [>CHCH$_3$]; 44.97 [C_2]; 67.49 [–CH_2O–]; 88.33 and 101.57 [2C, –C≡C–TMS]; 120.43 [C_8]; 121.64 [2C, *C ortho* of Ph]; 123.33, 124.80, 127.32 and 129.54 [4C, C_3, C_5, C_6, C_7]; 125.64 [*C para* of Ph]; 128.36 [C_{4a}]; 129.31 [2C, *C meta* of Ph]; 134.16 [C_4]; 138.16 [C_{8a}]; 151.00 [*C ipso* of Ph]; 151.90 [CO].

4.14.5. 4-{(*S)-[2-Hydroxy-1-methyl]ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8d and its epimer, 9d**. Pure **8d** and **9d** have been isolated by chromatography with PE/Et_2O (4:6) as solids. Both have been crystallized from Et_2O/PE to give white solids. R_f 0.39 (**8d**) and 0.47 (**9d**) (PE/Et_2O 6:4, **A**, **B**). **Characterization of 8d**: Mp 109.3–110.7°C (Et_2O/PE). IR: ν_{max} 3621, 2961, 2929, 2169, 1715, 1383, 1191, 1024. GC–MS: R_t 11.62; m/z 406 (9.5), 405 (M^+, 28), 404 (10), 374 (11), 360 (8.2), 348 (9.7), 347 (30), 346 (100), 329 (12), 328 (53), 313 (5.7), 312 (26), 284 (12), 267 (5.5), 254 (14), 253 (6.5), 252 (15), 238 (7.9), 226 (12), 222 (5.2), 208 (9.9), 194 (11), 180 (19), 156 (5.6), 77 (22), 75 (12), 74 (5.5), 73 (57). ^{1}H NMR: 0.04 [9H, s, –Si(CH_3)$_3$]; 1.34 [3H, d, >CHCH_3, J=6.8]; 3.16 [1H, sextuplet, >CHCH$_3$, J=6.6]; 3.64 [2H, m, became an AB part of ABX system at 3.54 and 3.72 after exchange with D_2O, >CHCH_2O–, J_{AB}=10.7, J_{AX} and J_{BX}=4.8, 6.2]; 5.94 and 5.98 [2H, AB system, H_2 and H_3, J_{AB}=7.0]; 7.16–7.46 [8H, m, H_5, H_6, H_7, Ph]; 7.76 [1H, broad d, H_8, J=8.2]. ^{13}C NMR: −0.22 [3C, –Si(CH_3)$_3$]; 15.81 [>CHCH_3]; 36.02 [>CHCH$_3$]; 45.15 [C_2]; 66.40 [–CH_2O–]; 88.72 and 101.26 [2C, –C≡C–TMS]; 121.52 [2C, *C ortho* of Ph]; 121.53 [C_8]; 123.05, 124.84 [most likely 2C] and 127.66 [4C, C_3, C_5, C_6, C_7]; 125.63 [*C para* of Ph]; 127.46 [C_{4a}]; 129.27 [2C, *C meta* of Ph]; 134.32 [C_4]; 136.69 [C_{8a}]; 150.88 [*C ipso* of Ph]; 151.76 [CO]. **Characterization of 9d**: Mp 112.3–113.0°C (Et_2O/PE). IR: ν_{max} 3611, 2963, 2929, 2393, 1715, 1484, 1300, 1207, 1024. GC–MS: R_t 11.66; m/z 406 (7.5), 405 (M^+, 24), 404 (8.4), 374 (9.8), 348 (7.5), 347 (28), 346 (100), 330 (5.0), 329 (12), 328 (49), 313 (5.9), 312 (25), 284 (12), 282 (10), 268 (5.1), 266 (19), 254 (14), 253 (7.7),

252 (18), 238 (9.3), 236 (5.6), 226 (12), 208 (8.9), 194 (10), 180 (17), 151 (6.4), 77 (20), 75 (9.3), 73 (53). ^{1}H NMR: 0.04 [9H, s, –Si(CH_3)$_3$]; 1.19 [3H, d, >CHCH_3, J=7.0]; 4.13 [1H, sextuplet, >CHCH$_3$, J=6.5]; 3.77 and 3.89 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=10.7, J_{AX} and J_{BX}=6.0, 6.3]; 5.95 and 5.98 [2H, AB system, H_2 and H_3, J_{AB}=6.8]; 7.17–7.48 [8H, m, H_5, H_6, H_7, Ph]; 7.75 [1H, broad d, H_8, J=7.7]. ^{13}C NMR: –0.23 [3C, –Si(CH_3)$_3$]; 17.14 [>CHCH$_3$]; 36.03 [>CHCH$_3$]; 44.81 [C_2]; 66.61 [–CH$_2$O–]; 88.76 and 101.60 [2C, –C≡C–TMS]; 120.64 [C_8]; 121.49 [2C, C *ortho* of Ph]; 122.96, 123.07 and 124.87 [most likely 2C] [4C, C_3, C_5, C_6, C_7]; 125.74 [C *para* of Ph]; 127.62 [C_{4a}]; 129.25 [2C, C *meta* of Ph]; 134.23 [C_4]; 137.44 [C_{8a}]; 150.86 [C *ipso* of Ph]; 151.77 [CO].

4.14.6. 4-{(*S)-[2-(*tert*-Butyldiphenylsilyloxy)-1-methyl]ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8e and its epimer, 9e**. Preparative thin layer chromatography was performed with PE/Et$_2$O (95:5) to give **8e** and **9e** as pale yellow oils. R_f 0.48 (**8e**) and 0.44 (**9e**) (PE/CH$_2$Cl$_2$/Et$_2$O 85:7:8, **A**, **B**). **Characterization of 8e**: IR: ν_{max} 2927, 2895, 2857, 2170, 1711, 1378, 1327, 1302, 1191, 1110. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.04 [9H, s, –Si(CH_3)$_3$]; 1.00 [9H, s, –C(CH)$_3$]; 1.38 [3H, d, >CHCH_3, J=7.1]; 3.12 [1H, center of m, >CHCH$_3$]; 3.51 and 3.71 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.7, J_{AX} and J_{BX}=4.2, 7.0]; 5.91 and 5.91 [2H, AB system, H_2 and H_3, J=7.5]; 7.04 [1H, dt, H_6, J=1.2, 8.1]; 7.07–7.75 [18H, m, aromatics]. ^{13}C NMR: –0.18 [3C, –Si(CH_3)$_3$]; 15.80 [>CHCH$_3$]; 19.26 [–C(CH$_3$)$_3$]; 26.78 [3C, –C(CH_3)$_3$]; 35.93 [>CHCH$_3$]; 45.15 [C_2]; 67.54 [–CH$_2$O–]; 88.43 and 101.62 [2C, –C≡C–TMS]; 120.76 [C_8]; 121.85 [2C, C *ortho* of –OPh]; 123.12, 124.81 [most likely 2C], and 127.33 [4C, C_3, C_5, C_6, C_7]; 125.59 [C *para* of –OPh]; 127.60 and 127.70 [5C, C *meta* to Si and, most likely, C_{4a}]; 129.28 [2C, C *meta* of –OPh]; 129.53 and 129.62 [2C, C *para* to Si]; 133.82 [C_4]; 135.53 and 135.61 [4C, C *ortho* to Si]; 135.70 and 135.80 [2C, C quat. of PhSi]; 137.00 [C_{8a}]; 151.02 [C *ipso* of –OPh]; 151.79 [CO]. **Characterization of 9e**: IR: ν_{max} 2953, 2926, 2854, 2170, 1724, 1378, 1326, 1304, 1233, 1107. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.02 [9H, s, –Si(CH_3)$_3$]; 1.08 [9H, s, –C(CH)$_3$]; 1.19 [3H, d, >CHCH_3, J=7.0]; 3.05 [1H, sextuplet, >CHCH$_3$, J=6.7]; 3.73 and 3.90 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=10.0, J_{AX} and J_{BX}=6.0, 7.1]; 5.93 [2H, s, H_2 and H_3]; 7.10 [1H, dt, H_6, J=1.2, 6.9]; 7.17–7.77 [18H, m, aromatics]. ^{13}C NMR: –0.21 [3C, –Si(CH_3)$_3$]; 17.43 [>CHCH$_3$]; 19.25 [–C(CH$_3$)$_3$]; 26.93 [3C, –C(CH_3)$_3$]; 36.28 [>CHCH$_3$]; 44.95 [C_2]; 67.84 [>CH$_2$O–]; 88.37 and 101.47 [2C, –C≡C–TMS]; 120.77 [C_8]; 121.66 [2C, C *ortho* of –OPh]; 123.22, 124.85 [most likely 2C], and 127.32 [4C, C_3, C_5, C_6, C_7]; 125.66 [C *para* of –OPh]; 127.71 and 127.76 [4C, C *meta* to Si]; 128.32 [C_{4a}]; 129.35 [2C, C *meta* of –OPh]; 129.62 and 129.72 [2C, C *para* to Si]; 133.67 [C_4]; 135.52 and 135.60 [2C, C quat. of PhSi]; 135.70 and 135.80 [4C, C *ortho* to Si]; 137.79 [C_{8a}]; 151.04 [C *ipso* of –OPh]; 151.91 [CO].

4.14.7. 4-{(*S)-[2-Methoxy-1-methyl]ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8f and its epimer, 9f**. Preparative thin layer chromatography was performed with PE/Et$_2$O (7:3) to give **8f** and **9f** as pale yellow oils. R_f 0.68 (**8f**) and 0.72 (**9f**) (PE/Et$_2$O 6:4, **A**, **B**). **Characterization of 8f**: IR: ν_{max} 2965, 2168, 1713, 1383, 1329, 1304, 1099. GC–MS: R_t 10.86; m/z 419 (M$^+$, 6.8), 347 (7.8), 346 (28), 342 (16), 326 (6.7), 298 (5.1), 254 (5.4), 252 (5.0), 226 (5.1), 222 (5.5), 194 (11), 180 (14), 77 (28), 75 (5.0), 74 (5.4), 73 (62). 59 (7.8), 51 (5.5), 45 (100). ^{1}H NMR: 0.04 [9H, s, –Si(CH_3)$_3$]; 1.34 [3H, d, >CHCH_3, J=6.2]; 3.11–3.23 (2H) and 3.45–3.56 (1H) [3H, 2 m, >CHCH_2O–]; 3.32 [3H, s, –OCH_3]; 5.92 and 5.96 [2H, AB system, H_2 and H_3, J_{AB}=6.8]; 7.17–7.47 [8H, m, H_5, H_6, H_7, Ph]; 7.75 [1H, broad d, H_8, J=7.2]. ^{13}C NMR: –0.25 [3C, –Si(CH_3)$_3$]; 16.33 [>CHCH$_3$]; 33.87 [>CHCH$_3$]; 45.10 [C_2]; 58.84 [–OCH$_3$]; 77.00 [–CH$_2$O–]; 88.57 and 101.36 [2C, –C≡C–TMS]; 121.29 [C_8]; 121.59 [2C, C *ortho* of Ph]; 122.95, 124.89 [most likely 2C] and 127.54 [4C, C_3, C_5, C_6, C_7]; 125.65 [C *para* of Ph]; 127.66 [C_{4a}]; 129.31 [2C, C *meta* of Ph]; 134.30 [C_4]; 136.96 [C_{8a}]; 150.95 [C *ipso* of Ph]; 151.82 [CO]. **Characterization of 9f**: IR: ν_{max} 2966, 2394, 1715, 1197, 1081, 1033. GC–MS: R_t 10.99; m/z 419 (M$^+$, 6.0), 347 (6.3), 346 (22), 342 (15), 326 (6.3), 254 (5.2), 226 (5.4), 222 (5.7), 194 (11), 180 (13), 77 (28), 75 (5.1), 74 (5.6), 73 (64). 59 (7.8), 51 (5.4), 45 (100). ^{1}H NMR: 0.04 [9H, s, –Si(CH_3)$_3$]; 1.19 [3H, d, >CHCH_3, J=6.9]; 3.11 [1H, center of m, >CHCH$_3$]; 3.42 [3H, s, –OCH_3]; 3.46 and 3.66 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=9.2, J_{AX} and J_{BX}=5.0, 7.4]; 5.91 [2H, apparent s, H_2 and H_3]; 7.16–7.46 [8H, m, H_5, H_6, H_7, Ph]; 7.73 [1H, broad d, H_8, J=6.8]. ^{13}C NMR: –0.24 [3C, –Si(CH_3)$_3$]; 17.69 [>CHCH$_3$]; 33.88 [>CHCH$_3$]; 44.88 [C_2]; 59.05 [–OCH$_3$]; 77.02 [–CH$_2$O–]; 88.55 and 101.52 [2C, –C≡C–TMS]; 120.44 [C_8]; 121.63 [2C, C *ortho* of Ph]; 123.10, 124.89 [most likely 2C] and 127.49 [4C, C_3, C_5, C_6, C_7]; 125.67 [C *para* of Ph]; 128.82 [C_{4a}]; 129.34 [2C, C *meta* of Ph]; 134.30 [C_4]; 137.86 [C_{8a}]; 151.00 [C *ipso* of Ph]; 151.89 [CO].

4.14.8. 4-{(*S)-[2-Acetoxy-1-methyl]ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8g and its epimer, 9g**. Preparative thin layer chromatography was performed with PE/Et$_2$O (8:2) to give **8g** and **9g** as pale yellow oils. R_f 0.29 (**8g**) and 0.33 (**9g**) (PE/Et$_2$O 8:2, **A**, **B**). **Characterization of 8g**: IR: ν_{max} 2957, 2173, 1725, 1377, 1196. GC–MS: R_t 11.99; m/z 447 (M$^+$, 8.1), 371 (7.2), 370 (28), 348 (6.7), 347 (28), 346 (100), 294 (17), 280 (5.1), 279 (9.5), 278 (17), 266 (19), 252 (9.7), 250 (9.7), 226 (10), 220 (5.9), 208 (7.0), 194 (17), 180 (20), 151 (6.6), 117 (12), 77 (25), 75 (20), 74 (5.9), 73 (64), 59 (5.2), 43 (52). ^{1}H NMR: 0.04 [9H, s, –Si(CH_3)$_3$]; 1.33 [3H, d, >CHCH_3, J=6.7]; 2.00 [3H, –COCH_3]; 3.30 [1H, sextuplet, >CHCH$_3$, J=6.5]; 3.87 and 4.22 [2H, AB part of ABX system, >CHCH_2O–, J_{AB}=10.8, J_{AX} and J_{BX}=5.0, 8.2]; 5.94 and 5.99 [2H, AB system, H_2 and H_3, J_{AB}=6.8]; 7.00–7.50 [8H, m, H_5, H_6, H_7, Ph]; 7.74 [1H, broad d, H_8, J=6.8]. ^{13}C NMR: –0.19 [3C, –Si(CH_3)$_3$]; 15.98 [>CHCH$_3$]; 20.83 [–COCH$_3$]; 32.93 [>CHCH$_3$]; 45.05 [C_2]; 68.16 [–CH$_2$O–]; 88.74 and 101.21 [2C, –C≡C–

TMS]; 121.58 [2C, *C ortho* of Ph]; 121.83 [C_8]; 123.01, 124.97, 125.14 and 127.69 [4C, C_3, C_5, C_6, C_7]; 125.64 [*C para* of Ph]; 127.53 [C_{4a}]; 129.30 [2C, *C meta* of Ph]; 134.33 [C_4]; 136.43 [C_{8a}]; 150.99 [*C ipso* of Ph]; 151.81 [–O*C*OPh]; 170.91 [–*C*OCH$_3$]. **Characterization of 9g**: IR: ν_{max} 2956, 2168, 1723, 1376, 1285, 1243. GC–MS: R_t 12.28; *m*/*z* 447 (M^+, 9.7), 371 (7.0), 370 (24), 347 (15), 346 (50), 295 (5.0), 294 (22), 280 (5.3), 279 (9.0), 278 (18), 266 (18), 252 (9.9), 250 (9.5), 236 (6.0), 226 (11), 220 (6.3), 208 (9.8), 194 (19), 193 (6.2), 180 (21), 156 (5.2), 154 (6.1), 151 (7.2), 117 (23), 97 (5.3), 77 (43), 75 (33), 73 (100), 65 (5.9), 59 (7.6), 51 (5.8), 45 (7.6), 43 (87). ^{1}H NMR: 0.04 [9H, s, –Si(C*H*$_3$)$_3$]; 1.20 [3H, d, >CHC*H*$_3$, J=7.0]; 2.09 [3H, –COC*H*$_3$]; 3.24 [1H, sextuplet, >C*H*CH$_3$, J=6.9]; 3.87 and 4.22 [2H, AB part of ABX system, >CHC*H*$_2$O–, J_{AB}=10.8, J_{AX} and J_{BX}= 5.0, 8.2]; 5.94 and 5.99 [2H, AB system, H_2 and H_3, J_{AB}=6.8]; 7.00–7.50 [8H, m, H_5, H_6, H_7, Ph]; 7.74 [1H, broad d, H_8, J=6.8]. ^{13}C NMR: –0.18 [3C, –Si(*C*H$_3$)$_3$]; 17.49 [>CH*C*H$_3$]; 20.95 [–CO*C*H$_3$]; 32.94 [>*C*HCH$_3$]; 44.92 [C_2]; 67.81 [–*C*H$_2$O–]; 88.76 and 101.24 [2C, –*C*≡*C*–TMS]; 120.96 [C_8]; 121.58 [2C, *C ortho* of Ph]; 122.96, 124.98 [most likely 2C] and 127.70 [4C, C_3, C_5, C_6, C_7]; 125.68 [*C para* of Ph]; 127.54 [C_{4a}]; 129.32 [2C, *C meta* of Ph]; 134.33 [C_4]; 136.88 [C_{8a}]; 150.98 [*C ipso* of Ph]; 151.84 [–O*C*OPh]; 170.95 [–*C*OCH$_3$].

4.14.9. 4-{(*S)-[2-(*p*-Methoxyphenoxy)-1-methyl]ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8h and its epimer, 9h**. Both components of the mixture **8**,**9h**, as a pale yellow oil, could not be separated. R_f 0.39 (**8h** and **9h**) (PE/Et$_2$O 8:2, **A**, **B**). Both compounds have however been characterized separately, by protection of **8d** and **9d** (see text and experimental below). **Characterization of 8h**: IR: ν_{max} 3014, 2956, 2169, 1713, 1380, 1301, 1014. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 14.62; *m*/*z* 512 (8.2), 511 (M^+, 20), 435 (14); 434 (48), 418 (14), 390 (14), 388 (7.4), 386 (6.6), 374 (8.6), 348 (7.6), 347 (30), 346 (100), 294 (8.1), 280 (6.1), 266 (12), 264 (6.4), 254 (6.2), 252 (14), 250 (8.1), 226 (11), 222 (8.0), 220 (6.1), 194 (28), 193 (6.2), 181 (6.1), 180 (19), 170 (10), 154 (6.8), 151 (11), 137 (20), 124 (15), 123 (14), 109 (18), 107 (19), 97 (6.8), 95 (6.5), 94 (6.6), 92 (7.9), 77 (52), 75 (6.7), 74 (6.7), 73 (73). ^{1}H NMR: 0.05 [9H, s, –Si(C*H*$_3$)$_3$]; 1.44 [3H, d, >CHC*H*$_3$, J=6.5]; 3.38 [1H, center of m, >C*H*CH$_3$]; 3.63 [1H, t, >CHC*H*HO–, J=8.8]; 3.75 [3H, –OC*H*$_3$]; 4.04 [1H, dd, >CHCH*H*O–, J=3.9, 9.0]; 5.94 and 6.03 [2H, AB system, H_2 and H_3, J_{AB}=6.7]; 6.80 [4H, s, *p*-anisyl]; 7.15–7.48 [8H, m, H_5, H_6, H_7, Ph]; 7.76 [1H, broad d, H_8, J=7.8]. ^{13}C NMR: –0.17 [3C, –Si(*C*H$_3$)$_3$]; 16.28 [>CH*C*H$_3$]; 33.79 [>*C*HCH$_3$]; 45.14 [C_2]; 55.71 [–OCH$_3$]; 72.85 [–*C*H$_2$O–]; 88.72 and 101.24 [2C, –*C*≡*C*–TMS]; 114.58 [2C, *C ortho* to –OMe]; 115.65 [2C, *C meta* to –OMe]; 121.59 [2C, *C ortho* of Ph]; 121.79 [C_8]; 122.95, 124.96 [most likely 2C] and 127.66 [4C, C_3, C_5, C_6, C_7]; 125.66 [*C para* of Ph]; 129.30 [3C, *C meta* of Ph and, most likely, C_{4a}]; 134.32 [C_4]; 136.59 [C_{8a}]; 150.91 [*C ipso* of Ph]; 151.79 [*C*O]; 152.99 and 153.83 [2*C* quat. of *p*-anisyl]. **Characterization of 9h**: IR: ν_{max} 3002, 2958, 2168, 1714, 1379, 1324, 1287, 1013. GC–MS: (usual conditions, but with fin. temp. 290°C) R_t 15.06; *m*/*z* 511 (M^+, 16), 435 (13); 434 (35), 418 (11), 390 (10), 388 (8.7), 374 (9.8), 347 (22), 346 (98), 294 (9.7), 266 (19), 252 (15), 250 (9.9), 226 (9.9), 222 (9.4), 204 (8.4), 194 (35), 180 (21), 179 (8.7), 170 (13), 151 (2), 137 (26), 124 (22), 123 (14), 109 (27), 107 (31), 94 (12), 92 (9.3), 77 (56), 75 (8.5), 74 (8.4), 73 (100), 43 (9.1). ^{1}H NMR: 0.05 [9H, s, –Si(C*H*$_3$)$_3$]; 1.38 [3H, d, >CHC*H*$_3$, J=7.0]; 3.33 [1H, sextuplet, >C*H*CH$_3$, J=6.6]; 3.78 [3H, –OC*H*$_3$]; 3.99 and 4.18 [2H, AB part of ABX system, >CHC*H*$_2$O–, J_{AB}=9.0 J_{AX} and J_{BX}=5.8, 7.2]; 5.94 and 5.97 [2H, AB system, H_2 and H_3, J_{AB}=6.0]; 6.80–6.93 [4H, m, *p*-anisyl]; 7.16–7.48 [8H, m, H_5, H_6, H_7, Ph]; 7.75 [1H, broad d, H_8, J=8.2]. ^{13}C NMR: –0.17 [3C, –Si(*C*H$_3$)$_3$]; 17.69 [>CH*C*H$_3$]; 33.65 [>*C*HCH$_3$]; 44.95 [C_2]; 55.71 [–OCH$_3$]; 72.56 [–*C*H$_2$O–]; 88.66 and 101.42 [2C, –*C*≡*C*–TMS]; 114.65 [2C, *C ortho* to –OMe]; 115.79 [2C, *C meta* to –OMe]; 120.79 [C_8]; 121.59 [2C, *C ortho* of Ph]; 123.03, 124.91 [most likely 2C] and 127.56 [4C, C_3, C_5, C_6, C_7]; 125.66 [*C para* of Ph]; 129.30 [3C, *C meta* of Ph and, most likely, C_{4a}]; 134.32 [C_4]; 136.59 [C_{8a}]; 150.91 [*C ipso* of Ph]; 151.79 [*C*O]; 153.06 and 153.96 [2*C* quat. of *p*-anisyl].

4.14.10. 4-{(*S)-[1-Methyl-2-(*p*-nitrophenoxy)]ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8i and its epimer, 9i**. Preparative thin layer chromatography was performed with PE/Et$_2$O (8:2) to give **8i** and **9i** as pale yellow oils. R_f 0.42 (**8i**) and 0.34 (**9i**) (PE/Et$_2$O 7:3, **A**, **B**). **Characterization of 8i**: IR: ν_{max} 2956, 2171, 1721, 1592, 1379, 1332, 1216, 1111, 986, 840. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.05 [9H, s, –Si(C*H*$_3$)$_3$]; 1.47 [3H, d, >CHC*H*$_3$, J=6.6]; 3.37–3.55 [1H, m, >C*H*CH$_3$]; 3.79 [1H, t, >CHC*H*HO–, J= 8.7]; 4.15 [1H, dd, >CHCH*H*O–, J=3.9, 8.9]; 5.96 and 6.07 [2H, AB system, H_2 and H_3, J_{AB}=6.8]; 6.90 [2H, dt, *H meta* to –NO$_2$, J=2.8, 9.3]; 7.15–7.48 [8H, m, H_5, H_6, H_7, Ph]; 7.78 [1H, broad d, H_8, J=7.7]; 8.16 [2H, dt, *H ortho* to –NO$_2$, J=2.8, 9.3]. ^{13}C NMR: –0.18 [3C, –Si(*C*H$_3$)$_3$]; 16.09 [>CH*C*H$_3$]; 33.52 [>*C*HCH$_3$]; 45.08 [C_2]; 72.70 [–*C*H$_2$O–]; 88.98 and 100.91 [2C, –*C*≡*C*–TMS]; 114.49 [2C, *C meta* to –NO$_2$]; 121.50 [2C, *C ortho* of Ph]; 122.35 [C_8]; 122.73, 125.07, 125.21 and 127.95 [4C, C_3, C_5, C_6, C_7]; 125.78 [*C para* of Ph]; 125.83 [2C, *C ortho* to NO$_2$]; 127.24 [C_{4a}]; 129.36 [2C, *C meta* of Ph]; 134.36 [C_4]; 135.92 [C_{8a}]; 141.50 [*C*NO$_2$]; 150.84 [*C ipso* of Ph]; 151.78 [*C*O]; 163.81 [*C para* to –NO$_2$]. **Characterization of 9i**: IR: ν_{max} 3002, 2177, 1717, 1593, 1342, 1257. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.07 [9H, s, –Si(C*H*$_3$)$_3$]; 1.33 [3H, d, >CHC*H*$_3$, J=6.9]; 3.42 [1H, sextuplet, >C*H*CH$_3$, J=6.6]; 4.14 and 4.31 [2H, AB part of ABX system, >CHC*H*$_2$O–, J_{AB}=9.0, J_{AX} and J_{BX}=5.6, 7.1]; 5.97 [2H, apparent s, H_2 and H_3]; 6.96–7.04 [2H, *H meta* to –NO$_2$]; 7.18–7.48 [8H, m, H_5, H_6, H_7, Ph]; 7.70 [1H, broad d, H_8, J=7.9]; 8.15–8.26 [2H, m, *H ortho* to –NO$_2$]. ^{13}C NMR: –0.20 [3C, –Si(*C*H$_3$)$_3$]; 17.62 [>CH*C*H$_3$]; 33.52 [>*C*HCH$_3$]; 44.91

[C_2]; 72.47 [–CH_2O–]; 88.95 and 101.22 [2C, –$C{\equiv}C$–TMS]; 114.55 [2C, *C meta* to –NO_2]; 121.14 [C_8]; 121.56 [2C, *C ortho* of Ph]; 122.84, 124.97, 125.15 and 127.88 [4C, C_3, C_5, C_6, C_7]; 125.75 [*C para* of Ph]; 125.92 [2C, *C ortho* to NO_2]; 127.36 [C_{4a}]; 129.36 [2C, *C meta* of Ph]; 134.44 [C_4]; 136.86 [C_{8a}]; 141.71 [CNO_2]; 150.96 [*C ipso* of Ph]; 151.84 [*C*O]; 163.85 [*C para* to –NO_2].

4.14.11. 4-{(*S)-[1-Methyl-2-trityloxy]ethyl}-2-{(*R**)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8j and its epimer, 9j**. Both components of the mixture **8**,**9j**, as a white foam, could not be separated. By crystallization with Et_2O/PE nearly pure **8j** (containing only 1% of **9j** by HPLC) was obtained. Mp 126.9–125.7°C (Et_2O/PE). R_f 0.35 (**8j** and **9j**) (PE/Et_2O 9:1, **A**, **B**). **Characterization of 8j**: IR: ν_{max} 2977, 1712, 1383, 1111, 1071. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.13 [9H, s, –Si(CH_3)$_3$]; 1.44 [3H, d, >CHCH_3, J=6.5]; 3.07–3.13 [1H, m, >CHCH$_3$]; 3.25–3.36 [2H, m, >CHCH_2O–]; 6.03 [2H, apparent s, H_2 and H_3]; 7.03 [1H, broad s, H_6]; 7.17–7.47 [22H, m, H_5, H_7, Ph, Tr]; 7.83 [1H, broad d, H_8, J=7.8]. ^{13}C NMR: –0.14 [3C, –Si(*C*H$_3$)$_3$]; 16.39 [>CH*C*H$_3$]; 34.25 [>*C*HCH$_3$]; 45.15 [C_2]; 67.26 [–CH_2O–]; 86.24 [–*C*Ph$_3$]; 88.43 and 101.64 [2C, –*C*≡*C*–TMS]; 121.38 [C_8]; 121.63 [2C, *C ortho* of Ph]; 123.25, 124.81, 125.04 and 127.26 [4C, C_3, C_5, C_6, C_7]; 125.47 [*C para* of Ph]; 126.74 [3C, *C para* of Tr]; 127.65 and 128.61 [12C, *C ortho* and *meta* of Tr]; 128.22 [C_{4a}]; 129.15 [2C, *C meta* of Ph]; 134.29 [C_4]; 137.72 [C_{8a}]; 144.13 [3C, *C ipso* of Tr]; 150.93 [*C ipso* of Ph]; 151.80 [*C*O]. **Characterization of 9j** (this compound was obtained pure after reduction of **30**, see experimental below): IR: ν_{max} 2955, 2922, 1708, 1377, 1305, 1190, 1066, 1017. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.07 [9H, s, –Si(CH_3)$_3$]; 1.19 [3H, d, >CHCH_3, J=6.6]; 3.08–3.36 [3H, m, >CHCH_2O–]; 5.82 and 5.89 [2H, AB system, H_2 and H_3, J_{AB}=7.0]; 7.10–7.50 [23H, m, H_5, H_6, H_7, Ph, Tr]; 7.72 [1H, broad d, H_8, J=7.8]. ^{13}C NMR: –0.32 [3C, –Si(*C*H$_3$)$_3$]; 18.06 [>CH*C*H$_3$]; 34.46 [>*C*HCH$_3$]; 44.92 [C_2]; 67.33 [–*C*H$_2$O–]; 86.50 [–*C*Ph$_3$]; 88.48 and 101.30 [2C, –*C*≡*C*–TMS]; 120.85 [C_8]; 121.66 [2C, *C ortho* of Ph]; 123.39, 124.84 [most likely 2C] and 127.36 [4C, C_3, C_5, C_6, C_7]; 125.67 [*C para* of Ph]; 126.87 [3C, *C para* of Tr]; 127.76 and 128.85 [12C, *C ortho* and *meta* of Tr]; 128.36 [C_{4a}]; 129.34 [2C, *C meta* of Ph]; 134.16 [C_4]; 138.02 [C_{8a}]; 144.15 [3C, *C ipso* of Tr]; 151.00 [*C ipso* of Ph]; 151.92 [*C*O].

4.14.12. 2-{(*R)-[3-(Benzyloxy)prop-1-ynyl]}-4-{(*S**)-[1-methyl-2-trityloxy]ethyl}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8k and its epimer, 9k**. Both components of the mixture **8**,**9k**, together with the excess of the starting alkyne, as a white foam, could not be separated. Thus only a partial characterization of them was possible. The two diastereoisomers were however separated and fully characterized after trityl and benzyl removal to give **26** and **27**, respectively (see experimental below). R_f 0.64 (**8k** and **9k**) (PE/Et_2O 6:4, **A**, **B**). **Characterization of 8**,**9k**: GC–MS: unsuitable for this analysis. ^{1}H NMR: 1.19 [3H, d, >CHCH_3 (**9k**), J=6.7]; 1.34 [3H, d, >CHCH_3 (**8k**), J=6.6]; 2.99–3.35 [3H, m, >CHCH_2O– (**8**,**9k**)]; 3.89 [2H, d, –OCH_2C≡C– (**9k**), J=1.3]; 4.02 [2H, d, –OCH_2C≡C– (**8k**), J=1.5]; 4.27 [2H, s, –OCH_2Ph (**9k**)]; 4.39 [2H, s, –OCH_2Ph (**8k**)]; 5.84–6.12 [2H, m, H_2 and H_3 (**8**,**9k**)]; 6.93 [1H, broad s, H_6 (**8**,**9k**)]; 7.08–7.48 [27H, m, H_5, H_6, H_7, –OPh, Ph, Tr (**8**,**9k**)]; 7.75 [1H, broad d, H_8, J=7.7 (**8**,**9k**)].

4.14.13. 2-{(*R)-[3-(4-Methoxybenzyloxy)prop-1-ynyl]}-4-{(*S**)-[1-methyl-2-trityloxy]ethyl}-2*H*-quinoline-1-carboxylic acid phenyl ester 8l and its epimer 9l**. Both purified components of the mixture **8**,**9k**, together with a small amount of the excess of the starting alkyne, as an ivory foam, could not be separated. Thus only a partial characterization of them was possible. The two diastereoisomers were however separated and fully characterized after trityl and 4-methoxybenzyl removal to give **26** and **27**, respectively (see experimental below). R_f 0.50 (**8l** and **9l**) (PE/Et_2O 6:4, **A**, **B**). **Characterization of 8**,**9l**: GC–MS: unsuitable for this analysis. ^{1}H NMR: 1.18 [3H, d, >CHCH_3 (**9l**), J=6.6]; 1.35 [3H, d, >CHCH_3 (**8l**), J=6.6]; 2.95–3.35 [3H, m, >CHCH_2O– (**8**,**9l**)]; 3.78 [3H, s, –OCH_3 (**9l**)]; 3.79 [3H, s, –OCH_3 (**8l**)]; 3.87 [2H, broad s, –OCH_2C≡C– (**9l**)]; 3.98 [2H, d, –OCH_2C≡C– (**8l**), J=1.5]; 4.18 [2H, s, –OCH_2Ar (**9l**)]; 4.28 [2H, s, –OCH_2Ar (**8l**)]; 5.84–6.08 [2H, m, H_2 and H_3 (**8**,**9l**)]; 6.75–7.48 [27H, m, H_5, H_6, H_7, –OPh, *p*-OMeC$_6$H$_4$, Tr (**8**,**9l**)]; 7.73 [1H, broad d, H_8, J=7.5 (**8**,**9l**)].

4.14.14. 4-{(*S*)-[1-(Acetoxy)methyl-2-trityloxy]ethyl}-2-{(*R*)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8m and its epimer, 9m. Diastereoisomers **8**,**9m** were in part separated by chromatography with PE/Et_2O 95:5→6:4 both as white foams. R_f 0.36 (**8m**) and 0.26 (**9m**) (PE/Et_2O 8:2, **A**, **B**). **Characterization of 8m**: $[\alpha]_D$=+115.1 (*c* 1.08, $CHCl_3$). IR: ν_{max} 2962, 2168, 1726, 1382, 1325, 1239, 1074, 1023. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.005 [9H, s, –Si(CH_3)$_3$]; 1.94 [3H, s, –COCH_3]; 3.21 [2H, apparent d, –CH_2OTr, J=4.8]; 3.38 [1H, quintuplet, –CH(CH$_2$O–)$_2$, J=5.7]; 4.45 and 4.92 [2H, AB part of ABX system, –CH_2OAc, J_{AB}=11.0, J_{AX} and J_{BX}=6.1, 6.7]; 5.93 [2H, apparent s, H_2 and H_3]; 6.91 [1H, broad d, H_6, J=7.2]; 7.08–7.34 [22H, m, H_5, H_7, Ph, Tr]; 7.73 [1H, broad d, H_8, J=7.5]. ^{13}C NMR: –0.26 [3C, –Si(*C*H$_3$)$_3$]; 20.81 [–CO*C*H$_3$]; 38.75 [–*C*H(CH$_2$O–)$_2$]; 44.81 [C_2]; 62.07 and 63.59 [2C, –CH(*C*H$_2$O–)$_2$]; 86.38 [–*C*Ph$_3$]; 88.64 and 101.05 [2C, –*C*≡*C*–TMS]; 115.28, 122.56, 123.03, 124.99 and 125.19 [5C, C_3, C_5, C_6, C_7, C_8]; 121.62 [2C, *C ortho* of Ph]; 125.62 [*C para* of Ph]; 126.90 [3C, *C para* of Tr]; 127.69 [C_{4a}]; 127.76 and 128.51 [12C, *C ortho* and *meta* of Tr]; 129.23 [2C, *C meta* of Ph]; 133.41 and 134.41 [2C, C_4 and C_{8a}]; 143.74 [3C, *C ipso* of Tr]; 150.83 [*C ipso* of Ph]; 151.82 [–O*C*OPh]; 170.92 [–*C*OCH$_3$]. **Characterization of 9m**: $[\alpha]_D$=−83.1 (*c* 0.79, $CHCl_3$). IR: ν_{max} 2959, 2169, 1715, 1380, 1240. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.00 [9H, s, –Si(CH_3)$_3$]; 2.01 [3H, s, –COCH_3]; 3.34–3.65 [3H, m, >CHCH_2OTr]; 4.31–4.46 [2H, m, –CH_2OAc]; 6.04 and 6.07 [2H, AB system, H_2 and H_3, J_{AB}=7.0]; 6.90–7.34 [23H, m, H_5, H_6, H_7, Ph, Tr]; 7.72 [1H, broad d, H_8, J=7.2]. ^{13}C NMR: –0.37 [3C, –Si(*C*H$_3$)$_3$]; 20.81 [–CO*C*H$_3$]; 39.18 [–*C*H(CH$_2$O–)$_2$];

44.85 [C_2]; 62.43 and 64.14 [2C, –CH(CH_2O–)$_2$]; 86.77 [–CPh_3]; 88.79 and 101.74 [2C, –C≡C–TMS]; 121.63 [2C, *C ortho* of Ph]; 122.92, 123.07, 125.01 [most likely 2C] [4C, *C*H of 1,2-dihydroquinoline]; 125.62 [*C para* of Ph]; 126.97 [3C, *C para* of Tr]; [C_{4a}: overlapped with other signals]; 127.82 and 128.78 [12C, *C ortho* and *meta* of Tr]; 129.37 [2C, *C meta* of Ph]; 133.26 and 134.21 [2C, C_4 and C_{8a}]; 143.80 [3C, *C ipso* of Tr]; 150.96 [*C ipso* of Ph]; 151.90 [–OCOPh]; 170.84 [–COCH$_3$].

4.14.15. 4-{(*S*)-[1-(Acetoxy)methyl-2-(*p*-methoxyphenyl)-diphenylmethoxy]ethyl}-2-{(*R*)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8n and its epimer, 9n. Diastereoisomers **8**,**9n** were in part separated by chromatography with PE/Et$_2$O 7:3→3:7 both as yellow foams. R_f 0.49 (**8n**) and 0.41 (**9n**) (PE/Et$_2$O 6:4, **A**, **B**). **Characterization of 8n**: $[\alpha]_D$ = +207.9 (*c* 1.46, CHCl$_3$). IR: ν_{max} 3006, 2393, 1722, 1379, 1189. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.03 [9H, s, –Si(CH_3)$_3$]; 1.97 [3H, s, –COCH_3]; 3.16–3.28 [2H, m, –CH_2OMMTr]; 3.39 [1H, quintuplet, –CH(CH_2O–)$_2$, J = 5.7]; 3.72 [3H, s, –OCH_3]; 4.47 and 4.52 [2H, AB part of ABX system, –CH_2OAc, J_{AB} = 10.8, J_{AX} and J_{BX} = 6.1, 6.7]; 5.95 [2H, s, H_2 and H_3]; 6.74 [2H, apparent d, *H ortho* to –OMe, J = 8.8]; 6.95 [1H, broad d, H_6, J = 7.0]; 7.11–7.43 [19H, m, H_5, H_7, Ph, 2 Ph of MMTr and *H meta* to –OMe]; 7.74 [1H, broad d, H_8, J = 8.0]. ^{13}C NMR: –0.24 [3C, –Si(CH$_3$)$_3$]; 20.84 [–COCH$_3$]; 38.79 [–CH(CH$_2$O–)$_2$]; 44.84 [C_2]; 55.15 [–OCH$_3$]; 62.03 and 63.67 [2C, –CH(CH$_2$O–)$_2$]; 86.11 [–CPh$_2$Ar]; 88.66 and 101.08 [2C, –C≡C–TMS]; 113.05 [2C, *C ortho* to –OMe]; 115.29, 122.54, 123.05, 124.98 and 125.20 [5C, C_3, C_5, C_6, C_7, C_8]; 121.65 [2C, *C ortho* of Ph]; 125.64 [*C para* of Ph]; 126.77 [2C, *C para* of Ph of MMTr]; 127.67 [C_{4a}]; 127.78, 128.23 and 128.28 [8C, *C ortho* and *meta* of Ph of MMTr]; 129.25 [2C, *C meta* of Ph]; 130.21 [2C, *C meta* to –OMe]; 133.44 and 134.43 [2C, C_4 and C_{8a}]; 135.43 [*C para* to –OMe]; 144.25 and 144.32 [2C, *C ipso* of MMTr]; 150.86 [*C ipso* of Ph]; 151.83 [–OCOPh]; 158.44 [COMe of MMTr]; 170.94 [–COCH$_3$]. **Characterization of 9n**: $[\alpha]_D$ = –179.3 (*c* 0.44, CHCl$_3$). IR: ν_{max} 2928, 2854, 2171, 1725, 1377, 1248, 1068, 1018. GC–MS: unsuitable for this analysis. ^{1}H NMR: –0.11 [9H, s, –Si(CH_3)$_3$]; 1.90 [3H, s, –COCH_3]; 3.32–3.50 [3H, m, >CHCH_2OMMTr]; 3.78 [3H, s, –OCH_3]; 4.26 and 4.26 [2H, AB part of ABX system, –CH_2OAc, J_{AB} = 11.6, J_{AX} and J_{BX} = 6.6, 6.6]; 5.92 and 5.95 [2H, AB system, H_2 and H_3 J_{AB} = 7.0]; 6.81 [2H, dt, *H ortho* to –OMe, J = 8.8]; 7.13–7.48 [20H, m, H_5, H_6, H_7, Ph, 2 Ph of MMTr and *H meta* to –OMe]; 7.30 [1H, broad d, H_8, J = 7.0]. ^{13}C NMR: –0.33 [3C, –Si(CH$_3$)$_3$]; 20.83 [–COCH$_3$]; 39.26 [–CH(CH$_2$O–)$_2$]; 44.87 [C_2]; 55.19 [–OCH$_3$]; 62.39 and 64.22 [2C, –CH(CH$_2$O–)$_2$]; 86.52 [–CPh$_2$Ar]; 88.80 and 101.82 [2C, –C≡C–TMS]; 113.09 [2C, *C ortho* to –OMe]; 121.66 [2C, *C ortho* of Ph]; 122.97, 123.11, 125.01 [most likely 2C] [4C, *C*H of 1,2-dihydroquinoline]; 125.75 [*C para* of Ph]; 126.85 [2C, *C para* of Ph of MMTr]; 127.67 [C_{4a}]; 127.82, and 128.53 [8C, *C ortho* and *meta* of Ph of MMTr]; 129.38 [2C, *C meta* of Ph]; 130.48 [2C, *C meta* to –OMe]; 133.35 and 134.24 [2C, C_4 and C_{8a}]; 135.55 [*C para* to –OMe]; 144.25 and 144.37 [2C, *C ipso* of MMTr]; 150.98 [*C ipso* of Ph]; 151.92 [–OCOPh]; 158.53 [COMe of MMTr]; 170.87 [–COCH$_3$].

4.14.16. 4-{(*S*)-[1-(Triethylsilyloxy)methyl-2-trityloxy]-ethyl}-2-{(*R*)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 8o and its epimer, 9o. Both components of the mixture **8**,**9o**, as a yellow oil, could not be separated. R_f 0.85 (**8o** and **9o**) (PE/Et$_2$O 6:4, **A**, **B**). **Characterization of 8**,**9o**: IR: ν_{max} 2950, 2313, 2170, 1712, 1594, 1447, 1380, 1304, 1084. GC–MS: unsuitable for this analysis. ^{1}H NMR: –0.14 [9H, s, –Si(CH_3)$_3$ (**9o**)]; 0.02 [9H, s, –Si(CH_3)$_3$ (**8o**)]; 0.50 [6H, broad q, –Si(CH_2CH$_3$)$_3$, J = 8.0 (**9o**)]; 0.56 [6H, broad q, –Si(CH_2CH$_3$)$_3$, J = 8.0 (**8o**)]; 0.83 [9H, t, –Si(CH$_2$CH_3)$_3$, J = 7.9 (**9o**)]; 0.91 [9H, t, –Si(CH$_2$CH_3)$_3$, J = 7.9 (**8o**)]; 3.12–3.38 [2H, m, –CH_2OTr (**8**,**9o**)]; 3.53–3.81 [1H, m, –CH(CH$_2$O–)$_2$ (**8**,**9o**)]; 3.90–4.04 [2H, m, –CH_2OTES]; 5.86 and 5.89 [2H, AB system, H_2 and H_3, J_{AB} = 6.8 (**9o**)]; 5.93 and 5.93 [2H, AB system, H_2 and H_3, J_{AB} = 6.4 (**8o**)]; 6.90 [1H, broad d, H_6, J = 6.6 (**8**,**9o**)]; 7.08–7.49 [22H, m, H_5, H_7, Ph, Tr (**8**,**9o**)]; 7.73 [1H, broad d, H_8, J = 7.0 (**8**,**9o**)]. ^{13}C NMR: –0.37 [3C, –Si(CH$_3$)$_3$ (**9o**)]; –0.24 [3C, –Si(CH$_3$)$_3$ (**8o**)]; 4.31 [3C, –Si(CH$_2$CH$_3$)$_3$ (**9o**)]; 4.40 [3C, –Si(CH$_2$CH$_3$)$_3$ (**8o**)]; 6.75 [3C, –Si(CH$_2$$CH_3$)$_3$ (**9o**)]; 6.88 [3C, –Si(CH$_2$$CH_3$)$_3$ (**8o**)]; 42.38 [–CH(CH$_2$O–)$_2$ (**8o**)]; 42.55 [–CH(CH$_2$O–)$_2$ (**9o**)]; 44.86 [C_2 (**8o**)]; 44.98 [C_2 (**9o**)]; 62.49, 62.82 and 62.98 [4C, –CH(CH$_2$O–)$_2$ (**8**,**9o**)]; 86.22 [–CPh$_3$ (**9o**)]; 86.55 [–CPh$_3$ (**8o**)]; 88.24 and 101.44 [2C, –C≡C–TMS (**8o**)]; 88.55 and 101.05 [2C, –C≡C–TMS (**9o**)]; 121.61 [2C, *C ortho* of Ph (**9o**)]; 121.67 [2C, *C ortho* of Ph (**8o**)]; 122.03, 123.33, 124.85, 127.30 and 128.88 [5C, C_3, C_5, C_6, C_7, C_8 (**8o**)]; 122.03, 123.45, 125.30, 127.46 and 128.88 [5C, C_3, C_5, C_6, C_7, C_8 (**9o**)]; 125.53 [*C para* of Ph (**8o**)]; 125.64 [*C para* of Ph (**9o**)]; 126.76 [3C, *C para* of Tr (**8**,**9o**)]; 127.66, 127.69 and 128.63 [12C, *C ortho* and *meta* of Tr (**8**,**9o**)]; 129.33 [2C, *C meta* of Ph (**8o**)]; 129.45 [2C, *C meta* of Ph (**9o**)]; 134.21 and 134.86 [2C, C_4 and C_{8a} (**9o**)]; 134.26 and 134.50 [2C, C_4 and C_{8a} (**8o**)]; 144.02 [3C, *C ipso* of Tr (**8o**)]; 144.11 [3C, *C ipso* of Tr (**9o**)]; 150.89 [*C ipso* of Ph (**8o**)], 151.00 [*C ipso* of Ph (**9o**)]; 151.86 [CO (**8**,**9o**)].

4.15. (2*S**,3*S**,4*R**)-3,4-Epoxy-4-{(*S**)-[1-methyl-2-trityloxy]ethyl}-2-[(trimethylsilyl)ethynyl]-3,4-dihydro-2*H*-quinoline-1-carboxylic acid phenyl ester, 11 and its epimer, 12

A solution of **8** or **9j** (324 mg, 500 μmol) in dry CH$_2$Cl$_2$ (10 ml) was cooled to 0°C and treated with *m*CPBA (1.0 mmol). After stirring until complete (about 3 h) the reaction was quenched with Me$_2$S (86 μl, 1.17 mmol) and stirred at rt in the presence of NaHCO$_3$ sat. sol. for an additional 15 min. Usual extraction with Et$_2$O was followed by chromatography with PE/Et$_2$O (85:15) to give **11** (92% yield) as a white solid, which was crystallized from PE/Et$_2$O, and **12** (90% yield) as a pale yellow oil. **Characterization of 11**: Mp: 151.5–151.9°C (PE/Et$_2$O). R_f 0.41 (PE/Et$_2$O 8:2, **A**, **B**). IR: ν_{max} 2963, 2928,

2176, 1721, 1488, 1191. GC–MS: unsuitable for this analysis. ^{1}H NMR: −0.02 [9H, s, –Si(CH_3)$_3$]; 1.27 [3H, d, >CHCH_3, J=6.2]; 2.94–3.06 and 3.43–3.53 [3H, m, >CHCH_2O–]; 3.88 [1H, d, H_3, J=3.2]; 5.71 [1H, d, H_2, J=3.0]; 7.08–7.50 [24H, m, aromatics]. ^{13}C NMR: −0.44 [3C, –Si(CH$_3$)$_3$]; 15.25 [>CHCH$_3$]; 33.02 [>CHCH$_3$]; 44.75 [C_2]; 58.65 [C_4]; 63.82 [C_3]; 64.01 [–CH$_2$O–]; 86.92 [–CPh$_3$]; 91.71 and 99.22 [2C, –C≡C–TMS]; 121.55 [2C, *C ortho* of Ph]; 125.49, 125.55, 127.29, 128.08 and 128.76 [5C, C_5, C_6, C_7, C_8, *C para* of Ph]; 127.00 [3C, *C para* of Tr]; 127.49 [C_{4a}]; 127.73 and 128.85 [12C, *C ortho* and *meta* of Tr]; 129.24 [2C, *C meta* of Ph]; 135.54 [C_{8a}]; 144.20 [3C, *C ipso* of Tr]; 151.20 [*C ipso* of Ph]; 153.43 [CO]. **Characterization of 12**: R_f 0.41 (PE/Et$_2$O 8:2, **A**, **B**). IR: ν_{max} 3005, 2396, 1716, 1379, 1323, 1190, 1065. GC–MS: unsuitable for this analysis. ^{1}H NMR: −0.01 [9H, s, –Si(CH_3)$_3$]; 1.16 [3H, d, >CHCH_3, J=6.8]; 2.81–2.91 [1H, m, >CHCH$_2$O–]; 3.16 and 3.30 [2H, AB part of ABX system, >CHCH$_2$O–, J_{AB}=9.7, J_{AX} and J_{BX}=5.5, 7.2]; 3.85 [1H, d, H_3, J=3.1]; 5.72 [1H, d, H_2, J=2.9]; 7.05–7.49 [24H, m, aromatics]. ^{13}C NMR: −0.49 [3C, –Si(CH$_3$)$_3$]; 12.76 [>CHCH$_3$]; 33.84 [>CHCH$_3$]; 44.80 [C_2]; 57.18 [C_4]; 63.52 [C_3]; 64.82 [–CH$_2$O–]; 86.88 [–CPh$_3$]; 91.35 and 98.97 [2C, –C≡C–TMS]; 121.58 [2C, *C ortho* of Ph]; 125.57 [most likely 2C], 127.02, and 127.27 [4C, 3C (between C_5, C_6, C_7, C_8, while one is overlapped with other signals), *C para* of Ph]; 127.50 [C_{4a}]; 127.86 [3C, *C para* of Tr]; 127.94 and 128.71 [12C, *C ortho* and *meta* of Tr]; 129.26 [2C, *C meta* of Ph]; 135.44 [C_{8a}]; 144.12 [3C, *C ipso* of Tr]; 146.88 [*C ipso* of Ph]; 151.11 [CO].

4.16. (2*S**,3*S**,4*S**)-3-Hydroxy-4-{(*R**)-[2-hydroxy-1-methyl]ethyl}-4-methoxy-2-[(trimethylsilyl)ethynyl]-3,4-dihydro-2*H*-quinoline-1-carboxylic acid phenyl ester, 13 and its epimer, 14

A suspension of **11** or **12** (122 mg, 184 μmol) in dry methanol (5 ml) was cooled to 0°C and treated with *p*TSA (35 mg, 184 μmol). After 5 min the reaction flask was allowed to stir at rt for 2 h and gradually a pale yellow solution was obtained. Neutralization with solid NaHCO$_3$ (16 mg, 184 μmol) was followed by careful evaporation of methanol under reduced pressure at ≈15°C. The residue was partitioned between water and Et$_2$O and extracted as usual. Chromatography with PE/Et$_2$O (1:1) gave the corresponding diols **13** (50 mg, 60% yield) or **14** (42 mg, 51% yield) as pale yellow oils. **Characterization of 13**: R_f 0.36 (PE/Et$_2$O 1:1, **A**, **B**). IR: ν_{max} 3309, 2964, 2174, 1723, 1368, 1324, 1098. GC–MS: R_t 13.48; m/z 404 (M$^+$–49, 5.6), 394 (5.3), 377 (8.5), 376 (30), 300 (14), 256 (7.5), 216 (6.1), 202 (13), 190 (6.6), 170 (5.6), 169 (6.6), 168 (44), 162 (7.8), 160 (5.1), 158 (15), 146 (14), 144 (5.5), 140 (5.6), 132 (6.5), 130 (24), 97 (9.8), 95 (8.0), 94 (28), 89 (8.2), 83 (7.7), 77 (31), 75 (16), 74 (9.1), 73 (100), 66 (5.2), 65 (7.7), 59 (12), 51 (5.4), 45 (8.7), 43 (7.3), 39 (6.1). ^{1}H NMR: 0.17 [9H, s, –Si(CH_3)$_3$]; 0.68 [3H, d, >CHCH_3, J=7.0]; 2.01 [1H, center of m, >CHCH$_2$O–]; 2.04 [1H, s, –OH]; 3.44 [3H, s, –OCH_3]; 3.50–3.88 [1H, m; became a dd at 3.52, J=2.5, 10.9, after exchange with D$_2$O, –CHHOH]; 3.98–4.10 [2H, m; became a t at 4.00, J=9.6, –CHHOH and a d at 4.02, J=9.4, H_3, after exchange with D$_2$O]; 4.96 [1H, d, H_2, J=9.4]; 5.97 [1H, broad s, –OH]; 7.16–7.42 [8H, m, H_5, H_6, H_7 and Ph]; 7.72 [1H, broad d, H_8, J=7.3]. ^{13}C NMR: −0.01 [3C, –Si(CH$_3$)$_3$]; 13.69 [>CHCH$_3$]; 38.45 [>CHCH$_3$]; 50.55 [–OCH_3]; 52.03 [C_2]; 63.62 [–CH$_2$O–]; 74.32 [C_3]; 80.71 [C_4]; 87.62 and 104.59 [2C, –C≡C–TMS]; 121.58 [2C, *C ortho* of Ph]; 124.82, 125.46, 126.02, and 127.38 [4C, C_5, C_6, C_7, C_8]; 125.71 [*C para* of Ph]; 129.34 [2C, *C meta* of Ph]; 133.07 and 134.40 [2C, C_{4a} and C_{8a}]; 151.14 [*C ipso* of Ph]; 152.56 [CO]. **Characterization of 14**: R_f 0.39 (PE/Et$_2$O 4:6, **A**, **B**). IR: ν_{max} 3302, 2170, 1725, 1365, 1088. GC–MS: R_t 13.52; m/z 404 (M$^+$–49, 6.1), 394 (13), 378 (8.4), 377 (27), 376 (100), 334 (9.2), 301 (5.3), 300 (18), 256 (19), 244 (5.4), 242 (6.8), 240 (5.3), 226 (5.6), 216 (6.1), 210 (6.8), 202 (13), 190 (6.9), 170 (6.7), 169 (6.8), 168 (49), 162 (8.1), 160 (5.8), 158 (14), 146 (16), 144 (6.7), 140 (5.9), 132 (5.9), 130 (23), 115 (5.5), 97 (8.6), 95 (7.6), 94 (29), 91 (5.3), 90 (5.2), 89 (8.6), 83 (7.5), 77 (30), 75 (15), 74 (7.6), 73 (89), 66 (6.0), 65 (7.6), 59 (11), 55 (5.2), 45 (7.5), 43 (6.4), 39 (5.9). ^{1}H NMR: 0.13 [9H, s, –Si(CH_3)$_3$]; 1.15 [3H, d, >CHCH_3, J=7.3]; 2.15 [1H, center of m, >CHCH$_2$O–]; 2.87 [1H, broad s, –OH]; 3.36 [3H, s, –OCH_3]; 3.32–3.43 [1H, m; became a dd at 3.38, J=5.5, 11.1, after exchange with D$_2$O, –CHHOH]; 3.82 [1H, broad d, J=10.7; became a dd, J=2.6, 11.1, after exchange with D$_2$O, –CHHOH]; 4.05 [1H, broad s, –OH]; 4.21–4.25 [1H, m, became a d at 4.23, J=7.6, after exchange with D$_2$O, H_3]; 5.07 [1H, d, H_2, J=7.7]; 7.14–7.43 [8H, m, H_5, H_6, H_7 and Ph]; 7.75 [1H, broad d, H_8, J=8.3]. ^{13}C NMR: −0.16 [3C, –Si(CH$_3$)$_3$]; 12.63 [>CHCH$_3$]; 41.09 [>CHCH$_3$]; 50.80 [–OCH_3]; 52.66 [C_2]; 64.79 [–CH$_2$O–]; 75.36 [C_3]; 81.86 [C_4]; 88.98 and 103.82 [2C, –C≡C–TMS]; 121.57 [2C, *C ortho* of Ph]; 124.91, 125.58, 125.72 [most likely 2C] and 127.80, [5C, C_5, C_6, C_7, C_8, *C para* of Ph]; 129.35 [2C, *C meta* of Ph]; 131.12 and 135.58 [2C, C_{4a} and C_{8a}]; 151.15 [*C ipso* of Ph]; 152.42 [CO].

4.17. (2*S**,3*S**,4*S**)-2-Ethynyl-3-hydroxy-4-{(*R**)-[2-hydroxy-1-methyl]ethyl}-4-methoxy-3,4-dihydro-2*H*-quinoline-1-carboxylic acid methyl ester, 15

The oxirane opening was performed under the same conditions described for the preparation of **13** and **14**, starting from 301 mg (453 μmol) of **11**. Crude product (or either chromatographed as previously reported), obtained after solvent removal, was dissolved in dry methanol (5 ml) and heated at 40°C for 3 h, after solid NaHCO$_3$ (241 mg, 2.87 mmol) has been added. The mixture was concentrated under reduced pressure, partitioned between water and Et$_2$O and extracted as usual. Chromatography with PE/Et$_2$O 1:1→Et$_2$O gave, as prevailing product, **15** (70 mg, 50% from **11**) as a pale yellow oil. R_f 0.14 (PE/Et$_2$O 4:6, **A**, **B**). IR: ν_{max} 3303, 2955, 1702, 1440, 1337, 1192, 1097. GC–MS: R_t 9.48; m/z 319 (M$^+$, 3.6), 271 (5.0), 270 (28), 261 (15), 260 (92), 258 (10), 243 (13), 242 (84), 232 (5.8), 228 (24),

209 (6.9), 202 (14), 201 (16), 200 (100), 192 (11), 187 (6.6), 186 (8.8), 185 (23), 184 (7.4), 177 (5.6), 174 (6.3), 172 (6.2), 170 (8.4), 169 (5.7), 168 (17), 167 (8.9), 162 (5.5), 158 (7.4), 156 (8.3), 154 (10), 146 (25), 144 (9.7), 143 (11), 142 (7.1), 141 (18), 140 (7.4), 132 (11), 130 (17), 129 (11), 128 (12), 117 (6.8), 116 (5.9), 115 (18), 91 (5.1), 77 (7.2), 59 (10). ^{1}H NMR: 0.66 [3H, d, >CHCH_3, J=7.1]; 1.90 [1H, broad s, –OH]; 1.93 [1H, center of m, >CHCH$_2$O–]; 2.41 [1H, d, –C≡CH, J=2.0]; 3.41 [3H, s, –OCH_3]; 3.58 [1H, dd, –CHHOH, J=2.9, 10.8]; 3.82 [3H, s, –CO$_2$CH_3]; 3.90–4.10 [2H, m; became a d at 4.02, J=9.5, H_3 and a t at 4.65, J=9.7, –CHHOH, after exchange with D$_2$O]; 4.81 [1H, dd, H_2, J=1.7, 9.5]; 6.13 [1H, broad s, –OH]; 7.14–7.38 [3H, m, H_5, H_6, H_7]; 7.59 [1H, broad d, H_8, J=7.7]. ^{13}C NMR: 13.56 [>CHCH$_3$]; 38.14 [>CHCH$_3$]; 50.45 [–OCH$_3$]; 50.85 [C_2]; 53.44 [–CO$_2$$CH_3$]; 63.41 [–$CH_2$O–]; 70.51 [–C≡$C$H]; 74.27 [$C_3$]; 80.43 [$C_4$]; 83.45 [–$C$≡CH]; 124.58, 125.41, 125.90 and 127.27, [4C, C_5, C_6, C_7, C_8]; 132.78 and 134.28 [2C, C_{4a} and C_{8a}]; 154.68 [CO].

4.18. (6*R**,6a*S**,11*R**,11a*S**)-6-Ethynyl-11a-methoxy-8,8,11-trimethyl-6a,10,11,11a-tetrahydro-6*H*-7,9-dioxa-5-aza-cyclohepta[*a*]naphthalene-5-carboxylic acid methyl ester, 16

A solution of **15** (54 mg, 170 μmol) in dry CH_2Cl_2 (4 ml) was cooled to 0°C and treated with 2-methoxypropene (33 μl, 341 μmol) and *p*-TSA (34 μml of a 0.1 M sol. in THF). After 10 min the solution was diluted with 5% aq $NaHCO_3$ and extracted with Et_2O. Chromatography with PE/Et_2O 7:3 furnished pure **16** as a pale yellow oil. R_f 0.14 (PE/Et_2O 4:6, **A**, **B**). IR: ν_{max} 3303, 2991, 2955, 2124, 1709, 1439, 1383, 1329, 1133, 1046. GC–MS: R_t 8.94; m/z 359 (M$^+$, 29), 301 (9.8), 286 (10), 273 (17), 272 (77), 258 (10), 242 (23), 240 (20), 234 (58), 232 (16), 231 (12), 230 (83), 229 (10), 218 (21), 215 (12), 212 (16), 205 (59), 202 (45), 198 (14), 192 (16), 187 (9.6), 184 (16), 182 (18), 181 (16), 180 (22), 174 (9.6), 172 (9.7), 170 (21), 168 (14), 167 (26), 160 (11), 156 (12), 154 (15), 146 (27), 144 (9.6), 143 (12), 142 (9.6), 141 (10), 140 (11), 130 (14), 129 (12), 128 (19), 127 (10), 115 (21), 101 (12), 91 (13), 90 (13), 77 (24), 73 (14), 69 (22), 59 (100), 51 (15), 45 (17), 43 (62), 42 (12), 41 (34), 39 (27). ^{1}H NMR: 0.59 [3H, d, >CHCH_3, J=6.8]; 1.45 and 1.43 [6H, 2 s, >C(CH_3)$_2$]; 2.17 [1H, d, –C≡CH, J=2.5]; 2.37 [1H, center of m, >CHCH$_2$O–]; 3.30 [3H, s, –OCH_3]; 3.65 and 3.67 [2H, AB part of ABX system, –CH_2O–, J_{AB}=12.0, J_{AX} and J_{BX}=3.9, 13.2]; 3.83 [3H, s, –CO$_2$CH_3]; 4.48 [1H, d, H_{6a}, J=3.0]; 5.44 [1H, t, H_6, J=2.7]; 7.15 [1H, dt, H_2, J=1.4, 7.4]; 7.24–7.34 [2H, m, H_1, H_3]; 7.53 [1H, broad d, H_4, J=8.5]. ^{13}C NMR: 12.64 [>CHCH$_3$]; 24.97 and 25.40 [2C, >C(CH_3)$_2$]; 39.82 [>CHCH$_3$]; 50.56 [C_6]; 51.46 [–OCH_3]; 53.14 [–CO$_2$$CH_3$]; 66.06 [–$CH_2$O–]; 73.21 [–C≡$C$H]; 77.24 [$C_{6a}$]; 79.70 [$C_{11a}$]; 80.74 [–$C$≡CH]; 101.87 [>$C$(CH$_3$)$_2$]; 123.57, 125.01, 127.42 and 128.20, [4C, C_1, C_2, C_3, C_4]; 130.66 and 136.59 [2C, C_{4a} and C_{11b}]; 154.43 [CO].

4.19. (2*S**,3*S**,4*S**)-3-Acetoxy-4-{(*R**)-[2-acetoxy-1-methyl]ethyl}-4-methoxy]-2-[(trimethylsilyl)ethynyl]-3,4-dihydro-2*H*-quinoline-1-carboxylic acid phenyl ester, 17

A solution of **13** (16 mg, 35 μmol) in dry CH_2Cl_2 (3 ml) was treated, at 0°C, with triethylamine (15 μl, 106 μmol), 4-dimethylaminopyridine (1.0 mg, 8.2 μmol) and acetic anhydride (10 μl, 106 μmol). After 5 min, the solution was stirred at rt until the reaction was complete (about 3 h), and then partitioned between water and Et_2O and finally extracted with the same solvent. Chromatography with PE/Et_2O (7:3) gave pure **17** (12 mg, 63%) as a pale yellow oil. R_f 0.57 (PE/Et_2O 1:1, **A**, **B**). IR: ν_{max} 3015, 2962, 2177, 1728, 1374, 1323, 1194, 1030. GC–MS: R_t 13.57; m/z 446 (M$^+$–91, 2.5), 376 (100), 268 (6.9), 210 (5.2), 202 (12), 170 (6.0), 117 (6.4), 77 (14), 75 (10), 73 (30), 43 (5.2). ^{1}H NMR: 0.07 [9H, s, –Si(CH_3)$_3$]; 0.90 [3H, d, >CHCH_3, J=6.9]; 2.03 and 2.19 [6H, 2 s, –COCH_3]; 2.28–2.45 [1H, m, >CHCH$_2$O–]; 3.24 [3H, s, –OCH_3]; 3.87 [1H, dd, –CHHOAc, J=9.3, 10.9]; 4.68 [1H, dd, –CHHOAc, J=3.7, 11.0]; 5.30 [1H, d, H_3, J=6.4]; 5.61 [1H, d, H_2, J=6.4]; 7.17–7.43 [8H, m, H_5, H_6, H_7 and Ph]; 7.72 [1H, broad d, H_8, J=8.0].

4.20. (1*S**,3a*S**,4*S**,9b*S**)-9b-Methoxy-1-methyl-2-oxo-4-[(trimethylsilyl)ethynyl]-1,3a,4,9b-tetrahydro-2*H*-furo[2,3-*c*]quinoline-5-carboxylic acid phenyl ester, 18 and its epimer, 19

A solution of **13** or **14** (35 mg, 77 μmol) in dry CH_2Cl_2 (2 ml) was stirred for 5 min at rt in the presence of powdered 4 Å molecular sieves (10 mg). Then 4-methylmorpholine-*N*-oxide (25 μl, 232 μmol) and tetrapropylammonium perruthenate (2.7 mg, 7.7 μmol) were added and the resulting mixture was stirred for 30 min. After concentration under reduced pressure, direct chromatography with PE/Et_2O (8:2) gave **18** (22 mg, 62% yield) or **19** (21 mg, 61% yield) as pale yellow oils. **Characterization of 18**: R_f 0.41 (PE/Et_2O 7:3, **A**, **B**). IR: ν_{max} 2960, 2180, 1784, 1727, 1381, 1327, 1246, 1045. GC–MS: R_t 12.90; m/z 449 (M$^+$, 18), 357 (13), 356 (48), 322 (13), 321 (37), 300 (24), 268 (8.8), 228 (11), 196 (19), 190 (18), 180 (9.5), 173 (11), 172 (8.2), 168 (9.1), 167 (14), 158 (8.2), 157 (7.7), 146 (40), 142 (9.7), 141 (29), 130 (11), 97 (58), 90 (9.1), 89 (15), 83 (12), 77 (47), 75 (13), 74 (8.6), 73 (100), 69 (7.3), 65 (9.6), 59 (19), 55 (8.1), 51 (8.3), 45 (9.0), 43 (13), 39 (8.2). ^{1}H NMR: –0.06 [9H, s, –Si(CH_3)$_3$]; 1.21 [3H, d, >CHCH_3, J=7.4]; 2.52 [1H, q, >CHCH$_3$, J=7.4]; 3.38 [3H, s, –OCH_3]; 5.10 [1H, s, H_{3a}]; 5.73 [1H, s, H_4]; 7.13–7.47 [8H, m, H_7, H_8, H_9 and Ph]; 7.66 [1H, broad d, H_6, J=7.4]. ^{13}C NMR: –0.65 [3C, –Si(CH$_3$)$_3$]; 7.20 [>CHCH$_3$]; 47.58 [>CHCH$_3$]; 50.82 [C_4]; 52.24 [–OCH$_3$]; 79.74 [C_{9b}]; 85.93 [C_{3a}]; 93.71 and 99.16 [2C, –C≡C–TMS]; 121.49 [2C, *C ortho* of Ph]; 124.43, 125.87, 125.97, 126.17 and 128.26 [5C, C_6, C_7, C_8, C_9, *C para* of Ph]; 129.46 [2C, *C meta* of Ph]; 131.68 and 135.27 [2C, C_{5a} and C_{9a}]; 151.14 [*C ipso* of Ph]; 152.56 [CO]; 176.12 [CO of lactone]. **Characterization of 19**: R_f 0.38 (PE/Et_2O 6:4, **A**, **B**). IR: ν_{max} 2425, 2182, 1784, 1727, 1381, 1330, 1314, 1250, 1053. GC–MS (this lactone, unlike **18**, partially epimerizes in the column): R_t 13.07; m/z 449 (M$^+$, 17), 357 (11), 356 (41), 324 (12), 321 (21), 300 (18),

268 (8.0), 228 (11), 196 (18), 190 (18), 180 (11), 173 (8.4), 172 (6.8), 168 (9.8), 167 (12), 158 (8.2), 146 (35), 142 (8.2), 141 (28), 130 (9.5), 97 (50), 90 (9.0), 89 (13), 83 (13), 77 (42), 75 (12), 74 (8.1), 73 (100), 65 (7.9), 59 (18), 50 (9.4), 45 (8.8), 43 (10). ^{1}H NMR: −0.05 [9H, s, –Si(CH_3)$_3$]; 0.77 [3H, d, >CHCH_3, J=7.8]; 3.15 [1H, q, >CHCH$_3$, J=7.8]; 3.35 [3H, s, –OCH_3]; 5.12 [1H, d, H_{3a}, J=1.5]; 5.73 [1H, d, H_4, J=1.5]; 7.12–7.42 [8H, m, H_7, H_8, H_9 and Ph]; 7.65 [1H, broad d, H_6, J=7.7]. ^{13}C NMR: −0.72 [3C, –Si(CH_3)$_3$]; 12.68 [>CHCH$_3$]; 48.03 [>CHCH$_3$]; 49.69 [C_4]; 52.80 [–OCH$_3$]; 82.56 [C_{9b}]; 85.67 [C_{3a}]; 93.61 and 99.03 [2C, –C≡C–TMS]; 121.63 [2C, *C ortho* of Ph]; 125.58, 125.90, 126.10, 127.00 and 128.65 [5C, C_6, C_7, C_8, C_9, *C para* of Ph]; 129.44 [2C, *C meta* of Ph]; 127.62 and 136.60 [2C, C_{5a} and C_{9a}]; 150.88 [*C ipso* of Ph]; 152.04 [CO]; 175.86 [CO of lactone].

4.21. 8,9d by deprotection of 8,9c, 8,9e and 8,9j

From 8,9c and 8,9e: protective group has been removed in both cases on **8c**,**e** and **9c**,**e**. A solution of substrate (100 μmol) in acetonitrile (1 ml) was cooled to −20°C and treated with ≈11% HF in acetonitrile. After 1.5 h a stoichiometric amount of solid $NaHCO_3$ with respect to HF was added and the mixture was diluted with water and extracted with Et_2O. Chromatography with PE/Et_2O (1:1) gave the corresponding alcohol **8d** or **9d** (yields, in the range 73–74% for both stereoisomers and whatever the starting silyl ether, have been improved up to 91%, performing the reaction on a 10 mmol scale of **8**,**9c** mixture).

From 8,9j: A solution of **8**,**9j** (65 mg, 100 μmol) in dry methanol (2 ml) was cooled to 0°C and treated with *p*TSA (19 mg, 100 μmol), then, after 5 min, the solution was allowed to stir at rt for 1.5 h. A stoichiometric amount of solid $NaHCO_3$ with respect to *p*TSA was added and the mixture was carefully concentrated under reduced pressure at ≈15°C. Then it was diluted with water and extracted with Et_2O. Chromatography with PE/Et_2O (1:1) gave the corresponding alcohols **8d** or **9d** with an overall 99% yield.

4.22. 8f by protection of 8d

A solution of **8d** (15 mg, 37 μmol) in chloroform (2 ml) was treated with 10 mg of powdered 4 Å molecular sieves, 2,6-di-*t*butyl-4-methylpyridine (61 mg, 296 μmol) and methyl triflate (17 μl, 148 μmol) and then heated at 60°C for 48 h (a second addition of an equivalent amount of both reagents was performed after 24 h). After dilution with water, the mixture was extracted with Et_2O and crude product was chromatographed with PE/Et_2O (6:4) to give **8f** (11 mg, 73% yield).

4.23. 8g by protection of 8d

The same procedure reported for the preparation of **5e** was followed starting from pure **8d** and the corresponding **8g** was obtained in 87% yield.

4.24. 8,9h by protection of 8,9d

The same procedure reported for the preparation of **5f** was followed starting from pure **8d** or **9d** and the corresponding **8h** and **9h** were obtained in 67–68% yield.

4.25. 2-[(*R**)-Ethynyl]-4-{(*S**)-[1-methyl-2-trityloxy]-ethyl}-2*H*-quinoline-1-carboxylic acid phenyl ester, 20

A solution of **8**,**9j** (with a 82:18 d.r.) (247 mg, 381 μmol) in dry MeOH (4 ml) was treated with $NaHCO_3$ (128 mg, 1.52 mmol) and heated at 40°C for 2.5 h. After addition of water, the mixture was extracted with Et_2O. Chromatography with PE/Et_2O 9:1→7:3 gave desired product (199 mg, 91%) as a white foam. Crystallization from Et_2O/PE gave diastereomerically pure **20** as a white solid. Mp 160.7–161.6°C (Et_2O/PE). R_f 0.34 (PE/Et_2O 8:2, **A**, **B**). IR: ν_{max} 3303, 2962, 2037, 1712, 1447, 1377, 1302, 1067. GC–MS: unsuitable for this analysis. ^{1}H NMR: 1.34 [3H, d, >CHCH_3, J=6.5]; 2.19 [1H, d, –C≡CH, J=1.8]; 2.97–3.06 [1H, m, >CHCH$_3$]; 3.13–3.29 [2H, m, >CHCH_2O–]; 5.93–6.01 [2H, m, H_2 and H_3]; 6.92 [1H, broad s, H_6]; 7.09–7.38 [22H, m, H_5, H_7, Ph, Tr]; 7.74 [1H, broad d, H_8, J=8.4]. ^{13}C NMR 16.28 [>CHCH$_3$]; 34.15 [>CHCH$_3$]; 44.09 [C_2]; 67.14 [–CH$_2$O–]; 71.55 [–C≡CH]; 80.20 [–C≡CH]; 86.19 [–CPh$_3$]; 120.82 [C_8]; 123.44, 125.08 [most likely 2C] and 127.60 [4C, C_3, C_5, C_6, C_7]; 121.60 [2C, *C ortho* of Ph]; 125.63 [*C para* of Ph]; 126.73 [3C, *C para* of Tr]; 127.70 and 128.58 [12C, *C ortho* and *meta* of Tr]; 128.83 [C_{4a}]; 129.24 [2C, *C meta* of Ph]; 134.11 [C_4]; 138.28 [C_{8a}]; 144.10 [3C, *C ipso* of Tr]; 150.83 [*C ipso* of Ph], 151.83 [CO].

4.26. 2-{(*R**)-[3-(Benzyloxy)prop-1-ynyl]}-4-{(*S**)-[(2-hydroxy-1-methyl)ethyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester 22 and its epimer 23 and 4-{(*S**)-[(2-hydroxy-1-methyl)ethyl]}-2-{(*R**)-[3-(*p*-methoxybenzyl-oxy)prop-1-ynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 24 and its epimer, 25

By reaction with *p*-TSA: the same procedure used for the transformation of **8**,**9j** into **8**,**9d**, but working at rt, was employed for the preparation of **22**,**23** and **24**,**25**, starting from **8**,**9k** and **8**,**9l**, respectively. Chromatography with the appropriate eluent based on PE/Et_2O gave the corresponding products as pale yellow oils and as inseparable diastereoisomeric mixtures (**22**,**23** in 63% yield and **24**,**25** in 78% yield). **By reaction with EtSH and boron trifluoride**: a solution of **8**,**9k** or **8**,**9l** (500 μmol) in dry CH_2Cl_2 (10 ml) was cooled to 0°C and treated with EtSH (185 μl, 2.5 mmol) and $BF_3{\cdot}Et_2O$ (127 μl, 1.0 mmol). After 1 h the reaction is usually complete. Quenching with NH_4Cl sat. sol. and extraction with Et_2O was followed by chromatography with PE/Et_2O to give the inseparable diastereoisomeric mixtures **22**,**23** in 89% yield from **8**,**9k**. When the reaction was performed on **8**,**9l** the 4-methoxybenzyl ether was also cleaved and **26**,**27** were isolated in 66% overall

yield. **Characterization of 22,23**: R_f 0.31 (**22,23**) (PE/Et_2O 4:6, **A**, **B**). IR (**22,23**): ν_{max} 3472, 2400, 1712, 1380, 1327, 1304, 1068. GC–MS: unsuitable for this analysis. ^{1}H NMR: 1.19 [3H, d, >CHCH_3, J=7.0 (**23**)]; 1.34 [3H, d, >CHCH_3, J=6.8 (**22**)]; 3.15 [1H, sextuplet, >CHCH$_2$O–, J=6.8 (**23**)]; 3.16 [1H, sextuplet, >CHCH$_2$O–, J=6.6 (**22**)]; 3.50–3.94 [2H, m, –CHCH_2O– (**22,23**)]; 4.03 [2H, s, –OCH_2C≡C– (**23**)]; 4.04 [2H, s, –OCH_2C≡C– (**22**)]; 4.27 [2H, s, –OCH_2Ph (**22,23**)]; 6.02 [2H, apparent s, H_2 and H_3 (**22,23**)]; 7.14–7.49 [13H, m, H_5, H_6, H_7, –OPh, Ph (**22,23**)]; 7.79 [1H, broad d, H_8, J=7.8 (**22,23**)]. ^{13}C NMR: 15.91 [>CHCH$_3$, (**22**)]; 17.25 [>CHCH$_3$, (**23**)]; 36.08 [>CHCH$_3$, (**22**)]; 36.22 [>CHCH$_3$, (**23**)]; 44.25 [C_2 (**23**)]; 44.56 [C_2 (**22**)]; 57.13 [–CH$_2$C≡C– (**22,23**)]; 66.51 [–CH$_2$OH (**22,23**)]; 71.04 [–OCH$_2$Ph (**22,23**)]; 79.62 and 82.90 [2C, –C≡C– (**22,23**)]; 121.58 [2C, *C ortho* of Ph (carbamate) (**22,23**)]; 123.27, 124.96, 125.07, 127.83, 127.92 and 127.98 [5C, aromatics (**22,23**)]; 125.78 [*C para* of Ph (carbamate) (**22,23**)]; 127.56 [C_{4a} (**22,23**)]; 128.23 and 128.35 [4C, *C ortho* and *meta* of Ph (Bn) (**22,23**)]; 129.40 [2C, *C meta* of Ph (carbamate) (**22,23**)]; 134.50 [C_4 (**22,23**)]; 137.13 and 137.22 [C_{8a} and *C ipso* of Ph (Bn) (**22,23**)]; 150.98 [*C ipso* of Ph (carbamate) (**22,23**)]; 151.83 [CO (**22,23**)]. **Characterization of 24,25**: R_f 0.30 (**24,25**) (PE/Et_2O 2:8, **A**, **B**). IR (**24,25**): ν_{max} 3008, 2411, 1714, 1384, 1303, 1234, 1071. GC–MS: unsuitable for this analysis. ^{1}H NMR: 1.20 [3H, d, >CHCH_3, J=7.0 (**25**)]; 1.35 [3H, d, >CHCH_3, J=6.7 (**24**)]; 3.07–3.25 [1H, m, >CHCH$_2$O– (**24,25**)]; 3.52–3.77 [2H, m, –CHCH_2O– (**24,25**)]; 3.79 [3H, s, –OCH_3 (**24,25**)]; 4.01 [2H, s, –OCH_2C≡C– (**24,25**)]; 4.31 [2H, s, –OCH_2Ar (**24,25**)]; 6.02 [2H, apparent s, H_2 and H_3 (**24,25**)]; 6.82 [2H, dt, *H ortho* to –OMe, J=2.4, 8.6 (**24,25**)]; 7.09 [2H, dt, *H meta* to –OMe, J=2.6, 8.7 (**24,25**)]; 7.18–7.48 [8H, m, H_5, H_6, H_7, –OPh (**24,25**)]; 7.80 [1H, broad d, H_8, J=6.6 (**24,25**)]. ^{13}C NMR: 15.89 [>CHCH$_3$, (**24**)]; 17.26 [>CHCH$_3$, (**25**)]; 35.99 [>CHCH$_3$, (**24**)]; 36.14 [>CHCH$_3$, (**25**)]; 44.16 [C_2 (**25**)]; 44.48 [C_2 (**24**)]; 55.24 [–OCH$_3$ (**24,25**)]; 56.65 [–CH$_2$C≡C– (**24,25**)]; 66.37 [–CH$_2$OH (**24,25**)]; 70.55 [–OCH$_2$Ar (**24,25**)]; 79.58 (**25**), 79.65 (**24**), 82.72 (**24**) and 82.96 (**25**) [2C, –C≡C–]; 113.68 [2C, *C ortho* to –OMe (**24,25**)]; 121.53 [2C, *C ortho* of Ph (**24,25**)]; 123.21, 124.86, 125.02, 127.82 (**24**) and 127.89 (**25**) [4C, aromatics (**24,25**)]; 125.74 [*C para* of Ph (**24,25**)]; 127.45 [≥CCH$_2$C≡C– (**24,25**)]; 129.03 [C_{4a} (**25**)]; 129.07 [C_{4a} (**24**)]; 129.34 [2C, *C meta* of Ph (**24,25**)]; 129.85 [2C, *C meta* to –OMe (**24,25**)]; 134.33 [C_4 (**24,25**)]; 136.93 [C_{8a} (**24**)]; 137.73 [C_{8a} (**25**)]; 150.78 [*C ipso* of Ph (**24,25**)]; 151.76 [CO (**24,25**)]; 159.25 [≥C-OMe (**24,25**)].

4.27. 4-{(*S**)-[(2-Hydroxy-1-methyl)ethyl]}-2-[(*R**)-3-hydroxyprop-1-ynyl]-2*H*-quinoline-1-carboxylic acid phenyl ester, 26 and its epimer, 27

From 20: (a) **Transformation of 20 into 21**. A solution of **20** (124 mg, 215 μmol) in dry THF (5 ml) was cooled to 0°C and treated with *t*BuMgCl (2 M sol in Et_2O, 107 μl). After 45 min the solution was stirred for additional 15 min at rt. Then paraformaldehyde (39 mg, 1.29 mg) was added and the slurry was stirred at rt for 17 h; after the addition of an equivalent amount of *t*BuMgCl and paraformaldehyde the reaction was refluxed for 22 h. Quenching with NH_4Cl sat. sol. was followed by extraction with Et_2O. (b) **Transformation of 21 into 26**. Crude mixture was treated with *p*-TSA in methanol as described for the transformation of **8**,**9j** into **8**,**9d**. Chromatography with PE/Et_2O (1:9) furnished **26** (11 mg) in 14% overall yield from **20**.

From 22,23 or 24,25: the same procedure described in the previous paragraph, using EtSH and $BF_3{\cdot}Et_2O$ was followed, performing the reaction at reflux (**22,23**) or at 0°C (**24,25**). The diols **26**,**27**, that have been separated, have been obtained in an overall yield of 50 and 99%, respectively, as pale yellow oils. **Characterization of 26**: R_f 0.47 (Et_2O 4:6, **A**, **B**). IR: ν_{max} 3461, 2960, 2391, 1713, 1328, 1303. GC–MS (analysis performed on the diastereomeric mixture **26**,**27**): (usual conditions, but with fin. temp. 290°C). R_t 12.05; m/z 363 (M^+, 9.8), 345 (15), 305 (11), 304 (52), 288 (12), 286 (14), 242 (11), 222 (25), 212 (12), 210 (14), 196 (11), 195 (10), 194 (46), 193 (12), 192 (13), 184 (20), 183 (8.8), 182 (17), 181 (9.9), 180 (25), 179 (11), 178 (15), 168 (12), 167 (31), 166 (40), 165 (17), 156 (18), 155 (7.0), 154 (22), 153 (9.1), 152 (18), 144 (10), 132 (14), 130 (11), 129 (9.3), 128 (22), 127 (14), 115 (19), 94 (20), 91 (9.5), 78 (10), 77 (100), 65 (25), 55 (11), 51 (24), 44 (16), 43 (10), 41 (10), 39 (25). ^{1}H NMR: 1.33 [3H, d, >CHCH_3, J=6.8] 3.11 [1H, sextuplet, >CHCH$_2$O–, J=6.2]; 3.48 and 3.69 [2H, AB part of ABX system, –CHCH_2OH, J_{AB}=9.8, J_{AX} and J_{BX}=6.1, 6.9]; 4.09 [2H, d, –OCH_2C≡C–, J=1.6]; 5.93 [1H, d, H_3, J=6.4]; 5.99 [1H, dt, H_2, J=1.4, 6.6]; 7.15–7.44 [8H, m, H_5, H_6, H_7, Ph]; 7.75 [1H, broad d, H_8, J=7.6]. ^{13}C NMR: 15.71 [>CHCH$_3$]; 35.92 [>CHCH$_3$]; 44.42 [C_2]; 50.97 [–CH$_2$C≡C–]; 66.35 [–CH$_2$OH]; 81.56 and 81.89 [2C, –C≡C–]; 121.40 [C_8]; 123.26, 124.87, 125.06 and 127.93 [4C, C_3, C_5, C_6, C_7]; 121.55 [2C, *C ortho* of Ph]; 125.82 [*C para* of Ph]; 127.32 [C_{4a}]; 129.39 [2C, *C meta* of Ph]; 134.18 [C_4]; 136.80 [C_{8a}]; 150.81 [*C ipso* of Ph]; 151.96 [CO]. **Characterization of 27**: R_f 0.36 (Et_2O 4:6, **A**, **B**). IR: ν_{max} 3426, 2398, 1713, 1380, 1303, 1188, 1135. GC–MS: see compound **26**. ^{1}H NMR: 1.17 [3H, d, >CHCH_3, J=6.8] 3.11 [1H, sextuplet, >CHCH$_2$O–, J=6.6]; 3.77 and 3.88 [2H, AB part of ABX system, –CHCH_2OH, J_{AB}=10.8, J_{AX} and J_{BX}=5.8, 6.2]; 4.12 [2H, d, –OCH_2C≡C–, J=1.8]; 5.95 [1H, d, H_3, J=6.6]; 6.02 [1H, dt, H_2, J=1.7, 6.6]; 7.18–7.55 [8H, m, H_5, H_6, H_7, Ph]; 7.76 [1H, broad d, H_8, J=6.1]. ^{13}C NMR: 17.25 [>CHCH$_3$]; 36.03 [>CHCH$_3$]; 44.14 [C_2]; 51.07 [–CH$_2$C≡C–]; 66.62 [–CH$_2$OH]; 81.86 and 81.97 [2C, –C≡C–]; 120.34 [C_8]; 123.19, 124.93, 125.11 and 127.92 [4C, C_3, C_5, C_6, C_7]; 121.60 [2C, *C ortho* of Ph]; 125.84 [*C para* of Ph]; 127.68 [C_{4a}]; 129.42 [2C, *C meta* of Ph]; 134.22 [C_4]; 137.66 [C_{8a}]; 150.90 [*C ipso* of Ph]; 152.00 [CO].

4.28. 4-{(*R*)-[1-Hydroxymethyl-2-trityloxy]ethyl}-2-{(*R*)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 28 and its epimer at C-2, 29

Triethylsilyl ether was removed under the same conditions used for the transformation of **8c** and **8e** into **8d**, starting from the diastereomeric mixture **8**,**9o**. After chromatography with PE/Et_2O 7:3→4:6 the two

epimeric alcohols **28** and **29** were separated and obtained in 97% overall yield as white foams. **Characterization of 28**: R_f 0.43 (PE/Et_2O 1:1, **A**, **B**). $[\alpha]_D$ = +255.0 (*c* 1.75, $CHCl_3$). IR: ν_{max} 3023, 2995, 2954, 2170, 1708, 1447, 1376, 1190, 1008. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.02 [9H, s, –Si(CH_3)$_3$]; 2.45 [1H, broad s, –CH_2OH]; 3.29–3.43 [3H, m, >$CHCH_2$OTr]; 4.00 [2H, apparent s; became a broad d, J = 4.0, after exchange with D_2O, –CH_2OH]; 5.88 and 5.88 [2H, AB system, H_2 and H_3, J_{AB} = 6.9]; 7.02 [1H, broad d, H_6, J = 7.6]; 7.13–7.41 [22H, m, H_5, H_7, Ph, Tr]; 7.74 [1H, broad d, H_8, J = 7.8]. ^{13}C NMR: −0.27 [3C, –Si(CH_3)$_3$]; 41.55 [–CH(CH_2O–)$_2$]; 44.72 [C_2]; 64.78 and 65.17 [2C, –CH(CH_2O–)$_2$]; 87.16 [–CPh_3]; 88.90 and 101.20 [2C, –C≡C–TMS]; 121.62 [2C, *C ortho* of Ph]; 122.35 [C_8]; 123.06, 125.04 [most likely 2C]; and 127.83 [4C, C_3, C_5, C_6, C_7]; 125.68 [*C para* of Ph]; 127.20 [3C, *C para* of Tr]; 127.48 [C_{4a}]; 127.96 and 128.50 [12C, *C ortho* and *meta* of Tr]; 129.28 [2C, *C meta* of Ph]; 133.69 [C_4]; 134.34 [C_{8a}]; 144.61 [3C, *C ipso* of Tr]; 150.85 [*C ipso* of Ph], 151.80 [*C*O]. **Characterization of 29**: R_f 0.29 (PE/Et_2O 2:8, **A**, **B**). $[\alpha]_D$ = −227.8 (*c* 1.16, $CHCl_3$). IR: ν_{max} 3044, 2981, 2305, 1714, 1379, 1327, 1255. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.08 [9H, s, –Si(CH_3)$_3$]; 2.22 [1H, broad s, –CH_2OH]; 3.27 [1H, quintuplet, >$CHCH_2$OTr, J = 6.0]; 3.51 and 3.57 [2H, AB part of ABX system, –$CHCH_2$OTr, J_{AB} = 9.2, J_{AX} and J_{BX} = 5.0, 8.1]; 3.77–3.84 [2H, m, –CH_2OH]; 5.82 and 5.88 [2H, AB system, H_2 and H_3, J_{AB} = 6.6]; 7.08–7.51 [23H, m, H_5, H_6, H_7, Ph, Tr]; 7.73 [1H, broad d, H_8, J = 7.7]. ^{13}C NMR: −0.37 [3C, –Si(CH_3)$_3$]; 41.92 [–CH(CH_2O–)$_2$]; 44.85 [C_2]; 64.46 and 64.90 [2C, –CH(CH_2O–)$_2$]; 87.29 [–CPh_3]; 87.29 and 101.90 [2C, –C≡C–TMS]; 121.58 [2C, *C ortho* of Ph]; 122.46 [C_8]; 123.12, 124.94 [most likely 2C]; and 127.78 [4C, C_3, C_5, C_6, C_7]; 125.71 [*C para* of Ph]; 127.11 [3C, *C para* of Tr]; 127.54 [C_{4a}]; 127.94 and 128.68 [12C, *C ortho* and *meta* of Tr]; 129.33 [2C, *C meta* of Ph]; 133.49 [C_4]; 134.20 [C_{8a}]; 144.68 [3C, *C ipso* of Tr]; 150.87 [*C ipso* of Ph], 151.83 [*C*O].

4.29. 8m by acetylation of 29

The same procedure reported for the preparation of **5f** was followed starting from **29** and the corresponding **8m** was obtained in 82% yield.

4.30. 4-{(*S*)-[1-(Toluene-4-sulfonyloxymethyl)-2-trityloxy]ethyl}-2-{(*S*)-[(trimethylsilyl)ethynyl]}-2*H*-quinoline-1-carboxylic acid phenyl ester, 30

A solution of **29** (202 mg, 304 μmol) in dry CH_2Cl_2 (3 ml) was cooled a t 0°C and treated with 4-dimethylaminopyridine (4 mg, 33 μmol), triethylamine (148 μl, 106 mmol) and freshly distilled *p*-TsCl (87 mg, 456 μmol). After 5 min the reaction was stirred at rt for 7 h. After addition of 5% aq $NH_4H_2PO_4$, the reaction was extracted as usual with Et_2O. Chromatography with PE/Et_2O 8:2→7:3 gave pure **30** (176 mg, 71% yield) as a white foam. R_f 0.44 (PE/Et_2O 6:4, **A**, **B**). $[\alpha]_D$ = −60.5 (*c* 1.32, $CHCl_3$). IR: ν_{max} 2954, 2170, 1720, 1377, 1326, 1291, 1174. GC–MS: unsuitable for this analysis. ^{1}H NMR: 0.13 [9H, s, –Si(CH_3)$_3$]; 2.36 [3H, s, –CH_3]; 3.27 [1H, quintuplet, –$CHCH_2$OTr, J = 5.7]; 3.27 and 3.43 [2H, AB part of ABX system, >$CHCH_2$OTr, J_{AB} = 9.0, J_{AX} and J_{BX} = 5.0, 6.8]; 4.18 and 4.24 [2H, AB part of ABX system, >$CHCH_2$OTs, J_{AB} = 9.6, J_{AX} and J_{BX} = 5.0, 5.9]; 5.77 and 5.84 [2H, AB system, H_2 and H_3, J_{AB} = 6.8]; 7.06–7.42 [25H, m, H_5, H_6, H_7, Ph, Tr, *H ortho* to –SO_2–]; 7.64 [2H, apparent d, *H ortho* to –SO_2–, J = 8.4]; 7.72 [1H, broad d, H_8, J = 8.2]. ^{13}C NMR: −0.41 [3C, –Si(CH_3)$_3$]; 39.37 [–CH(CH_2O–)$_2$]; 44.76 [C_2]; 62.11 and 69.18 [2C, –CH(CH_2O–)$_2$]; 86.96 [–CPh_3]; 88.94 and 100.48 [2C, –C≡C–TMS]; 121.61 [2C, *C ortho* of Ph]; 122.69, 123.30, and 124.87 [most likely 2C] [4C, 4*C* (between C_3, C_5, C_6, C_7, C_8, while one is overlapped with another signal)]; 125.77 [*C para* of Ph]; 127.05 [3C, *C para* of Tr]; 127.79 [2C, *C ortho* to –SO_2–]; 127.85 and 128.69 [12C, *C ortho* and *meta* of Tr]; 128.47 [C_{4a}]; 129.38 [2C, *C meta* of Ph]; 129.80 [2C, *C meta* to –SO_2–]; 131.87 [C_4]; 132.50 [–CSO_2–]; 134.16 [C_{8a}]; 143.58 [3C, *C ipso* of Tr]; 144.73 [–*C*Me of Ts]; 150.88 [*C ipso* of Ph], 151.78 [*C*O].

4.31. 9j by reduction of 30

A solution of **30** (48 mg, 59 μmol) in dry THF (3 ml) was treated with NaI (198 mg, 132 μmol) and AIBN [2,2′-azobis(2-methylpropionitrile)] (2.5 mg, 15 μmol). Then nBu$_3$SnH (24 μl, 89 μmol) was added via syringe and the resulting mixture was heated at 85°C in a sealed tube for 19 h. After diluting with water, an extraction was performed with Et_2O. Chromatography with PE/Et_2O 9:1→6:4 gave **9j** as a pale yellow oil [11 mg, 29% yield (39% on unrecovered starting material)].

4.32. NOE difference experiments on 16, 18, 19

The samples were prepared (20 mg/ml) using $CDCl_3$ previously dried on 3 Å molecular sieves, and freshly passed through alumina. The tubes were placed under nitrogen and kept for 30 min in an ultrasound bath, in order to remove oxygen. NOEDIF spectra were acquired at 200 MHz, using a delay of 3.9 s and 256 transients. A decoupling power so that γH_2 = 3–4 Hz was used. The NOEs were calculated on the basis of the integrals for the 'normal' spectrum and the decoupled one. **Compound 16**: irradiation of OMe gave, at 49% saturation, NOEs of 5.5, 2.5 and 1.0 for H_{6a}, ≡C–*H* and H_1, respectively, corresponding to effective NOEs of 11.2, 5.2 and 2.1. **Compound 18**: (a) irradiation of OMe gave, at 44% saturation, NOEs of 8.0, 3.4 and 0.8 for H_{3a}, H_9, and CH_3CHCO, respectively, corresponding to effective NOEs of 18.3, 7.8 and 1.8; (b) Irradiation of CH_3CHCO gave, at 31 saturation, NOEs of 1.3, 0.7 and 0.6 for H_9, H_{3a} and OCH_3, respectively, corresponding to effective NOEs of 4.2, 2.2 and 1.8; (c) Irradiation of CH_3CHCO gave, at 43 saturation, NOEs of 0.9, 0.5 and 0.5 for H_9, H_4 and H_{3a}, respectively, corresponding to effective NOEs of 2.0, 1.2 and 1.1. **Compound 19**: (a) irradiation of OMe gave, at 50% saturation, NOEs of 8.6, and 3.8 for H_{3a} and H_9, respectively, corresponding to effective NOEs of 17.1 and 7.6; (b) Irradiation of CH_3CHCO gave, at 73 saturation, a NOE of 4.5 for H_9, corresponding to an

effective NOE of 6.2; (c) Irradiation of CH_3CHCO gave, at 73 saturation, NOEs of 5.3 and 1.9 for H_{3a} and H_9, respectively, corresponding to effective NOEs of 7.3 and 2.6.

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