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Unusual Reactivity of Isoquinolinones Generated by Silver-Catalyzed Cycloisomerizations of Imines Derived from *ortho*-Alkynylsalicylaldehydes

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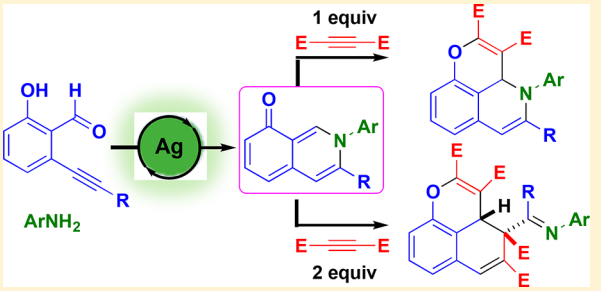
Supporting Information

ABSTRACT: 8-Isoquinolinones derived from a silver-catalyzed cycloisomerization of in situ formed *ortho*-alkynylsalicylaldimines react with 1 equiv of acetylenedicarboxylate derivatives to give pyrano[2,3,4-*ij*]isoquinolines through a [4 + 2]-cycloaddition reaction. When 2 equiv of the alkyne are used, structurally complex benzo[*de*]chromenes are obtained through an intricate cascade process comprising unusual formal [4 + 2]- and [2 + 2]-cycloadditions followed by several ring-opening and ring-closing processes.



INTRODUCTION

Coinage metal-catalyzed cycloisomerization reactions of *ortho*-alkynylbenzaldehydes performed in the presence of different reagents have become valuable tools for the synthesis of a wide range of interesting complex molecules.[1−3] Although the imine derivatives of *ortho*-alkynylbenzaldehydes are also known to suffer cycloisomerization processes under catalytic conditions, its reactivity has been much lesser studied than that of their parent aldehydes.[4] In this context, we have recently reported the silver-catalyzed reaction of imines derived from *ortho*-alkynylsalicylaldehydes **1**, a particular type of *ortho*-alkynylbenzaldimines, to obtain azaphilone derivatives (Scheme 1a).[5] This reaction proceeds through an initial cycloisomerization reaction to generate the 8-isoquinolinone derivative **2** that, surprisingly, performs as a nucleophile in a subsequent formal dimerization reaction.[5] Interestingly, isoquinolinone derivative **2** also contains in its structure a 1,4-heterodiene and an alkene (highlighted in color in Scheme 1b) that might participate in [4 + 2]- and/or [2 + 2]-cycloaddition processes, respectively.[6] Thus, apart from being a nucleophile at *α*-position, this molecule **2** could also be an appropriate partner for new cycloaddition reactions with alkynes (Scheme 1b).

With this idea in mind, we initiated a study on the in situ generation of 8-isoquinolinone derivatives from *ortho*-alkynylsalicylaldehydes and its subsequent reaction with alkynes. Our results are presented herein.

RESULTS AND DISCUSSION

Considering that imines **1** are easily formed from the corresponding aldehyde through a condensation reaction with appropriate amines, we started our investigation by studying the multicomponent reaction of *ortho*-alkynylsalicylaldehyde derivatives **3**, anilines **4**, and dimethyl acetylenedicarboxylate **5a** (Table 1). Thus, when a 1:1:1 mixture of these three reagents was dissolved in tetrahydrofuran in the presence of 5 mol % of silver triflate and was heated at reflux for 3 h, it was possible to gain the desired multicomponent coupling products **6** in moderate yields (Table 1). As shown, different substitution was allowed at the aldehyde **3** and aniline **4** but, unfortunately, the reaction did not proceed with other alkynes lacking the two electron-withdrawing groups. Structural

Scheme 1. 8-Isoquinolinones Derived from *ortho*-Alkynylsalicylaldimines: Previous Work and Our Proposal

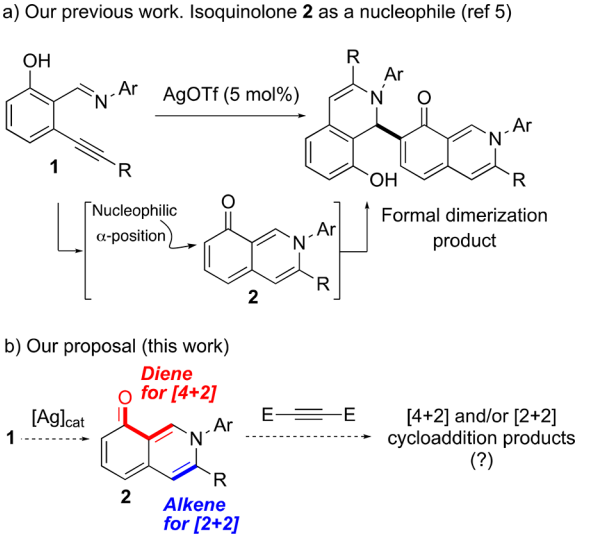


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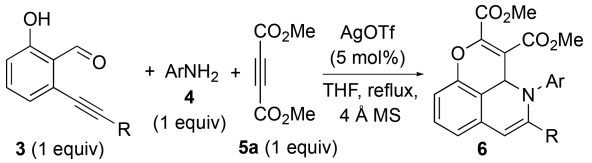
Table 1. Synthesis of Pyrano[2,3,4-*ij*]isoquinolines 6



3 (1 equiv) 5a (1 equiv) 6

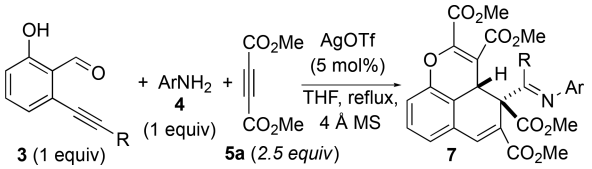
ent	3	R	4	Ar	6	yield[a]
1	3a	Bu	4a	4-MeC_6H_4	6a	62%
2	3a	Bu	4b	4-ClC_6H_4	6b	56%
3	3a	Bu	4c	4-$MeOC_6H_4$	6c	62%
4	3a	Bu	4d	3-$NO_2C_6H_4$	6d	58%
5	3a	Bu	4e	2-PhC_6H_4	6e	59%
6	3a	Bu	4f	2-MeC_6H_4	6f	56%[b]
7	3a	Bu	4g	2-BrC_6H_4	6g	59%[c]
8	3a	Bu	4h	2-Br,3-MeC_6H_3	6h	57%[c]
9	3b	*c*-C_5H_9	4a	4-MeC_6H_4	6i	55%
10	3b	*c*-C_5H_9	4e	2-PhC_6H_4	6j	58%
11	3c	Ph	4a	4-MeC_6H_4	6k	62%
12	3d	4-MeC_6H_4	4b	4-ClC_6H_4	6l	58%
13	3d	4-MeC_6H_4	4i	4-MeC_6H_4	6m	56%
14	3d	4-MeC_6H_4	4j	4-BrC_6H_4	6n	58%
15	3d	4-MeC_6H_4	4d	3-$NO_2C_6H_4$	6o	55%
16	3e	3-Thienyl	4a	4-MeC_6H_4	6p	62%
17	3f	2-MeC_6H_4	4e	2-PhC_6H_4	6q	65%
18	3f	2-MeC_6H_4	4g	2-BrC_6H_4	6r	57%[d]

[a]Isolated yield based on 3. [b]3.5:1 mixture of rotamers. [c]2.6:1 mixture of rotamers. [d]8:1 mixture of rotamers.

assignments of all these new compounds were based on a series of NMR studies. Additionally, the structure of **6l** was confirmed by single-crystal X-ray diffraction analysis.[7]

As previously noted, all these reactions were executed with equimolecular quantities of all three reagents. However, interesting results were observed when the reaction of *ortho*-alkynylsalicylaldehyde derivatives **3** and anilines **4** was performed in the presence of an excess of dimethyl acetylenedicarboxylate **5a** (2.5 equiv) in tetrahydrofuran as solvent at reflux for 12 h (Table 2). Under these conditions, the expected pyrano[2,3,4-*ij*]isoquinolines **6** were not obtained, and instead, formation of benzo[*de*]chromene derivatives **7**, incorporating two molecules of dimethyl acetylenedicarboxylate **5a** in their structure, was observed. These one-pot four-component coupling products **7** were isolated as single diastereoisomers. The complex structure and the apparent intricate skeletal rearrangement observed in benzo[*de*]chromene derivatives **7** should be remarked upon at this point. The structure of these compounds was determined by NMR studies and confirmed by single-crystal X-ray diffraction analysis performed on **7d**.[7]

Table 2. Synthesis of Benzo[*de*]chromene Derivatives 7



3 (1 equiv) 5a (2.5 equiv) 7

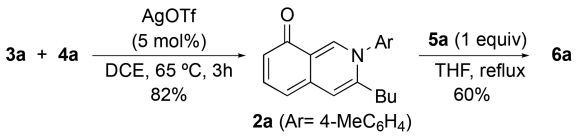
ent	3	R	4	Ar	7	yield[a]
1	3a	Bu	4a	4-MeC_6H_4	7a	42%
2	3a	Bu	4e	2-PhC_6H_4	7b	41%
3	3a	Bu	4f	2-MeC_6H_4	7c	40%
4	3a	Bu	4g	2-BrC_6H_4	7d	42%
5	3a	Bu	4h	2-Br,3-MeC_6H_3	7e	41%
6	3a	*c*-C_5H_9	4g	2-BrC_6H_4	7f	48%
7	3a	Pr	4g	2-BrC_6H_4	7g	46%

[a]Isolated yield based on 3.

Controlled experiments were conducted to gain insights into the reaction mechanisms. First, the isoquinolinone derivative **2a** was synthesized by reacting aldehyde **3a** and aniline **4a** in 1,2-dichloroethane (DCE) at 65 °C for 3 h. Interestingly, we observed that the reaction of isolated **2a** with dimethyl acetylenedicarboxylate **5a** in tetrahydrofuran at reflux led to pyrano[2,3,4-*ij*]isoquinoline **6a** (60% yield) in the absence of any additional reagent or catalyst (Scheme 2a). This

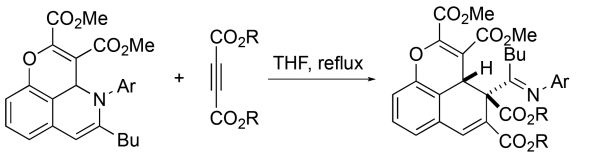
Scheme 2. Controlled Experiments

a) Synthesis of isoquinolinone **2a** and its thermal reaction with **5a**



2a (Ar= 4-MeC_6H_4)

b) Thermal reaction of isolated **6g** with alkynes **5a,b**



6g (Ar= 2-BrC_6H_4) **5a** (R= Me) **5b** (R= Et) **7d** (Ar= 2-BrC_6H_4, R= Me; 78%) **7h** (Ar= 2-BrC_6H_4, R= Et; 78%)

experiment not only indicated that 8-isoquinolinones **2** were intermediates of the reaction but also that their reaction with alkyne **5a** may not necessarily be a catalytic process.

We also verified that the reaction of isolated pyrano[2,3,4-*ij*]isoquinoline derivative **6g** and dimethyl acetylenedicarboxylate **5a** in tetrahydrofuran at reflux cleanly led to benzo[*de*]chromene derivative **7d** (Scheme 2b). Again, this reaction did not require any catalyst or additional reagent and it went to completion by simple heating. Under similar conditions, pyrano[2,3,4-*ij*]isoquinoline derivative **6g** reacted with diethyl acetylene dicarboxylate **5b** to generate the new benzo[*de*]chromene derivative **7h** in high yield (78%; Scheme 2b).

A plausible mechanism for the formation of pyrano[2,3,4-*ij*]isoquinolines **6** and benzo[*de*]chromene derivatives **7** is shown in Scheme 3. Thus, the initial coordination of the catalyst to the triple bond of the imines **1**, derived from the condensation between *ortho*-alkynylsalicylaldehydes **3** and anilines **4**, generates the first intermediates **8**. This coordination favors the intramolecular addition of the nitrogen of the imine to the alkyne to form the isoquinolinium intermediates **9**. The subsequent formal intramolecular protodemetalation reaction regenerates the silver catalyst and delivers the 8-isoquinolinone derivatives **2**. These intermediates can participate as the heterodiene partners of [4 + 2] thermal cycloaddition reactions with dimethyl acetylenedicarboxylate **5a** to deliver the pyrano[2,3,4-*ij*]isoquinolines **6**.

Compounds **6** are the final products of the process when equimolecular quantities of the reactants are used. However, when an excess of dimethyl acetylenedicarboxylate **5a** is employed, the pyrano[2,3,4-*ij*]isoquinolines **6** may further

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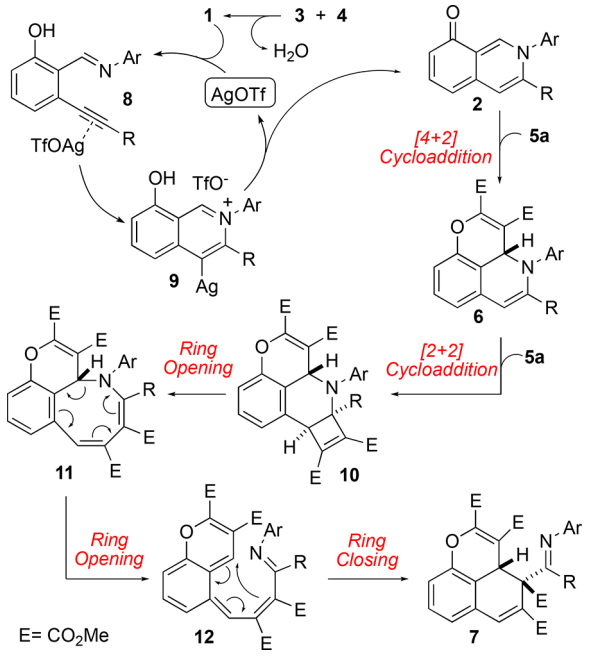
Scheme 3. Mechanistic Proposal



react with alkyne **5a** through a formal [2 + 2] cycloaddition reaction to obtain the cyclobutene derivatives **10**. A subsequent formal electrocyclic ring opening of the cyclobutene results in the formation of the new tricyclic intermediates **11**. These chromeno[4,5-*bc*]azocine derivatives **11** may evolve through another ring-opening process of the eight-membered ring to give the bicyclic intermediates **12**. Finally, a formal electrocyclic ring-closing process on these highly conjugated molecules would explain the formation of benzo[*de*]chromene derivatives **7**.

It should be noted that the proposed sequence from isoquinolinone **2** to the final product **7** consists of five consecutive and different formal pericyclic reactions. This proposal offers an attractive opportunity for computational studies. Thus, density functional theory (DFT) calculations [at the b3lyp/6-31G* and M06-2X/6-311++G** levels (PCM/THF)] were performed. A summary of the results of this investigation is shown in Figure 1 (see Supporting Information for details).

We initially investigated the [4 + 2] cycloaddition reaction between the model 8-isoquinolinone **2b** (Ar = Ph; R = Me) and dimethyl acetylenedicarboxylate **5a** to give the pyrano-[2,3,4-*ij*]isoquinoline **6ab**. As shown, this reaction was characterized as a highly asynchronous concerted process, as deduced from the comparison of the forming C−C bonds at the transition state **TS1** (1.78 and 2.82 Å). Although the process is exergonic, it features a relatively high activation energy (28.6 or 27.1 kcal mol^{-1} depending on the level of theory used) typical of highly ordered transition states of concerted cycloaddition reactions.

Next, we computationally studied the [2 + 2] carbocyclization reaction of the previously formed pyrano[2,3,4-*ij*]-isoquinoline **6ab** and dimethyl acetylenedicarboxylate **5a** to give the corresponding cyclobutene derivative **10ab**. This reaction was characterized as a stepwise process, proceeding via the zwitterionic intermediate **13** formed by addition of the nucleophilic enaminic *β*-carbon of **6ab** to one of the highly electrophilic carbons of alkyne **5a**. An activation energy of 26.3 kcal mol^{-1} to reach transition state **TS2** was found for this

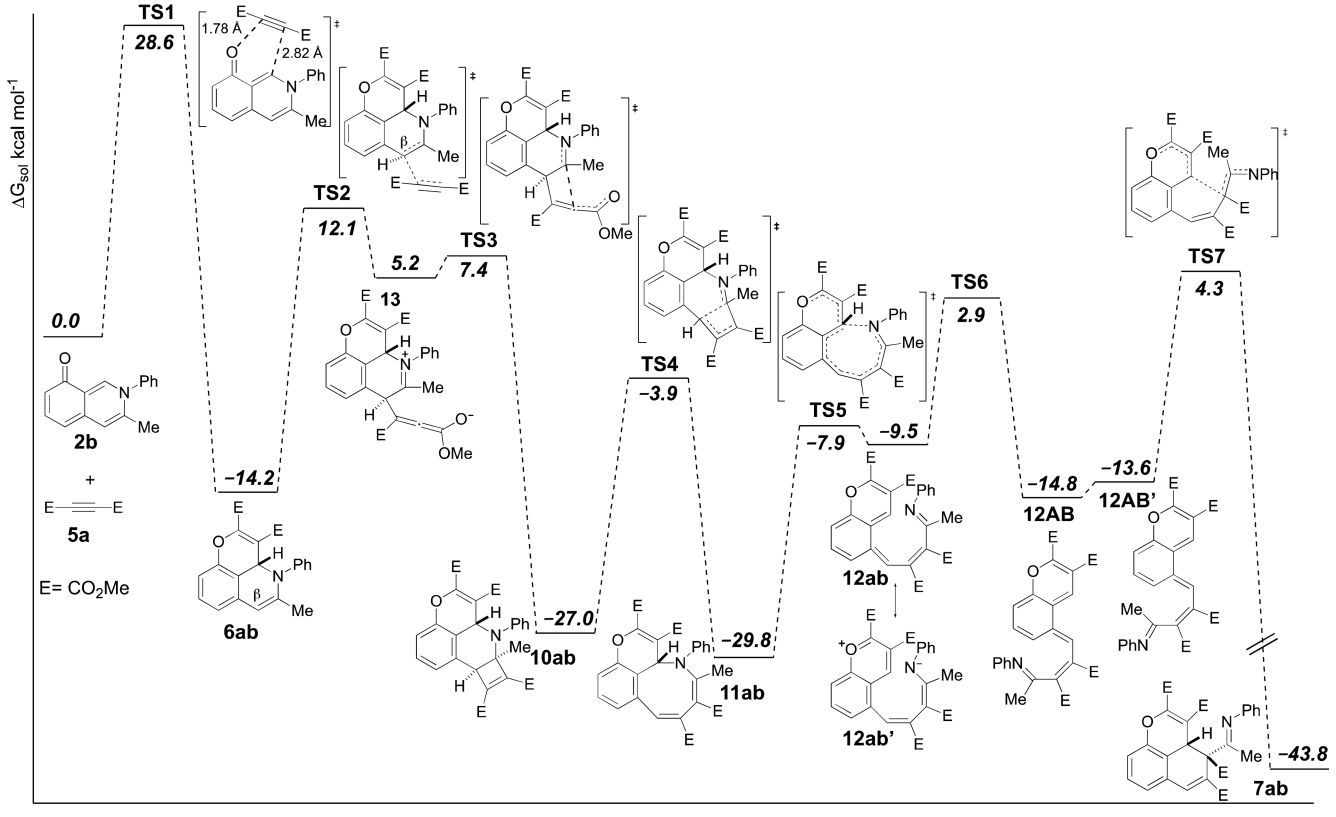


Figure 1. Energy profile for the reaction of isoquinolinone **2b** and dimethyl acetylenedicarboxylate **5a** at the b3lyp/6-31G* level (PCM/THF).

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step. This transition state results from the approach of alkyne **5a** to the apparently less hindered face of enamine **6ab**. This approach was computed to be energetically favored over the alternative approach of **5a** to the other face of enamine **6ab**. Once intermediate **13** was formed, we found that it could undergo cyclization to provide the cyclobutene derivative **10ab** through transition state **TS3** with very low activation energy (2.2 kcal mol^{-1}). The overall [2 + 2] carbocyclization reaction from **6ab** to **10ab** was found to be a highly exergonic process by 12.8 kcal mol^{-1}.

The subsequent ring opening of the cyclobutene of **10ab** to give the eight-membered-containing tricyclic compound **11ab** was characterized as a formally disrotatory process that proceeded through transition state **TS4**.[8] The computed barrier for this transformation was 23.1 kcal mol^{-1}, and the process was exergonic by 2.8 kcal mol^{-1}. It was found that intermediate **11ab** might evolve through a typical 8π-electrons conrotatory electrocyclic ring-opening reaction to give the new intermediate **12ab**, which features a helicoidal arrangement of the side chain. The activation energy we calculated for this process was 21.9 kcal mol^{-1}, and the transition state (**TS5**) was found to be very close to the intermediate **12ab**. Interestingly, intermediate **12ab** can be represented by the alternative resonance form **12ab′** featuring an aromatic zwitterionic structure. Inspection of bond distances on this intermediate clearly indicated a substantial contribution of this latter canonical form. In consequence, intermediate **12ab** may undergo structural changes by means of bond rotations to render more stable isomers such as **12AB** and **12AB′**.

Finally, we evaluated the last cyclization process to give benzo[*de*]chromene derivative **7ab**. It should be noted that attending to the stereochemistry of products **7**, the direct cyclization from intermediate **12ab** would imply a forbidden 6π-electrons conrotatory electrocyclic reaction. So, as expected, we were not able to locate a transition state for this process (from **12ab** to **7ab**). However, we found that the reaction could proceed from isomer **12AB′** through the transition state **TS7** with an activation energy of 17.9 kcal mol^{-1} in a process that was highly exergonic (30.2 kcal mol^{-1}). Interestingly, the structure of early transition state **TS7** looks like a zwitterionic species comprising a chromenium cation and an enamine. Therefore, this final cyclization could be seen as an intramolecular nucleophilic addition of the enamine to the chromenium ion.

Globally, the rate-determining step for the complete sequence is the initial [4 + 2] cycloaddition of isoquinolinone **2b** and dimethyl acetylenedicarboxylate **5a**. The highly exergonic nature of the overall process should also be noted.

■ CONCLUSIONS

In summary, complex polyheterocyclic molecules such as pyrano[2,3,4-*ij*]isoquinolines and benzo[*de*]chromenes could be easily synthesized from the reaction of simple *ortho*-alkynylsalicylaldehydes, anilines, and dimethyl acetylenedicarboxylate in the presence of silver triflate as a catalyst. Supported by computational studies, it is proposed that these products are generated through a complex sequence that implies the initial formation of an 8-isoquinolinone derivative that further evolves by several formal consecutive cycloadditions and electrocyclic processes. The rich and atypical reactivity of the in situ generated 8-isoquinolinone should be noted. Indeed, it is shown that this multitalented molecule, apart from behaving as nucleophile in some reactions, contains in its simple structure a heterodiene that participates in formal [4 + 2] cycloadditions and an alkene that participates in [2 + 2] cycloaddition processes.

■ EXPERIMENTAL SECTION

General Experimental Methods. All reactions were conducted in dried glassware under an inert atmosphere of argon. Solvents were dried with a PureSolv column system before use. Starting materials were prepared according to methods reported in the literature. Purification of the final products was performed by column chromatography employing silica gel 60 (230−240 mesh, Aldrich) as the stationary phase. ^{1}H NMR spectra were recorded on a Bruker AV-400 (400 MHz) and Bruker AV-300 (300 MHz). Chemical shifts are reported in ppm from tetramethylsilane with the residual solvent resonance as the internal standard ($CHCl_3$: δ = 7.26 ppm). Data are reported as follows: chemical shift, multiplicity: (app) = apparent, (s) = singlet, (d) = doublet, (t) = triplet, (m) = multiplet, (bs) = broad singlet, (td) = triplet of doublets, (dd) = doublet of doublets, (ddd) = doublet doublet of doublets; coupling constants (J in Hz), integration and assignment. ^{13}C NMR spectra were recorded on a Bruker AV-400 (100 MHz) or Bruker AV-300 (75 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$: δ = 77.16 ppm). High-resolution mass spectrometry was carried out on a Micromass AutoSpec device employing electrospray ionization methods (ESI). Melting points have been measured in a Gallenkamp device and have not been corrected.

Synthesis of Compounds 6. 4 Å Molecular sieves (50 mg) and the corresponding *ortho*-alkynylsalicylaldehyde **3** (0.15 mmol) and aniline **4** (0.15 mmol) were suspended in tetrahydrofuran (1 mL) in a glass reaction tube equipped with a magnetic stirring bar under an argon atmosphere. The mixture was stirred at room temperature for 5 h, and then alkyne **5a** (0.15 mmol) and silver triflate (5 mol %) were added. The mixture was heated at 65 °C for 3 h. Then, the reaction was filtered through a path of Celite, the solvent was removed *in vacuo*, and the resulting crude was purified by flash column chromatography on silica gel using mixtures of hexane and ethyl acetate as eluent to give the corresponding pure products **6.**

*Dimethyl 5-Butyl-4-(p-tolyl)-3a,4-dihydropyrano[2,3,4-ij]-isoquinoline-2,3-dicarboxylate (**6a**).* Brown solid (40 mg, 62%). R_f = 0.23 (hexane/ethyl acetate 5:1). Melting point: 77−79 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.21 (app t, J = 7.7 Hz, 1H), 6.95 (d, J = 8.0 Hz, 2H), 6.91 (dd, J = 7.6, 0.8 Hz, 1H), 6.86 (d, J = 8.0 Hz, 1H), 6.62 (d, J = 8.0 Hz, 2H), 6.16 (s, 1H), 5.31 (s, 1H), 3.83 and 3.75 (2 s, 6H), 2.27 (s, 3H), 2.14−1.98 (m, 2H), 1.59−1.48 (m, 2H), 1.43−1.22 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.1, 162.9, 153.7, 150.9, 146.5, 139.1, 136.6, 135.8, 130.1, 129.2, 128.4, 118.5, 112.4, 108.0, 107.7, 105.7, 53.0, 52.0, 51.8, 33.6, 30.9, 22.2, 21.0, 13.4. HMRS (ESI): calculated for $C_{26}H_{28}NO_5$ [M + H]$^+$ 434.1961, found 434.1949.

*Dimethyl 5-Butyl-4-(4-chlorophenyl)-3a,4-dihydropyrano[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6b**).* Orange solid (38 mg, 56%). R_f = 0.44 (hexane/ethyl acetate 5:1). Melting point: 79−81 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.21 (app t, J = 7.9 Hz, 1H), 7.10 (d, J = 8.6 Hz, 2H), 6.92 (d, J = 7.1 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.63 (d, J = 8.6 Hz, 2H), 6.22 (s, 1H), 5.29 (s, 1H), 3.84 and 3.76 (2 s, 6H), 2.12−1.97 (m, 2H), 1.62−1.22 (m, 4H), 0.89 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.0, 162.8, 153.3, 151.4, 146.5, 140.5, 135.4, 132.5, 131.2, 128.8, 128.6, 118.9, 113.0, 109.6, 107.8, 105.3, 53.1, 52.2, 52.0, 33.5, 30.8, 22.2, 13.9. HMRS (ESI): calculated for $C_{25}H_{25}ClNO_5$ [M + H]$^+$ 454.1415, found 454.1410.

*Dimethyl 5-Butyl-4-(4-methoxyphenyl)-3a,4-dihydropyrano-[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6c**).* Brown solid (42 mg, 62%). R_f = 0.27 (hexane/ethyl acetate 5:1). Melting point: 80−82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.19 (app t, J = 7.9 Hz, 1H), 6.89 (d, J = 7.5 Hz, 1H), 6.85 (d, J = 8.2 Hz, 1H), 6.65 (app s, 4H), 6.10 (s, 1H), 5.29 (s, 1H), 3.81, 3.73, and 3.72 (3 s, 9H), 2.15−1.92 (m, 2H), 1.56−1.44 (m, 2H), 1.39−1.22 (m, 2H), 0.87 (t, J = 7.3 Hz,

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3H). $^{13}C\{^1H\}$-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.1, 162.9, 158.3, 153.8, 150.8, 146.5, 135.8, 134.5, 131.7, 128.4, 118.5, 113.7, 112.4, 107.5, 107.5, 105.8, 55.2, 53.0, 52.0, 51.8, 33.5, 30.9, 22.2, 14.0. HMRS (ESI): calculated for $C_{26}H_{28}NO_7$ $[M + OH]^+$ 466.1860, found 466.1868.

*Dimethyl 5-Butyl-4-(3-nitrophenyl)-3a,4-dihydropyrano[2,3,4-ij]-isoquinoline-2,3-dicarboxylate (**6d**).* Yellow solid (40 mg, 58%). R_f = 0.43 (hexane/ethyl acetate 3:1). Melting point: 86−89 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.00 (ddd, J = 8.0, 2.1, 0.9 Hz, 1H), 7.63 (app t, J = 2.1 Hz, 1H), 7.31 (app t, J = 8.1 Hz, 1H), 7.25 (app t, J = 8.0 Hz, 1H), 6.99 (d, J = 7.5 Hz, 1H), 6.94 (ddd, J = 7.9, 2.1, 1.0 Hz, 1H), 6.90 (d, J = 8.1 Hz, 1H), 6.39 (s, 1H), 5.35 (s, 1H), 3.86 and 3.83 (2 s, 6H), 2.10 (t, J = 7.3 Hz, 2H), 1.65−1.51 (m, 2H), 1.46−1.25 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 165.9, 162.6, 152.6, 152.0, 148.2, 146.6, 143.4, 135.3, 134.9, 129.5, 129.0, 124.2, 121.5, 119.5, 113.6, 112.2, 108.0, 104.8, 53.1, 52.6, 52.3, 33.5, 30.8, 22.1, 13.9. HMRS (ESI): calculated for $C_{25}H_{24}N_2NaO_7$ $[M + Na]^+$ 487.1475, found 487.1480.

*Dimethyl 4-([1,1′-Biphenyl]-2-yl)-5-butyl-3a,4-dihydropyrano-[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6e**).* Yellow solid (44 mg, 59%). R_f = 0.3 (hexane/ethyl acetate 7:1). Melting point: 200−202 °C. ^1H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.39 (dd, J = 7.4, 1.6 Hz, 1H), 7.37−7.27 (m, 3H), 6.99−6.97 (m, 2H), 6.92 (app t, J = 7.8 Hz, 1H), 6.91−6.88 (m, 3H), 6.67 (d, J = 7.5 Hz, 1H), 6.39 (d, J = 8.1 Hz, 1H), 5.83 (s, 1H), 5.37 (s, 1H), 3.84 and 3.44 (2 s, 6H), 2.39 (ddd, J = 15.5, 10.3, 5.3 Hz, 1H), 2.32 (m, 1H), 1.71−1.62 (m, 1H), 1.58−1.49 (m, 1H), 1.44−1.35 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$-NMR (151 MHz, $CDCl_3$) δ (ppm) 166.1, 163.0, 150.2, 149.8, 144.7, 144.6, 139.5, 138.5, 136.6, 136.4, 131.4, 128.6, 127.9, 127.3, 127.2, 126.8, 117.1, 111.2, 106.0, 104.7, 99.8, 53.0, 51.7, 51.7, 33.7, 30.5, 22.9, 14.1. HMRS (ESI): calculated for $C_{31}H_{30}NO_5$ $[M + H]^+$ 496.2118, found 496.2113.

*Dimethyl 5-Butyl-4-(o-tolyl)-3a,4-dihydropyrano[2,3,4-ij]-isoquinoline-2,3-dicarboxylate (**6f**).* Yellow solid (36 mg, 56%). R_f = 0.60 (hexane/ethyl acetate 3:1). Melting point: 189−191 °C. Rotamers mixture (3.5:1). Only representative signals are listed: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.30−7.11 (m, 9H), 6.91−6.79 (m, 4H), 6.55 (d, J = 6.7 Hz, 1H), 5.92 (s, 1H), 5.86 (s, 1H), 5.62 (s, 1H), 5.56 (s, 1H), 3.81 and 3.45 (2 s, 6H), 3.80 and 3.46 (2 s, 6H), 2.15−1.85 (m, 4H), 1.44−1.14 (m, 8H), 0.84−0.73 (m, 6H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.2, 165.8, 162.7, 162.5, 153.6, 150.1, 149.6, 145.7, 140.8, 140.4, 140.0, 139.1, 137.1, 136.5, 135.4, 132.0, 130.3, 128.8, 128.5, 128.2, 127.8, 127.7, 126.6, 125.3, 117.8, 117.4, 116.1, 111.9, 110.9, 110.1, 107.9, 106.5, 105.7, 105.6, 103.5, 100.8, 53.1, 52.9, 52.5, 51.9, 51.7, 51.6, 33.3, 32.3, 30.9, 30.4, 22.4, 22.3, 18.6, 18.2, 13.8. HMRS (ESI): calculated for $C_{26}H_{28}NO_5$ $[M + H]^+$ 434.1962, found 434.1968.

*Dimethyl 4-(2-Bromophenyl)-5-butyl-3a,4-dihydropyrano[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6g**).* Yellow solid (44 mg, 59%). R_f = 0.47 (hexane/ethyl acetate 3:1). Melting point: 205−207 °C. Rotamers mixture (2.6:1). Only representative signals are listed: ^1H NMR (300 MHz, $CDCl_3$, 298 K) δ (ppm) 7.42 (dd, J = 7.8, 1.7 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 6.82 (d, J = 8.1 Hz, 1H), 6.67−6.62 (m, 1H), 6.00 (s, 1H), 5.89 (s, 1H), 5.69 (s, 1H), 5.61 (s, 1H), 3.83 and 3.45 (2 s, 6H), 3.80 and 3.61 (2 s, 6H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$, 298 K) δ (ppm) 166.3, 165.7, 162.7, 162.3, 153.8, 150.5, 148.7, 147.5, 146.6, 145.8, 141.4, 139.6, 137.4, 136.8, 136.0, 133.5, 133.2, 133.0, 129.2, 128.8, 128.3, 128.1, 127.9, 126.7, 118.2, 117.6, 112.5, 111.1, 108.4, 106.9, 106.7, 105.5, 104.8, 101.8, 53.0, 52.8, 52.3, 51.7, 33.2, 32.6, 31.0, 30.2, 22.4, 22.3, 13.8, 13.8. ^1H NMR (400 MHz, Toluene-d8, 343 K) δ (ppm) 7.28−7.22 (m, 1H), 7.04−6.94 (m, 3H), 6.75 (d, J = 8.1 Hz, 1H), 6.74 (d, J = 7.5 Hz, 1H), 6.63 (app t, J = 7.1 Hz, 1H), 5.91 (s, 1H), 5.66 (s, 1H), 3.40 (s, 3H), 3.34 (brs, 3H), 2.03−1.89 (m, 1H), 1.37−1.25 (m, 1H), 1.23−1.09 (m, 4H), 0.75 (t, J = 7.2 Hz, 3H). HMRS (ESI): calculated for $C_{25}H_{25}BrNO_6$ $[M + OH]^+$ 514.0859, found 514.0855.

*Dimethyl 4-(2-Bromo-3-methylphenyl)-5-butyl-3a,4-dihydro-pyrano[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6h**).* Orange solid (43 mg, 57%). R_f = 0.34 (hexane/ethyl acetate 4:1). Melting point: 205−207 °C. Rotamers mixture (2.6:1). Only representative signals are listed: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.27−7.11 (m, 5H), 6.99 (app t, J = 7.7 Hz, 1H), 6.91−6.79 (m, 5H), 6.50 (dd, J = 7.7, 1.2 Hz, 1H), 5.95 (s, 1H), 5.87 (s, 1H), 5.72 (s, 1H), 5.61 (s, 1H), 3.82 and 3.45 (2 s, 6H), 3.80 and 3.55 (2 s, 6H), 2.45 (s, 3H), 2.37 (s, 3H), 2.07−1.80 (m, 4H), 1.45−1.14 (m, 8H), 0.86−0.72 (m, 6H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.4, 165.7, 162.7, 162.2, 153.6, 150.2, 148.8, 146.5, 145.8, 141.5, 139.9, 139.7, 139.2, 137.0, 136.2, 134.5, 131.0, 130.4, 130.2, 130.0, 128.7, 128.0, 127.4, 125.8, 117.9, 117.5, 112.2, 111.0, 108.7, 106.7, 106.6, 105.0, 104.5, 101.3, 52.9, 52.8, 52.2, 51.7, 51.7, 33.2, 32.5, 31.1, 30.2, 24.2, 22.4, 22.3, 13.8. HMRS (ESI): calculated for $C_{26}H_{27}BrNO_6$ $[M + OH]^+$ 528.1016, found 528.1017.

*Dimethyl 5-Cyclopentyl-4-(p-tolyl)-3a,4-dihydropyrano[2,3,4-ij]-isoquinoline-2,3-dicarboxylate (**6i**).* Brown solid (37 mg, 55%). R_f = 0.4 (hexane/ethyl acetate 5:1). Melting point: 93−95 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.19 (app t, J = 7.9 Hz, 1H), 6.94−6.90 (m, 3H), 6.84 (d, J = 8.1 Hz, 1H), 6.57 (d, J = 8.2 Hz, 2H), 6.26 (s, 1H), 5.25 (s, 1H), 3.81 and 3.78 (2 s, 6H), 2.39 (quint, J = 7.9 Hz, 1H), 2.24 (s, 3H), 2.00−1.90 (m, 1H), 1.73−1.62 (m, 3H), 1.60−1.43 (m, 4H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.2, 163.0, 157.9, 151.1, 146.5, 139.5, 136.5, 135.8, 129.9, 129.2, 128.3, 118.9, 112.6, 108.1, 106.3, 105.7, 53.0, 52.3, 51.9, 43.4, 33.5, 30.9, 25.1, 24.9, 21.0. HMRS (ESI): calculated for $C_{27}H_{28}NO_6$ $[M + OH]^+$ 462.1911, found 462.1910.

*Dimethyl 4-([1,1′-Biphenyl]-2-yl)-5-cyclopentyl-3a,4-dihydro-pyrano[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6j**).* Orange solid (44 mg, 58%). R_f = 0.31 (hexane/ethyl acetate 4:1). Melting point: 188−190 °C. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.46−7.39 (m, 1H), 7.37−7.27 (m, 3H), 7.02−6.84 (m, 6H), 6.66 (d, J = 7.0 Hz, 1H), 6.38 (d, J = 8.0 Hz, 1H), 5.90 (s, 1H), 5.35 (s, 1H), 3.83 and 3.45 (2 s, 6H), 2.84−2.63 (m, 1H), 2.22−2.09 (m, 1H), 1.94−1.46 (m, 7H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.1, 162.9, 154.2, 150.1, 144.9, 144.5, 139.3, 138.6, 136.7, 136.3, 131.4, 128.5, 127.8, 127.2, 127.2, 127.0, 126.7, 117.2, 111.1, 106.0, 104.7, 97.3, 52.9, 51.8, 51.6, 42.2, 33.8, 32.3, 25.4, 25.1. HMRS (ESI): calculated for $C_{32}H_{30}NO_5$ $[M + H]^+$ 508.2118, found 508.2114.

*Dimethyl 5-Phenyl-4-(p-tolyl)-3a,4-dihydropyrano[2,3,4-ij]-isoquinoline-2,3-dicarboxylate (**6k**).* Brown solid (42 mg, 62%). R_f = 0.19 (hexane/ethyl acetate 5:1). Melting point: 90−92 °C. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.74 (dd, J = 7.9, 1.6 Hz, 2H), 7.34−7.24 (m, 4H), 7.16 (d, J = 7.1 Hz, 1H), 6.94 (d, J = 8.2 Hz, 1H), 6.92 (s, 1H), 6.79 (d, J = 8.2 Hz, 2H), 6.53 (d, J = 8.2 Hz, 2H), 5.42 (s, 1H), 3.98 and 3.87 (2 s, 6H), 2.14 (s, 3H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.4, 163.0, 152.2, 151.6, 147.0, 139.1, 136.7, 135.9, 135.7, 129.2, 128.8, 128.5, 128.4, 128.2, 119.9, 113.8, 111.5, 109.4, 105.1, 53.1, 52.8, 52.2, 20.9. HMRS (ESI): calculated for $C_{28}H_{24}NO_5$ $[M + H]^+$ 454.1648, found 454.1650.

*Dimethyl 4-(4-Chlorophenyl)-5-(p-tolyl)-3a,4-dihydropyrano-[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6l**).* Brown solid (42 mg, 58%). R_f = 0.38 (hexane/ethyl acetate 4:1). Melting point: 199−201 °C. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.60 (d, J = 8.0 Hz, 2H), 7.30 (app t, J = 7.8 Hz, 1H), 7.16 (d, J = 7.3 Hz, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.00−6.91 (m, 4H), 6.57 (d, J = 8.7 Hz, 2H), 5.39 (s, 1H), 3.98 and 3.89 (2 s, 6H), 2.26 (s, 3H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.3, 162.9, 152.6, 151.2, 146.9, 140.6, 139.1, 135.5, 133.4, 131.6, 129.5, 129.1, 128.7, 128.1, 120.0, 113.9, 111.6, 109.2, 104.8, 53.1, 52.8, 52.3, 21.3. HMRS (ESI): calculated for $C_{28}H_{23}ClNO_5$ $[M + H]^+$ 488.1259, found 488.1251.

*Dimethyl 4,5-Di-p-tolyl-3a,4-dihydropyrano[2,3,4-ij]-isoquinoline-2,3-dicarboxylate (**6m**).* Brown solid (39 mg, 56%). R_f = 0.38 (hexane/ethyl acetate 5:1). Melting point: 92−94 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.62 (d, J = 8.0 Hz, 2H), 7.27 (app t, J = 7.8 Hz, 1H), 7.13 (d, J = 7.5 Hz, 1H), 7.08 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.1 Hz, 1H), 6.87 (s, 1H), 6.78 (d, J = 8.1 Hz, 2H), 6.51 (d, J = 8.1 Hz, 2H), 5.38 (s, 1H), 3.89 and 3.87 (2 s, 6H), 2.29 and 2.13 (2 s, 6H). $^{13}C\{^1H\}$-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.4, 163.1, 152.2, 151.7, 147.0, 139.2, 138.8, 135.9, 135.8, 133.9, 129.2, 129.0, 128.5, 128.3, 128.3, 119.7, 113.6, 110.8, 109.4, 105.2, 53.1, 52.7, 52.1, 21.2, 20.9. HMRS (ESI): calculated for $C_{29}H_{26}NO_5$ $[M + H]^+$ 468.1805, found 468.1810.

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*Dimethyl 4-(4-Bromophenyl)-5-(p-tolyl)-3a,4-dihydropyrano-[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6n**).* Brown solid (46 mg, 58%). R_f = 0.29 (hexane/ethyl acetate 5:1). Melting point: 196−198 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.57 (d, J = 7.9 Hz, 2H), 7.28 (app t, J = 7.8 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 7.12−7.07 (m, 4H), 6.96−6.89 (m, 2H), 6.49 (d, J = 8.4 Hz, 2H), 5.37 (s, 1H), 3.97 and 3.89 (2 s, 6H), 2.30 (s, 3H). ^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.3, 162.9, 152.6, 151.1, 146.9, 141.2, 139.1, 135.5, 133.3, 131.7, 129.8, 129.1, 128.7, 128.1, 120.0, 119.7, 114.0, 111.7, 109.3, 104.8, 53.1, 52.8, 52.3, 21.3. HMRS (ESI): calculated for $C_{28}H_{23}BrNO_5$ [M + H]$^+$ 532.0754, found 532.0749.

*Dimethyl 4-(3-Nitrophenyl)-5-(p-tolyl)-3a,4-dihydropyrano-[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6o**).* Yellow solid (41 mg, 55%). R_f = 0.26 (hexane/ethyl acetate 5:1). Melting point: 209−211 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.82 (ddd, J = 8.0, 2.2, 1.0 Hz, 1H), 7.63−7.56 (m, 3H), 7.31 (app t, J = 7.5 Hz, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.14 (t, J = 8.0 Hz, 1H), 7.10 (d, J = 7.9 Hz, 2H), 7.03 (s, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.89 (ddd, J = 8.0, 2.1, 1.0 Hz, 1H), 5.46 (s, 1H), 4.02 and 3.87 (2 s, 6H), 2.29 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.1, 162.6, 152.8, 150.4, 148.2, 146.8, 143.6, 139.5, 135.2, 133.9, 132.8, 129.3, 129.1, 128.1, 123.0, 120.8, 120.5, 114.4, 112.9, 109.2, 104.6, 53.2, 53.1, 52.6, 21.3. HMRS (ESI): calculated for $C_{28}H_{23}N_2O_7$ [M + H]$^+$ 499.1499, found 499.1500.

*Dimethyl 5-(Thiophen-3-yl)-4-(p-tolyl)-3a,4-dihydropyrano-[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6p**).* Orange solid (42 mg, 62%). R_f = 0.26 (hexane/ethyl acetate 5:1). Melting point: 91−93 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.49 (dd, J = 3.0, 0.8 Hz, 1H), 7.33 (dd, J = 5.0, 0.8 Hz, 1H), 7.26 (app t, J = 7.9 Hz, 1H), 7.18 (dd, J = 5.0, 3.0 Hz, 1H), 7.11 (d, J = 7.5 Hz, 1H), 6.90 (d, J = 8.1 Hz, 1H), 6.87 (s, 1H), 6.81 (d, J = 8.2 Hz, 2H), 6.52 (d, J = 8.2 Hz, 2H), 5.36 (s, 1H), 3.96 and 3.86 (2 s, 6H), 2.15 (s, 3H). ^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.4, 163.0, 152.2, 147.0, 146.7, 139.4, 139.1, 136.0, 135.5, 129.3, 128.5, 128.0, 126.6, 125.4, 124.9, 119.9, 113.8, 111.2, 109.4, 105.1, 53.1, 52.7, 52.2, 20.9. HMRS (ESI): calculated for $C_{26}H_{22}NO_5S$ [M + H]$^+$ 460.1213, found 460.1207.

*Dimethyl 4-([1,1′-Biphenyl]-2-yl)-5-(o-tolyl)-3a,4-dihydro-pyrano[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6q**).* Yellow solid (51 mg, 65%). R_f = 0.52 (hexane/ethyl acetate 4:1). Melting point: 197−199 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) δ 7.24−6.83 (m, 13H), 6.75 (d, J = 7.2 Hz, 1H), 6.67 (dd, J = 8.0, 0.9 Hz, 1H), 6.45 (d, J = 8.1 Hz, 1H), 5.91 (s, 1H), 5.66 (s, 1H), 3.83 and 3.37 (2 s, 6H), 2.64 (s, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ (ppm) 165.8, 162.9, 150.4, 148.4, 144.8, 143.9, 139.9, 138.7, 138.3, 137.2, 135.4, 135.3, 131.3, 129.8, 129.2, 128.8, 128.4, 127.5, 127.3, 127.3, 127.2, 126.6, 125.4, 118.2, 112.7, 107.7, 105.2, 104.5, 53.0, 51.9, 51.6, 20.3. HMRS (ESI): calculated for $C_{34}H_{27}NNaO_5$ [M + Na]$^+$ 552.1781, found 552.1779.

*Dimethyl 4-(2-Bromophenyl)-5-(o-tolyl)-3a,4-dihydropyrano-[2,3,4-ij]isoquinoline-2,3-dicarboxylate (**6r**).* Yellow solid (45 mg, 57%). R_f = 0.33 (hexane/ethyl acetate 4:1). Melting point: 179−181 °C. Rotamers mixture (8:1). Only signals of the major rotamer are listed: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.46−7.37 (m, 1H), 7.24 (app t, J = 7.8 Hz, 1H), 7.14−7.06 (m, 2H), 7.01−6.85 (m, 7H), 6.02 (s, 1H), 5.88 (s, 1H), 3.84 and 3.47 (2 s, 6H), 2.47 (brs, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ (ppm) 166.1, 162.7, 150.9, 147.4, 146.0, 139.8, 137.1, 136.8, 136.5, 136.3, 133.2, 129.6, 128.7, 128.2, 127.3, 126.3, 125.0, 118.6, 112.3, 107.6, 106.4, 104.5, 53.0, 51.9, 51.7, 19.8. HMRS (ESI): calculated for $C_{28}H_{23}BrNO_6$ [M + OH]$^+$ 548.0703, found 548.0703.

Synthesis of Compounds 7. 4 Å Molecular sieves (50 mg) and the corresponding *ortho*-alkynylsalicylaldehyde **3** (0.15 mmol) and aniline **4** (0.15 mmol) were suspended in tetrahydrofuran (1 mL) in a glass reaction tube equipped with a magnetic stirring bar under an argon atmosphere. The mixture was stirred at room temperature for 5 h, and then alkyne **5a** (0.38 mmol) and silver triflate (5 mol %) were added. The mixture was heated at 65 °C for 12 h. Then, the reaction was filtered through a path of Celite, the solvent was removed *in vacuo*, and the resulting crude was purified by flash column chromatography on silica gel using mixtures of hexane and ethyl acetate as eluent to give the corresponding pure products **7**.

Tetramethyl (3aS,4R*)-4-[(E)-1-(p-Tolylimino)pentyl]-3a,4-dihydrobenzo[de]chromene-2,3,4,5-tetracarboxylate (**7a**).* Yellow solid (36 mg, 42%). R_f = 0.32 (hexane/ethyl acetate 2:1). Melting point: 142−145 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.52 (s, 1H), 7.40−7.24 (m, 1H), 7.17−7.10 (m, 2H), 7.04 (d, J = 7.0 Hz, 2H), 6.47 (d, J = 7.0 Hz, 2H), 5.09 (s, 1H), 3.93, 3.84, 3.82, and 3.58 (4 s, 12H), 2.29 (s, 3H), 2.27−2.15 (m, 1H), 2.08−1.88 (m, 1H), 0.95−0.63 (m, 4H), 0.41 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$) δ (ppm) 170.7, 168.1, 166.2, 165.5, 162.1, 149.1, 147.8, 145.4, 133.3, 133.0, 132.1, 131.6, 129.8, 129.2, 125.4, 118.4, 118.0, 115.7, 113.1, 53.1, 52.4, 52.2, 52.0, 49.3, 44.7, 29.2, 28.9, 22.7, 20.8, 13.0. HMRS (ESI): calculated for $C_{32}H_{34}NO_9$ [M + H]$^+$ 576.2225, found 576.2214.

Tetramethyl (3aS,4R*)-4-{(E)-1-([1,1′-Biphenyl]-2-ylimino)-pentyl}-3a,4-dihydrobenzo[de]chromene-2,3,4,5-tetracarboxylate (**7b**).* Yellow solid (39 mg, 41%). R_f = 0.24 (hexane/ethyl acetate 3:1). Melting point: 85−87 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.73 (s, 1H), 7.32−6.96 (m, 12H), 5.01 (s, 1H), 3.84, 3.79, 3.72, and 3.60 (4 s, 12H), 2.09 (dd, J = 13.4, 5.6 Hz, 2H), 0.86−0.69 (m, 4H), 0.48 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ (ppm) 171.9, 167.5, 166.9, 165.8, 161.6, 148.6, 147.7, 140.5, 139.7, 138.0, 132.2, 130.9, 130.3, 130.2, 128.8, 128.4, 128.1, 127.4, 126.1, 123.8, 123.3, 119.8, 118.5, 116.3, 61.4, 52.7, 52.3, 52.2, 40.8, 32.4, 28.0, 22.9, 13.1. HMRS (ESI): calculated for $C_{37}H_{36}NO_9$ [M + H]$^+$ 638.2384, found 638.2367.

Tetramethyl (3aS,4R*)-4-[(E)-1-(o-Tolylimino)pentyl]-3a,4-dihydrobenzo[de]chromene-2,3,4,5-tetracarboxylate (**7c**).* Orange solid (34 mg, 40%). R_f = 0.43 (hexane/ethyl acetate 2:1). Melting point: 96−98 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) δ 7.82 (s, 1H), 7.27 (t, J = 8.0 Hz, 1H), 7.21 (d, J = 7.7 Hz, 1H), 7.07−6.95 (m, 3H), 6.86 (t, J = 7.5 Hz, 1H), 6.25 (d, J = 7.5 Hz, 1H), 5.05 (s, 1H), 3.83, 3.81, 3.79, 3.78 (4 s, 12H), 2.49−2.30 (m, 2H), 0.95−0.68 (m, 4H), 0.52 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ (ppm) 171.9, 167.3, 166.9, 166.0, 161.5, 148.9, 148.6, 139.1, 138.4, 131.3, 130.7, 129.8, 128.5, 126.3, 125.8, 123.9, 122.6, 118.8, 60.8, 52.7, 52.4, 52.3, 52.1, 40.1, 31.1, 28.4, 22.8, 16.8, 13.1. HMRS (ESI): calculated for $C_{32}H_{34}NO_9$ [M + H]$^+$ 576.2228, found 576.2218.

Tetramethyl (3aS,4R*)-4-{(E)-1-[(2-Bromophenyl)imino]pentyl}-3a,4 dihydrobenzo[de]chromene-2,3,4,5-tetracarboxylate (**7d**).* White solid (40 mg, 42%). R_f = 0.34 (hexane/ethyl acetate 3:1). Melting point: 136−138 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.83 (s, 1H), 7.33 (dd, J = 8.0, 1.2 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.16 (app td, J = 7.6, 1.2 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 6.80 (app td, J = 7.7, 1.6 Hz, 1H), 6.54 (dd, J = 7.9, 1.5 Hz, 1H), 5.07 (s, 1H), 3.81, 3.79, 3.78, and 3.76 (4 s, 12H), 2.52−2.37 (m, 2H), 0.97−0.79 (m, 4H), 0.52 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ (ppm) 171.8, 169.2, 167.3, 166.0, 161.5, 148.7, 148.7, 138.9, 132.4, 130.9, 130.1, 128.5, 127.6, 124.4, 123.8, 119.3, 119.2, 116.6, 116.4, 112.8, 60.4, 52.7, 52.5, 52.4, 52.1, 40.1, 31.3, 28.3, 22.9, 13.1. HMRS (ESI): calculated for $C_{31}H_{31}BrNO_9$ [M + H]$^+$ 640.1176, found 640.1158.

Tetramethyl (3aS,4R*)-4-{(E)-1-[(2-Bromo-3-methylphenyl)-imino]pentyl}-3a,4-dihydrobenzo[de]chromene-2,3,4,5-tetracarboxylate (**7e**).* Yellow solid (40 mg, 41%). R_f = 0.33 (hexane/ethyl acetate 5:1). Melting point: 67−69 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.86 (s, 1H), 7.20 (t, J = 7.7 Hz, 1H), 7.09−6.99 (m, 3H), 6.83 (d, J = 6.8 Hz, 1H), 6.39 (d, J = 7.5 Hz, 1H), 5.10 (s, 1H), 3.83, 3.81, 3.80, and 3.78 (4 s, 12H), 2.47 (t, J = 8.0 Hz, 2H), 2.28 (s, 3H), 0.98−0.79 (m, 4H), 0.54 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$) δ (ppm) 171.9, 168.7, 167.4, 166.0, 161.5, 149.1, 148.7, 138.9, 138.3, 130.9, 128.4, 126.9, 124.6, 124.4, 119.3, 116.7, 116.5, 115.4, 60.4, 52.7, 52.5, 52.3, 52.1, 40.0, 31.2, 28.2, 23.2, 13.1. HMRS (ESI): calculated for $C_{32}H_{33}BrNO_9$ [M + H]$^+$ 654.1333, found 654.1315.

Tetramethyl (3aS,4R*)-4-{(E)-[(2-Bromophenyl)imino](cyclo-pentyl)methyl}-3a,4-dihydrobenzo[de]chromene-2,3,4,5-tetracarboxylate (**7f**).* Yellow solid (47 mg, 48%). R_f = 0.40 (hexane/ethyl acetate 2:1). Melting point: 128−130 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.82 (s, 1H), 7.29 (dd, J = 7.9, 1.2 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.09−6.97 (m, 3H), 6.71 (app td, J = 7.8, 1.5 Hz, 1H), 6.43 (d, J = 7.8 Hz, 1H), 5.10 (s, 1H), 3.82 (s, 12H), 3.33−3.17

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(m, 1H), 1.72−1.43 (m, 4H), 1.32−1.13 (m, 4H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 172.0, 170.1, 167.1, 166.1, 161.5, 148.5, 148.0, 139.8, 138.2, 132.4, 131.7, 131.3, 128.5, 126.8, 124.3, 122.8, 119.4, 118.9, 116.3, 116.2, 111.0, 62.4, 52.8, 52.4, 52.4, 52.3, 45.6, 40.6, 32.5, 31.2, 25.6, 25.4. HMRS (ESI): calculated for $C_{32}H_{31}BrNO_9$ $[M + H]^+$ 652.1175, found 652.1176.

Tetramethyl (3aS,4R*)-4-{(E)-1-[(2-Bromophenyl)imino]butyl}-3a,4-dihydrobenzo[de]chromene-2,3,4,5-tetracarboxylate (**7g**).* Yellow solid (43 mg, 46%). R_f = 0.39 (hexane/ethyl acetate 2:1). Melting point: 134−136 °C. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.85 (s, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.24−7.11 (m, 2H), 7.06−7.00 (m, 2H), 6.82 (t, J = 7.6 Hz, 1H), 6.55 (d, J = 7.8 Hz, 1H), 5.09 (s, 1H), 3.83, 3.81, 3.80, and 3.79 (4 s, 12H), 2.54−2.38 (m, 2H), 1.13−0.83 (m, 2H), 0.53 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$-NMR (100 MHz, $CDCl_3$) δ (ppm) 171.8, 169.1, 167.3, 166.1, 161.5, 148.8, 148.7, 139.2, 138.9, 132.4, 130.9, 130.3, 128.5, 127.6, 124.4, 123.8, 119.3, 119.1, 116.4, 116.3, 112.7, 60.4, 52.7, 52.5, 52.4, 52.1, 40.0, 33.8, 20.0, 14.6. HMRS (ESI): calculated for $C_{30}H_{29}BrNO_9$ $[M + H]^+$ 626.1015, found 626.1020.

4,5-Diethyl 2,3-Dimethyl (3aS,4R*)-4-{(E)-1-[(2-bromophenyl)-imino]pentyl}-3a,4-dihydrobenzo[de]chromene-2,3,4,5-tetra-carboxylate (**7h**).* Yellow solid. Yield (78 mg, 78%). R_f = 0.36 (hexane/ethyl acetate 2:1). Melting point: 78−80 °C. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) δ 7.82 (s, 1H), 7.33 (dd, J = 7.9, 1.1 Hz, 1H), 7.21−7.09 (m, 2H), 7.04−6.97 (m, 2H), 6.79 (td, J = 7.9, 1.6 Hz, 1H), 6.53 (d, J = 6.7 Hz, 1H), 5.07 (s, 1H), 4.34−4.14 (m, 4H), 3.78 and 3.75 (2 s, 6H), 2.58−2.36 (m, 2H), 1.39−1.27 (m, 6H), 0.99−0.80 (m, 4H), 0.52 (t, J = 6.9 Hz, 3H). $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$) δ (ppm) 171.3, 169.4, 167.4, 165.6, 161.6, 148.8, 148.7, 138.6, 132.4, 130.9, 128.4, 127.5, 124.3, 123.8, 119.2, 119.2, 116.7, 116.5, 112.8, 61.7, 61.3, 52.7, 52.1, 40.1, 31.3, 28.4, 22.9, 14.3, 13.7, 13.1. HMRS (ESI): calculated for $C_{33}H_{35}BrNO_9$ $[M + H]^+$ 668.1489, found 668.1473.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b03081.

Optimization studies, NMR spectra, computational data, and X-ray crystallographic data (PDF)

Crystallographic data for **6l** (CIF)

Crystallographic data for **7d** (CIF)

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Notes

The authors declare no competing financial interest.

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