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Direct Synthesis of Benzhydryl-Functionalized 3,4-Dihydropyridin-2-Ones from 2-Pyridones and Their Use in the Formation of Bridged δ-Lactams

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Abstract: A method for the synthesis of C4-benzhydryl functionalized 3,4-dihydropyridin-2-ones using complementary addition of benzhydryllithium and/or benzhydrylmagnesiate reagents to 2-pyridones, with high regioselectivity triggered by substituents, is described. A partially stereoselective cyclization was successfully demonstrated using TfOH and/or TIPSOTf as Brønsted and Lewis acids, respectively, leading to C6-phenyl functionalized 7,8-benzomorphanones. It is also shown that the use of functionalized δ-enelactams obtained with an active methoxy-substituted benzyl group at C3, enabled the preparation of a new C3-C6 bridged system within δ-lactam framework.

Keywords: 2-pyridones; enelactams; bridged lactams; benzhydryllithium; magnesiates; 3,4-dihydropyridin-2-ones; TIPSOTf; benzomorphanones

1. Introduction

A broad spectrum of biological activity and their unique reactivity of different nature make 2-pyridones privileged scaffolds in drug discovery [1–3] and valuable precursors for synthesizing natural and naturally inspired compounds [4]. 3,4-Dihydropyridin-2-ones – partially saturated derivatives of 2-pyridones, belonging to the group of δ-enelactams, have also attracted much attention as pharmacophores and as functional building units applicable in synthesis, mainly because of the presence of the double bond adjacent to a nitrogen atom [5]. From among the variety of methods of their synthesis that have been reported, the addition of organometallic species to 2-pyridones is of fundamental importance, even though the reactions proceed with different C4 vs. C6 regioselectivity, leading to 3,4- or 3,6-dihydropyridin-2-ones, respectively.

Seebach and co-workers have reported the first regioselective nucleophilic 1,4-addition to 2-pyridone. The sole product – C4-functionalized 3,4-dihydropyridin-2-one – was obtained using a chiral, non-racemic large lithium enolate as a nucleophilic reagent [6]. Other reports on the intermolecular addition of organometallic compounds to non-activated 2---pyridones comprise the addition of *n*-BuLi to *N*H 2-pirydones [7] and the addition of phenyl Grignard reagents to *N*R 2-pyridones in the presence of iron salts [8], both leading regioselectively to C6-adduct. In order to extend the range of the applicability of the above synthetic methods, we have reported on the nucleophilic addition of lithium magnesiates of type R_3MgLi to 2-pyridones, permitting straightforward access to allyl [9–14], vinyl [15], and benzyl/benzyl-type [16–20] functionalized dihydropyridones. However, concerning regioselectivity, it should be noted that in these reactions, in general, *N*-alkyl 2-pyridones gave mainly C6 addition products. In contrast, *N*H(Li) 2-pyridones led regioselectively to C4 adduct (except for the vinylation reaction). Comparatively, the *N*-phenyl substituent led to an almost equimolar mixture of C6 and C4 regioisomeric adducts, except for the

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additions of vinylmagnesiate, as in these cases the addition occurred selectively at C6, regardless of the type of substituent at the nitrogen atom.

Continuing our studies on the synthesis of functionalized 3,4-dihydropyridon-2-ones, we were encouraged to check whether it would be possible to introduce a benzhydryl moiety into a 2-pyridone ring by using benzhydryllithium and benzhydrylmagnesium "ate" reagents, bearing in mind that benzhydryl group is a common structural motif present in a variety of bioactive compounds including commercial drugs (Figure 1) and that C4-benzhydryl functionalized 3,4-dihydropyridin-2-ones could be potentially used in cyclization reactions leading to i.e., functionalized benzomorphanones [21].

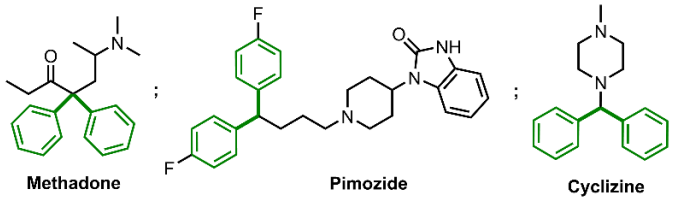

Figure 1. Representative commercial drugs bearing benzhydryl moiety: Methadone, which is the chemically simplest opioid drug known; Pimozide, the first antipsychotic drug for the treatment of Tourette syndrome [22]; and Cyclizine that exhibited anticholinergic and antihistamine activity [23].

2. Results and Discussion

At the first stage of our study, which aimed at the synthesis of C4-benzhydryl functionalized 3,4-dihydropyridin-2-ones, diphenylmethyllithium (**BzhLi**), easily generated from diphenylmethane using *n*-BuLi in THF at 0°C [24], was taken. However, in the first attempt, no expected reaction effect between *N*-lithiated 2-pyridone **1a** and **BzhLi** was observed, even when a 2-fold molar excess of the latter was used. Followingly, the other *N*-substituted 2-pyridones were tested under treatment with **BzhLi** (Scheme 1). After a short optimization, the best reaction conditions were: generation of **BzhLi** at 0°C for 25 min and its use in the addition reaction in 1.5 fold excess at -80°C for 70 min. Both steps were performed in THF as a solvent. Under these conditions, *N*-Ph substituted 2-pyridone **1d** gave a sole C4-adduct **2d** in 78% yield, while *N*-Me (**1b**) and *N*-Bn (**1c**) led to a mixture of C4 and C6 adducts at the ratios 33 : 67 and 61 : 39, respectively, however, in good total yields. The use of *N*-Bn derivative, equipped with a C5-Cl group (**1g**) disclosed the lack of significant changes in the regioselectivity of this addition in comparison to the addition to **1c**, while the presence of C5-Me substituent (**1e**) shifted the regioselectivity to favour C4 adduct (Scheme 1). In contrast, comparing C4- vs C6-adducts distribution for *N*-Ph substrates (**1d** and **1f**, **1h**), the tendency to increase regioselectivity towards C6-adduct was observed for C5-Me 2-pyridone **1f**. In comparison, for C5-Cl derivative **1h**, the formation of a sole C4-adduct was observed. However, it should be noted, that amongst the tested C5-functionalized derivatives in the reaction with **BzhLi**, the presence of a secondary amide group (substrate **1i**) had the most significant impact on obtaining C6 adduct. Only C6-adduct **3i** was obtained in this case, but in a low 27% yield.

At the end of this part of the study, it was found that the use of 2-pyridone **1k** with a benzhydryl substituent at the nitrogen atom resulted in the formation of C4 adduct (**2k**) as the only product. This result indicates that the steric effect of the benzhydryl group is responsible for the full regioselectivity, which could be confirmed by the lower regioselectivity in the case of the addition reaction to derivative **1j** with a smaller *N*-PMB group (Scheme 1).

Encouraged by the successful addition of **BzhLi** to *N*-substituted 2-pyridone, we were next prompted to check whether it would be possible to add fluorenyllithium (**FluLi**) and trityllithium (**TrLi**) reagents, which can also be generated by lithiation of fluorene [25] and triphenylmethane [26], respectively. The results are presented in Scheme 2. The reactions tested using 2-pyridone **1f** revealed the lack of reactivity when treated with **TrLi**.

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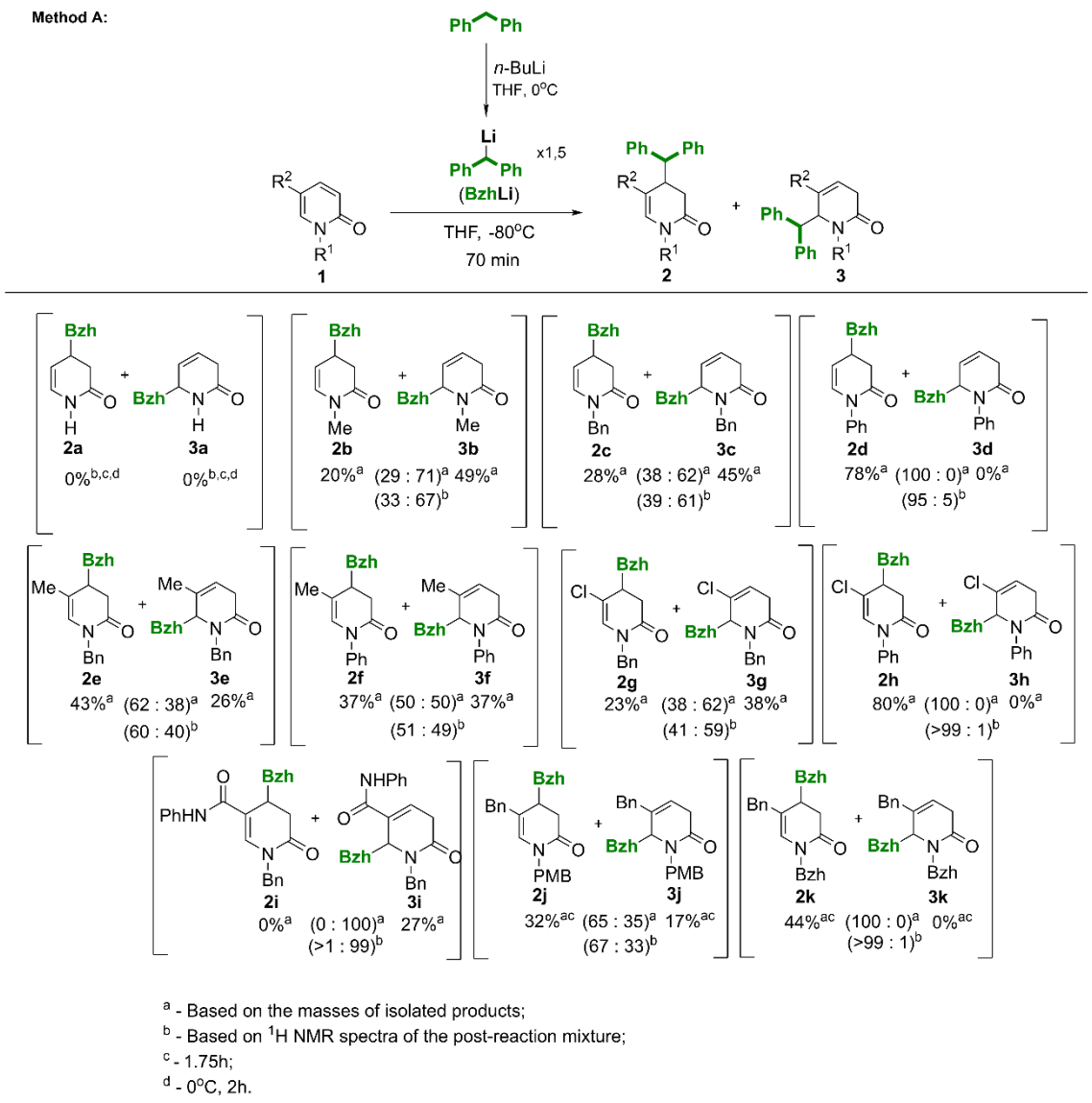
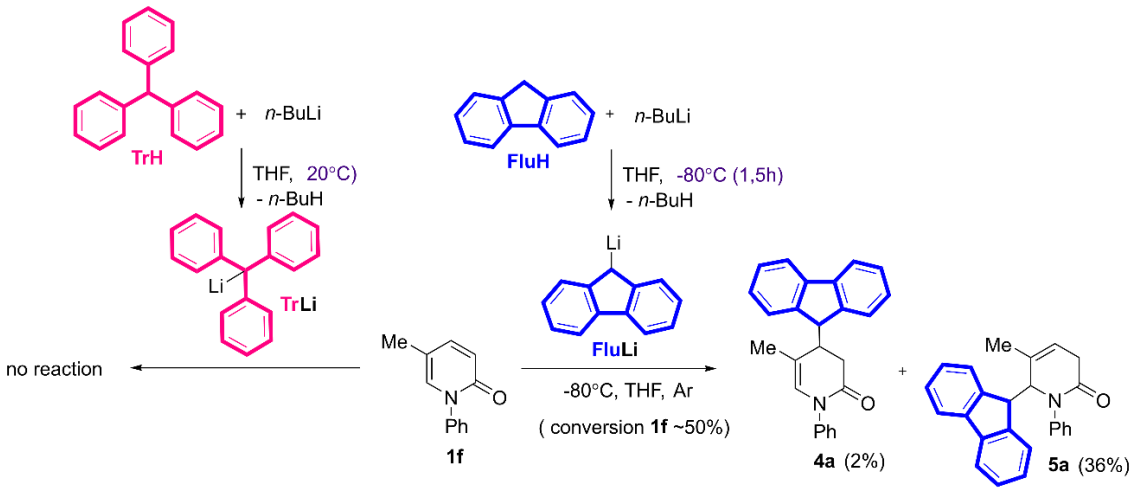


Scheme 1. Addition of diphenylmethyllithium (BzhLi) to 2-pyridones (Method A).



Scheme 2. Attempts **TrLi** and **FluLi** addition to 2-pyridone **1f**.

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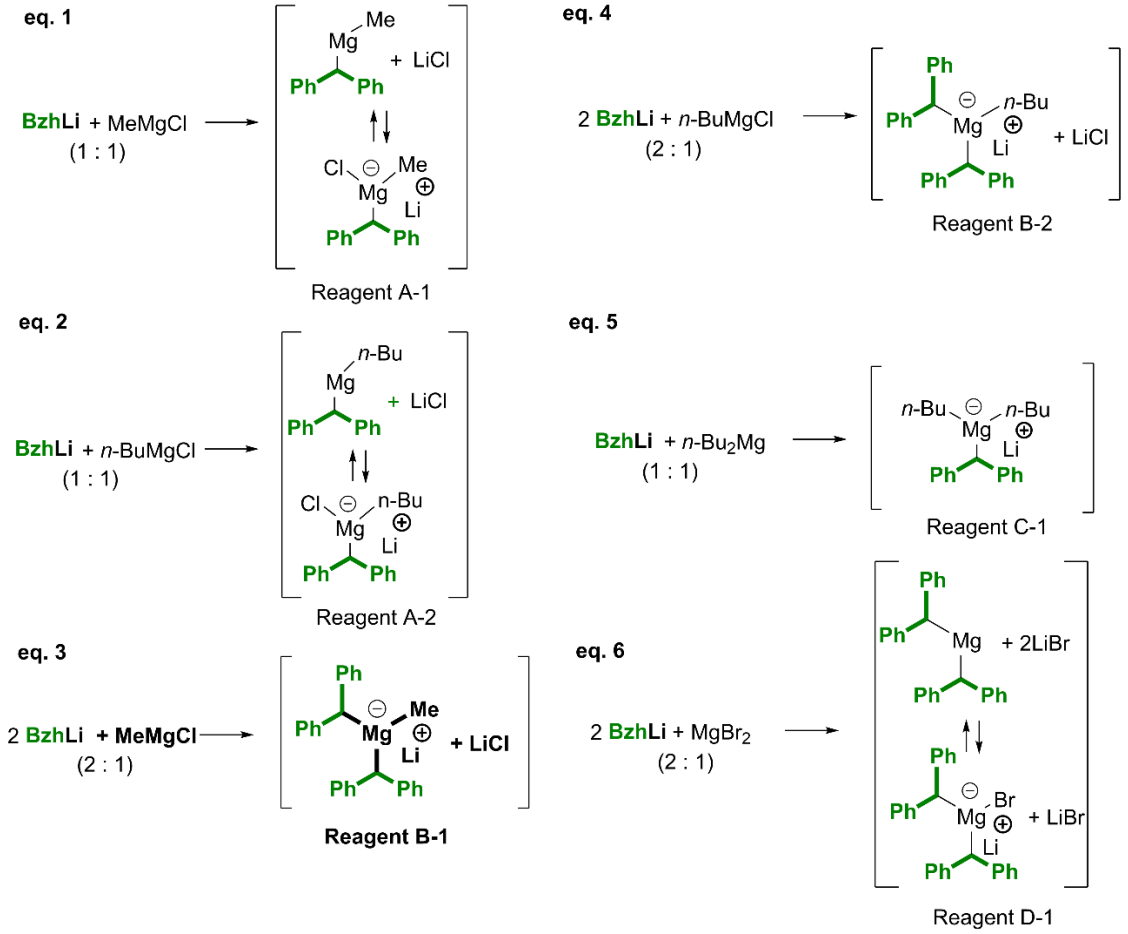
Application of **FluLi** yielded 36% of C6-adduct and only 2% of C4-adduct, with no full conversion. Because these results were not satisfactory regarding the reactivity and regioselectivity, **TrLi** and **FluLi** were not used in further study.

Nevertheless, building the research plan on the previous success of adding benzylmagnesiates to *N*-substituted 2-pyridone [16–20], we decided to check the reactivity of benzhydrylmagnesiates as a novel addition reagent. Given our promising results using benzylmagnesiates, an attempt to apply benzhydrylmagnesiates was planned as a consistent step in our research. However, in contrast to the previously applied magnesiate preparation method, consisting of mixing of benzyl magnesium chloride (as a donor of benzyl group) and alkyllithium compounds at 1 : 2 molar ratio, in this attempt we mixed – easily generated – **BhzLi** reagent with various magnesium compounds, including Grignards, *n*-Bu$_2$Mg and MgBr$_2$ at 1 : 1 and/or 2 : 1 molar ratio, respectively. The probable structures of lithium magnesiates formed in the mixture in THF at 0°C are shown in Scheme 3. From among the reagents tested in the reactions with 2-pyridone **1f** in THF at -80°C (Table 1), the complex **B-1** formed by combining **BzhLi** and MeMgLi at the molar ratio of 2 : 1 gave the best results in terms of yield and regioselectivity, when used in a concentration of 0.08 mol/mL (Table 1, entry 3), which could be further improved slightly by reducing the concentration more than twice (Table 1, entry 5).



Scheme 3. Variety of benzhydrylmagnesiates potentially formed between **BzhLi** and magnesium compounds.

Interestingly, good results were also achieved for reagents **C-1** and **D-1**, obtained by mixing **BzhLi** and *n*-Bu$_2$Mg at the molar ratio of 1 : 1 and MgBr$_2$ at the molar ratio of 2 : 1, respectively. In these cases, the yields of 81% (**C-1**) and 76% (**D-1**) were attained upon full conversion, but with worse regioselectivity than when reagent **B-1** was used. It is worth noting that the obtained result is better than that reached using **BzhLi** alone in terms of efficiency and selectivity (see Scheme 1).

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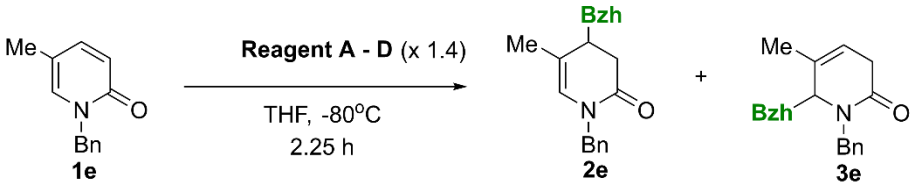
Table 2. Addition of benzhydrylmagnesiates **A**-**D** (Scheme 3) to 2-pyridone **1e**.



	Reagenta	Conversion[a,b] of 1e [%}	2e Yield[c] [%]	3e Yield[c] [%]	2e, 3e Total Yield[c] [%]	2e : 3e
1	**A-1**	99	39	19	58	67 : 33[c]
2	**A-2**	88	-	-	-	63 : 37[b]
3	**B-1**	95	59	22	81	73 : 27[c]
4	**B-1**	99	57	24	81[d]	70 : 30[c]
5	**B-1**	**99**	**67**	**22**	**89[e]**	**75 : 25[c]**
6	**B-2**	28	-	-	-	67 : 33[b]
7	**C-1**	99	51	31	82	62 : 38[c]
8	**D-1**	99	45	31	76	59 : 41[c]

[a] – Concentration of 0.08 mol/dm^3 was applied unless otherwise specified; [b] – Assigned by ^{1}H NMR;[c] – Yields of isolated products; [d] – Concentration of 0.06 mol/dm^3 was applied; [e] - Concentration of 0.034 mol/dm^3 was applied.

After establishing the best reaction conditions, we evaluated the scope and limitations of reagent **B-1** addition to various *N*- and C5-substituted 2-pyridones (see Scheme 4). Our findings showed that the optimized protocol enables benzhydrylation only for *N*-substituted 2-pyridones because *N*Li 2-pyridone derived from *N*H derivative remained unchanged. The results demonstrated that the yield and product distributions are dependent on the nature of the substituents. Regarding the substituents on the nitrogen atom, the regioselectivity is generally similar to that observed for the addition of **BzhLi**. Specifically, 2-pyridones with *N*-alkyl groups produced a mixture of 1,4- and 1,6-adducts, whereas *N*-Ph 2-pyridones generally only yielded C4-benzhydrylated products. Similarly to the reaction of **BzhLi** with *N*-Bzh substituted 2-pyridone **1k** (Scheme 1), the reactions of magnesiate **B-1** with **1k**, selectively provided 1,4-addition products, albeit with better yields (see Scheme 4). The other *N*-Bzh derivatives of 2-pyridone (**1n**, **1p**, **1r** and **1t**) also led regioselectively to C-4 additions products, generally in good yields, except for **1r**.

The influence of the substituents at the C5 atom depends on their electronic nature. Generally, it can be assumed that electron-donating substituents favour the increase in the yield of 1,4-adduct, while electron-withdrawing substituents cause the addition to C6 carbon atom to be preferred. However, the reactions with 2-pyridones having a bulky benzhydryl group at the nitrogen atom are exceptions. In the case of these 2-pyridones, regardless of the nature of the substituent at C5 atom, the only product is the C4-benzhydrylated compound, as mentioned earlier. This result indicates a predominant steric effect on the distribution of products. A striking example is the complete regioselectivity reversal in the case of derivatives with 5-dimethylaminocarbonyl groups and with an *N*-benzyl (**1q**) and *N*-benzhydryl (**1r**) substituent, respectively (Scheme 4).

However, a few differences were noted between the reactions with addition of **B-1** reagent and those with the use of **BzhLi**. The most significant difference was the unexpected appearance of additional products **6f**, **6g**, and **6h** (each isolated in 10% yield), which contained two benzhydryl groups in the 2-pyridone ring (Scheme 4) when applying **B-1**. Based on their structures, it can be assumed that these products were likely formed as a result of the decomposition of the organomagnesium addition product **IP-1** through β-elimination towards the intermediate 2-pyridone (**IP-2**). This intermediate then takes part in the subsequent addition of excess magnesiate **B-1**, as shown in Scheme 5. Examples of β-elimination involving Grignard compounds are described in

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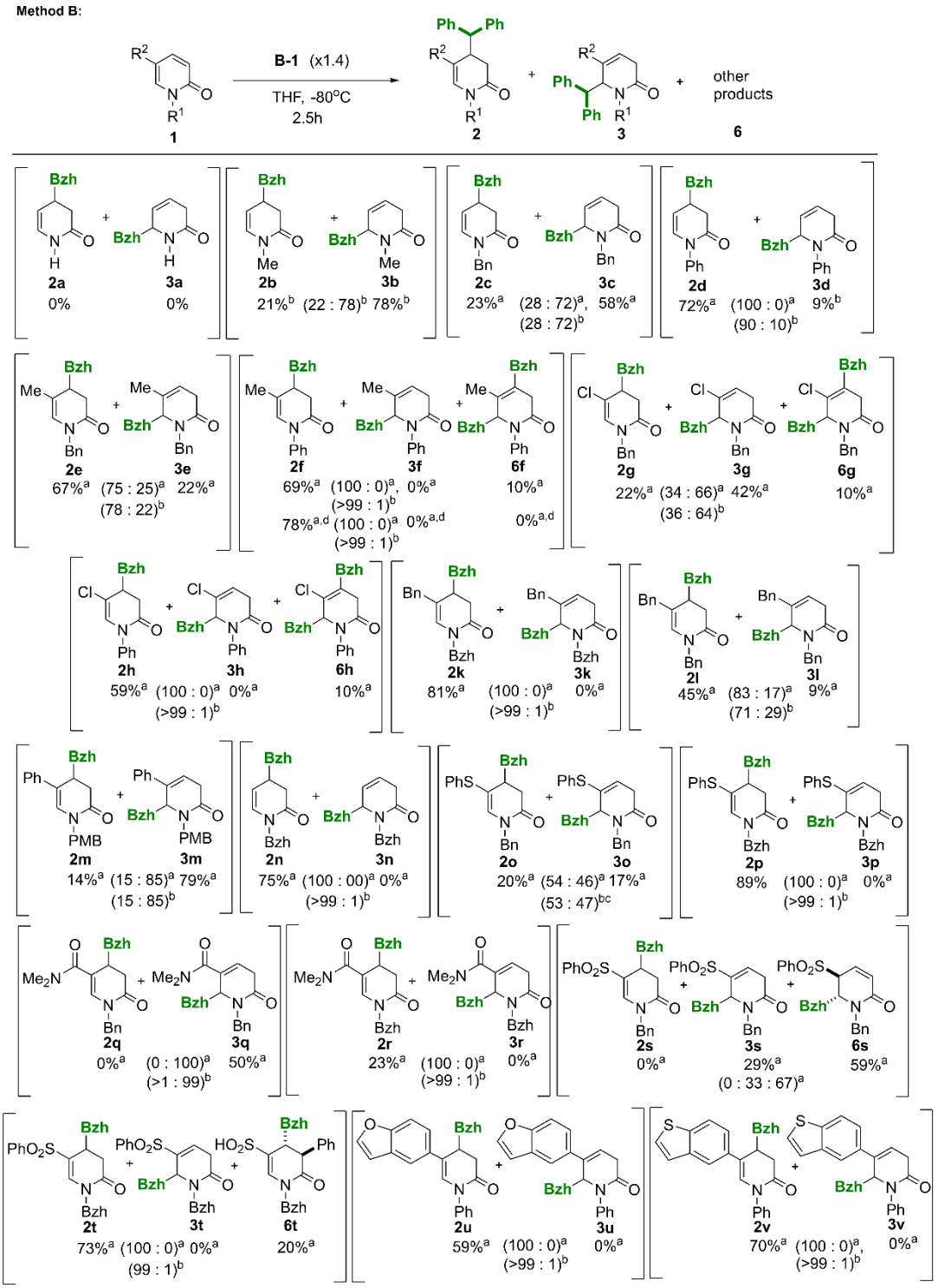
literature [27]. However, it should be noted that by using reagent **C-1** in the reaction with **2f**, the formation of product **6f** (Scheme 4) was avoided.



[a] – Yields of isolated products; [b] – Assigned by ^{1}H NMR; [c] - A small amount of an unidentified product is present; [d] - Reagent **C-1** was applied.

Scheme 4. Addition of benzhydrylmagnesiate **B-1** to 2-pyridones in the optimized conditions (Method B).

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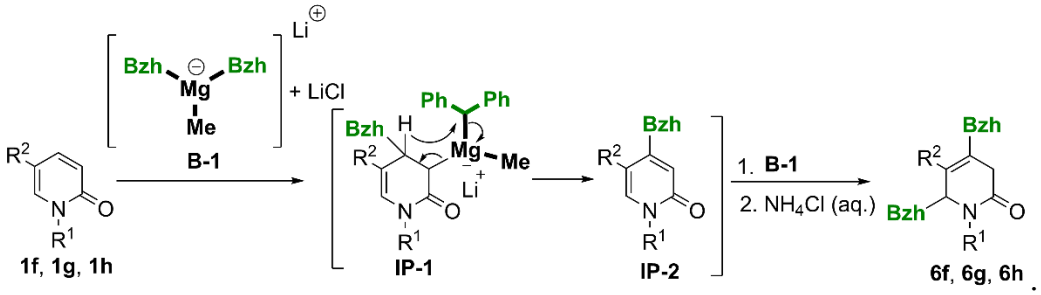
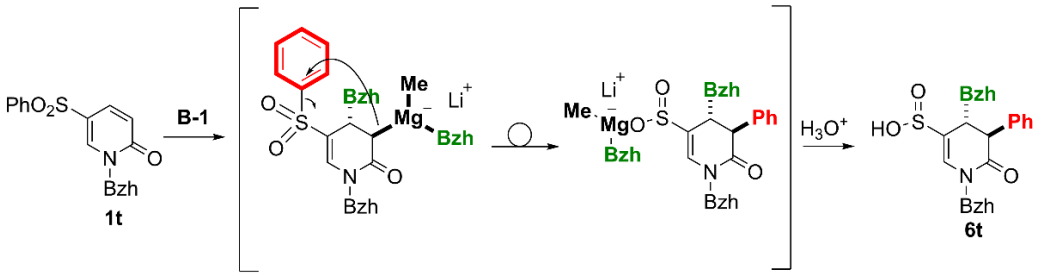


Scheme 5. Probable mechanism of formation of by-products **6f**, **6g** and **6h**.

Furthermore, 2-pyridones **1s** and **1t**, equipped with a 5-phenylsulfonyl group, upon treatment with magnesiate **B-1** led to formation of the most intriguing by-products. On the one hand, for *N*-Bn 2-pyridone **1s**, 1,4-adduct (**2s**) is absent, while 1,6-adduct (**3s**) is present, along with its **6s** isomer with a shifted double bond. On the other hand, in the reaction with *N*-Bzh 2-pyridone **1t**, apart from the C4-product **2t** formation (**3t** is absent), the rearrangement product **6t**, with a benzene ring transferred from the phenylsulfone group to the C3 position of the lactam, was formed. This type of rearrangement can be classified as one of the variants of the Truce–Smiles rearrangement, whose main stages are shown in Scheme 6. It should be noted that, although many examples of this type of rearrangement using organolithium compounds are known [28,29], the Truce–Smiles rearrangement initiated by organomagnesium compounds of the "ate" type is described in this work for the first time. Moreover, because of a significant amount of the obtained product (yield 20%), further studies on this rearrangement are worth continuing within another project.



Scheme 6. Proposed mechanism of **6t** product formation as a variant of the Truce-Smiles rearrangement.

The origin of compound **6s** is depicted in Scheme 7. The formation of both isomers **3s** and **6s** can be explained by the difference in anion stabilization by the carbonyl and sulfonic groups in the intermediate magnesium **IP-3** and **IP-4**, respectively, formed by addition of **B-1** to 2-pyridone. An additional observation that product **6s** is less stable and transforms into isomer **3s** on heating indicates that product **3s** is thermodynamically more stable than **6s**.

In the next phase of the study on the reaction of introducing a benzhydryl group at C4 position of the 2-pyridone ring, we attempted to combine this process with the introduction of a benzyl group at C-3 position using a one-pot method. We used an organo-lithium reagent (**BzhLi**) and *N*-Ph 2-pyridones **1d**, primarily due to the high yield of addition product **2d** and the complete regioselectivity of the addition at C4 atom (Scheme 1). Considering the regioselectivity of the addition and the predicted mechanism of the entire transformation, it was expected that the organolithium addition products would form intermediate product **IP-5** with the lithium atom located at C3 carbon atom thanks to stabilization by the carbonyl group. It is worth noting that this reaction sequence involving a benzhydryl nucleophile has not been reported as yet. In the alkylation step, BnBr and benzyl bromides substituted with methoxy groups as electrophiles were used (Scheme 8). As a result, the reaction proceeded in a chemo-, regio- and stereoselective manner, leading to 3,4-*trans*-disubstituted products as sole isomers in good yields (products **7a**, **7b**, and **7c**).

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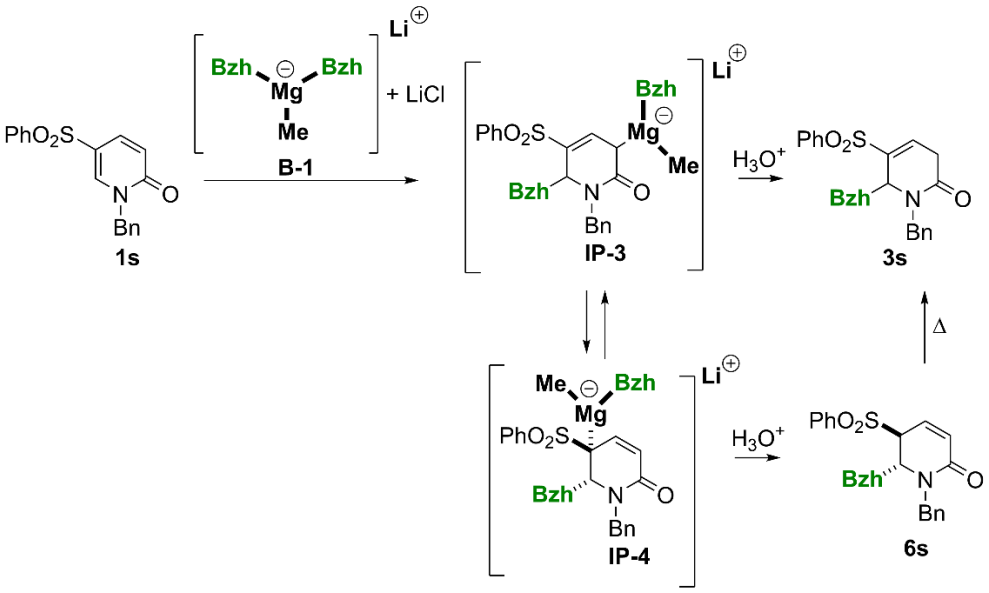
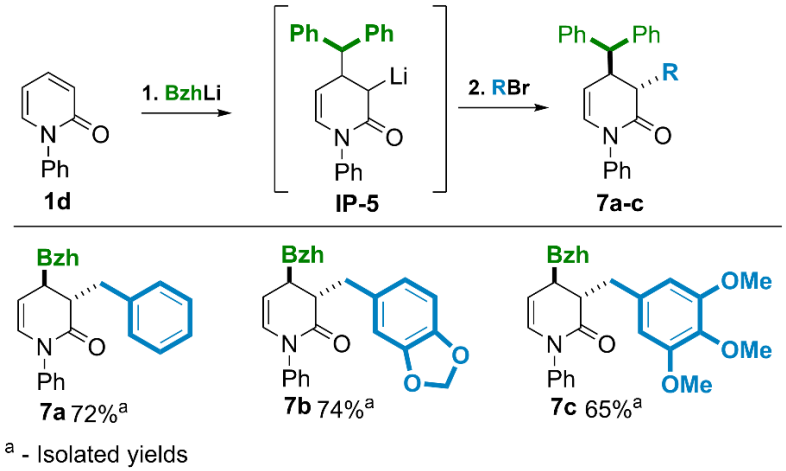


Scheme 7. Probable mechanism formation of products **3s** and **6s**.



Scheme 8. Chemo-, regio- and stereoselective one-pot synthesis of 3,4-*trans*-disubstituted δ-enelactams.

With a relatively wide range of 3,4-dihydropyridones at our disposal, we proceeded to perform cyclization reactions via the acyliminium cation, generated using Brøensted and Lewis acids, in the hope of obtaining 6-phenyl-7,8-benzomorphanone derivatives. A literature survey indicated that such a cyclization of 4-benzyl-3,4-dihydropyridones can be achieved using tin(IV) chloride in a mixture with hydrochloric acid [21]. Additionally, we have recently identified triisopropylsilyltrifluoromethanesulfonate (TIPSOTf) as a potent reagent for cyclization in various δ-enelactams, including 4-benzyl derivatives [5].

Following a brief screening of the reaction of **2d** with available acids, we selected H_3PO_4 and CF_3SO_3H as Brøensted acids and TIPSOTf as a Lewis acid. After adjusting the reaction conditions, we found that for H_3PO_4, the best conditions include the use of a 60-fold excess of 85% phosphoric(V) acid without solvent at 120°C and the reaction time of 2-3 h (Method A). When using triflic acid, the use of a 7.5-fold excess and CH_3CN as a solvent is necessary, and the reaction should be carried out for 20-24 h at room temperature (Method B). In the case of TIPSOTf, the best conditions were those used earlier for 4-benzyl-3,4-dihydropyridones [18], i.e., reflux for 24 h of a mixture consisting of **2d**, a 2.5-fold excess of TIPSOTF and acetonitrile as a solvent (Method C). Under these conditions, for derivative **2d**, products **8a** and **9a** were obtained partially stereoselective in yields of 43% and 22% (Method A) or 64% and 20% (Method B) or 27% and 12% (Method C), respectively (Scheme 9).

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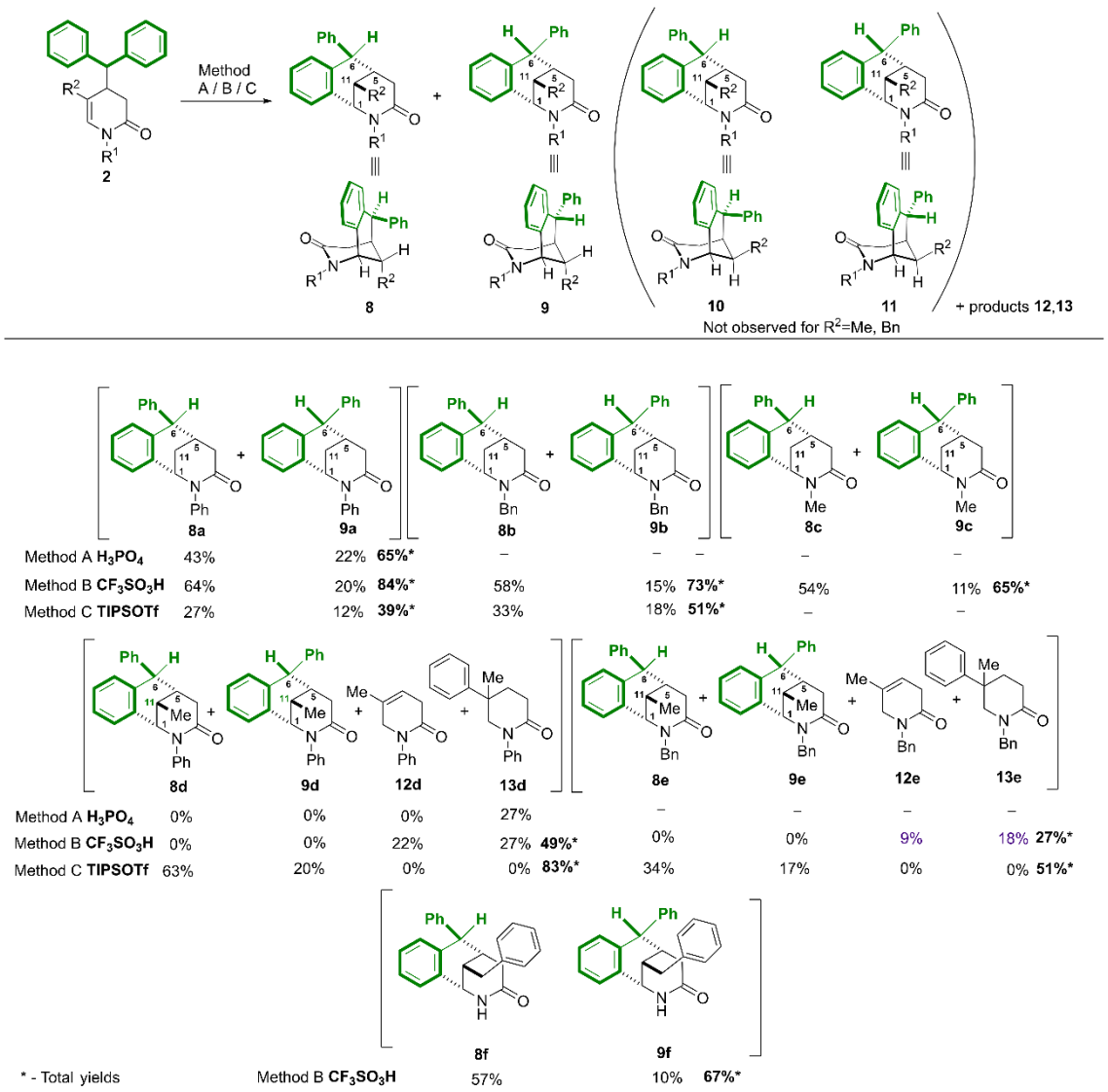

Scheme 9. Cyclization of 4-benzhydryl-3,4-dihydropyridin-2-ones upon treatment with H_3PO_4 (Method A) and CF_3SO_3H (Method B) as Brøensted acids and TIPSOTf (Method C) as a Lewis acid towards 6-phenyl-7,8-benzomorphanones **8** and **9**.

Next, we tested the cyclization reactions of *N*-Me, *N*-Bn, and C5-H/Me substituted δ-enelactams using all or selected developed methods, considering that 5-substituted substrates can theoretically lead to four isomeric products **8**-**11** (Scheme 9). The results led to a conclusion that triflic acid (TfOH) is a good choice for cyclization of C5-H substituted substrates, while C5-Me derivatives decompose upon treatment with TfOH to give products **12** and **13**. In contrast, in the case of C5-Me derivatives, the TIPSOT reagent works better, with no decomposition products observed. This effect is probably a result of two different reaction mechanisms occurring under the influence of TfOH and TIPSOTf, as discussed earlier [5]. It is important to note that derivative **2k** cyclizes to *N*H benzomorphanones **8f** and **9f** when treated with CF_3SO_3H, removing the *N*-Bzh group.

The above data indicate that isomer **8** is the dominant species obtained by all the methods used, when the formation of two isomers **8** and **9** is possible (C5-H substrates) or when two isomers **8** and **9** are formed from the theoretically four possible ones (**8-11**, C5-Me substrates). We could determine their structures through extensive and precise NMR structural analyses of derivatives **8** and **9** (see below) and identify a simple parameter for their easy recognition using ^{1}H NMR spectra. Thus, for derivative **8**, the ^{1}H NMR signal from the CH-6 carbon atom (labelled as CHα-6) is a singlet, occurring in the range of 4.14-4.32 ppm. Meanwhile, for derivative **9**, the ^{1}H NMR signal from CH-6 carbon

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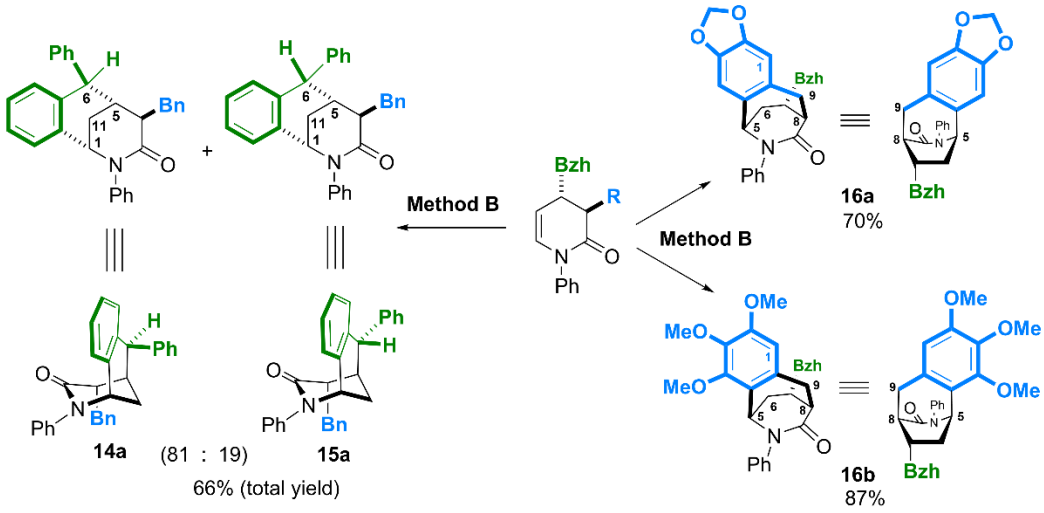
atom (labelled as CHβ-6) is a doublet, occurring in the range of 4.57-4.63 ppm, with a coupling constant ^{3}J ranging from 5.6-6.4 Hz.

In the cyclization reaction group, we conducted an interesting test to determine the direction of bridge formation in 3,4-disubstituted derivatives containing C3-methoxybenzyl groups (**7b**-**7c**) in comparison to that in compound **7a**, which has an unsubstituted C3-benzyl group. As expected, the increased nucleophilicity of benzene rings due to the presence of methoxy groups caused this ring to participate in cyclization in derivatives **7b** and **7c**, forming a rare polycyclic system **16** in good yields, while, in contrast, compound **7a**, with unsubstituted benzene ring, provided 7,8-benzomorphans **14a** and **15a** at the ratio of 81 : 19 (Scheme 10).



Scheme 10. Two directions of cyclization observed in 3,4-disubstituted δ-enelactams **7a**-**7c**, caused by the lack or presence of methoxy groups in the benzyl group.

The structures of all compounds were elucidated based on the analyses of 1D NMR (^{1}H, ^{13}C and ^{13}C-DEPT-135) and 2D NMR (^{1}H,^{1}H DFQ-COSY, ^{13}C,^{1}H COSY, ^{1}H,^{1}H NOESY, ^{1}H,^{13}C HMQC and ^{1}H,^{13}C HMBC spectra, recorded in $CDCl_3$ or toluene-d_8 solutions, and by HRMS analyses. The product configurations were established by comparing the experimental vicinal coupling constants, refined from the ^{1}H NMR spectra, with the theoretical values calculated using Haasnoot correlation [30] based on dihedral angles found in PM3-optimized structures [31]. Simultaneously, the proposed configurations were verified by the ^{1}H,^{1}H NOESY through-space interactions between the juxtaposed hydrogen atoms. The diagnostic NOEs found in the NOESY spectra and vicinal coupling constants for the representative compounds are presented in supplementary materials.

3. Materials and Methods

3.1. General Chemical Procedures

Melting points were determined on a Boetius hot stage apparatus. ^{1}H, ^{13}C NMR spectroscopic measurements were performed on a Bruker DPX 400 Avance III HD spectrometer, operating at 400.2, 100.6 MHz, respectively. TMS was used as internal standard and spectra were acquired in 5 mm probes at 21°C. For NMR analyses MestReNova (version: 12.0.4) program was used. Conformational analyses were performed on the basis of PM3 calculated structures (HyperChem 7.52) and calculated vicinal coupling constants by MSpin program (version: 2.3.4.). For detailed peak assignments, 2D spectra were acquired using standard Bruker software (^{1}H,^{1}H DFQCOSY; ^{13}C,^{1}H COSY; ^{1}H, ^{13}C HMQC; ^{1}H,^{1}H NOESY; ^{1}H,^{13}C HMBC). In the ^{1}H,^{1}H NOESY spectra the optimized mixing time, varied from 0.7 s to 0.8 s, was used. The ^{1}H,^{13}C HMBC long-range correlations were acquired for $J_{C,H}$=10 Hz. The standard abbreviation for multiplicities were used (s = singlet, d =doublet, t = triplet, q =quartet, quint = quintet, m = multiplet, sxt = sextet, spt = septet, etc. Gas chromatography-mass spectrometry (GC-MS) measurements were carried out on an Agilent 7820B GC system equipped with a mass

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(Agilent 5977E MSD) and FID detectors. HRMS analyses (ESI+) were performed on a Agilent 6546 LC/Q-TOF using acetonitrile or mixture of acetonitrile/methanol as solvent.

Reactions in tetrahydrofuran (THF), acetonitrile (MeCN) were performed under argon in flame-dried flasks and liquid components were added from a syringe. Anhydrous toluene and THF were purified by distillation over sodium metal under argon prior to use. Anhydrous MeCN was purified by filtration through a pad of Al_2O_3. Products were purified by flash column chromatography on silica gel (63-200 μm, Merck) using appropriate solvents. Crude post-reaction mixtures were analyzed by GC-MS and ^{1}H NMR spectroscopy. *n*-BuLi (2.5 M in hexane), MeMgCl (3.0 M in THF), 2-pyridones **1a**, **1b** and benzyl bromide were purchased from Aldrich. 2-Methoxypyridine, TIPSOTf, TfOH were purchased from Fluorochem. Diphenylmethane was purchased from Acros Organics. (Bromomethyl)-1,2,3-trimethoxybenzene [32], piperonyl bromide [33], methoxy-*N*-phenylnicotinamide [34], 5-(phenylthio)-2-methoxypyridnie [34], 6-methoxy-*N*,*N*-dimethylnicotinamide [34], 2-methoxy-5-phenyl-pyridine [14] and 5-(benzofuran-5-yl)pyridin-2(1*H*)-one [20] as substrates were obtained according to procedure described earlier.

3.2. Synthesis of 4-Benzhydryl-3,4-dihydropyridin-2(1H)-ones (2) / 6-Benzhydryl-3,6-dihydropyridin-2(1H)-ones (3) and by-Products 6

Method A (addition of BzhLi to 2-pyridones).

A 25 mL Schlenk flask was charged with 16 mL of anhydrous THF, placed in an ice bath at 0°C, 0.815g of diphenylmethane (1.5 equiv, 4.858 mmol) was added, and subsequently 2.04 mL of *n*-BuLi (2.5 M in hexanes, 1.575 equiv, 5.102 mmol) was carefully added dropwise with a syringe and stirred for 25 min at 0°C. The orange-red solution was then transferred with a syringe to a second 50 mL flask placed in a -80°C bath in which 2-pyridone (3.239 mmol) had been previously dissolved in 16 mL of anhydrous tetrahydrofuran. The reaction was carried out for 70 min at -80°C, after which saturated ammonium chloride solution (ca 5 mL) was added. The solution was warmed to rt, extracted with ethyl acetate (3 x 80 mL), and the organic layer was dried over anhydrous magnesium sulfate, concentrated, and purified by column chromatography using silica gel as the stationary phase.

Method B (addition of magnesiate **B-1** to 2-pyridones).

A 50 mL Schlenk flask was charged with 10.7 mL of anhydrous THF under argon, placed in an ice bath, and then 0.8g of diphenylmethane (2.8 equiv, 4.756 mmol) and 2 mL of *n*-BuLi (2.94 equiv, 4.993 mmol, 2.5M solution in hexanes) were added dropwise with a syringe and stirred for 25 min maintaining the temperature at 0°C. Then 0.8 mL of MeMgCl (1.4 equiv, 3.0 M solution in THF) was added and stirred at 0°C for a further 25 min (a slight color change to carmine red was observed). The solution was then transferred with a syringe to a 100 mL Schlenk flask placed in a -80°C bath, in which 1.698 mmol of 2-pyridone was dissolved in 36 mL of anhydrous tetrahydrofuran. The reactions were carried out for 2.5-3 h. Further procedure as in method A.

(Note: In the syntheses of the compounds listed below, proportional amounts of reagents and solvents were used in relation to the amount of starting 2-pyridone.)

(4*RS*)-4-Benzhydry-1-methyl-3,4-dihydropyridin-2(1*H*)-one (**2b**).

Yield 20% (method A, 0.127g, from 0.25g of **1b**); yield 21% (method B. Yield determined by internal standard method using ^{1}H NMR). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 3:1) gave a beige solid, m.p. 103−105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (dd, J = 16.2, 10.0 Hz, 1H, C<u>H</u>H-3), 2.46 (dd, J = 16.2, 6.4 Hz, 1H, CHH-3), 3.03 (s, 3H, NCH_3), 3.37 (ddddd, J = 11.0, 10.0, 6.4, 3.5, 2.0 Hz, 1H, CH-4), 3.72 (d, J = 11.2 Hz, 1H, 4-CH), 4.93 (ddd, J = 7.8, 3.5, 0.8 Hz, 1H, =CH-5), 5.95 (dd, J = 7.8, 1.8 Hz, 1H, =CH-6), 7.11 – 7.34 (m, 10H, 2 x C_6H_5). ^{13}C{H} NMR (100.6 MHz, $CDCl_3$): δ 33.47 (NCH_3), 36.07 (CH-4), 36.42 (CH_2-3), 56.10 (4-CH), 109.29 (=CH-5), 126.59, 126.70, 127.85 (2C), 128.21 (2C), 128.65 (2C), 128.79 (2C), ArH, 130.50 (=CH-6), 142.35, 142.52 (Ar), 169.16 (C=O). GC−MS (EI, 70 eV) m/z: 277 (<1) [$M^{+\bullet}$], 167 (41), 165 (30), 152 (13), 110 (100). HRMS (ESI-TOF): m/z Calcd for $C_{19}H_{20}NO$[M + H]$^+$, 278.1545; Found 278.1539.

(6*RS*)-6-Benzhydryl-1-methyl-3,6-dihydropyridin-2(1*H*)-one (**3b**).

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Yield 49% (method A, 0.31g from 0.25g of **1b**); yield 78% (method B. Yield determined by internal standard method using ^{1}H NMR). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 3:1) gave a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08 (dq, J = 22.0, 3.4 Hz, 1H, CHH-3), 2.68 (ddd, J = 22.0, 4.9, 2.2 Hz, 1H, CHH-3), 2.93 (s, 3H, NCH3), 4.41 (d, J = 5.5 Hz, 1H, 6-CH), 4.63 – 4.72 (m, 1H, CH-6), 5.73 (dddd, J = 10.1, 5.0, 2.2, 0.7 Hz, 1H, =CH-5), 5.89 (ddd, J = 10.1, 4.6, 3.1 Hz, 1H, =CH-6), 7.19 – 7.35 (m, 10H, 2 x Ph). ^{13}C{H} NMR (100.6 MHz, $CDCl_3$): δ 32.17 (CH_2-3), 33.98, NCH_3, 54.49 (6-CH), 64.68 (CH-6), 124.13 (=CH-4), 125.35 (=CH-5), 126.87, 127.21, 128.23, 128.53, 128.60, 129.74, 138.82, 140.22 (2 x Ph), 168.82 (C=O). GC−MS (EI, 70 eV) m/z: 277 (<1) [$M^{+\bullet}$], 202 (100), 167 (17), 165 (16), 110 (100). HRMS (ESI-TOF): m/z Calcd for $C_{19}H_{20}NO[M + H]^+$, 278.1545; Found, 278.1539.

(4*RS*)-4-Benzhydryl-1-benzyl-3,4-dihydropyridin-2(*1H*)-one (**2c**).

Yield 28% (method A, 0.114g from 0.234g of **1c**); yield 23% (method B, 0.138g from 0.315 g of **1c**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 3:1) gave a white solid, m.p. = 105-114°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (dd, J = 16.1, 9.7 Hz, 1H, CHH-3), 2.53 (dd, J = 16.1, 6.2 Hz, 1H, CHH-3), 3.26 – 3.45 (m, 1H, CH-4), 3.69 (d, J = 11.3 Hz, 1H, 4-CH), 4.62 – 4.72 (m, 2H, NCH_2), 4.93 (dd, J = 7.9, 3.6 Hz, 1H, =CH-5), 5.97 (dd, J = 7.9, 1.7 Hz, 1H, =CH-6), 7.09 – 7.41 (m, 15H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$): δ 36.02 (CH-4), 36.62 (CH_2-3), 48.79 (NCH_2), 55.99 (4-CH_2),109.99 (=CH-5), 126.56, 126.72, 127.57, 127.77, 127.85, 128.15, 128.62, 128.69, 128.81 (ArH), 129.03 (=CH-6), 137.22, 142.27, 142.51 (Ar), 168.84 (C=O). GC−MS (EI, 70 eV) m/z: 353 (>1) [$M^{+\bullet}$], 186 (100) [M-167(benzhydryl radical)], 165 (15), 91 (97). HRMS (ESI-TOF): m/z Calcd for $C_{25}H_{24}NO[M + H]^+$, 354.1858; Found 354.1852.

(6*RS*)-6-Benzhydryl-1-benzyl-3,6-dihydropyridyn-2(*1H*)-one (**3c**).

Yield 45% (method A, 0.2g); yield 58% (0.346g, method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 3:1) gave a white solid, m.p. = 124-125°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.23 (dq, J = 21.2, 2.8 Hz, 1H, CHH-3), 2.82 (ddd, J = 21.1, 5.1, 1.8 Hz, 1H,CHH-3), 3.53 (d, J = 15.3 Hz, 1H, NCHH), 4.41 (d, J = 6.1 Hz, 1H, 6-CH), 4.52-4.63 (m, 1H, CH-6), 5.54 (d, J = 15.3 Hz, 1H,NCHH), 5.77 (ddd, J = 10.0, 5.1, 2.0 Hz, 1H, =CH-4), 5.85 (ddd, J = 10.0, 4.8, 3.1 Hz, 1H, =CH-5), 7.09-7.18 (m, 2H, ArH), 7.19 – 7.37 (m, 13H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$): δ 32.63 (CH_2-2), 47.12 (NCH_2), 54.54 (6-CH), 60.47 (CH-6), 125.13 (=CH-5), 125.29 (=CH-4), 126.93, 127.19, 127.41, 127.81, 128.30, 128.61, 128.69. 129.70 (ArH), 136.89, 139.10, 140.27 (Ar), 169.25 (C=O). GC−MS (EI, 70 eV) m/z: 353 (<1) [$M^{+\bullet}$], 186 (76) [$M^{+\bullet}$-167(benzhydryl radical)], 165 (20), 91 (100). HRMS (ESI-TOF): m/z Calcd for $C_{25}H_{24}NO[M + H]^+$, 354.1858; Found 354.1852.

(4*RS*)-4-Benzhydryl-1-phenyl-3,4-dihydropyridin-2(*1H*)-one (**2d**).

Yield 78% (3.088g, method A, from 2 g of **1d**); yield 72% (0.339g, method B, from 0.29 g of **1d**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave a pink solid, m.p. = 100-106°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (dd, J = 15.9, 9.9 Hz, 1H, CHH-3), 2.65 (ddd, J = 15.9, 6.1, 1.0 Hz, 1H, CHH-3), 3.41 – 3.59 (m, 1H, CH-4), 3.81 (d, J = 11.1 Hz, 1H, 4-CH), 5.09 (ddd, J = 7.9, 3.6, 1.0 Hz, 1H, =CH-5), 6.23 (dd, J = 7.9, 1.8 Hz, 1H, =CH-6), 7.03 – 7.45 (m, 15H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$): δ 36.00 (CH-4), 37.49 (CH_2-3), 56.21 (4-CH), 110.14 (=CH-5), 125.91 (2C), 126.67, 126.77, 127.01, 127.89 (2C), 128.24 (2C), 128.72 (2C), 128.83 (2C), 129.06 (2C), 130.51 (=CH-6), (ArH) 140.29, 142.20, 142.43 (Ar), 168.54 (C=O). GC−MS (EI, 70 eV) m/z: 339 (<1), [$M^{+\bullet}$], 172 (100) [$M^{+\bullet}$-167(benzhydryl radical)], 144 (8), 77 (10). HRMS (ESI-TOF): m/z Calcd for $C_{24}H_{22}NO[M + H]^+$, 340.1701; Found 340.1696.

(4*RS*)-4-Benzhydryl-1-benzyl-5-methyl-3,4-dihydropyridin-2(1*H*)-one (**2e**).

Yield 43% (0.198g, method A, from z 0.25g of **1e**); yield 67% (0.246g, method B, from 0.2g of **1e**); The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave a white solid, m.p. = 132-134°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (d, J = 1.5 Hz, 3H, 5-CH_3), 2.44 (dd, J = 16.0, 1.8 Hz, 1H, CHH-3), 2.61 (dd, J = 16.0, 6.3 Hz, 1H, CHH-3), 2.88 (ddd, J = 11.2, 6.3, 1.8 Hz, 1H, CH-4), 3.69 (d, J = 11.2 Hz, 1H, 4-CH), 4.33 (d, J = 14.6 Hz, 1H, NCHH), 5.00 (d, J = 14.6 Hz, 1H, NCHH), 5.79 (d, J = 1.5 Hz, 1H, =CH-6), 6.76 – 7.01 (m, 2H, ArH), 7.04 – 7.49 (m, 13H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 19.88 (5-CH_3), 35.81 (CH_2-3), 41.36 (CH-4), 48.65 (NCH_2), 53.13 (4-CH), 120.52 (=C-5), 124.57 (=CH-6), 126.35, 126.69, 127.71, 128.11 (2C), 128.22 (2C), 128.29 (2C), 128.37 (2C), 128.71 (2C),

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128.75 (2C), ArH), 137.74, 141.61, 143.05 (Ar), 167.83 (C=O). GC–MS (EI, 70 eV) *m/z*: 367 (<1), [M$^{+\bullet}$], 200 (68) [M$^{+\bullet}$-167(benzhydryl radical)], 165 (14), 158 (12), 91 (100). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{26}H_{25}NO$ 368.2014; Found 368.2009.

(6*RS*)-6-Benzhydryl-1-benzyl-5-methyl-3,6-dihydropyridin-2(1*H*)-one (**3e**).

Yield 26% (0.12g, method A, from z 0.25g of **1e**); yield 22% (0.08g, method B, from 0.2g of **1e**); The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.47 (p, *J* = 1.2 Hz, 3H, 5-CH_3), 2.04 (dq, *J* = 20.7, 2.6 Hz, 1H, C<u>H</u>H-3), 2.70 (ddt, *J* = 20.7, 5.9, 1.0 Hz, 1H, CH<u>H</u>-3), 3.30 (d, *J* = 15.4 Hz, 1H, NC<u>H</u>H), 4.22 – 4.44 (m, 2H, CH-6, 6-CH), 5.33 – 5.53 (m, 2H, NCH<u>H</u>, =CH-4), 6.97 – 7.04 (m, 2H, ArH), 7.21 – 7.38 (m, 13H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 21.45 (5-CH_3), 32.86 (CH_2-3), 47.80 (NCH_2), 54.46 (6-CH), 65.66 (CH-6), 120.89 (=CH-4), 127.11, 127.26 (2C), 127.54 (2C), 128.42 (2C), 128.45 (2C), 128.60 (2C), 129.09 (2C), 129.75 (2C), (ArH), 134.23 (=C-5), 137.07, 138.51, 139.57 (Ar), 170.27 (C=O). GC-MS: m/z = 367 (<1), [M$^{+\bullet}$], 200 (69) [M$^{+\bullet}$-167(benzhydryl radical)], 165 (18), 91 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{26}H_{25}NO$ 368.2014; Found 368.2009.

(4*RS*)-4-Benzhydryl-5-methyl-1-phenyl-3,4-dihydropyridin-2(1*H*)-one (**2f**).

Yield 37% (0.42g, method A, from z 0.6g of 1f); yield 69% (method B, from 0.3146g of 1e), yield 78% (magnesiate C-1 was used). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave a white solid, m.p. = 154-155°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (d, J = 1.3 Hz, 3 H, 5-CH_3), 2.59 (dd, *J* = 15.9, 1.6Hz, 1 H, CHH-3), 2.81 (dd, *J* = 15.9, 6.5 Hz, 1 H, CHH-3), 3.04 (ddd, 1 H, *J* = 10.4, 6.5, 1.6 Hz, CH-4), 4.01 (d, *J* = 10.4 Hz, 1 H, 4-CH), 6.06 (q, *J* = 1.3 Hz, 1 H, =CH-6), 7.16 – 7.22 (m, 2 H, ArH), 7.24 – 7.33 (m, 11 H, ArH), 7.38 – 7.43 (m, 2 H, ArH). ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 19.84 (5-CH_3), 36.59 (CH2-3), 41.27 (CH-4), 53.55 (4-CH),120.31 (C-5), 125.65 (ArH), 126.34 (=CH-6), 126.58, 126.69, 126.80, 128.35, 128.42, 128.47, 128.71, 128.96 (ArH), 140.35, 141.38, 142.98 (Ar), 167.50 (C=O). GC-MS (EI, 70eV) m/z: 353 (<1), [M$^{+\bullet}$], 186 (100) [M+•-167(benzhydryl radical)], 158 (12), 143 (15), 77 (11). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{25}H_{23}NO$ 354.1858; Found 354.1852.

(6*RS*)-6-Benzhydryl-5-methyl-1-phenyl-3,6-dihydropyridin-2(1*H*)-one (**3f**).

Yield 37% (0.42g, method A, from z 0.6g of **1f**); yield 0% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave yellow oil.^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (dt, *J* = 2.6, 1.1 Hz, 3H, CH_3), 2.38 (dq, *J* = 20.4, 2.6 Hz, 1H, C<u>H</u>H-3), 2.76 (ddt, *J* = 20.4, 5.8, 1.1 Hz, 1H, CH<u>H</u>-3), 4.35 (d, *J* = 5.9 Hz, 1H, 6-CH), 5.03 (dd, *J* = 5.9, 2.6 Hz, 1H, CH-6), 5.58 (dt, *J* = 5.8, 1.7 Hz, 1H, =CH-4), 7.10 – 7.37 (m, 15H, 3 x C_6H_5). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 22.14 (CH_3), 33.51 (CH_2-3), 54.66 (6-CH), 71.33 (CH-6), 121.67 (=CH-4), 126.65 , 126.67, 127.32, 127.50 (2C), 128.26 (4C), 128.34 (2C), 128.95 (2C), 130.10 (2C), (ArH), 134.29 (=C-5), 137.92, 139.91, 141.79 (Ar), 168.96 (C=O). GC-MS (EI, 70eV) *m/z:* 353 (<1) [M$^{+\bullet}$], 186 (100) [M$^{+\bullet}$-167(benzhydryl radical)], 158 (13), 143 (14). HRMS (ESI-TOF) *m/z:* [M + H]$^+$ Calcd for $C_{25}H_{23}NO$ 354.1858; Found 354.1852.

(6*RS*)-4,6-Dibenzhydryl-5-methyl-1-phenyl-3,6-dihydropyridin-2(1*H*)-one (**6f**).

Yield 0% (method A); yield 10% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave a white solid, m.p.= 128 – 129°C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 1.47 (d, *J* = 2.4 Hz, 3H, CH_3), 2.42 (dt, *J* = 19.9, 2.4 Hz, 1H, C<u>H</u>H-3), 2.92 (d, *J* = 19.9 Hz, 1H, CH<u>H</u>-3), 4.26 (d, *J* = 7.5 Hz, 1H, 6-CH), 5.08 (dd, *J* = 7.5, 1.7 Hz, 1H, CH-6), 5.27 (s, 1H, 4-CH), 6.95 – 7.00 (m, 2H, C_6H_5), 7.03 – 7.44 (m, 23H, 5 x C_6H_5). ^{13}C{H} NMR (101 MHz, $CDCl_3$) *δ* 18.52 (CH_3), 36.07 (CH_2-3), 51.76 (4-CH), 55.57 (6-CH), 72.38 (CH-6), 126.41, 126.53, 126.72, 126.82, 127.09, 127.23 (2C), 128.26 (2C), 128.28 (2C), 128.36 (2C), 128.53 (2C), 128.58 (2C), 128.60 (2C), 128.76 (2C), 129.51 (2C), 129.68 (2C), (ArH), 130.35 (C-5), 131.72, 138.81, 139.78, 140.70, 141.53, 141.87 (Ar, C-4), 169.40 (C=O). GC-MS (EI, 70eV) *m/z* = 519 (>1), [M$^{+\bullet}$], 351 (100) [M$^{+\bullet}$-1 -167 (benzhydryl radical)], 350 (68), 246 (45), 208 (32), 165 (23), 77(51). HRMS (ESI-TOF) *m/z:* [M + H]$^+$ Calcd for $C_{38}H_{34}NO$: 520.2640; Found 520.2635.

(4*RS*)-4-Benzhydryl-1-benzyl-5-chloro-3,4-dihydropyridin-2(1*H*)-one (**2g**).

Yield 23% (0.08g, method A, from 0.2g of **1g**); yield 22% (0.15g, method B, from 0.373g of **1g**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave a white solid, m.p. = 127-131°C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 2.66 (dd, *J* = 16.5, 1.9 Hz, 1H, C<u>H</u>H-3),

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2.88 (dd, *J* = 16.5, 7.5 Hz, 1H, CHH-3), 3.32 (td, *J* = 8.8, 7.5, 1.9 Hz, 1H, CH-4), 4.00 (d, *J* = 8.8 Hz, 1H, 4-CH), 4.40 (d, *J* = 14.7 Hz, 1H, NCHH), 4.57 (d, *J* = 14.7 Hz, 1H, NCHH), 6.14 (s, 1H, =CH-6), 6.96 – 7.10 (m, 2H, ArH), 7.12 – 7.45 (m, 13H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 35.32 (CH_2-3), 43.28 (CH-4), 48.81 (NCH_2), 52.31 (4-CH), 116.89 (=C-5), 126.62, 126.91, 127.09, 127.96, 128.19 (2C), 128.22 (2C), 128.49 (2C), 128.61 (2C), 128.72 (2C), 128.85 (2C), (ArH), 136.60, 140.41, 141.35 (Ar), 166.59 (C=O). GC-MS (EI 70eV) *m/z:* 387 (<1) [$M^{+\bullet}$], 222 (12), 220 (35) [$M^{+\bullet}$-167(benzhydryl radical)], 167 (49), 165 (23), 152 (12), 91 (100). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{25}H_{22}ClNO$ 388.1468; Found 388.1463.

(6*RS*)-6-Benzhydryl-1-benzyl-5-chloro-3,6-dihydropyridin-2(1*H*)-one (**3g**).

Yield 38% (0.133g, method A); yield 42% (0.274g, method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave a semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61 (dt, *J* = 21.1, 2.5 Hz, 1H, CHH-3), 2.63 (ddd, *J* = 21.1, 5.9, 1.0 Hz, 1H, CHH-3), 3.35 (d, *J* = 15.3 Hz, 1H, NCHH), 4.62 – 4.68 (m, 2H, CH-6, 6-CH), 5.52 (d, *J* = 15.3 Hz, 1H, NCHH), 5.68 (dd, *J* = 5.9, 2.5 Hz, 1H, =CH-4), 6.90 (dd, *J* = 7.3, 2.2 Hz, 2H, ArH), 7.21 – 7.41 (m, 13H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 32.80 (CH_2-3), 47.71 (NCH_2), 52.98 (6-CH), 66.58 (CH-6), 122.94 (=CH-4), 127.06, 127.51, 127.66 (2C), 127.79 (ArH), 127.91 (=C-5), 128.28 (2C), 128.37 (2C), 128.62 (2C), 128.70 (2C), 131.03 (2C), (ArH), 135.75, 136.20, 139.54 (Ar), 168.25 (C=O). GC-MS (EI 70eV) *m/z:* 387 (<1) [$M^{+\bullet}$], 222 (12), 220 (36) [$M^{+\bullet}$-167(benzhydryl radical)],167 (47), 165 (21), 152 (11), 91 (100). HRMS (ESI-TOF) *m/z:* [M + H]$^+$ Calcd for $C_{25}H_{22}ClNO$ 388.1468; Found 388.1463.

(6*RS*)-4,6-Dibenzhydryl-1-benzyl-5-chloro-3,6-dihydropyridin-2(1*H*)-one (**6g**).

Yield 0% (method A); yield 10% (0.095g, method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 5:1) gave a white solid, m.p. = 171-174°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (dd, *J* = 20.5, 2.8 Hz, 1H, CHH-3), 2.66 (d, *J* = 20.5 Hz, 1H, CHH-3), 3.30 (d, *J* = 15.3 Hz, 1H, NCHH), 4.66 (d, *J* = 2.8 Hz, 1H, 6-CH), 4.73 (t, *J* = 2.8 Hz, 1H, CH-6), 5.48 (d, *J* = 15.3 Hz, 1H, NCHH), 5.51 (s, 1H, 4-CH), 6.84 – 6.95 (m, 4H, ArH), 7.01 (d, *J* = 7.5 Hz, 2H, ArH), 7.16 – 7.38 (m, 19H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 35.05 (CH_2-5), 47.77 (NCH_2), 52.22 (4-CH), 53.38 (6-CH), 67.14 (CH-6), 124.84 (=C-5), 126.82, 126.94, 127.02, 127.48 (2C), 127.55, 127.66, 128.18 (2C), 128.26 (2C), 128.42 (2C), 128.45 (2C), 128.63 (2C), 128.70 (4C), 129.43 (2C), 130.79 (2C), (ArH), 133.42, 136.03, 136.31, 139.67 (2C), 139.80 (Ar), 169.12 (C=O). GC-MS (EI, 70eV) *m/z*: 553 (<1), [$M^{+\bullet}$], 387 (14) [$M^{+\bullet}$-167 (benzhydryl radical) 385 (30), 384 (18), 165 (11), 91 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{38}H_{32}ClNO$ 554.2251; Found 554.2245.

(4*RS*)-4-Benzhydryl-5-chloro-1-phenyl-3,4-dihydropyridin-2(1*H*)-one (**2h**).

Yield 80% (0.269g, method A, from 0.185g of **1h**); yield 59% (0.377g, method B, from 0.349g of **1h**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 3:1) gave a white solid, m.p. = 117-119°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.88 (dd, *J* = 16.6, 1.6 Hz, 1 H, CHH-3), 3.10 (dd, *J* = 16.6, 8.2 Hz, 1 H, CHH-3), 3.52 (ddd, *J* = 8.2, 6.9, 1.6 Hz, 1 H, CH-4), 4.36 (d, *J* = 6.9 Hz, 1H), 6.38 (s, 1 H =CH-6), 6.90 – 7.01 (m, 2 H, C_6H_5), 7.20 – 7.37 (m, 13 H, ArH). ^{13}C({H} NMR (101 MHz, $CDCl_3$) δ 35.47 (CH_2-3), 43.15 (CH-4), 51.88 (4-CH), 116.55 (=C-5), 125.82 (2C), 126.72, 127.26, 127.34, 128.43 (2C), 128.50 (2C), 128.54 (2C), (ArH), 128.82 (=CH-6), 129.02 (2C), 129.32 (2C), 139.43, 140.15, 141, 27 (Ar), 165.99 (C=O). GC-MS (EI 70eV) *m/z:* 373 (1) [$M^{+\bullet}$], 208 (46), 207 (26), 206 (100), 168 (15), 167 (83), 165 (31), 152 (18), 77 (13). HRMS (ESI-TOF) *m/z:* [M + H]$^+$ Calcd for $C_{24}H_{20}ClNO$ 374.1312; Found 374.1306.

(6*RS*)-4,6-dibenzhydryl-5-chloro-1-phenyl-3,6-dihydropyridin-2(1*H*)-one (**3h**).

Yield 0% (method A); yield 10% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.97 (dd, *J* = 20.2, 2.5 Hz, 1H, CHH-3), 2.86 (d, *J* = 20.2 Hz, 1H, CHH-3), 4.52 (d, *J* = 4.5 Hz, 1H, 6-CH), 5.46 (dd, *J* = 4.5, 2.5 Hz, 1H, CH-6), 5.60 (s, 1H, 4-CH), 6.95 – 7.37 (m, 25H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 35.80 (CH_2-3), 52.33 (4-CH), 54.24 (6-CH), 71.51 (CH-6), 124.86 (=C-5), 126.82, 127.00, 127.05 (2C), 127.14, 127.40 (2C), 128.16 (2C), 128.19 (2C), 128.31 (2C), 128.61 (2C), 128.67 (2C), 129.04 (2C), 129.21 (2C), 129.46 (2C), 129.66 (2C), (ArH), 133.88, 137.39, 138.23, 139.62, 139.70, 140.89 (Ar), 167.89 (C=O). GC-MS (EI 70eV) *m/z:* 539 (<1), [$M^{+\bullet}$], 374 (10), 373 (52), 372 (42), 371 (100), 370 (55), 336 (27), 308 (17), 306 (32), 307 (11), 266 (20), 130(20), 202 (25), 167 (15), 165 (45), 152 (22), 141 (10), 104 (23), 77 (64), 51 (17). HRMS (ESI-TOF) *m/z:* [M + H]$^+$ Calcd for $C_{37}H_{30}ClNO$ 540.2094; Found 540.2089.

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(6*RS*)-2-Benzhydryl-1-benzyl-6-oxo-*N*-phenyl-1,2,5,6-tetrahydropyridine-3-carbox-amide (**3i**).

Yield 27% (0.0633g method A, using 0.154g of **1i**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 1:1) gave a white solid, m.p. = 206 – 210°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (br s, 3H, NCH_3), 2.67 (br s, 3H, NCH_3), 2.86 (d, J = 15.4 Hz, 1H, NCHH), 2.96 (ddd, J = 20.7, 2.2, 1.6 Hz, 1H, CHH-3), 3.10 (dd, J = 20.7, 6.2 Hz, 1H, CHH-3), 4.23 (d, J = 9.0 Hz, 1H, 6-CH), 5.08 (d, J = 15.4 Hz, 1H, NCHH), 5.17 (dd, J = 9.0, 1.6 Hz, 1H, CH-6), 5.92 (dd, J = 6.2, 2.2 Hz, 1H, =CH-4), 7.01 – 7.10 (m, 2H, ArH), 7.17 – 7.38 (m, 13H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 33.03 (CH_3-2), 34.90 (br, NCH_3), 38.08 (br, NCH_3), 49.33 (NCH_2), 57.29 (6-CH), 62.57 (CH-6), 126.30 (=CH-4), 127.35, 127.38, 127.46, 127.75 (2C), 128.48 (2C), 128.53 (2C), 128.77 (2C), 128.81 (2C), 129.12 (2C), 135.93, 136.63, 139.59, 139.79 (Ar), 168.63 (C=O), 168.69 (C=O). GC-MS (EI 70eV) m/z: 472 (<1), [$M^{+\bullet}$], 305 (43) [$M^{+\bullet}$- benzhydryl radical (167)], 91 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{32}H_{28}N_2O_2$ 473.2229; Found 473.2224.

(4*RS*)-4-Benzhydryl-5-benzyl-1-(4-methoxybenzyl)-3,4-dihydropyridin-2(1*H*)-one (**2j**).

Yield 32% (0.159g method A, using 0.32g of **1i**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 6:1) gave a white solid, m.p. = 70 – 72°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (dd, J = 15.5, 1.7 Hz, 1H, 5-CHH), 2.36 (dd, J = 15.9, 2.1 Hz, 1H, CHH-3), 2.43 (dd, J = 15.9, 5.7 Hz, 1H, CHH-3), 2.71 (d, J = 15.5 Hz, 1H, 5-CHH), 2.80 (ddd, J = 11.7, 5.7, 2.1 Hz, 1H, CH-4), 3.65 (d, J = 11.7 Hz, 1H, 4-CH), 4.15 (d, J = 14.4 Hz, 1H, NCHH), 3.85 (s, 3H, OCH_3), 5.11 (d, J = 14.4 Hz, 1H, NCHH), 5.80 (d, J = 1.7 Hz, 1H, =CH-6), 6.85 – 7.03 (m, 6H, ArH), 7.12 – 7.30 (m, 11H, ArH), 7.30 – 7.40 (m, 2H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 36.34 (CH_2-3), 38.52 (CH-4), 39.69 (5-CH_2), 48.26 (NCH_2), 53.20 (4-CH), 55.40 (OCH_3), 114.11 (2C, ArH), 124.54 (=C-5), 126.16 (=CH-6), 126.32, 126.62, 126.72, 128.14 (2C), 128.22 (2C), 128.39 (2C), 128.53 (2C), 128.76 (2C), 128.82 (2C), 129.74 (2C), (ArH), 129.93, 139.29, 141.48, 143.11, 159.32 (Ar), 167.83 (C=O). GC-MS (EI 70eV) *m/z*: 473 (<1) [$M^{+\bullet}$], 306 [$M^{+\bullet}$-167(benzhydryl radical)], 207 (12), 121 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{33}H_{31}NO_2$ 474.2433; Found 474.2428.

(6*RS*)-6-Benzhydryl-5-benzyl-1-(4-methoxybenzyl)-3,6-dihydropyridin-2(1*H*)-one (**3j**).

Yield 17% (0.084g method A). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 6:1) gave brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.00 (d, J = 20.7 Hz, 1H, CHH-3), 2.71 (dd, J = 20.7, 5.9 Hz, 1H, CHH-3), 2.87 (ddd, J = 15.3, 2.4, 1.5 Hz, 1H, 5-CHH), 3.14 (d, J = 15.3 Hz, 1H, 5-CHH), 3.18 (d, J = 14.9 Hz, 1H, NCHH), 3.78 (s, 3H, OCH_3), 4.34 (d, J = 5.1 Hz, 1H, 6-CH), 4.38 (dd, J = 5.1, 1.5 Hz, 1H, CH-6), 5.28 (d, J = 14.9 Hz, 1H, NCHH), 5.44 (dd, J = 5.8, 1.5 Hz, 1H, =CH-3), 6.68 (d, J = 8.4 Hz, 2H, ArH), 6.74 – 6.84 (m, 4H, ArH), 7.08 – 7.16 (m, 3H, ArH), 7.26 – 7.38 (m, 10H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 33.03 (CH_2-3), 40.97 (5-CH_2), 47.37 (NCH_2), 54.63 (6-CH), 55.19 (OCH_3), 63.21, 113.81 (2C), 122.64 (=CH-4), 126.30, 127.18, 127.29, 128.35 (2C), 128.46 (2C), 128.48 (2C), 128.73 (2C), (ArH), 128.77 (=C-5), 129.01 (2C), 129.26 (2C), 129.82 (2C), (ArH), 137.75, 138.01, 138.41, 139.42, 158.68 (Ar), 170.14 (C=O). GC-MS (EI 70eV) *m/z*: 473 (<1) [$M^{+\bullet}$], 306 (8) [$M^{+\bullet}$-167 (benzhydryl radical)], 281 (37), 253 (15), 208 (12), 207 (100), 191 (11), 133 (12), 121 (62), 73 (26). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{33}H_{31}NO_2$ 474.2433; Found 474.2428.

(4*RS*-)-1,4-Dibenzhydryl-5-benzyl-3,4-dihydropyridin-2(1*H*)-one (**2k**).

Yield 44% (0.065g method A, using 0.1g of **1k**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 8:1) gave solid, m.p. = 153–155°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.07 (dd, J = 15.5, 1.7 Hz, 1H, 5-CHH), 2.42 (dd, J = 15.9, 1.9 Hz, 1H, CHH-3), 2.54 (dd, J = 15.9, 5.9 Hz, 1H, CHH-3), 2.67 (d, J = 15.5 Hz, 1H, 5-CHH), 2.81 (ddd, J = 11.8, 5.9, 1.9 Hz, 1H, CH-4), 3.63 (d, J = 11.8 Hz, 1H, 4-CH), 5.85 (d, J = 1.7 Hz, 1H, =CH-6), 6.79 – 6.87 (m, 2H, ArH), 6.90 – 6.96 (m, 2H, ArH), 7.12 – 7.37 (m, 17H, ArH, NCH), 7.39 – 7.56 (m, 5H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 36.60 (CH_3-2), 38.03 (CH-4), 39.92 (5-CH_2), 53.22 (4-CH), 58.58 (NCH), 123.94 (=CH-6), 124.35 (=C-5), 126.28, 126.63, 126.73, 127.38, 127.96, 128.12 (4C), 128.22 (2C), 128.36 (2C), 128.49 (2C), 128.53 (2C), 128.72 (2C), 128.76 (2C), 128.80 (2C), 129.24 (2C), (ArH), 138.41, 139.28, 140.06, 141.48, 143.13 (Ar), 168.00 (C=O). GC-MS (EI 70eV) *m/z*: 519 (<1) [$M^{+\bullet}$], 352 (18) [$M^{+\bullet}$-167 (benzhydryl radical], 207 (21), 167 (100), 165 (20). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{38}H_{34}NO$ 520.2640; Found 520.2635.

(6*RS*)-4-benzhydryl-1,5-dibenzyl-3,4-dihydropyridin-2(1*H*)-one (**2l**).

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Yield 45% (0.1383g method B, using 0.1g of **1l**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 8:1) gave white solid, m.p. = 184–187°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (dd, J = 15.5, 1.7 Hz, 1H, 5-CHH), 2.38 (dd, J = 15.9, 2.1 Hz, 1H, CHH-3), 2.45 (dd, J = 15.9, 5.7 Hz, 1H, CHH-3), 2.71 (d, J = 15.5 Hz, 1H, 5-CHH), 2.81 (ddd, J = 11.6, 5.7, 2.1 Hz, 1H, CH-4), 3.66 (d, J = 11.6 Hz, 1H, 4-CH), 4.19 (d, J = 14.5 Hz, 1H, NCHH), 5.20 (d, J = 14.4 Hz, 1H, NCHH), 5.81 (d, J = 1.7 Hz, 1H, =CH-6), 6.87 – 6.97 (m, 4H, ArH), 7.13 – 7.29 (m, 11H, ArH), 7.36 – 7.49 (m, 5H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 36.29 (CH_2-3), 38.52 (CH-4), 39.67 (5-CH_2), 48.88 (NCH_2), 53.22 (4-CH), 124.58 (=C-5), 126.22 (=CH-6), 126.33, 126.62, 126.73, 127.82, 128.13 (2C), 128.23 (2C), 128.41 (4C), 128.50 (2C), 128.78 (4C), 128.82 (2C), (ArH), 137.76, 139.27, 141.47, 143.10 (Ar), 167.89 (C=O). GC-MS (EI 70eV) m/z: 443 (<1), [$M^{+\bullet}$], 277 (17) [$M^{+\bullet}$-167 (benzhydryl radical)], 276 (77), 91 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{32}H_{29}ClNO$ 444.2327; Found 444.2322.

(6*RS*)-6-Benzhydryl-1,5-dibenzyl-3,6-dihydropyridin-2(1*H*)-one (**3l**).

Yield 9% (0.029g method B, using 0.1g of **1l**). White solid, m.p. = 148–150°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04 (d, J = 20.7 Hz, 1H, CHH-3), 2.74 (dd, J = 20.7, 5.8 Hz, 1H, CHH-3), 2.89 (dt, J = 16.2, 3.0, 2.0 Hz, 1H, 5-CHH), 3.18 (d, J = 16.2 Hz, 1H, 5-CHH), 3.23 (d, J = 15.7 Hz, 1H, NCHH), 4.35 (d, J = 5.1 Hz, 1H, 6-CH), 4.40 (dd, J = 5.1, 2.0 Hz, 1H, CH-6), 5.32 (d, J = 15.3 Hz, 1H, NCHH), 5.45 (d, J = 5.8 Hz, 1H, =CH-4), 6.78 – 6.89 (m, 4H, ArH), 7.11 – 7.20 (m, 6H, ArH), 7.24 – 7.37 (m, 10H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 33.03 (CH_2-3), 41.00 (5-CH_2), 48.10 (NCH_2), 54.71 (6-CH), 63.73 (CH-6), 122.64 (=CH-4), 126.42, 127.12, 127.21, 127.34, 127.60 (2C), 128.42 (4C), 128.49 (2C), 128.51 (2C), 128.79 (2C), 129.22 (2C), 129.85 (2C), (ArH), 136.78, 137.83, 137.97, 138.40, 139.45 (Ar, =C-5), 170.19 (C=O). GC-MS (EI 70 eV) m/z: 443 (<1) [$M^{+\bullet}$], 276 (100) [$M^{+\bullet}$-167(benzhydryl radical)], 91 (86). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{32}H_{29}NO$ 444.2327; Found 444.2322.

(4*RS*)-4-Benzhydryl-1-(4-methoxybenzyl)-5-phenyl-3,4-dihydropyridin-2(1*H*)-one (**2m**).

Yield 14% (0.426g method B, using 1.94g of **1m**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 8:1) gave a white solid, m.p. = 122–124°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.70 (dd, J = 16.1, 1.7 Hz, 1H, CHH-3), 2.81 (dd, J = 16.1, 6.4 Hz, 1H, CHH-3), 3.74 (ddd, J = 9.6, 6.4, 1.7 Hz, 1H, CH-4), 3.81 (d, J = 9.6 Hz, 1H, 4-CH), 3.83 (s, 3H, OCH_3), 4.43 (d, J = 14.5 Hz, 1H, NCHH), 4.80 (d, J = 14.5 Hz, 1H, NCHH), 6.23 (s, 1H, =CH-6), 6.78 – 6.83 (m, 2H, ArH), 6.88 (ddd, J = 8.0, 4.3, 1.8 Hz, 5H, ArH), 6.91 – 6.96 (m, 2H, ArH), 7.02 – 7.11 (m, 3H, ArH), 7.16 – 7.34 (m, 7H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 35.70 (CH_2-3), 38.89 (CH-4), 48.42 (NCH_2), 53.18 (4-CH), 55.37 (OCH_3), 114.19 (2C, ArH), 123.90 (=C-5), 125.85 (2C), 126.06, 126.21 (ArH), 126.31 (=CH-6), 126.82, 127.64 (2C), 128.08 (2C), 128.46 (2C), 128.58 (4C), (ArH), 129.51 (Ar), 129.63 (2C, ArH), 138.81, 141.35, 141.89, 159.32 (Ar), 167.96 (C=O). GC-MS (EI 70eV) m/z: 459 (<1) [$M^{+\bullet}$], 292 (15) [$M^{+\bullet}$-167 (benzhydryl radical)], 207 (16), 167 (10), 121 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{32}H_{29}NO_2$ 460.2277; Found 360.2271.

(6*RS*)-6-Benzhydryl-1-(4-methoxybenzyl)-5-phenyl-3,6-dihydropyridin-2(1*H*)-one (**3m**).

Yield 79% (2.41g method B, using 1.94g of **1m**).). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 4:1) gave yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17 (dt, J = 20.8, 2.4 Hz, 1H, CHH-3), 2.92 (dd, J = 20.8, 6.0 Hz, 1H, CHH-3), 3.11 (d, J = 15.1 Hz, 1H, NCHH), 3.82 (s, 3H, OCH_3), 4.15 (d, J = 4.8 Hz, 1H, 6-CH), 5.11 (dd, J = 4.8, 2.4 Hz, 1H, CH-6), 5.52 (d, J = 15.1 Hz, 1H, NCHH), 5.76 (dd, J = 6.0, 2.4 Hz, 1H, =CH-4), 6.83 – 6.96 (m, 6H, ArH), 7.11 – 7.40 (m, 13H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 33.37 (CH_2-3), 47.46 (NCH_2), 54.98 (6-CH), 55.33 (OCH_3), 63.89 (CH-6), 114.05 (2C), 122.28, 126.34 (2C), 126.65, 127.49, 127.54, 128.20 (2C), 128.24 (2C), 128.40 (2C), 128.64 (2C), 128.87 (=C-5), 129.06 (2C), 130.50 (2C), (ArH), 137.75, 139.21, 139.63, 140.24, 158.97 (Ar), 170.08 (C=O). (EI 70eV) m/z: 459 (<1) [$M^{+\bullet}$], 458 (3), 292 (15) [$M^{+\bullet}$-167 (benzhydryl radical)], 291 (56), 121 (100), 116 (20), 89 (53), 73 (17), 51 (38). HRMS (ESI-TOF) m/z: [M + H]+ Calcd for $C_{32}H_{21}NS$ 460.2277; Found 460.2271.

(4*RS*)-1,4-Dibenzhydryl-3,4-dihydropyridin-2(1*H*)-one (**2n**).

Yield 75% (0.436g method B, using 0.35g of **1n**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 7:1) gave transparent oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (dd, J = 16.1, 9.2 Hz, 1H, CHH-3), 2.60 (dd, J = 16.1, 6.1 Hz, 1H, CHH-3), 3.25 – 3.42 (m, 1H, CH-4), 3.68 (d, J = 11.5 Hz, 1H, 4-CH), 4.92 (dd, J = 8.1, 3.8 Hz, 1H, =CH-5), 5.95 (dd, J = 8.1, 1.5 Hz, 1H,

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=CH-6), 6.52 – 7.53 (m, 21H, 4 x C_6H_5, NCH). $^{13}C\{H\}$ NMR (101 MHz, $CDCl_3$) δ 35.74 (CH-4), 36.85 (CH_2-3), 55.91 (4-CH), 58.97 (NCH), 109.64 (=CH-5), 126.55, 126.73 (ArH), 126.92 (=CH-6), 127.59, 127.66, 127.88 (2C), 128.13 (2C), 128.56 (4C), 128.60 (4C), 128.63 (2C), 128.81 (2C), (ArH), 139.18, 139.40, 142.23, 142.62 (Ar), 168.80 (C=O). GC-MS (EI 70eV) *m*/*z*: 429 (<1) [$M^{+\bullet}$], 262 (21) [$M^{+\bullet}$-167 (benzhydryl radical)], 167 (100), 165 (24), 152 (13). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{31}H_{27}NO$ 430.2171; Found 430.2165.

(4*RS*)-4-Benzhydryl-1-benzyl-5-(phenylthio)-3,4-dihydropyridin-2(1*H*)-one (**2o**).

Yield 20% (0.05g method B, using 0.155g of **1o**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 6:1) gave a white solid, m.p. 168-170°C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.68 (dd, *J* = 16.4, 2.7 Hz, 1H, CHH-3), 2.74 (dd, *J* = 16.4, 6.2 Hz, 1H, CHH-3), 3.17 (ddd, *J* = 8.9, 6.3, 2.6 Hz, 1H, CH-4), 3.99 (d, *J* = 8.9 Hz, 1H, 4-CH), 4.38 (d, *J* = 14.6 Hz, 1H, NCHH), 4.69 (d, *J* = 14.7 Hz, 1H, NCHH), 6.46 (s, 1H, =CH-6), 6.97 (dd, *J* = 7.6, 1.9 Hz, 2H, ArH), 7.11 – 7.44 (m, 18H, ArH). $^{13}C\{H\}$ NMR (101 MHz, $CDCl_3$) δ 36.02 (CH_2-3), 40.44 (CH-4), 48.94 (NCH_2), 52.71 (4-CH), 115.03 (=C-5), 126.39, 126.48, 126.92, 127.95, 128.08 (2C), 128.27 (2C), 128.50 (2C), 128.55 (2C), 128.56 (2C), 128.75 (2C), 128.86 (2C), 129.11 (2C), 135.29 (=CH-6), 136.22, 136.81, 140.84, 141.86 (Ar), 167.49 (C=O). GC-MS (EI 70eV) *m*/*z*: 461 (3) [$M^{+\bullet}$], 294 (97) [$M^{+\bullet}$-167 (benzhydryl radical)], 91 (100). HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{31}H_{27}NOS$ 462.1892; Found 462.1886.

(6*RS*)-6-Benzhydryl-1-benzyl-5-(phenylthio)-3,6-dihydropyridin-2(1*H*)-one (**3o**).

Yield 17% (0.0324g method B, using 0.155g of **1o**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 6:1) gave a brown oil. ^1H NMR (400 MHz, $CDCl_3$) δ 1.47 (dt, *J* = 21.2, 2.2 Hz, 1H, CHH-3), 2.68 (ddd, *J* = 21.2, 5.8, 1.2 Hz, 1H, CHH-3), 3.12 (d, *J* = 14.9 Hz, 1H, NCHH), 4.49 – 4.63 (m, 1H, CH-6), 4.84 (d, *J* = 2.1 Hz, 1H, 6-CH), 5.49 (d, *J* = 14.9 Hz, 1H, NCHH), 5.98 (dd, *J* = 5.8, 2.2 Hz, 1H, =CH-4), 6.81 (dd, *J* = 7.3, 1.7 Hz, 2H, ArH), 6.98 – 7.10 (m, 6H, ArH), 7.12 – 7.41 (m, 12H, ArH). $^{13}C\{H\}$ NMR (101 MHz, $CDCl_3$) δ 33.60 (CH_2-3), 47.66 (NCH_2), 53.17 (6-CH), 64.28 (CH-6), 126.67, 127.06, 127.37, 127.68, 128.01 (2C), 128.06 (2C), 128.29 (2C), 128.41 (2C), 128.56 (2C), 129.24 (2C), 130.20 (3C), (ArH, =CH-4), 130.91 (Ar), 131.32 (2C, ArH), 132.75, 135.99, 136.74 (Ar), 140.46 (=C-5), 169.11 (C=O). GC-MS (EI 70eV) *m*/*z*: 461 (3) [$M^{+\bullet}$], 294 (97) [$M^{+\bullet}$-167 (benzhydryl radical)], 91 (100). HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{31}H_{27}NOS$ 462.1892; Found 462.1886.

(4*RS*)-1,4-Dibenzhydryl-5-(phenylthio)-3,4-dihydropyridin-2(1*H*)-one (**2p**).

Yield 89% (0.387g method B, using 0.3g of **1p**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate = 8:1) gave a white solid, m.p. 63–65°C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.67 (dd, *J* = 16.2, 2.0 Hz, 1H, CHH-3), 2.78 (dd, *J* = 16.2, 6.8 Hz, 1H, CHH-3), 3.16 (ddd, *J* = 10.0, 6.8, 2.0 Hz, 1H, CH-4), 3.89 (d, *J* = 10.0 Hz, 1H, 4-CH), 6.44 (s, 1H, =CH-6), 6.87 – 7.02 (m, 2H, ArH), 7.06 – 7.53 (m, 24H, ArH, NCH). $^{13}C\{H\}$ NMR (101 MHz, $CDCl_3$) δ 36.52 (CH_2-3), 40.32 (CH-4), 53.10 (4-CH), 59.23 (NCH), 115.32 (=C-5), 126.40, 126.51, 126.89, 127.72, 128.02 (3C), 128.18 (2C), 128.50 (2C), 128.58 (2C), 128.70 (6C), 128.81 (2C), 128.91 (2C), 129.07 (2C), 132.86 (=CH-6), 136.13, 138.22, 139.17, 141.02, 141.93 (Ar), 167.62 (C=O). GC-MS (EI 70eV): decomposition. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{37}H_{31}NOS$ 538.2205; Found 538.2199.

(6*RS*)-2-Benzhydryl-1-benzyl-N,N-dimethyl-6-oxo-1,2,5,6-tetrahydropyridine-3-carboxamide (**3q**).

Yield 50% (0.085g method B, using 0.103g of **1q**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate) gave a white solid, m.p. 204–208°C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.30 (br. s, 3H, NCH_3), 2.67 (br. s, 3H, NCH_3), 2.86 (d, *J* = 15.4 Hz, 1H, NCHH), 2.96 (ddd, *J* = 20.6, 2.1, 1.6 Hz, 1H, CHH-5), 3.10 (dd, *J* = 20.6, 6.2 Hz, 1H, CHH-5), 4.23 (d, *J* = 9.1 Hz, 1H, 2-CH), 5.08 (d, *J* = 15.4 Hz, 1H, NCHH), 5.17 (dd, *J* = 9.1, 1.6 Hz, 1H, CH-2), 5.92 (dd, *J* = 6.2, 2.1 Hz, 1H, =CH-4), 7.01 – 7.11 (m, 2H, ArH), 7.18 – 7.37 (m, 13H, ArH). $^{13}C\{H\}$ NMR (101 MHz, $CDCl_3$) δ 33.03 (CH_2-5), 34.90 br. (NCH_3), 38.08 br. (NCH_3), 49.33 (NCH_2), 57.29 (2-CH), 62.57 (CH-2), 126.30 (=CH-4), 127.35, 127.38, 127.46, 127.75 (2C), 128.48 (2C), 128.53 (2C), 128.77 (2C), 128.81 (2C), 129.12 (2C), 135.93, 136.63, 139.59, 139.79 (Ar, =C-3), 168.63 (C=O), 168.69 (C=O). GC-MS (EI 70eV) *m*/*z*: 424 (<1) [$M^{+\bullet}$], 257 [$M^{+\bullet}$ - 167] (82), 207(44), 167 (32), 91 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{28}H_{28}N_2O_2$ 425.2229; Found 425.2224.

(4*RS*)-1,4-Dibenzhydryl-*N*,*N*-dimethyl-6-oxo-1,4,5,6-tetrahydropyridine-3-carboxamide (**2r**).

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Yield 23% (method B, using 0.165g of **1r**). White solid, m.p. = 212–213°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.75 (br s, 3H, CH_3), 2.52 (dd, J = 16.3, 1.7 Hz, 1H, CHH-3), 2.32 – 2.73 (br s, 3H, CH_3), 2.84 (dd, J = 16.3, 6.5 Hz, 1H, CHH-3), 3.75 (d, J = 12.3 Hz, 1H, 4-CH), 3.91 (ddd, J = 12.3, 6.5, 1.7 Hz, 1H, CH-4), 6.08 (s, 1H, =CH-6), 7.04 – 7.20 (m, 8H, ArH, NCH), 7.24 – 7.45 (m, 13H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$)* δ 35.79 (CH_2-3), 35.94 (CH-4), 54.54 (4-CH), 58.94 (NCH), 117.44 (=C-5), 126.79, 126.92 (2C), 127.83 (2C), 127.94, 128.05 (2C), 128.18 (2C), 128.30, 128.80 (2C), 128.83 (2C), 128.89 (2C), 128.95 (2C), 129.35 (ArH), 137.53, 140.34, 141.85, 142.35 (Ar), 168.42 (C=O), 169.83 (C=O). (*Note: signals for $N(CH_3)_2$ groups are invisible). GC-MS (EI 70eV): decomposition. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{34}H_{33}N_2O_2$ 501.2542; Found 501.2537.

(6*RS*)-6-Benzhydryl-1-benzyl-5-(phenylsulfonyl)-3,6-dihydropyridin-2(1*H*)-one (**3s**).

Yield 29% (0.0654g method B, using 0.149g of **1s**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1) gave a white solid, m.p. 167–176°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (dt, J = 21.7, 2.0, 1.5 Hz, 1H, CHH-3), 2.67 (dd, J = 21.7, 6.3 Hz, 1H, CHH-3), 3.20 (d, J = 15.0 Hz, 1H, NCHH), 4.88 (dd, J = 1.5, 1.2 Hz, 1H, CH-6 or 6-CH), 4.98 (d, J = 1.2 Hz, 1H, CH-6 or 6-CH), 5.42 (d, J = 15.0 Hz, 1H, NCHH), 6.46 (d, J = 7.6 Hz, 2H, ArH), 6.93 (dd, J = 6.3, 2.0 Hz, 1H, =CH-4), 6.94 – 7.00 (m, 2H, ArH), 7.10 (t, J = 7.3 Hz, 1H, ArH), 7.28 – 7.48 (m, 12H, ArH), 7.55 – 7.61 (m, 1H, ArH), 7.70 – 7.77 (m, 2H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 32.89 (CH_2-3), 48.01 (NCH_2), 54.49, 61.14 (CH-6, 6-CH), 126.97, 127.27, 127.35 (2C), 127.58 (2C), 127.73 (2C), 128.11, 128.40 (2C), 128.59 (2C), 128.86 (2C), 129.48 (2C), 132.37 (2C), 133.80 (ArH), 134.63, 135.76 (Ar), 138.56 (=CH-4), 138.86, 139.45, 140.07 (Ar, =C-5), 167.86 (C=O). GC-MS (EI 70eV) m/z: 493 (<1) [M$^{+\bullet}$], 325 (32) [M$^{+\bullet}$-167], 91 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{31}H_{27}NO_3S$ 494.1790; Found 494.1784.

(5*SR*,6*RS*)-6-Benzhydryl-1-benzyl-5-(phenylsulfonyl)-5,6-dihydropyridin-2(1*H*)-one (**6s**).

Yield 59% (0.1338g method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1) gave a white solid, m.p. 180–182°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (d, J = 14.8 Hz, 1H, NCHH), 3.82 (d, J = 6.0 Hz, 1H, CH-5), 4.22 (d, J = 10.0 Hz, 1H, 6-CH), 4.65 (dd, J = 10.0, 1.5 Hz, 1H, CH-6), 5.02 (d, J = 14.8 Hz, 1H, NCHH), 6.20 (ddd, J = 9.8, 6.0, 1.5 Hz, 1H, =CH-4), 6.40 (dd, J = 9.8, 0.9 Hz, 1H, =CH-3), 6.86 – 6.93 (m, 2H, ArH), 7.07 – 7.14 (m, 2H, ArH), 7.15 – 7.41 (m, 15H), 7.57 – 7.67 (m, 1H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 48.93 (NCH_2), 55.12 (6-CH), 56.97 (CH-6), 62.35 (CH-5), 127.36 (=CH-4), 127.55, 127.67, 127.90, 128.09 (2C), 128.36 (2C), 128.92 (2C), 128.94 (2C), 129.03 (2C), 129.27 (2C), 129.34 (2C), 130.57 (2C), (ArH), 131.53 (=CH-3), 134.06 (ArH), 135.86, 137.00, 139.59, 139.82 (Ar), 161.43 (C=O). GC-MS (EI 70eV) m/z: 493 (<1) [M$^{+\bullet}$], 325 (48) [M$^{+\bullet}$-167], 91 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{31}H_{27}NO_3S$ 494.1790; Found 494.1784.

(4*RS*)-1,4-Dibenzhydryl-5-(phenylsulfonyl)-3,4-dihydropyridin-2(1*H*)-one (**2t**).

Yield 73% (0.0942g method B, using 0.091g of **1t**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1) gave a white solid, m.p. 154–156°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (dd, J = 17.2, 9.3 Hz, 1H, CHH-3), 3.02 (dd, J = 17.2, 1.1 Hz, 1H, CHH-3), 3.73 (dud, J = 9.3, 4.3, 1.1 Hz, 1H, CH-4), 4.41 (d, J = 4.3 Hz, 1H, 4-CH), 6.58 – 6.65 (m, 2H, ArH), 6.67 (s, 1H,NCH), 6.88 – 6.98 (m, 2H, ArH), 7.01 – 7.13 (m, 4H, ArH), 7.13 – 7.39 (m, 13H, ArH, =CH-6), 7.49 (t, J = 7.8 Hz, 2H, ArH), 7.55 – 7.67 (m, 3H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 34.01 (CH_2-3), 35.49 (CH-4), 51.59 (4-CH), 60.14 (NCH), 118.45 (=C-5), 126.56, 127.43, 127.45 (2C), 127.64 (2C), 128.10 (2C), 128.15 (2C), 128.34 (2C), 128.46 (2C), 128.81 (2C), 128.90 (2C), 129.00 (2C), 129.31 (2C), 130.22 (2C), 133.05 (ArH) , 137.67, 138.15, 139.15 (Ar), 139.56 (=CH-6), 141.37, 141.54 (Ar), 167.43 (C=O). GC-MS (EI 70eV) m/z: 569 (<1), (M$^{+\bullet}$), 535 (12) [569 (M$^{+\bullet}$) - H_2S], 207 (11), 168 (17), 167 (100), 165 (33), 152 (19). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{37}H_{31}NO_3S$ 570.2103; Found 570.2097.

(4*RS*,5*SR*)-1,4-Dibenzhydryl-6-oxo-5-phenyl-1,4,5,6-tetrahydropyridine-3-sulfinic acid (**6t**).

Yield 20% (0.026g method B, using 0.091g of **1t**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1) gave a white solid, m.p. 208–210°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 – 2.44 (m, 1H, OH), 3.58 (dd, J = 4.2, 1.3 Hz, 1H, CH-4), 4.59 (dd, J = 3.7, 1.3 Hz, 1H, 4-CH), 4.66 (d, J = 4.1 Hz, 1H, CH-5), 6.54 (s, 1H, NCH), 6.69 – 6.76 (m, 2H, ArH), 6.92 – 7.00 (m, 2H, ArH), 7.00 – 7.06 (m, 2H, ArH), 7.10 – 7.40 (m, 15H, ArH, =CH-2), 7.46 – 7.54 (m, 2H, ArH), 7.58 – 7.64 (m, 1H, ArH), 7.69 – 7.75 (m, 2H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 43.55 (CH-4), 49.45 (CH-5), 60.31 (NCH), 69.60 (4-CH), 117.01 (=C-3), 126.62, 127.40 (2C), 127.48, 127.57 (2C), 127.99 (2C),

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128.02, 128.34 (2C), 128.40, 128.51 (2C), 128.85 (2C), 128.92 (2C), 129.18 (2C), 129.28 (2C), 129.89 (2C), 133.10 (ArH), 137.18 (Ar), 137.59 (=CH-2), 137.90, 139.27, 140.46, 141.17 (Ar), 167.32 (C=O). GC-MS (EI 70eV): decomposition. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{37}H_{31}NO_3S$ 570.2103; Found 570.2097.

(4*RS*)-4-Benzhydryl-5-(benzofuran-5-yl)-1-phenyl-3,4-dihydropyridin-2(1*H*)-one (**2u**).

Yield 59% (0.15g method B, using 0.160g of **1u**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 4 : 1) gave a white solid, m.p. 148–149°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.96 (dd, J = 16.3, 1.6 Hz, 1H, CHH-3), 3.09 (dd, J = 16.3, 7.3 Hz, 1H, CHH-3), 3.99 (ddd, J = 7.9, 7.3, 1.6 Hz, 1H, CH-4), 4.15 (d, J = 7.9 Hz, 1H, 4-CH), 6.48 (s, 1H, =CH-6), 6.67 (dd, J = 2.2, 1.0 Hz, 1H, ArH), 6.94 – 7.09 (m, 4H, ArH), 7.11 – 7.19 (m, 4H, ArH), 7.19 – 7.35 (m, 8H, ArH), 7.37 – 7.45 (m, 2H, ArH), 7.59 (d, J = 2.2 Hz, 1H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 35.93 (CH_2-3), 39.36 (CH-4), 53.15 (4-CH), 106.54, 111.17, 118.66, 122.88 (ArH), 123.29 (=C-5), 126.08 (2C), 126.26, 126.98, 127.12 (ArH), 127.57 (Ar), 127.96 (3C, ArH, =CH-6), 128.47 (2C), 128.51 (2C), 129.08 (2C), 129.13 (2C), (ArH), 133.53, 140.36, 141.10, 142.07 (Ar), 145.46 (ArH), 153.96 (Ar), 167.55 (C=O). GC-MS (EI 70eV) *m*/*z*: 455 (<1) [$M^{+\bullet}$], 287 (36) [$M^{+\bullet}$- 168], 167 (100), 77 (28). HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{25}NO_2$ 456.1964; Found 456.1958.

(4*RS*)-4-Benzhydryl-5-(benzo[b]thiophen-5-yl)-1-phenyl-3,4-dihydropyridin-2(1*H*)-one (**2v**).

Yield 70% (0.13g method B, using 0.119g of **1v**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 4 : 1) gave a solid, m.p. 90–92°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.86 (dd, J = 16.0, 1.7 Hz, 1H, CHH-3), 3.16 (dd, J = 16.1, 6.8 Hz, 1H, CHH-3), 3.96 (ddd, J = 9.7, 6.8, 1.7 Hz, 1H, CH-4), 4.12 (d, J = 9.7 Hz, 1H, 4-CH), 6.46 (s, 1H, =CH-6), 6.76 – 6.88 (m, 4H, ArH), 6.98 (dd, J = 6.5, 3.1 Hz, 2H, ArH), 7.10 (t, J = 7.7 Hz, 1H, ArH), 7.16 – 7.34 (m, 9H, ArH), 7.37 (d, J = 5.6 Hz, 1H, ArH), 7.45 (t, J = 7.8 Hz, 2H, ArH), 7.66 (d, J = 8.0 Hz, 1H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 36.44 (CH_2-3), 40.63 (CH-4), 54.41 (4-CH), 121.02, 122.64 (ArH), 123.33 (=C-5), 123.70, 123.97, 125.98 (3C), 126.15, 126.92, 127.21, 127.79 (2C), 128.12 (2C), 128.48 (2C), 128.70 (2C), 129.21 (2C), (ArH), 129.85 (=CH-6), 135.10, 137.27, 140.06, 140.19, 141.60, 141.78 (Ar), 167.75 (C=O). GC-MS *m*/*z*: 470 (<1), ($M^{+\bullet}$) (304 (6), ($M^{+\bullet}$-167), 303 (49), 275 (12), 171 (26), 168 (39), 167 (100), 165 (33), 152 (13), 77 (17). HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{32}H_{26}NOS$ 472.1735; Found 472.1729.

3.3. Synthesis of Compounds 7

A 25 mL Schlenk flask was charged with 16 mL of anhydrous THF, placed in an ice bath at 0°C, 0.815g of diphenylmethane (1.5 equiv, 4.858 mmol) was added, and subsequently 2.04 mL of *n*-BuLi (2.5 M in hexanes, 1.575 equiv, 5.102 mmol) was carefully added dropwise from a syringe and stirred for 25 min at 0°C. The orange-red solution was then transferred with a syringe to a second 50 mL flask placed in a -80°C bath in which 2-pyridone **1d** (3.239 mmol) had been previously dissolved in 16 mL of anhydrous tetrahydrofuran. The reaction was carried out for 70 min at -80°C, after which, a 1.2-fold molar excess of the appropriate alkyl bromide was added and the reaction was continued for an additional 2 h. Then saturated ammonium chloride solution (ca. 5 mL) was added and the solution was warmed to rt, extracted with ethyl acetate (3 x 80 mL), and the organic layer was dried over anhydrous magnesium sulfate, concentrated, and purified by column chromatography using silica gel as the stationary phase.

(3*SR*,4*RS*)-4-Bnzhydryl-3-benzyl-1-phenyl-3,4-dihydropyridin-2(1*H*)-one (**7a**).

Yield 72% (1.08g, using 0.6g of **1d**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 7 : 1) gave a white solid, m.p. 109 – 110°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.82 (dddd, J = 11.5, 3.4, 1.6, 1.1 Hz, 1H, CH-3), 2.89 (dd, J = 12.4, 11.6 Hz, 1H, 3-CHH), 2.96 (ddd, J = 11.4, 6.3, 1.1 Hz, 1H, CHH), 3.11 (dd, J = 12.5, 3.4 Hz, 1H, CH-4), 3.81 (d, J = 11.4 Hz, 1H, 4-CH), 4.97 (td, J = 7.8, 6.3, 1.6 Hz, 1H, =CH-5), 6.29 (d, J = 7.8 Hz, 1H, =CH-6), 6.80 – 6.89 (m, 2H, ArH), 7.05 – 7.17 (m, 8H, ArH), 7.18 – 7.38 (m, 8H, ArH), 7.38 – 7.47 (m, 2H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 36.27 (3-CH_2), 38.30 (CH-4), 46.89 (CH-3), 55.13 (4-CH), 107.70 (=CH-5), 125.91 (2C), 126.41, 126.58, 126.73, 127.03, 127.96 (2C), 128.02 (2C), 128.46 (2C), 128.48 (2C), 128.61 (2C), 129.07 (2C), 129.50 (2C), (ArH), 129.55 (=CH-5), 138.02, 140.43, 141.49, 142.94 (Ar), 170.41 (C=O). GC-MS (EI 70eV) *m*/*z*: 429 (<1)

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[$M^{+\bullet}$], 262 (64) [$M^{+\bullet}$-167 (benzhydryl radical)], 165 (10). HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{31}H_{28}NO$ 430.2171; Found 430.2166.

(3*SR*,4*RS*)-4-Benzhydryl-3-(benzo[*d*][1,3]dioxol-5-ylmethyl)-1-phenyl-3,4-dihydropyridin-2(1*H*)-one (**7b**).

Yield 74% (0.61g, using 0.3g of **1d**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 5 : 1) gave a white solid, m.p. 218 – 220°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 – 2.86 (m, 2H, CH-3, 3-CHH), 2.98 (dd, *J* = 11.3, 6.3 Hz, 1H, CH-4), 3.02 (dd, *J* = 11.3, 2.4 Hz, 1H, 3-CHH), 3.82 (d, *J* = 11.3 Hz, 1H, 4-CH), 4.96 (ddd, *J* = 7.8, 6.3, 1.4 Hz, 1H, =CH-5), 6.01 (dd, *J* = 3.8, 1.4 Hz, 2H, OCH_2O), 6.28 (d, *J* = 7.8 Hz, 1H, =CH-6), 6.54 – 6.62 (m, 2H, ArH), 6.80 (d, *J* = 8.3 Hz, 1H, ArH), 6.90 – 6.99 (m, 2H, ArH), 7.06 – 7.33 (m, 11H, ArH), 7.37 – 7.48 (m, 2H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 36.09 (3-CH_2), 38.40 (CH-4), 47.02 (CH-3), 55.17 (4-CH), 101.00 (OCH_2O), 107.65 (=CH-5), 108.17, 109.77, 122.48, 125.91 (2C), 126.46, 126.68, 127.04, 128.01 (2C), 128.09 (2C), 128.49 (2C), 128.63 (2C), 129.08 (2C),(ArH), 129.56 (=CH-6), 131.76, 140.41, 141.54, 142.90, 146.33, 147.73 (Ar), 170.32 (C=O). GC-MS (EI 70eV): decomposition. HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{32}H_{28}NO_3$ 474.2069; Found 474.2064.

(3*SR*,4*RS*)-4-benzhydryl-1-phenyl-3-(3,4,5-trimethoxybenzyl)-3,4-dihydropyridin-2(1*H*)-one (**7c**).

Yield 65% (0.59g, using 0.3g of **1d**). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 5 : 1) gave a white solid, m.p. 91 – 93°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.74 – 2.86 (m, 2H, 3-CHH, CH-3), 2.96 (dd, *J* = 11.5, 6.3 Hz, 1H, CH-4), 3.07 (d, *J* = 9.0 Hz, 1H, 3-CHH), 3.78 – 3.85 (m, 7H, 2 x OCH_3, 4-CH), 3.91 (s, 3H, OCH_3), 4.97 (td, *J* = 7.8, 6.3, 1.3 Hz, 1H, =CH-5), 6.29 (d, *J* = 7.8 Hz, 1H, =CH-6), 6.33 (s, 2H, ArH), 6.87 – 6.93 (m, 2H, ArH), 7.07 – 7.18 (m, 6H, ArH), 7.20 – 7.27 (m, 2H, ArH), 7.27 – 7.36 (m, 3H, ArH), 7.40 – 7.49 (m, 2H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 36.60 (3-CH_2), 38.23 (CH-4), 47.02 (CH-3), 55.19 (4-CH), 56.18 (2C, 2 x OCH_3), 60.99 (OCH_3), 106.25 (2C, ArH), 107.68 (=CH-5), 125.94 (2C), 126.47, 126.62, 127.17, 127.94 (2C), 128.15 (2C), 128.52 (2C), 128.57 (2C), 129.15 (2C), (ArH), 129.59 (=CH-6), 133.75, 136.68, 140.37, 141.55, 142.84 (Ar), 153.21 (2C, Ar), 170.46. GC-MS (EI 70eV): decomposition. HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{34}H_{34}NO_4$: 520.2488; Found: 520.2482.

3.4. Synthesis of Compounds 8, 9

Method A: In a round-bottomed flask fitted with a reflux condenser and an argon balloon, 3,4-dihydropyridin-2-one (0.295 mmol) and 6 mL (18.24 mmol) of 85% phosphoric(V) acid were placed, heated to 120°C and stirred for 2-3 h. After this time, the reaction mixture was cooled, the flask was placed in an ice bath and saturated sodium bicarbonate solution was carefully added, extracted with ethyl acetate (3 x 20 mL), the organic layer was dried over anhydrous magnesium sulfate, filtered and the solvent was distilled off under reduced pressure. The crude product was purified by column chromatography (SiO_2) using a mixture of hexane and ethyl acetate as eluent.

Method B: The procedure was similar to method A, except that 0.295 mmol of 3,4-dihydropyridin-2-one was dissolved in 4 mL of anhydrous acetonitrile. Then, 0.21 mL of triflic acid (7.5-fold excess, 2.21 mmol) was slowly added dropwise and the reaction was carried out for 24 h at room temperature. After this time, while cooling the flask, a saturated solution of $NaHCO_3$ was slowly added. The further procedure is the same as in method A.

Method C: The procedure was similar to method A, except that 0.587 mmol of 3,4-dihydropyridin-2-one was dissolved in 8 mL of anhydrous acetonitrile in the flask and 2.5-fold excess of TIPSOTf (1.469 mmol) was added dropwise from a syringe then the mixture was refluxed for 24 h (monitoring by ^{1}H NMR). Then the reaction mixture was cooled to room temperature and 10 mL of saturated $NaHCO_3$ solution was added and the aqueous layer was extracted with ethyl acetate (3 x 40 mL). The further procedure is the same as in method A.

(1*SR*,5*SR*,6*RS*)-2,6-Diphenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[c]azocin-3(2*H*)-one (**8a**).

Yield 43% (method A), 64% (method B) 27% (method C). White solid, m.p. 183 – 185°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (dt, *J* = 13.3, 3.2 Hz, 1H, CHH_{ax}-11), 2.39 (dtd, *J* = 13.3, 3.2, 1.4 Hz, 1H, CHH_{eq}-11), 2.60 – 2.67 (m, 1H, CH-5), 2.74 (dt, *J* = 18.8, 1.4 Hz, 1H, CHH_{eq}-4), 3.11 (dd, *J* = 18.8, 8.3 Hz, 1H,

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CHH_{ax}-4), 4.26 (s, 1H, CH_{α}-6), 4.74 (td, *J* = 3.2, 1.4 Hz, 1H, CH-1), 6.59 (dd, *J* = 7.7, 1.2 Hz, 1H, ArH), 6.90 – 6.96 (m, 2H, ArH), 7.01 – 7.06 (m, 4H, ArH), 7.16 – 7.33 (m, 5H, ArH), 7.37 – 7.44 (m, 2H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 25.57 (CH_2-11), 35.06 (CH-5), 39.98 (CH_2-4), 52.08 (CH-6), 59.24 (CH-1), 126.33, 126.41, 127.27, 128.02 (2C), 128.39 (2C), 128.43, 128.53 (2C), 128.58, 129.26 (2C), 132.05 (ArH), 134.87, 136.55, 142.09, 146.61 (Ar), 169.51 (C=O). GC-MS (EI 70eV) *m*/*z*: 339 (100) [$M^{+\bullet}$], 204 (44), 178 (28), 141 (35), 135 (83). HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{24}H_{22}NO$ 340.1701; Found 340.1696.

(1*SR*,5*SR*,6*SR*)-2,6-Diphenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[c]azocin-3(2*H*)-one (**9a**).

Yield 22% (method A), 20% (method B) 12% (method C). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1) gave a white solid, m.p. 218 – 220°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 – 2.53 (m, 3H, CH_2-4, CHH-11), 2.68 – 2.81 (m, 2H, CHH-11, CH-5), 4.63 (d, *J* = 6.1 Hz, 1H, CH_b-6), 4.70 – 4.76 (m, 1H, CH-1), 6.49 (dd, *J* = 7.6, 1.4 Hz, 1H, ArH), 6.93 – 7.22 (m, 6H, ArH), 7.25 – 7.43 (m, 7H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 31.68 (CH_2-11), 33.33 (CH-5), 33.83 (CH_2-4), 50.67 (CH-6), 59.53 (CH-1), 125.85, 126.84, 127.22, 128.22 (4C), 128.47, 128.72 (2C), 129.23 (2C), 129.83 (br), 130.63 (ArH), 136.23, 137.08, 142.08, 143.16 (Ar), 169.48 (C=O). GC-MS (EI 70eV) *m*/*z*: 339 (100) [$M^{+\bullet}$], 204 (45), 178 (27), 135 (93). HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{24}H_{22}NO$ 340.1701 Found 340.1696.

(1*SR*,5*SR*,6*RS*)-2-Benzyl-6-phenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[c]azocin-3(2*H*)-one (**8b**).

Yield 58% (method B), 33% (method C). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 3 : 1) gave a white solid, m.p. 149 – 151°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (dt, *J* = 13.3, 3.4 Hz, 1H, CHH_{ax}-11), 2.19 (dq, *J* = 13.0, 2.6 Hz, 1H, CHH_{eq}-11), 2.46 – 2.59 (m, 1H, CH-5), 2.68 (d, *J* = 18.6 Hz, 1H, CHH_{eq}-4), 3.06 (dd, *J* = 18.6, 8.0 Hz, 1H, CHH_{ax}-4), 3.81 (d, *J* = 15.4 Hz, 1H, NCHH), 4.18 (s, 1H, CH_{α}-6), 4.23 (td, *J* = 3.2, 1.3 Hz, 1H, CH-1), 5.56 (d, *J* = 15.4 Hz, 1H, NCHH), 6.83 – 6.92 (m, 2H, ArH), 6.96 – 7.04 (m, 1H, ArH), 7.14 – 7.27 (m, 6H, ArH), 7.30 – 7.43 (m, 5H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 25.60 (CH_2-11), 35.09 (CH-5), 40.00 (CH_2-4), 46.99 (NCH_2), 52.00 (CH-6), 52.49 (CH-1), 126.36, 126.51, 127.46, 127.82, 128.15 (2C), 128.39 (4C), 128.50, 128.81 (2C), 132.22 (ArH), 135.82, 136.92, 137.19, 147.00 (Ar), 169.49 (C=O). GC-MS (EI 70eV) *m*/*z*: 353 (78) [$M^{+\bullet}$], 206 (100), 148 (75), 106 (61), 91 (85). HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{25}H_{24}NO$ 354.1858 Found 354.1852.

(1*SR*,5*SR*,6*SR*)-2-Benzyl-6-phenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[c]azocin-3(2*H*)-one (**9b**).

Yield 15% (method B), 18% (method C). The crude product purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 3 : 1) gave a white solid, m.p. 150 – 152°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 – 2.38 (m, 3H, CHH_{eq}-4, CH_2-11), 2.44 (dd, *J* = 19.0, 7.3 Hz, 1H, CHH_{ax}-4), 2.59 – 2.76 (m, 1H, CH-5), 3.83 (d, *J* = 15.3 Hz, 1H, NCHH), 4.20 (td, *J* = 3.1, 1.3 Hz, 1H, CH-1), 4.57 (d, *J* = 6.3 Hz, 1H, CH_{β}-6), 5.62 (d, *J* = 15.3 Hz, 1H, NCHH), 6.95 – 7.46 (m, 14H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 31.49 (CH_2-11), 33.22 (CH-5), 33.51 (CH_2-4), 46.77 (NCH_2), 50.76 (CH-6), 52.80 (CH-1), 126.21, 126.84, 127.48, 128.01, 128.11 (2C), 128.28, 128.70 (2C), 128.84 (2C), 129.84 br (2C), 130.84 (ArH), 136.89, 137.22, 137.28, 143.14 (Ar), 169.86 (C=O). GC-MS (EI 70eV) *m*/*z*: 353 (99) [$M^{+\bullet}$], 204 (57), 148 (47), 128 (44), 106 (78), 91 (100). HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{25}H_{24}NO$ 354.1858; Found 354.1852.

(1*SR*,5*SR*,6*RS*)-2-Methyl-6-phenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[c]azocin-3(2*H*)-one (**8c**).

Yield 54% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1 then 1 : 1) gave a white solid, m.p. 164 – 166°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.06 (dt, *J* = 13.1, 3.3 Hz, 1H, CHH_{ax}-11), 2.26 (dq, *J* = 13.1, 2.7 Hz, 1H, CHH_{eq}-11), 2.48 – 2.55 (m, 1H, CH-5), 2.56 (d, *J* = 18.5 Hz, 1H, CHH_{eq}-4), 2.92 (dd, *J* = 18.5, 7.9 Hz, 1H, CHH_{ax}-4), 3.00 (s, 3H, NCH_3), 4.14 (s, 1H, CH_{α}-6), 4.25 (td, *J* = 3.3, 1.3 Hz, 1H, CH-1), 6.87 – 6.94 (m, 2H, ArH), 6.96 – 7.02 (m, 1H, ArH), 7.17 – 7.30 (m, 6H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 25.33 (CH_2-11), 33.66 (NCH_3), 35.37 (CH-5), 39.83 (CH_2-4), 51.92 (CH-6), 57.27 (CH-1), 126.36, 126.51, 127.69, 128.41 (4C), 128.49, 132.25 (ArH), 135.48, 136.83, 147.05 (Ar), 169.61 (C=O). GC-MS (EI 70eV) *m*/*z*: 277 (23) [$M^{+\bullet}$], 204 (48), 73 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{19}H_{20}NO$ 278.1545; Found 278.1539.

(1*SR*,5*SR*,6*SR*)-2-Methyl-6-phenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[c]azocin-3(2*H*)-one (**9c**).

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Yield 11% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1 then 1 : 1) gave a white solid, m.p. 192 – 193°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (dt, J = 18.5, 1.7 Hz, 1H, CHH_{eq}-11), 2.30 (dd, J = 18.5, 7.3 Hz, 1H, CHH_{ax}-11), 2.36 (dq, J = 13.0, 2.8 Hz, 1H, CHH_{eq}-4), 2.50 (dt, J = 13.0, 3.5 Hz, 1H, CHH_{ax}-4), 2.61 – 2.70 (m, 1H, CH-5), 3.03 (s, 3H, NCH_3), 4.23 (td, J = 3.2, 1.3 Hz, 1H, CH-1), 4.57 (d, J = 6.4 Hz, 1H, CH_β-6), 7.02 – 7.28 (m, 7H, ArH), 7.32 (t, J = 7.4 Hz, 2H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 31.26 (CH_2-11), 33.46 (2C), (CH_3, CH_2-4), 33.50 (CH-5), 50.72 (CH-6), 57.55 (CH-1), 126.15, 126.77, 127.81, 128.22, 128.63 (2C), 129.80 br, (2C), 130.82 (ArH), 136.61, 137.25, 143.16 (Ar), 169.92 (C=O). GC-MS (EI 70eV) m/z: 277 (23) [$M^{+\bullet}$], 204 (48), 73 (100). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{19}H_{20}NO$ 278.1545; Found 278.1539.

(1*SR*,5*SR*,6*RS*,11*SR*)-11-Methyl-2,6-diphenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[*c*]azocin-3(2*H*)-one (**8d**).

Yield 63% (method C). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 3 : 1) gave a white solid, m.p. 170 – 172°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (d, J = 6.9 Hz, 3H, 11-CH_3), 2.37 (ddd, J = 8.6, 2.7, 1.7 Hz, 1H, CH-5), 2.53 (qt, J = 6.9, 2.7 Hz, 1H, CH-11), 2.60 (d, J = 19.1 Hz, 1H, CHH_{eq}-4), 3.08 (dd, J = 19.1, 8.6 Hz, 1H, CHH_{ax}-4), 4.32 (s, 1H, CH_a-6), 4.46 (dd, J = 2.7, 1.7 Hz, 1H, CH-1), 6.63 (dd, J = 7.6, 1.4 Hz, 1H, ArH), 6.88 – 6.95 (m, 2H, ArH), 7.02 – 7.13 (m, 4H, ArH), 7.17 – 7.35 (m, 5H), 7.36 – 7.47 (m, 2H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 17.06 (11-CH_3), 27.28 (CH-11), 36.65 (CH_2-4), 41.02 (CH-5), 53.92 (CH_a-6), 64.89 (CH-1), 126.40 (2C), 127.13, 128.06 (2C), 128.31 (2C), 128.42, 128.56, 128.70 (2C), 129.25 (2C), 132.09 (ArH), 134.31, 137.85, 142.31, 146.44 (Ar), 169.07 (C=O). GC-MS (EI 70eV) m/z: 353 (86) [$M^{+\bullet}$], 338 (39) [$M^{+\bullet}$- Me], 218 (100), 203 (46), 178 (33), 135 (77), 92 (35), 77 (23). HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{25}H_{24}NO$ 354.1858; Found 354.1852.

(1*SR*,5*SR*,6*SR*,11*SR*)-11-Methyl-2,6-diphenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[*c*]azocin-3(2*H*)-one (**9d**).

Yield 20% (method C). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 3 : 1) gave a white solid, m.p. 220 – 222°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52 (d, J = 6.9 Hz, 3H, 11-CH_3), 2.35 – 2.41 (m, 2H, CH_2-4), 2.43 – 2.51 (m, 1H, CH-5), 2.60 (qt, J = 6.9, 2.4 Hz, 1H, CH-11), 4.45 (t, J = 2.2 Hz, 1H, CH-1), 4.62 (d, J = 5.6 Hz, 1H, CH_b-6), 6.55 (dd, J = 7.6, 1.4 Hz, 1H, ArH), 7.00 – 7.23 (m, 6H), 7.24 – 7.46 (m, 7H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 17.37 (11-Me), 29.45 (CH_2-4), 34.45 (CH-11), 39.44 (CH-5), 52.47 (CH-6), 65.26 (CH-1), 126.00, 126.85, 127.15, 128.17, 128.21 (3C), 128.52, 128.66 (2C), 129.25 (2C), 130.02, 130.61 (ArH), 135.62, 138.12, 142.32, 142.86 (Ar), 169.21 (C=O). GC-MS (EI 70eV) *m*/*z*: 353 (100) [$M^{+\bullet}$], 218 (38), 178 (23), 133 (32), 91 (24); HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{25}H_{24}NO$ 354.1858; Found 354.1852.

(1*SR*,5*SR*,6*RS*,11SR)-2-Benzyl-11-methyl-6-phenyl-1,4,5,6-tetrahydro-1,5-methano-benzo[*c*]azocin-3(2*H*)-one (**8e**).

Yield 34% (method C). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 3 : 1) gave a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, J = 6.9 Hz, 3H, 11-CH_3), 2.22 (dd, J = 8.2, 2.3 Hz, 1H, CH-5), 2.27 – 2.35 (m, 1H, CH-11), 2.54 (d, J = 18.9 Hz, 1H, CHH_{eq}-4), 3.03 (dd, J = 18.9, 8.2 Hz, 1H, CHH_{ax}-4), 3.75 (d, J = 14.8 Hz, 1H, NCHH), 3.96 (t, J = 2.3 Hz, 1H, CH-1), 4.24 (s, 1H, CH_α-6), 5.58 (d, J = 14.9 Hz, 1H, NCHH), 6.80 – 6.90 (m, 2H, ArH), 6.98 – 7.04 (m, 1H, ArH), 7.11 – 7.26 (m, 6H, ArH), 7.28 – 7.41 (m, 5H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 16.42 (11-CH_3), 27.24 (CH-11), 36.47 (CH_2-4), 40.84 (CH-5), 46.98 (NCH_2), 53.84 (CH-6), 57.61 (CH-1), 126.30, 126.46, 127.58, 127.76, 128.28 (2C), 128.43, 128.52 (2C), 128.61 (2C), 129.16 (2C), 132.28, (ArH), 135.26, 136.91, 138.19, 146.91 (Ar), 169.12 (C=O). GC-MS *m*/*z*: 367 (82) [$M^{+\bullet}$], 220 (100), 205 (78), 146 (23), 25 (78), 146 (23), 106 (25), 91 (55). HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ Calcd for $C_{26}H_{26}NO$ 368.2014 Found 368.2009.

(1*SR*,5*SR*,6*SR*,11*SR*)-2-Benzyl-11-methyl-6-phenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[*c*]azocin-3(2*H*)-one (**9e**).

Yield 17% (method C). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 3 : 1) gave a white solid, m.p. = 220 - 221°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (d, J = 6.8 Hz, 3H, 11-CH_3), 2.25 (d, J = 17.6 Hz, 1H, CHH-4), 2.31 – 2.47 (m, 3H, CHH-4, CH-5, CH-11), 3.77 (d, J = 14.8 Hz, 1H, NCHH), 3.93 (t, J = 2.1 Hz, 1H, CH-1), 4.56 (d, J = 5.6 Hz, 1H, CH-6$_b$), 5.65 (d, J = 14.9 Hz, 1H, NCHH), 7.05 – 7.45 (m, 14H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 16.86 (11-

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CH_3), 29.25 (CH_2-4), 34.21 (CH-11), 39.16 (CH-5), 46.72 (NCH_2), 52.51 (CH-6), 57.88 (CH-1), 126.18, 126.80, 127.57, 127.98, 128.15, 128.65 (4C), 129.05 (2C), 130.01 (2C, br), 130.81 (ArH), 136.40, 137.05, 138.41, 142.95 (Ar), 169.41 (C=O). ^{1}H NMR (400 MHz, Toluene-d_8) δ 0.74 (d, J = 6.9 Hz, 3H, 11-CH_3), 1.74 – 1.83 (m, 1H, CH-11), 1.83 – 1.90 (m, 1H, CH-5), 2.18 (dd, J = 19.0, 7.3 Hz, 1H, CHH_{ax}-4), 2.28 (d, J = 19.0 Hz, 1H, CHH_{eq}-4), 3.58 (d, J = 14.8 Hz, 1H, NCHH), 3.65 (t, J = 2.2 Hz, 1H, CH-1), 4.14 (d, J = 6.2 Hz, 1H, CH-6$_b$), 5.83 (d, J = 14.8 Hz, 1H, NCHH), 6.87 – 7.32 (m, 14H, ArH). GC-MS (EI 70eV): m/z= 367 (100) [$M^{+\bullet}$], 220 (37), 205 (34), 179 (19), 143 (21), 106 (43), 91 (71). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{26}H_{26}NO$ 368.2014 Found 368.2009.

(1*SR*,5*SR*,6*RS*,11*SR*)-11-Benzylo-6-fenylo-1,4,5,6-tetrahydro-1,5-metanobenzo[*c*]azocyn-3(2*H*)-on (**8f**).

Yield 57% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1) gave a white semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (d, J = 8.2 Hz, 1H, CH-5), 2.47 (d, J = 19.1 Hz, 1H, CHH-4), 2.56 – 2.62 (m, 1H, CH-11), 2.66 (dd, J = 13.7, 6.3 Hz, 1H, 11-CHH), 2.88 (dd, J = 13.7, 9.6 Hz, 1H, 11-CHH), 2.95 (dd, J = 19.1, 8.3 Hz, 1H, CHH-4), 4.02 (dt, J = 4.6, 2.1 Hz, 1H, CH-1), 4.24 (s, 1H, CH-6), 6.45 (d, J = 4.6 Hz, 1H, NH), 6.83 – 6.92 (m, 2H, ArH), 6.96 – 7.05 (m, 3H, ArH), 7.05 – 7.10 (m, 1H, ArH), 7.17 – 7.30 (m, 8H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 33.56 (CH-11), 36.07 (CH_2-4), 36.51 (11-CH_2), 39.18 (CH-5), 52.66 (CH-6), 53.84 (CH-1), 126.42, 126.45, 127.35, 127.99, 128.34 (2C), 128.44, 128.56 (2C), 128.59 (2C), 128.73 (2C), 132.10 (ArH), 134.34, 138.91, 140.14, 146.35 (Ar), 172.13 (C=O). GC-MS (EI 70eV) m/z: 353 (2) [$M^{+\bullet}$- benzhydryl radical), 294 (100), 217 (31), 91 (37). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{25}H_{24}NO$ 354.1858; Found 354.1852.

(1*SR*,5*SR*,6*SR*,11*SR*)-11-Benzylo-6-fenylo-1,4,5,6-tetrahydro-1,5-metanobenzo[*c*]azocyn-3(2*H*)-on (**9f**).

Yield 10% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 2 : 1) gave a white semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18 (d, J = 19.2 Hz, 1H, CHH), 2.34 (dd, J = 19.2, 7.5 Hz, 1H, CHH-4), 2.45 (dd, J = 9.1, 6.8 Hz, 1H, CH-11), 2.57 – 2.66 (m, 1H, CH-5), 2.92 (dd, J = 13.7, 6.8 Hz, 1H, 11-CHH), 3.02 (dd, J = 13.7, 9.1 Hz, 1H. 11-CHH), 4.08 (dt, J = 4.3, 2.0 Hz, 1H, CH-1), 4.57 (d, J = 6.1 Hz, 1H, CH-6), 6.33 (d, J = 4.3 Hz, 1H, NH), 6.97 – 7.08 (m, 3H, ArH), 7.07 – 7.18 (m, 3H, ArH), 7.22 – 7.30 (m, 5H, ArH), 7.31 – 7.38 (m, 3H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 29.08 (CH_2-4), 37.18 (CH-11), 37.28 (11-CH_2), 40.88 (CH-5), 52.40 (CH-6), 53.59 (CH-1), 126.63, 126.91 (2C), 127.67, 128.16, 128.66 (2C), 128.78 (2C), 128.98 (2C), 129.99 br (2C), 130.75 (ArH), 135.62, 139.06, 140.42, 142.75 (Ar), 172.35 (C=O). GC-MS (EI 70eV) m/z: 353 (4) [$M^{+\bullet}$- benzhydryl radical], 294 (100), 217 (20), 91 (42). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{25}H_{24}NO$ 354.1858; Found 354.1852.

(1*SR*,4*RS*,5*RS*,6*RS*)-4-Benzyl-2,6-diphenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[c]azocin-3(2*H*)-one (**14a**)**.** Major isomer.

Total yield of **14a** and **15a** (80 : 20) 66% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 5 : 1) gave a white semi, m.p. = 187–190°C. Spectral data for **14a** refined from spectra of mixture **14a** : **15a** (80 : 20). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.04 (dt, J = 13.4, 3.6 Hz, 1H, CHH-11), 2.15 (dt, J = 13.4, 3.0 Hz, 1H, CHH-11), 2.36 – 2.43 (m, 1H, CH-5), 2.79 – 2.92 (m, 2H, CH-4, 4-CHH), 3.59 (d, J = 10.9 Hz, 1H, 4-CHH), 3.90 (s, 1H, CH-6), 4.70 (q, J = 2.6 Hz, 1H, CH-1), 6.43 (dd, J = 6.6, 2.9 Hz, 2H, ArH), 6.64 (dd, J = 7.7, 1.4 Hz, 1H, ArH), 6.96 (d, J = 7.5 Hz, 1H, ArH), 7.03 – 7.45 (m, 15H, ArH). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 23.70 (CH_2-11), 38.66 (CH-5), 39.44 (4-CH_2), 50.60 (CH-4), 52.58 (CH-6), 59.25 (CH-1), 126.15, 126.48, 126.51, 127.16, 127.92 (2C), 128.11 (2C), 128.49 (2C), 128.53, 128.61 (3C), 129.26 (2C), 129.52 (2C), 132.06 (ArH), 134.56, 136.66, 140.04, 142.57, 146.03 (Ar), 171.74 (C=O). HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{31}H_{28}NO$ 430.2171; Found 430.2166.

(1*SR*,4*RS*,5*RS*,6*SR*)-4-Benzyl-2,6-diphenyl-1,4,5,6-tetrahydro-1,5-methanobenzo[c]azocin-3(2*H*)-one (**15a**). Minor isomer.

Spectral data for **15a** refined from spectra of mixture **14a** : **15a** (80 : 20). ^{1}H NMR (400 MHz, CDCl3) δ 2.26 (dt, J = 13.1, 3.0 Hz, 1H, CHH-11), 2.43 – 2.50 (m, 1H, CH-5), 2.56 (dt, J = 13.1, 3.6 Hz, 1H, CHH-11), 2.72 (dd, J = 10.3, 4.0 Hz, 1H), 2.79 – 2.92 (m, 1H, CH-4,), 3.05 (dd, J = 13.7, 4.0 Hz, 1H), 4.49 (d, J = 6.3 Hz, 1H, CH-6), 4.66 (t, J = 3.3 Hz, 1H, CH-1), 6.45 – 6.50 (m, 1H, ArH), 6.75 – 6.85 (m,

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1H, ArH), 6.98 – 7.02 (m, 1H, ArH), 7.03 – 7.45 (m, 16H). $^{13}C\{H\}$ NMR (101 MHz, $CDCl_3$) δ 28.65, 35.53, 39.68, 42.55, 50.70, 59.62, 125.82, 126.03, 126.62, 128.17, 128.26 (3C), 128.53 (4C), 128.61 (2C), 128.99 (2C), 129.19 (2C), 129.26, 130.45, 136.00, 137.16, 139.25, 142.24, 142.43, 172.11.

(5*RS*,7*RS*,8*RS*)-7-Benzhydryl-12-phenyl-6,7,8,9-tetrahydro-5*H*-5,8-(epiminomethano)cyclohepta [4,5]benzo [1,2-*d*][1,3]dioxol-11-one (**16a**).

Yield 70% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 4 : 1) gave a white semi, 151–153°C. ^1H NMR (400 MHz, $CDCl_3$) δ 1.95 (ddd, *J* = 14.0, 8.3, 4.6 Hz, 1H, CHH_β-6), 2.25 (ddd, *J* = 14.0, 9.1, 2.5 Hz, 1H, CHH_α-6), 2.92 (dd, *J* = 5.1, 2.6 Hz, 1H, CH-8), 2.97 (dd, *J* = 17.4, 5.1 Hz, 1H, CHH_β -9), 3.12 (ddd, *J* = 12.0, 9.1, 8.3 Hz, 1H, CH-7), 3.31 (dd, *J* = 17.4, 2.6 Hz, 1H, CHH_α-9), 3.87 (d, *J* = 12.0 Hz, 1H, 7-CH), 4.43 (dd, *J* = 4.6, 2.5 Hz, 1H, CH_b-5), 5.94 (d, *J* = 1.1 Hz, 1H, OCHHO), 5.94 (d, *J* = 1.1 Hz, 1H, OCHHO), 6.51 (d, *J* = 1.0 Hz, 1H, CH-4), 6.66 (d, *J* = 1.1 Hz, 1H, CH-1), 7.02 – 7.46 (m, 15H, ArH). $^{13}C\{H\}$ NMR (101 MHz, $CDCl_3$) δ 37.40 (CH_2-9), 39.48 (CH_2-6), 39.52 (CH-7), 44.42 (CH-8), 59.14 (7-CH), 64.19 (CH-5), 101.18 (OCH_2O), 107.98 (CH-4), 110.86 (CH-1), 124.82 (2C), 126.30, 126.55, 126.71, 127.88 (2C), 128.07 (2C), 128.65 (2C), (ArH), 128.89 (Ar), 128.95 (4C), 131.58, 142.19, 142.94, 143.45, 145.78, 147.57 (Ar), 172.29 (C=O). GC-MS (EI 70eV): decomposition. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{32}H_{28}NO_3$ 474.2069; Found 474.2064.

(5RS,7RS,8RS)-7-Benzhydryl-2,3,4-trimethoxy-11-phenyl-6,7,8,9-tetrahydro-5*H*-5,8-(epiminomethano)benzo [7]annulen-10-one (**16b**).

Yield 87% (method B). The crude product purified by column chromatography (SiO_2, hexane/ethyl acetate, 4 : 1) gave a white semi, 205–207°C. ^1H NMR (400 MHz, $CDCl_3$) δ 2.00 (ddd, *J* = 14.0, 8.3, 4.8 Hz, 1H, CHH_β-6), 2.16 (ddd, *J* = 14.0, 9.1, 2.6 Hz, 1H, CHH_α-6), 2.92 (dd, *J* = 4.8, 3.0 Hz, 1H, CH-8), 3.03 (dd, *J* = 17.9, 4.9 Hz, 1H, CHH_β -9), 3.13 (ddd, *J* = 12.0, 9.1, 8.3 Hz, 1H, CH-7), 3.36 (ddd, *J* = 17.9, 3.0, 0.8 Hz, 1H, CHH_α-9), 3.61 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.88 (d, *J* = 12.0 Hz, 1H, 7-CH), 5.29 (dd, *J* = 4.7, 2.6 Hz, 1H, CH-5), 6.49 (s, 1H, CH-1), 7.09 – 7.46 (m, 15H, ArH). $^{13}C\{H\}$ NMR (101 MHz, $CDCl_3$) δ 37.54 (CH_2-9), 39.20 (CH_2-6), 39.86 (CH-7), 44.51 (CH-8), 54.66 (CH-5), 55.89 (OCH_3), 59.18 (7-CH), 60.85 (OCH_3), 61.44 (OCH_3), 109.41 (CH-1), 124.62 (Ar), 124.82 (2C), 126.17, 126.50, 126.65, 127.89 (2C), 128.07 (2C), 128.63 (2C), 128.86 (2C), 128.91 (2C), (ArH), 131.44, 139.97, 142.11, 143.00, 143.57, 149.78, 152.83 (Ar), 172.72 (C=O). GC-MS (EI 70eV): decomposition. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{34}H_{34}NO_4$ 520.2488; Found 520.2482.

4. Conclusions

To sum up, we have demonstrated that the 1,4-addition of diphenylmethyllithium (**BzhLi**) or benzhydrylmagnesiate reagents to *N*1/C5-functionalized 2-pyridones provided reliable access to racemic, benzhydryl-functionalized 3,4-dihydropyridin-2-ones in good yields and high regioselectivity. Both methods can be used complementarily based on specific differences. The influence of substituents on regioselectivity has been noted, allowing control over the regioselectivity of addition. The treatment of δ-enelactams with TfOH and/or TIPSOTf results in the partially stereoselective synthesis of 6-phenyl functionalized 7,8-benzomorphanones, indicating its potential in pharmaceutical research. The described cyclization protocol can be extended for the synthesis of novel C3-C6 bridged δ-lactams by using a methoxy-substituted benzyl group at C3 in the substrate.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org. Spectroscopic data and procedures for the synthesis of compounds: **1c**, **1e** and **1g** (Scheme S1**:** Synthesis of compounds **1c**, **1e** and **1g)**; compounds **1d**, **1f**, **1h**, **1u** and **1v** (Scheme S2: Synthesis of **1d**, **1f**, **1h**, **1u** and **1v**); compounds **1i-1t** (Scheme S3: Synthesis of **1i-1t**); 5-benzyl-2-methoxypyridine and 2-methoxy-5-(phenylsulfonyl)pyridine; compounds **4a**, **5a** (Scheme S4: Synthesis of **4a** and **5a**); compounds **12** and **13**. Structural analysis of bridged δ-lactams **8**, **9** and **16**. Figure S1: $J^3_{H,H}$ refined from ^1H NMR spectra and calculated based on Haasnoot equation [30] (in round brackets) using structures optimized by the PM3 method for all possible isomers **8**-**11**, together with Overhouser effects derived from $^1H,^1H$ NOESY spectra for **8** and **9**; Figure S2: $^1H,^1H$ NOESY spectra of compound **8b** ($CDCl_3$); Figure S3: $^1H,^1H$ NOESY spectra of compound **9b** ($CDCl_3$); Figure S4: $^1H,^1H$ NOESY spectra of compound **9b** (Toluene-d_8); Figure S5: $J^3_{H,H}$ refined from ^1H NMR spectra and calculated based on Haasnoot equation [30] (in round brackets) using structures optimized by the PM3 method for compounds **16a** and **16b**; Figure S6. $^1H,^1H$ NOESY spectra of compound **16a** ($CDCl_3$); Figure S7.

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^{1}H,^{1}H NOESY spectra of compound **16b** ($CDCl_3$). Copies of the ^{1}H NMR and ^{13}C NMR spectra for all new compounds **1**-**16**.

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