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Regioselective Synthesis of 6-Vinyl-3,6-dihydropyridine-2(1*H*)-ones through Simple Addition of a Vinylmagnesium "Ate" Complex to 2-Pyridones

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Dedicated to Professor Jürgen Liebscher on the occasion of his 70th birthday

Keywords: Nucleophilic addition / Nitrogen heterocycles / Lactams / Magnesium / Substituent effects

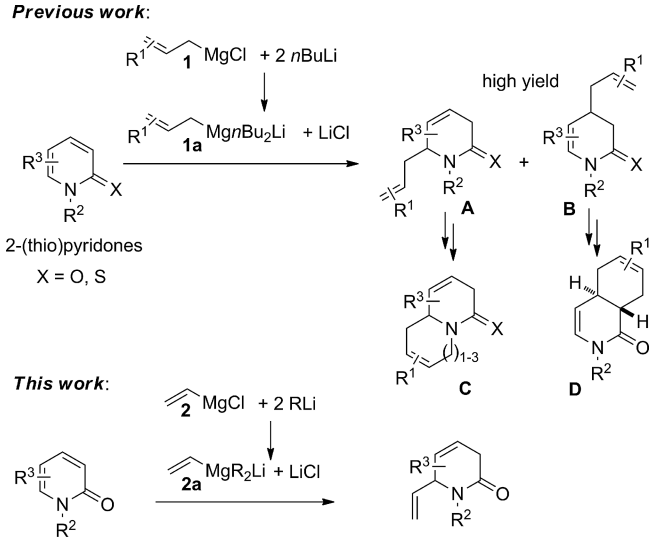
A highly nucleophilic vinylation reagent, lithium vinyldimethylmagnesate (vinylMe_2MgLi), is obtained by mixing vinylmagnesium chloride (1 equiv.) and MeLi (in diethoxymethane; 2 equiv.). The application of this new reagent in the completely regioselective synthesis of 6-vinyl-3,6-dihydro-1*H*-pyridin-2(1*H*)-ones by simple 1,6-additions to 2-pyridones is described. Examination of the scope and limitations of the addition revealed the influence on the efficiency of the 6-vinylation reaction of substituents on the nitrogen atom and on the 2-pyridone ring.

Introduction

Functionalized piperidin-2(1*H*)-ones have become important since it was recognized that compounds of this class show a wide range of pharmacological activities,[1] including anticancer,[1a] antidiabetic,[1b] and anti-HIV[1c] activities. It has also been shown that such compounds can act as neurokinin-2 receptor antagonists,[1d] glycosidase inhibitors,[1e] and fibrinogen receptor antagonists,[1f] among other roles. In addition to their applications as biologically active compounds, they have been used as building blocks for the synthesis of a wide range of naturally occurring alkaloids,[2] and also of potential pharmaceuticals based on a piperidine skeleton,[3] and their commonly used precursors.[4]

Among the variety of approaches to the synthesis of functionalized piperidin-2(1*H*)-ones that have been reported, the nucleophilic addition of organometallic species to 2-pyridones [pyridin-2(1*H*)-ones] is fundamentally important, because of the high availability of the substrates and the possibility of synthesizing functionalized dihydropyridin-2(1*H*)-ones, which are capable of undergoing further transformations.[5] However, it should be emphasized that unactivated 2-pyridones react effectively only with organolithium[5a–5c,5f,5g] reagents; it has been shown that they are inert towards Grignard reagents, and in order to overcome this lack of reactivity, the 2-pyridones must be transformed into highly electrophilic pyridinium salts by *O*-silylation.[6]

As a result of our recent work aimed at the synthesis of functionalized piperidin-2(1*H*)-(thi)ones, we have reported on the nucleophilic properties of lithium allyldi-*n*-butylmagnesates ([allyl*n*Bu_2Mg]Li [**1a**]), which are prepared simply by mixing allylmagnesium chloride (**1**) (or 2-methylallylmagnesium chloride or 3,3-dimethylallylmagnesium bromide) and *n*-butyllithium in a 1:2 molar ratio at 0 °C in THF solution (Scheme 1).[7] The magnesium "ate" complexes that are formed allowed the fairly regioselective introduction of an allyl substituent into a 2-(thio)pyridone. This gave 6-allyl-3,6-dihydropyridin-2(1*H*)-(thi)ones (**A**) or 4-allyl-3,4-dihydropyridin-2(1*H*)-(thi)ones (**B**), depending on



Scheme 1. The addition of allylmagnesates to 2-(thio)pyridones and further transformations (previous work), and the addition of vinyl magnesates to 2-pyridones (this work).

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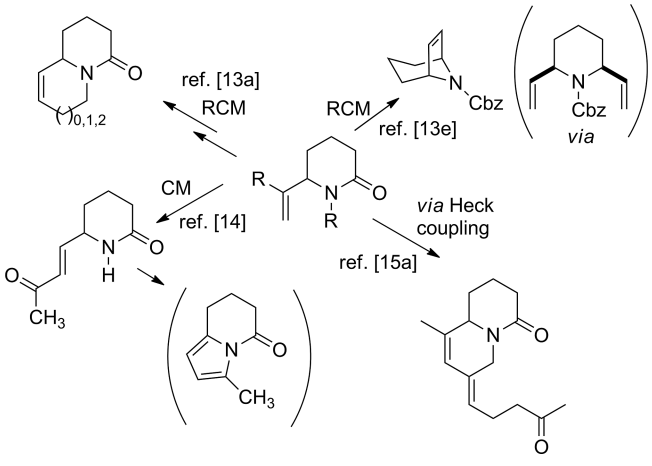
whether *N*R- or *N*H-substituted pyridin(e)-2(1*H*)-(thi)ones and allyl(2-methylallyl)di-*n*-butylmagnesate or 3,3-dimethylallyldi-*n*-butylmagnesate were used. Furthermore, the variable regioselectivity of the addition of allyl moieties enabled us to obtain substituted 3,6,9,9a-tetrahydroquinolizin-4-ones[8] (**C**) and *trans*-4a,5,8,8a-tetrahydro-2*H*-isoquinolin-1-ones[9] (**D**) by using ring-closing metathesis (Scheme 1). It should be noted that with the exception of the above-mentioned lithium allylmagnesates, which are monoanionic allylmagnesium compounds,[10] and which belong to the relatively new and useful family of "ate" complexes,[11] no further examples of the addition of magnesates to pyridin-2(1*H*)-ones have been reported. Furthermore, although the first preparation of vinylmagnesium "ate" complexes from vinyl iodides by iodine–magnesium exchange using *i*Pr*n*Bu$_2$MgLi as an exchange reagent has been reported by Oshima and coworkers,[12] the preparation of vinylmagnesates directly from Grignard reagents has not been described to date.

Encouraged by the successful use of allylmagnesates in the functionalization of piperidin-2(1*H*)-ones, we were prompted to check whether it would be possible to introduce a vinyl substituent into a piperidin-2(1*H*)-one ring by using a vinylmagnesate reagent. This is not only an interesting issue from the point of view of the fundamental chemistry of magnesium "ate" complexes. It could also be attractive from a synthetic point of view, because 6-vinyl-substituted piperidin-2(1*H*)-ones and piperidines could be further functionalized in many ways by reaction of the vinyl moiety by ring-closing[13] or cross[14] metathesis reactions, Heck reaction,[15] reduction,[16] cleavage by ozonolysis,[17] or other transformations.[18] A few examples of transformations of 6-vinylpiperidin-2-ones into other piperidine derivatives are shown in Scheme 2. Furthermore, the anticipated products of the vinylation reaction, vinyldihydropyridin-2(1*H*)-ones, in addition to the exocyclic C=C double bond (vinyl moiety) would also contain a C=C double bond inside the ring. This would allow additional transformations, and these products seem to be even more valuable building blocks than the compounds shown in Scheme 2. A simple route to 6-vinyl-3,6-dihydropyridin-2(1*H*)-ones would also be valuable because the 6-vinylpiperidine moiety is found in certain naturally occurring compounds, including (±)-pinidine,[19] (+)-caulophyllumine B,[20] (+)-dienomycin C,[21] and galbulimima alkaloids[22] (himbeline and himbacine), and also in some synthetic derivatives showing e.g., anticancer[15b] and antibacterial[23] activity. Thus, in this paper we describe the results of the first attempts to activate vinylmagnesium chloride by its conversion into "ate" complexes of type R_3MgLi by the addition of organolithium reagents, and the application of these "ate" complexes in nucleophilic addition to 2-pyridones, which in turn enables easy access to 6-vinyl-3,6-dihydropyridin-2-ones.



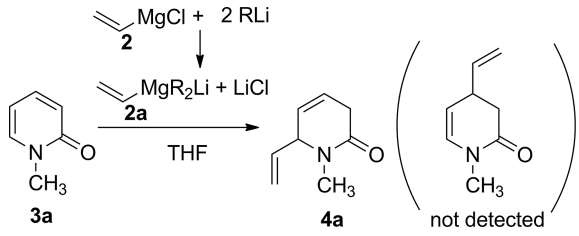
Scheme 2. Examples of the application of 6-vinylpiperidin-2-ones in the synthesis of functionalized piperidin-2-ones and piperidines. RCM = ring-closing metathesis; CM = cross metathesis.

Results and Discussion

For our first tests, we used commercially available *N*-methyl-2-pyridone. Treatment with vinylmagnesium chloride (**2**; 1.6 M solution in THF) alone at 0 °C gave only traces of 6-vinyl-3,6-dihydropyridine-2(1*H*)-one (**4a**) but with a high consumption of the substrate; this reagent showed a complete lack of reactivity at –80 °C (Table 1, entries 1 and 2). However, when vinylmagnesium chloride was converted into magnesate **2a** by the addition of 2 equiv. *n*BuLi, this reagent yielded **4a** in up to 49% isolated yield, although the substrate conversion was still unsatisfactory (Table 1, entries 3–6). Subsequent optimization of the reaction conditions involved testing other commercially available lithium reagents, and adjusting the temperature and reaction time. MeLi [3 M in DEM (diethoxymethane)] was the best choice among the organolithium reagents tested, and it was advantageous to change the temperature from –80 to 0 °C during the reaction (Table 1, entries 7–9). Furthermore, by using 1.4 equiv. of lithium dimethylvinylmagnesate, and increasing the scale of the reaction by a factor of three (up to 6.9 mmol of **3a**), we were able to obtain **4a** in a best isolated yield of 79% (Table 1, entry 9). It should be noted that in all attempts, only the 6-vinyl-substituted product (i.e., **4a**) was formed, as shown by ^{1}H NMR spectroscopic analysis of the crude reaction mixtures (the 4-vinyl isomer, which could potentially also be formed, was not detected). The choice of MeLi for the activation of vinylmagnesium chloride was also justified from a practical point of view, as its use led to a minimum number of by-products, as observed by ^{1}H NMR spectroscopy and GC–MS analysis of the crude reaction mixtures (see footnote in Table 1). In the light of the above results, it should be mentioned that the activation of aryl and alkyl Grignard reagents towards Michael addition to α,β-unsaturated *N*H amides by treatment with MeLi (in diethyl ether) has been reported earlier.[24]

Next, we were driven to check the level of influence of diethoxymethane (DEM; introduced into the reaction environment together with MeLi) on the product yield. When we ran the reaction using a diethyl ether solution of MeLi (1.6 M), another commercially available reagent, the yield

Table 1. Optimization of reaction conditions for the 6-vinylation of **3a**. The effect of varying the organolithium reagents on the efficiency of the vinyl addition.

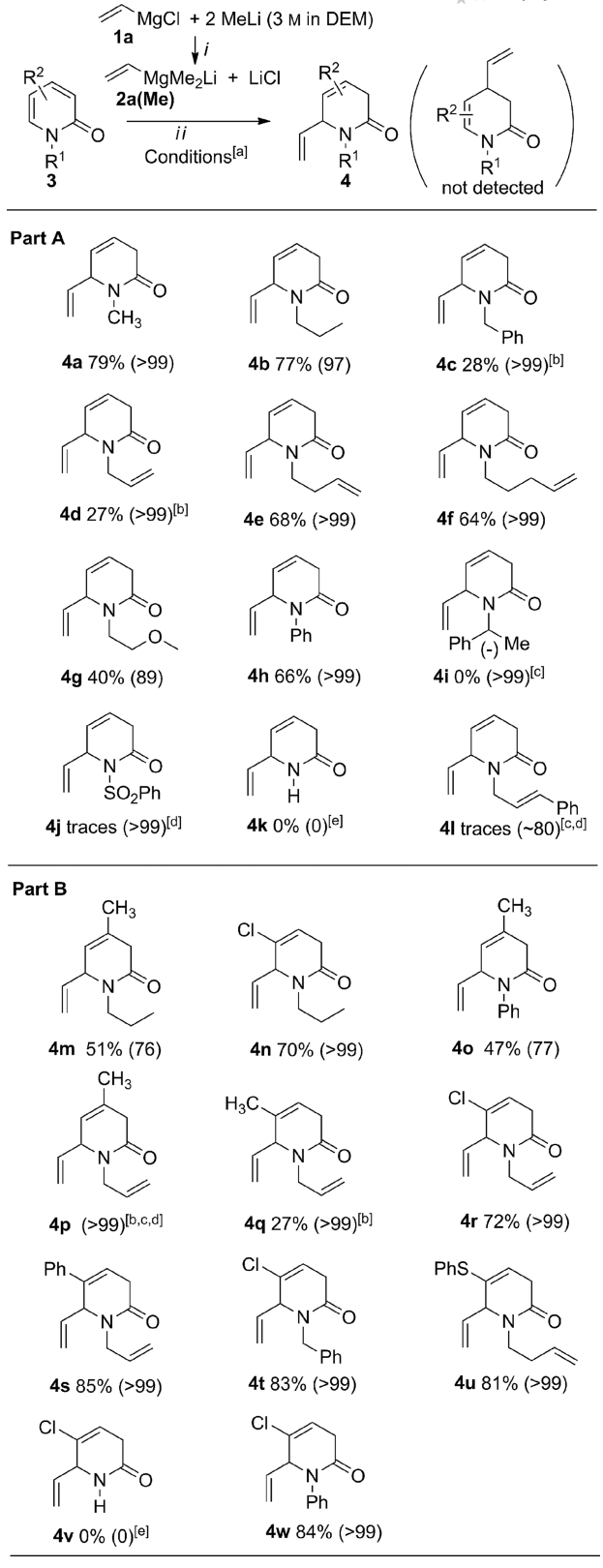


Entry	**2** equiv.	RLi (equiv.)	*T* [°C]/ *t* [min.]	**3a**[a] Conv. [%][b]	**4** Yield [%][c]
1	1.3	–	0/90	88	(2)[1]
2	1.3	–	–80/90	0	0
3	1.2	*n*BuLi[d] (2.4)	0/30	95	31 (34)[1]
4	1.2	*n*BuLi[d] (2.4)	–80/30	44	(18)[1]
5	1.4	*n*BuLi[d] (2.8)	–80/60 –80→23/15 0/45	87	49 (54)[1]
6	2.0	*n*BuLi[d] (4.0)	–80/90 –80→23/15 0/30	93	48
7	1.2	MeLi[e] (2.4)	–80/60 –80→23/15 0/45	93	(59)[2]
8	1.4	MeLi[e] (2.8)	as above	>99	(68)[2][f]
9	1.4	MeLi[e] (2.8)	as above	>99	79[f,g]
10	1.4	MeLi[h] (2.8)	as above	>99	60[g]
11	1.2	*sec*-BuLi[i] (2.4)	as above	81	(36)[1][j]
12	1.2	*tert*-BuLi[k] (2.4)	as above	93	(22)[1][j]
13	1.2	PhLi[l] (2.4)	as above	95	(44)[1][m]

[a] 2.3 mmol of **3a** (1.0 equiv.) was used unless otherwise stated. [b] Conversion of **3a** [%] estimated by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c] Isolated yield [%], yield estimated by ^{1}H NMR spectroscopy using an internal reference is given in parentheses. The number of determinations is given in the upper index. [d] 2.5 M *n*-hexane solution. [e] 3 M diethoxymethane solution. [f] The minimum number of by-products was observed by ^{1}H NMR spectroscopy and GC–MS analysis of the crude reaction mixture. [g] The reaction scale was increased threefold (6.9 mmol of **3a**). [h] 1.6 M diethyl ether solution. [i] 1.4 M cyclohexane solution. [j] The product of addition of the organolithium to **2a** was detected by GC–MS (*m*/*z* = 167), among other by-products. [k] 1.7 M pentane solution. [l] 1.8 M dibutyl ether solution. [m] Biphenyl was detected by GC–MS as the main by-product.

decreased significantly by 19%. This indicates that DEM is a better cosolvent, and that it is responsible for an additional activation effect (Table 1, entry 10).

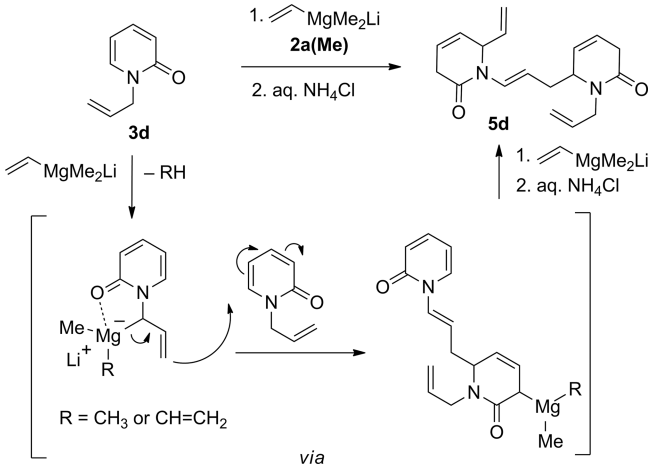
Having established optimal reaction conditions, we went on to evaluate the scope and limitations of the vinylation reaction in terms of substituted 2-pyridones. First, we examined 2-pyridones bearing various substituents on the nitrogen atom only, and then we tested derivatives with various substituents on both the nitrogen atom and the ring. The results of the first part of the study are presented in Scheme 3 (Part A). We found that the optimized protocol described above permits the 6-vinylation of *N*-substituted 2-pyridones; the *N*-Li 2-pyridone derived from *N*-H substrate **3k** remained intact. However, among the *N*-substituted 2-pyridones tested, only the derivatives with an *N*-phenyl group (**3h**) and with less bulky *N*-alkyl groups (**3a**–



Scheme 3. Scope of the addition of vinyl$MgMe_2Li$ + LiCl to substituted 2-pyridones. [a] Conditions are as follows: i) THF, 5 min at 0 °C; ii) 60 min at –80 °C, then warming at room temp. over 15 min, then 45 min at 0 °C. [b] High mass product detected by GC–MS analysis of the crude reaction mixture. [c] complex mixture observed by ^{1}H NMR spectroscopy. [d] Product not isolated. [e] Through *N*-Li salt.

3g) gave satisfactory yields. Derivatives with *N*-phenylsulfonyl (**3j**) and *N*-(3-phenylallyl) (**3l**) substituents gave only traces of the products or underwent degradation.

N-Benzyl- (**3c**) and *N*-allyl-substituted (**3d**) 2-pyridones constitute a separate group; they gave the products in lower yields (**4c**, 28%; and **4d**, 27%, respectively) due to the competitive formation of benzyl and allyl anions, which led to self-addition products. These undesirable by-products were detected by ^{1}H NMR spectroscopy and GC–MS analysis of the crude reaction mixtures. Their presence was confirmed by the successful isolation of one such by-product (i.e., **5d**; Scheme 4), whose purity was high enough to permit its structural analysis by ^{1}H and ^{13}C NMR spectroscopy and HRMS (ESI-TOF).



Scheme 4. Formation of by-product **5d** by competitive formation of a stabilized allyl anion and subsequent addition.

The above observations imply that the nucleophilic behaviour of vinylmagnesate **2a**, which leads to the addition products, competes with its behaviour as a base, manifested by proton abstraction from the *N*-CH moiety, and enabling self-addition through the formation of a stabilized anion. The above results show that the behaviour of **2a** is in distinct contrast to the reactivity of allyldi-*n*-butylmagnesate (**1a**), which yielded the addition product exclusively in its reactions with the corresponding *N*-allyl-2-pyridone (i.e., **3d**).[8d]

The results obtained from the second set of reactions (Scheme 3, B) indicate that the substituents on the 2-pyridone ring have a substantial influence on the yield of the 6-vinylation products (i.e., **4**), compared to the yields obtained for the ring-unsubstituted analogues. Judging by the conversion of the substrates and the yield of the products (i.e., **4**), it is clear that a 4-Me group decreases the reactivity of the 2-pyridone ring, whereas a 3-Me group does not influence the reactivity. 3-Cl, 3-Ph, and 3-PhS substituents make the 2-pyridone ring more reactive towards addition, except for 3-Cl, *N*-H substituted derivative **3v**, which, similarly to unsubstituted *N*-H 2-pyridone **3k**, remained intact. The influence of substituents on the 2-pyridone ring on the reactivity towards addition is the most pronounced for *N*-allyl (**3r** and **3s**) and *N*-benzyl (**3t**) substrates; the corresponding products (i.e., **4r**–**4t**) were obtained in good yields, and no self-condensed by-products were formed. This observation is very important, because in the light of the observed competition between the nucleophilic and basic behaviour of vinylmagnesate **2a**, the influence of the ring substituent enables a shift of the reactivity of 2-pyridones towards nucleophilic addition.

The lack of success in the addition reactions of 2-pyridones with bulky nitrogen substituents can be attributed to steric hindrance between the nucleophile and the large nitrogen substituents. The experimentally observed relationship between the structures of *N*-alkyl and *N*-aryl 2-pyridones and their reactivity towards addition can be rationalized in terms of classical frontier molecular orbital (FMO) theory.[25] LUMO energies were calculated using the PM3 method[26] for acceptors **3** for the prepared *N*-Me (**3a**) and *N*-Ph substituted (**3h**, **3o**, **3w**) derivatives, and also for theoretical structures **3Ta**–**3Td** similar to those obtained (*N*-alkyl or alkenyl) but with an *N*-Me group (Figure 1). The structures were simplified for the calculations in order to avoid interruption of the calculations at local energy minima due to *N*-alkyl-chain rotation. The results showed that the LUMO energies change in parallel to the experimentally observed reactivities of the acceptors. Derivatives with 3-Ph and 3-Cl substituents have LUMOs with significantly lower energies compared to the LUMO of **3a**, which makes them more reactive towards addition (Figure 1, structures **3Ta**, **3Tb**, and **3a**, respectively). The presence of a methyl substituent on the ring slightly increases the energy of LUMO, thus decreasing the reactivity (Figure 1, structures **3Tc** and **3Td**). The same substituent effect was observed in the *N*-Ph series. The highest reactivity was noted for 5-Cl-substituted 2-pyridone **3w**, whose LUMO energy had the lowest value; 4-Me derivative **3o** led to the lowest yield and conversion. These tentative results may indicate that orbital overlap is the main factor that controls the reactivity of **3**. However, more detailed calculations need to be carried out to support this hypothesis.

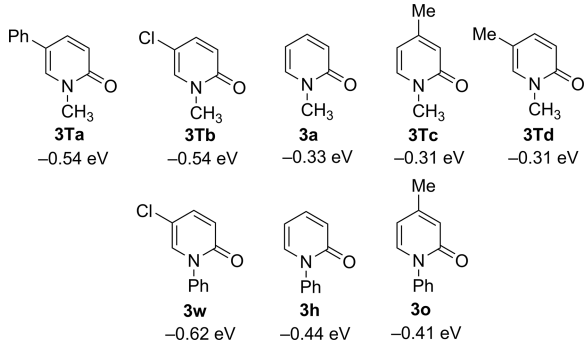
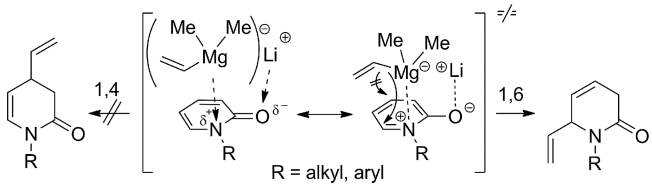


Figure 1. PM3-calculated energies of LUMO orbitals of selected *N*-Me and *N*-Ph 2-pyridones arranged in order of decreasing energy values for the two types of *N*-substituent.

It is not trivial to explain the regioselectivity of the addition of vinylmagnesium "ate" complexes to *N*-alkyl or *N*-aryl 2-pyridones; it requires detailed high-level calculations within e.g., FMO theory or another theory. Without using

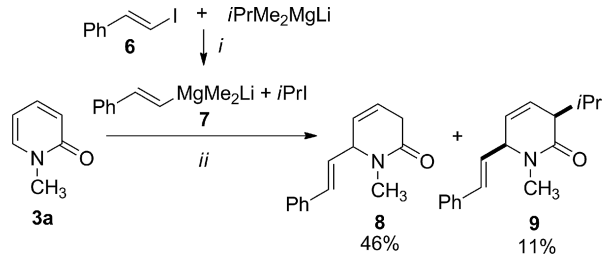
calculations, our current idea to explain the complete 1,6-regioselectivity in the addition reactions involves the existence of a polarized transition state, in which the amide functionality of the 2-pyridone interacts with the vinylmagnesate in the manner shown in Scheme 5. The postulated existence of such a complex, with a charge-driven orientation of the two components, is based on the assumption that the magnesate could be regarded as a contact or separated ion pair,[11b] and that the 2-pyridone is polarized due to the presence of an amide functionality.[27] The proposed interaction may result in a decrease of the electron density in the pyridone ring, which would increase its reactivity towards the addition of the vinyl nucleophile. More importantly, it seems that this proposed interaction is crucial for obtaining complete 1,6-regioselectivity in the addition reaction. This explanation may be confirmed by the failure of the reaction between *N*-methyl 2-pyridone and standard vinylmagnesium chloride, which has a different electron distribution compared to the vinylmagnesate. The final point is the fact that *N*-lithiated pyridones (which could be regarded as nitrogen-electron-rich variants of 2-pyridone) do not react on treatment with vinylmagnesate.



Scheme 5. The electrostatic interaction between vinylmagnesate **2a** and *N*-alkyl (or phenyl) substituted 2-pyridones as the potential reason for the total 1,6-regioselectivity.

Next, we studied the activation of vinylMgCl by MeLi (in DEM) by ^{1}H and ^{13}C NMR spectroscopy, performed at 22 °C in a coaxial probe using CD_3COCD_3 as an external lock and reference (Figure 2). The ^{1}H and ^{13}C spectra of vinylMgCl in THF (Figure 2, part a) and of 1:1 and 1:2 molar mixtures of vinylMgCl (in THF) and MeLi (in DEM) (Figure 2, c and d, respectively) clearly indicated that there was an interaction between vinylMgCl and MeLi, especially in a 1:2 molar ratio. [The highest chemical shift differences were observed for the 1:2 molar ratio mixture: $\delta \approx 0.5$ ppm in the ^{1}H NMR spectra, and $\delta \approx 5.8$ ppm (C=) in the ^{13}C NMR spectra.] Additional experiments showed only a weak interaction between vinylMgCl and diethoxymethane (DEM).

Finally, we checked the possibility of functionalizing 2-pyridones by the addition of vinyl magnesate prepared by Oshima's Mg–I exchange method. Thus, β-styrylmagnesate **7**, prepared from easily available β-iodostyrene[28] (**6**) using *i*PrMe$_2$MgLi as an exchange reagent (instead of the *i*Pr*n*Bu$_2$MgLi used in Oshima's original method), was treated with 2-pyridone **3a**, and gave product **8** in 46% yield, together with by-product **9** (11% yield; Scheme 6). It should be noted that undesired product **9** was formed as the result of alkylation of **8** by isopropyl iodide, which was released during the exchange process (Scheme 6). [The ease of alkylation of 3,6-dihydropyridin-2(1*H*)-one by alkyl iod-



Scheme 6. Attempted use of magnesate derived from styryl iodide by the I–Mg exchange method. The *cis*-configuration of product **9** was assigned from ^{1}H,^{1}H NOESY spectra (see Supporting Information). i) THF, 5 min at –10 °C; ii) 60 min at –80 °C then warming at room temp. over 15 min, then 60 min at 0 °C.

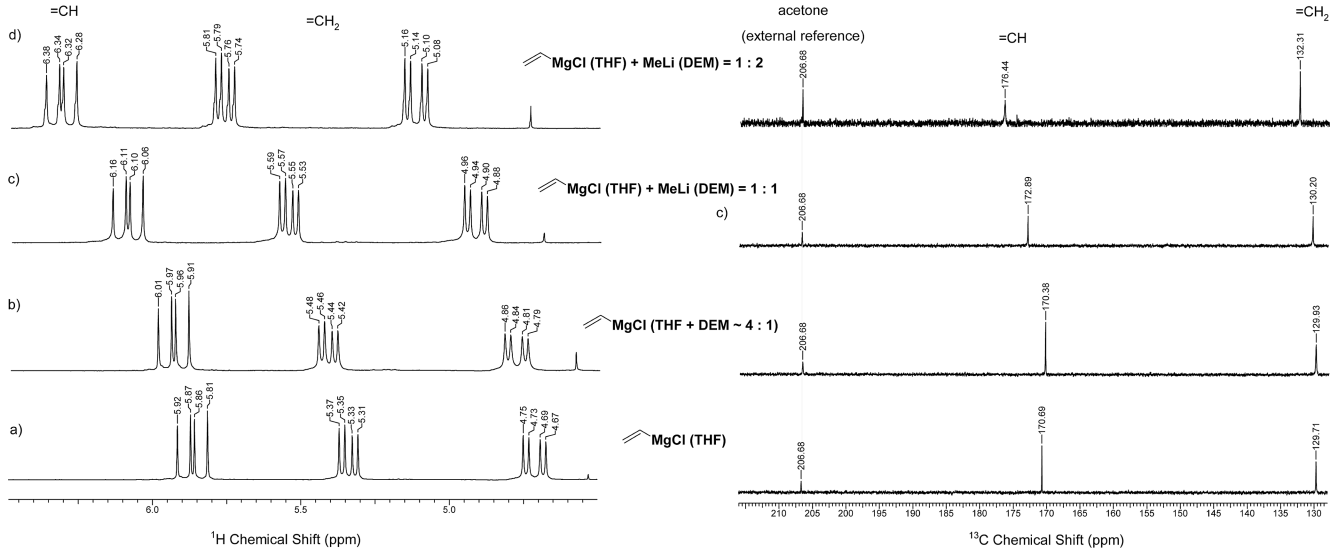


Figure 2. The additive effect of MeLi (c, d) and DEM (b) on ^{1}H (400 MHz; left) and ^{13}C (100 MHz; right) NMR spectra of vinylmagnesium chloride in THF (a) at 22 °C using CD_3COCD_3 as external lock and reference.

ides using magnesates has already been reported by us.][7c] These results indicate that the direct styrylation of 2-pyridones using magnesates obtained by the exchange method is also a promising prospect, but the reaction conditions should be optimized to minimize formation of the alkylated by-product.

Conclusions

We have demonstrated that lithium vinyldimethylmagnesate can be formed directly by mixing of 1 equiv. of vinylMgCl and 2 equiv. of MeLi. The vinyl "ate" complex, although less nucleophilic than the corresponding allylmagnesate, is capable of addition to *N*-substituted 2-pyridones regioselectively through C-6(sp^3)–C-vinyl(sp^2) bond formation. The presence on the 2-pyridone ring of substituents such as 3-Cl, 3-Ph, and 3-PhS enhances the reactivity of the 2-pyridone towards the addition reaction, helping to overcome the undesired basic properties of the vinyl magnesate, and thus improving the yields of the 6-vinyl-3,6-dihydropyridin-2(1*H*)-one addition products. We postulate that the LUMO energy of the 2-pyridones, which is dependent on the type of substituents on the 2-pyridone ring, is the main factor influencing the reactivity of the addition of lithium dimethylvinylmagnesate. The observed direction of activation can be used to design new reactive acceptors. The possible extension of the above reactions to magnesates obtained by an Mg–I exchange process indicates the great potential of these reactions. We are currently studying how the substituted vinylmagnesates obtained from Grignard reagents as well as by the Mg–I exchange process can be applied in addition reactions to 2-pyridones and to other acceptors.

Experimental Section

Typical Procedure for the Synthesis of 6-Vinyl-3,6-dihydropyridine-2(1*H*)-ones 4: A stirred solution of vinylMgCl (1.6 M in THF; 9.7 mmol, 6 mL) in dry THF (18 mL) in a Schlenk flask was cooled to 0 °C under argon, and MeLi (3.0 M in DEM; 19.5 mmol, 6.5 mL) was added by syringe over 3 min. The resulting solution was stirred for 5 min, and then it was cooled to –80 °C. The solution containing lithium vinyldimethylmagnesate was then transferred by syringe to a precooled (–80 °C) solution of 2-pyridone (**3**; 6.9 mmol) in THF (40 mL) in another Schlenk flask. The resulting solution was stirred for 60 min at –80 °C. After this time, the mixture was removed from the bath and allowed to warm up for 15 min, and then the flask was put into an ice-water bath (0 °C) for 45 min. The mixture was carefully quenched with saturated aqueous NH_4Cl (15 mL), then it was allowed to warm up to room temp., and diluted with water (ca. 20 mL). The aqueous layer was extracted with ethyl acetate (2 × 40 mL), and the combined organic layers were dried with $MgSO_4$. The mixture was filtered, and the solvents were evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using a mixture of *n*-hexane and ethyl acetate as eluent to give the desired product.

(±)-1-Methyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4a): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:10) to give **4a** (79%) as a pale yellow oil that darkened on standing. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 2.92–3.00 (m, 5 H, CH_2-3, NCH_3), 4.28 (dq, J = 8.1, 3.9 Hz, 1 H, CH-6), 5.18–5.26 (m, 2 H, =CH_2), 5.53–5.6 (ddd, J = 17.0, 9.8, 8.1 Hz, 1 H, =CH), 5.62–5.68 (m, 1 H, =CH-5), 5.77 (dtd, J = 10.0, 3.5, 1.3 Hz, 1 H, =CH-4) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 31.76 (CH_2-3), 32.28 (NCH_3), 64.19 (CH-6), 117.22 (=CH_2), 122.20 (=CH-4), 124.39 (=CH-5), 136.61 (=CH), 167.41 (C-2) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 137 (29) $[M]^+$, 137 (80), 110 (100), 79 (50), 68 (20). IR (film): $\tilde{\nu}$ = 3084 (w), 3048 (w), 2932, 1660 (s), 1484 (m), 1398 (m), 1312 (m), 1244 (w), 1120 (w), 1064 (w), 988 (w), 932 (m), 716 (w), 664 (w) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_8H_{12}NO$ $[M + H]^+$ 138.0919; found 138.0911.

(±)-1-Propyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4b): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:7) to give **4b** (77%) as a pale yellow oil that darkened on standing. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 0.89 (t, J = 7.5 Hz, 3 H, CH_3), 1.53–1.65 (m, 2 H, CH_2), 2.88 (ddd, J = 13.4, 8.9, 6.0 Hz, 1 H, NC*H*H), 2.94–3.00 (m, 2 H, CH_2-3), 3.82 (ddd, J = 13.4, 9.1, 6.8 Hz, NCH*H*), 4.35 (dq, J = 7.8, 3.6 Hz, 1 H, CH-6), 5.15–5.24 (m, 2 H, =CH_2), 5.60 (ddd, J = 17.1, 9.9, 8.1 Hz, 1 H, =CH), 5.63–5.68 (m, 1 H, =CH-5), 5.77 (dddd, J = 10.0, 4.2, 3.2, 1.2 Hz, 1 H, =CH-4) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 11.35 (CH_3), 20.35 (CH_2), 32.19 (CH_2-3), 46.10 (NCH_2), 61.96 (CH-6), 116.74 (=CH_2), 122.43 (=CH-4), 124.70 (=CH-5), 136.91 (=CH), 167.25 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 165 (27) $[M]^+$, 164 (100), 150 (13), 148 (16), 138 (31), 136 (28), 122 (18), 107 (61), 96 (58), 94 (20), 80 (32), 79 (76), 77 (30), 67 (15), 53 (12), 41 (28), 39 (24). IR (film): $\tilde{\nu}$ = 3084 (w), 3048 (w), 2964 (s), 2932 (m), 2876 (m), 1642 (s), 1466 (s), 1432 (m), 1410 (s), 1320 (m), 1262 (m), 1206 (m), 1168 (w), 1124 (w), 1080 (m), 990 (m), 926 (m), 714 (m), 664 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{10}H_{16}NO$ $[M + H]^+$ 166.1232; found 166.1228.

(±)-1-Benzyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4c): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:10) to give **4c** (28%) as a pale yellow oil that darkened on standing. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 3.05–3.10 (m, 2 H, CH_2-3), 3.83 (d, J = 14.9 Hz, 1 H, NC*H*H), 4.23 (dq, J = 8.0, 3.9 Hz, 1 H, CH-6), 5.17 (dt, J = 17.0, 0.8 Hz, 1 H, =C*H*H), 5.22 (d, J = 10.0 Hz, 1 H, =CH*H*), 5.55–5.65 (m, 3 H, NCH*H*, =CH-5, =CH), 5.78 (dddd, J = 9.9, 4.0, 3.2, 1.2 Hz, 1 H, =CH-4), 7.21–7.34 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 32.09 (CH_2-3), 46.20 (NCH_2), 60.55 (CH-6), 117.62 (=CH_2), 122.24 (=CH-4), 124.75 (=CH-5), 127.36, 128.09, 128.62 (C_6H_5), 136.30 (=CH), 136.88 (C_6H_5), 167.57 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 213 (45) $[M]^+$, 132 (20), 106 (30), 91 (100), 80 (20), 79 (32), 77 (17), 65 (24). IR (film): $\tilde{\nu}$ = 3028 (w), 2928 (w), 1644 (s), 1496 (w), 1452 (s), 1408 (m), 1356 (w), 1318 (m), 1252 (m), 1182 (w), 1148 (w), 1072 (w), 1028 (w), 990 (w), 962 (w), 930 (w), 772 (w), 702 (m), 668 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{14}H_{15}NNaO$ $[M + Na]^+$ 236.1051; found 236.1051.

(±)-1-Allyl-6-vinyl-3,6-dihydropyridin-2(H)-one (4d): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:7) to give **4d** (27%) as a pale yellow oil that darkened on standing. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 2.98–3.02 (m, 2 H, CH_2-3), 3.40 (dd, J = 15.4, 7.6 Hz, 1 H, NC*H*H), 4.36 (dq, J = 8.1, 3.4 Hz, 1 H, CH-6), 4.75 (ddt, J = 15.4, 4.1, 1.7, Hz, 1 H, NCH*H*), 5.10–5.23 (m, 4 H, 2 =CH_2), 5.58 (ddd, J = 17.3, 9.7, 8.1 Hz, 1 H, =CH), 5.67 (dquint, J = 10.0, 2.1 Hz, 1 H, =CH-5), 5.71–5.81 (m, 2 H, =CH-4, =CH) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 32.06 (CH_2-3), 45.94 (NCH_2), 60.93 (CH-6), 117.27, 117.38 (2 =CH_2), 122.32 (=CH-4), 124.67 (=CH-5),

132.59, 136.47 (2 =CH), 167.17 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 162 (74) $[M]^+$, 148 (40), 136 (56), 134 (40), 120 (31), 106 (16), 96 (65), 80 (44), 79 (100), 77 (35), 67 (26), 53 (15), 41 (64), 39 (44). IR (film): $\tilde{\nu}$ = 3084 (w), 3048 (w), 2980 (w), 2924 (w), 1658 (s), 1460 (s), 1408 (s), 1318 (m), 1264 (m), 1194 (w), 1120 (w), 992 (m), 926 (m), 716 (m) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{10}H_{14}NO$ $[M + H]^+$ 164.1075; found 164.1077.

(±)-1-But-3-enyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4e): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:8) to give **4e** (68%) as a pale yellow oil that darkened on standing. ^1H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 2.26–2.42 (m, 2 H, CH_2), 2.90–3.04 (m, 3 H, CH_2-3, NC*H*H), 3.93 (ddd, *J* = 13.5, 8.5, 6.4 Hz, 1 H, NC*H*H), 4.36 (dq, *J* = 7.6, 3.6 Hz, 1 H, CH-6), 5.02 (dm, *J* ≈ 10.0 Hz, 1 H, =C*H*H), 5.07 (dq, *J* = 17.1, 1.7 Hz, 1 H, =CH*H*), 5.17–5.24 (m, 2 H, $=CH_2$), 5.55–5.67 (m, 2 H, =CH-5, =CH), 5.73–5.84 (m, 2 H, =CH-4, =CH) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 31.70 (CH_2), 32.15 (CH_2-3), 43.98 (NCH_2), 62.32 (CH-6), 116.66, 116.92 (2 $=CH_2$), 122.37 (=CH-4), 124.59 (=CH-5), 135.32, 136.82 (2 =CH), 167.33 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 177 (8) $[M]^+$, 176 (22), 136 (100), 107 (94), 94 (19), 79 (51), 77 (25), 41 (13), 39 (17). IR (film): $\tilde{\nu}$ = 3080 (w), 3048 (w), 2976 (w), 2932 (w), 1646 (s), 1466 (m), 1410 (m), 1320 (w), 1246 (w), 1192 (w), 1124 (w), 1086 (w), 992 (m), 918 (m), 714 (m) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{11}H_{16}NO$ $[M + H]^+$ 178.1232; found 178.1240.

(±)-1-Pent-4-enyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4f): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:10) to give **4f** (64%) as a yellow oil that darkened on standing. ^1H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 1.67 (quint, *J* = 7.3 Hz, 2 H, CH_2), 2.06 (q, *J* = 7.6 Hz, 2 H, CH_2), 2.89–3.03 (m, 3 H, CH_2-3, NC*H*H), 3.84 (dt, *J* = 13.6, 7.8 Hz, 1 H, NCH*H*), 4.34 (dq, *J* = 7.6, 3.6 Hz, 1 H, CH-6), 4.97 (ddt, *J* = 10.1, 2.0, 1.2 Hz, 1 H, =C*H*H), 5.03 (dq, *J* = 17.2, 1.8 Hz, 1 H, =CH*H*), 5.16–5.23 (m, 2 H, $=CH_2$), 5.59 (ddd, *J* = 17.1, 9.8, 8.1 Hz, 1 H, =CH), 5.65 (ddt, *J* = 10.0, 4.1, 1.8 Hz, 1 H, =CH-5), 5.75–5.86 (m, 2 H, =CH, =CH-4) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 26.23 (CH_2), 31.07 (CH_2), 32.18 (CH_2-3), 44.11 (NCH_2), 62.07 (CH-6), 114.91, 116.87 (2 $=CH_2$), 122.43 (=CH-4), 124.66 (=CH-5), 136.88, 137.91 (2 =CH), 167.24 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 191 (15) $[M]^+$, 190 (83), 176 (25), 162 (25), 148 (28), 136 (82), 122 (53), 107 (88), 96 (59), 79 (100), 77 (42), 67 (31), 53 (22), 41 (65), 39 (42). IR (film): $\tilde{\nu}$ = 3080 (w), 3048 (w), 2976 (w), 2928 (m), 1648 (s), 1466 (m), 1410 (m), 1320 (m), 1280 (m), 1244 (w), 1184 (w), 1124 (w), 990 (m), 916 (m), 714 (m) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{12}H_{18}NO$ $[M + H]^+$ 192.1388; found 192.1382.

(±)-1-(2-Methoxyethyl)-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4g): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:20) to give **4g** (40%) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 2.90–3.05 (m, 2 H, CH_2-3), 3.12 (ddd, *J* = 14.0, 8.5, 4.8 Hz, 1 H, NC*H*H), 3.33 (s, 3 H, OCH_3), 3.52 (dt, *J* = 10.0, 4.6 Hz, 1 H, OC*H*H), 3.61 (ddd, *J* = 10.0, 8.3, 4.6 Hz, 1 H, OCH*H*), 4.05 (dt, *J* = 14.0, 4.6 Hz, 1 H, NCH*H*), 4.56 (dq, *J* = 8.0, 3.9 Hz, 1 H, CH-6), 5.16–5.25 (m, 2 H, $=CH_2$), 5.58 (ddd, *J* = 17.0, 10.0, 8.0 Hz, 1 H, =CH), 5.66 (dddd, *J* = 10.0, 3.9, 2.4, 1.5 Hz, 1 H, =CH-5), 5.76 (dddd, *J* = 10.0, 4.2, 3.2, 1.2 Hz, 1 H, =CH-4) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 32.16 (CH_2-3), 44.02 (NCH_2), 58.89 (CH_3), 63.25 (CH-6), 70.93 (OCH_2), 117.12 ($=CH_2$), 122.04 (=CH-4), 124.89 (=CH-5), 136.72 (=CH), 167.56 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 181 (15) $[M]^+$, 180 (89), 149 (32), 148 (45), 136 (28), 122 (48), 107 (100), 94 (25), 79 (69), 77 (32). IR (film): $\tilde{\nu}$ = 3048 (w), 2980 (w), 2932 (w), 2896 (w), 1648 (s), 1464 (m), 1410 (m), 1360 (w), 1320 (m), 1280 (m), 1188 (w), 1154 (w), 1120 (s), 1070 (w), 994 (w), 930 (w), 716 (w), 664 (w) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{10}H_{16}NO_2$ $[M + H]^+$ 182.1181; found 182.1177.

(±)-1-Phenyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4h): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:20) to give **4h** (66%) as a yellow oil that darkened on standing. ^1H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 3.09–3.23 (m, 2 H, CH_2-3), 4.71 (dq, *J* = 7.6, 3.6 Hz, 1 H, CH-6), 4.97 (dt, *J* = 16.9, 0.8 Hz, 1 H, =C*H*H), 5.03 (br. d, *J* = 10.0 Hz, 1 H, =CH*H*), 5.68 (ddd, *J* = 17.0, 9.9, 8.3 Hz, 1 H, =CH), 5.81 (ddt, *J* = 10.0, 4.0, 2.1 Hz, 1 H, =CH-5), 5.91 (dddd, *J* = 10.0, 4.0, 3.2, 1.0 Hz, 1 H, =CH-4), 7.18–7.23 (m, 2 H, C_6H_5), 7.29 (tt, *J* = 7.6, 1.2 Hz, 1 H, C_6H_5), 7.36–7.42 (m, 2 H, C_6H_5) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 32.70 (CH_2-3), 65.46 (CH-6), 117.33 ($=CH_2$), 122.52 (=CH-4), 125.08 (=CH-5), 127.38, 127.99, 129.14 (C_6H_5), 136.31 (=CH), 140.98 (C_6H_5), 167.53 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* = 199 (100) $[M]^+$, 198 (59), 172 (71), 170 (29), 156 (22), 144 (22), 130 (26), 119 (14), 104 (18), 91 (17), 80 (57), 79 (82), 77 (70), 51 (28), 39 (19). IR (film): $\tilde{\nu}$ = 3048 (w), 1654 (s), 1596 (m), 1496 (m), 1428 (m), 1402 (s), 1290 (m), 1282 (m), 1240 (w), 1168 (w), 1144 (m), 1074 (w), 986 (m), 926 (m), 832 (w), 762 (m), 696 (s) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{13}H_{13}NNaO$ $[M + Na]^+$ 222.0895; found 222.0899.

(±)-4-Methyl-1-propyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4m): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:2) to give **4w** (51%) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 0.88 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.51–1.63 (m, 2 H, CH_2), 1.73 (s, 3 H, 4-CH_3), 2.77–2.95 (m, 3 H, CH_2-3, NC*H*H), 3.81 (ddd, *J* = 13.4, 9.0, 6.8 Hz, 1 H, NCH*H*), 4.28 (br. dquint, *J* = 4.2 Hz, ca. 2.8 Hz, 1 H, CH-6), 5.11–5.19 (m, 2 H, -CH_2), 5.35 (br. s, 1 H, CH-5), 5.55 (ddd, *J* = 17.0, 9.8, 8.2 Hz, 1 H, =CH) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 11.35 (CH_3), 20.35 (CH_2), 21.80 (4-CH_3), 36.83 (CH_2-3), 45.85 (NCH_2), 61.91 (CH-6), 116.18 ($=CH_2$), 118.87 (=CH-5), 130.75 (=C-4), 137.49 (=CH-5), 167.43 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 179 (44) $[M]^+$, 178 (98), 164 (54), 162 (32), 152 (81), 150 (53), 136 (31), 122 (35), 121 (41), 110 (100), 108 (21), 94 (33), 93 (37), 79 (57), 77 (34), 67 (17), 53 (14), 41 (26). IR (film): $\tilde{\nu}$ = 2968 (m), 2932 (m), 2876 (w), 1654 (s), 1466 (m), 1408 (m), 1380 (w), 1292 (m), 1262 (m), 1204 (w), 1136 (w), 990 (w), 926 (w), 832 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{11}H_{18}NO$ $[M + H]^+$ 180.1388; found 180.1396.

(±)-5-Chloro-1-propyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4n): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:20) to give **4n** (70%) as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 0.90 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.53–1.64 (m, 2 H, CH_2), 2.81 (ddd, *J* = 13.6, 8.6, 6.4 Hz, 1 H, NC*H*H), 3.05 (dd, *J* = 3.9, 2.9 Hz, 2 H, CH_2-3), 3.84 (ddd, *J* = 13.6, 8.7, 7.2 Hz, 1 H, NCH*H*), 4.25 (dm, *J* = 7.8 Hz, 1 H, CH-6), 5.30–5.37 (m, 2 H, $=CH_2$), 5.66 (ddd, *J* = 16.9, 10.0, 7.8 Hz, 1 H, =CH), 5.88 (t, *J* = 3.9 Hz, 1 H, CH-4) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 11.26 (CH_3), 20.36 (CH_2), 32.91 (CH_2-3), 46.44 (NCH_2), 65.65 (CH-6), 119.60 ($=CH_2$), 120.74 (=CH-4), 127.15 (C-5), 133.97 (=CH), 165.97 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 201 (6) [M + 2], 200 (37) [M + 1], 199 (20) $[M]^+$, 198 (100), 184 (16), 172 (27), 164 (31), 156 (14), 143 (25), 141 (37), 130 (39), 113 (38), 79 (84), 77 (54), 51 (14), 39 (15). IR (film): $\tilde{\nu}$ = 3084 (w), 3064 (w), 2968 (s), 2936 (m), 2876 (m), 1658 (br. s), 1460 (m), 1430 (m), 1408 (s), 1380 (w), 1302 (w), 1250 (s), 1200 (m), 1124 (m), 1084 (w), 1014 (m), 986 (w), 930 (m), 874 (w), 812 (m), 796 (w), 776 (w), 694 (w) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{10}H_{14}ClNNaO$ $[M + Na]^+$ 222.0662; found 222.0699.

(±)-4-Methyl-1-phenyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4o): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:7) to give **4o** (32%) as a red-orange oil. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 1.82 (s, 3 H, CH_3), 2.99 (ddt, *J* = 21.5, 2.7, 0.7 Hz, 1 H, C*H*H-3), 3.12 (dspt, *J* = 21.5, 1.1 Hz, 1 H, CH*H*-3), 4.64 (br. s, 1 H, CH-6), 4.92 (dt, *J* = 17.0, 0.8 Hz, 1 H, =C*H*H), 4.99 (d, *J* = 10.0 Hz, 1 H, =CH*H*), 5.48–5.52 (m, 1 H, =CH-5), 5.64 (ddd, *J* = 17.0, 10.0, 8.2 Hz, 1 H, =CH), 7.17–7.21 (m, 2 H, C_6H_5), 7.25–7.30 (m, 1 H, C_6H_5), 7.35–7.41 (m, 2 H, C_6H_5) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 21.91 (CH_3), 37.36 (CH_2-3), 65.36 (CH-6), 116.74 (=CH_2), 119.23 (=CH-5), 127.29, 127.98, 129.10 (C_6H_5), 130.93 (=C-4), 136.88 (=CH), 140.95 (C_5H_6), 167.73 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* = 213 (100) $[M]^+$, 212 (30), 198 (37), 186 (72), 170 (24), 158 (11), 143 (19), 130 (23), 104 (16), 94 (34), 91 (19), 79 (80), 77 (62), 51 (17). IR (film): $\tilde{\nu}$ = 3064 (w), 2976 (w), 2912 (w), 1660 (s), 1596 (m), 1494 (s), 1428 (s), 1402 (s), 1280 (s), 1240 (w), 1176 (m), 1072 (w), 988 (w), 924 (m), 832 (w), 762 (m), 696 (s) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{14}H_{15}NNaO$ $[M + Na]^+$ 236.1051; found 236.1046.

(±)-1-Allyl-5-methyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4q): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:5) to give **4q** (27%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 1.72 (q, *J* = 1.6 Hz, 3 H, CH_3), 2.93–2.98 (m, 2 H, CH_2-3), 3.35 (dd, *J* = 15.4, 7.4 Hz, 1 H, NC*H*H), 4.03 (dt, *J* = 8.3, 2.7 Hz, 1 H, CH-6), 4.76 (ddt, *J* = 15.4, 4.0, 1.8 Hz, 1 H, NCH*H*), 5.09–5.29 (m, 4 H, 2 =CH_2), 5.48–5.50 (m, 1 H, =CH-4), 5.53 (ddd, *J* = 17.1, 10.0, 8.8 Hz, 1 H, =CH), 5.70–5.80 (m, 1 H, =CH) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 19.73 (CH_3), 32.24 (CH_2-3), 45.94 (NCH_2), 64.77 (CH-6), 117.30 (=CH_2), 118.02 (=CH-4), 118.21 (=CH_2), 131.07 (=C-5), 132.78, 135.73 (2 =CH), 167.57 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* = 177 (32) $[M]^+$, 176 (43), 162 (52), 150 (55), 153 (21), 134 (25), 110 (56), 93 (30), 91 (21), 79 (100), 77 (33), 41 (39), 39 (24). IR (film): $\tilde{\nu}$ = 3080 (w), 2976 (w), 2916 (w), 1660 (s), 1462 (m), 1410 (m), 1302 (m), 1258 (m), 1172 (w), 1122 (w), 1066 (m), 992 (m), 926 (m), 798 (w), 736 (w) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{11}H_{16}NNO$ $[M + H]^+$ 178.1232; found 178.1240.

(±)-1-Allyl-5-chloro-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4r): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:1) to give **4r** (72%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 3.09 (dd, *J* = 3.9, 3.2 Hz, 2 H, CH_2-3), 3.34 (dd, *J* = 15.4, 7.7 Hz, 1 H, NC*H*H), 4.27 (dt, *J* = 8.0, 2.8 Hz, 1 H, CH-6), 4.78 (ddt, *J* = 15.4, 4.3, 1.7 Hz, 1 H, NCH*H*), 5.17 (dq, *J* = 17.1, 1.4 Hz, 1 H, =C*H*H), 5.22 (dq, *J* = 10.0, 1.3 Hz, 1 H, =CH*H*), 5.32 (dt, *J* = 16.9, 0.9 Hz, 1 H, =C*H*H), 5.38 (d, *J* = 10.0 Hz, 1 H, =CH*H*), 5.64 (ddd, *J* = 16.9, 9.9, 7.9 Hz, 1 H, =CH), 5.74 (dddd, *J* = 17.1, 10.1, 7.8, 4.4 Hz, 1 H, =CH), 5.89 (t, *J* = 3.9 Hz, 1 H, =CH-4) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 32.78 (CH_2-3), 46.22 (NCH_2), 64.47 (CH-6), 118.18, 120.21 (2 =CH_2), 120.58 (=CH-4), 127.23 (=C-5), 132.09, 133.61 (2 =CH), 165.81 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 199 (5) $[M + 2]^+$, 198 (9) $[M + 1]^+$, 197 (17) $[M]^+$, 196 (26), 182 (18), 170 (25), 162 (58), 134 (16), 130 (23), 113 (13), 79 (100), 77 (54), 51 (17), 41 (39). IR (film): $\tilde{\nu}$ = 3084 (w), 2984 (w), 2924 (w), 1660 (s), 1456 (m), 1408 (m), 1320 (w), 1248 (m), 1184 (w), 1122 (w), 1016 (w), 992 (w), 930 (m), 814 (w), 712 (w) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{10}H_{12}ClNNaO$ $[M + Na]^+$ 220.0505; found 220.0510.

(±)-1-Allyl-5-phenyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4s): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:1) to give **4s** (85%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 3.12 (dt, *J* = 21.2, 2.7 Hz, 1 H, C*H*H-3), 3.21 (ddd, *J* = 21.2, 5.4, 1.7 Hz, 1 H, CH*H*-3), 3.42 (ddq, *J* = 15.8, 7.2, 0.6 Hz, 1 H, NC*H*H), 4.80 (dsxt, *J* = 7.0, 1.1, Hz, 1 H, CH-6), 4.90 (ddt, *J* = 15.8, 3.9, 1.9 Hz, 1 H, NCH*H*), 5.08–5.16 (m, 2 H, =CH_2), 5.18–5.25 (m, 2 H, =CH_2), 5.65 (ddd, *J* = 17.0, 10.1, 7.0 Hz, 1 H, =CH), 5.77–5.88 (m, 1 H, =CH), 6.07 (dd, *J* = 5.4, 2.7 Hz, 1 H, =CH-4), 7.28–7.38 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 33.01 (CH_2-3), 46.39 (NCH_2), 61.90 (CH-6), 117.15, 117.40 (2 =CH_2), 120.41 (=CH-4), 126.07, 127.92, 128.62 (C_6H_5), 132.83, 134.30 (2 CH), 136.63, 137.69 (C-5, C_6H_5), 168.00 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 239 (90) $[M]^+$, 238 (88), 224 (22), 212 (69), 210 (25), 196 (25), 171 (72), 156 (61), 155 (87), 141 (95), 128 (75), 115 (100), 91 (38), 77 (22), 41 (25). IR (film): $\tilde{\nu}$ = 3080 (w), 2980 (w), 2920 (w), 1658 (s), 1496 (w), 1464 (m), 1408 (m), 1260 (m), 1184 (w), 1122 (w), 990 (w), 926 (m), 824 (w), 758 (s), 698 (m) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{16}H_{18}NO$ $[M + H]^+$ 240.1388; found 240.1395.

(±)-1-Benzyl-5-chloro-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4t): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:1) to give **4t** (83%) as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 3.16 (dd, *J* = 3.7, 3.0 Hz, 2 H, CH_2-3), 3.78 (d, *J* = 15.1 Hz, 1 H, NC*H*H), 4.14 (dt, *J* = 8.0, 2.8 Hz, 1 H, CH-6), 5.31 (d, *J* = 16.9 Hz, 1 H, =C*H*H), 5.42 (d, *J* = 10.0 Hz, 1 H, =CH*H*), 5.55 (d, *J* = 15.1 Hz, 1 H, NCH*H*), 5.66 (ddd, *J* = 16.9, 10.0, 8.1 Hz, 1 H, =CH), 5.89 (t, *J* = 3.9 Hz, 1 H, =CH-4), 7.23 (br. d, *J* ≈ 6.8 Hz, 2 H, C_6H_5), 7.26–7.37 (m, 3 H, C_6H_5) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 32.79 (CH_2-3), 46.60 (NCH_2), 64.26 (CH-6), 120.54 (=CH-4), 120.58 (=CH_2), 127.22 (=C-5), 127.66, 128.08, 128.78 (C_6H_5), 133.53 (=CH), 136.19 (C_6H_5), 166.12 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 249 (6) $[M + 2]^+$, 248 (5) $[M + 1]^+$, 247 (21) $[M]^+$, 212 (74), 184 (56), 132 (26), 117 (14), 106 (32), 91 (100), 79 (43), 77 (32), 65 (29), 51 (12), 39 (12). IR (film): $\tilde{\nu}$ = 3060 (w), 3032 (w), 2928 (w), 1656 (s), 1496 (w), 1450 (m), 1408 (m), 1356 (w), 1328 (w), 1246 (m), 1156 (w), 1074 (w), 1016 (w), 936 (w), 816 (w), 704 (s) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{14}H_{15}ClNO$ $[M + H]^+$ 248.0842; found 248.0838.

(±)-1-But-3-enyl-5-phenylsulfanyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4u): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:7) to give **4u** (81%) as a yellow oil that darkened on standing. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 2.15–2.22 (m, 2 H, CH_2), 2.74 (dt, *J* = 13.7, 7.2 Hz, 1 H, NC*H*H), 3.03 (dt, *J* = 21.2, 2.7 Hz, 1 H, C*H*H-3), 3.13 (ddd, *J* = 21.2, 5.6, 1.7 Hz, 1 H, CH*H*-3), 4.00 (ddd, *J* = 13.7, 7.8, 6.8 Hz, 1 H, NCH*H*), 4.13 (ddt, *J* = 5.6, 2.7, 1.2 Hz, 1 H, CH-6), 4.93–5.02 (m, 2 H, =CH_2), 5.10 (dt, *J* = 17.0, 0.9 Hz, 1 H, =C*H*H), 5.23 (d, *J* = 10.0 Hz, 1 H, =CH*H*), 5.66 (ddt, *J* = 17.1, 10.0, 6.8 Hz, 1 H, =CH), 5.73 (ddd, *J* = 17.1, 10.0, 6.8 Hz, 1 H, =CH), 6.09 (dd, *J* = 5.4, 2.7 Hz, 1 H, =CH-4), 7.26–7.40 (m, 5 H, C_6H_5) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 31.89 (CH_2), 33.91 (CH_2-3), 44.60 (NCH_2), 63.56 (CH-6), 116.82, 117.34 (2 =CH_2), 127.51 (C_6H_5), 128.25 (=CH-4), 129.31 (C_6H_5), 130.58 (C-5), 130.70 (C_6H_5), 133.30 (C_6H_5), 134.11, 135.00 (2 =CH), 167.37 (C=O) ppm. GC–MS (EI, 70 eV): *m*/*z* (%) = 285 (42) $[M]^+$, 284 (55), 244 (100), 230 (15), 216 (12), 187 (65), 176 (27), 154 (14), 111 (25), 109 (21), 106 (26), 77 (25). IR (film): $\tilde{\nu}$ = 3072 (w), 2980 (w), 2936 (w), 1658 (s), 1582 (w), 1468 (m), 1440 (m), 1406 (m), 1248 (m), 994 (w), 920 (m), 816 (w), 746 (m), 692 (m) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{17}H_{20}NOS$ $[M + H]^+$ 286.1266; found 286.1274.

(±)-5-Chloro-1-phenyl-6-vinyl-3,6-dihydropyridin-2(1*H*)-one (4w): The crude product was purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate, 1:7) to give **4w** (84%) as a thick brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, 23 °C): δ = 3.16–3.31 (m, 2 H, CH_2-3), 4.59 (dm, *J* = 7.8 Hz, 1 H, CH-6), 5.11 (d, *J* = 17.1 Hz, 1 H,

=C*H*H), 5.24 (d, J = 10.0 Hz, 1 H, =CH*H*), 5.75 (ddd, J = 16.9, 10.0, 7.8 Hz, 1 H, =CH), 6.01 (dd, J = 5.1, 3.2 Hz, 1 H, =CH-4), 7.19–7.24 (m, 2 H, C_6H_5), 7.28–7.33 (m, 1 H, C_6H_5), 7.37–7.43 (m, 2 H, C_6H_5) ppm. ^{13}C NMR (100.6 MHz $CDCl_3$): δ = 33.42 (CH_2-3), 69.28 (CH-6), 120.18 (=CH_2), 120.80 (=CH-4), 127.54 (=C-5), 127.71, 127.84, 129.28 (C_6H_5), 133.47 (=CH), 140.43 (C_6H_5), 166.19 (C=O) ppm. GC–MS (EI, 70 eV): *m/z* (%) = 235 (26) [M + 2]$^+$, 234 (18) [M + 1]$^+$, 233 (78) [M]$^+$, 206 (36), 198 (21), 143 (24), 119 (18), 115 (17), 79 (100), 77 (74), 51 (23). IR (film): $\tilde{\nu}$ = 3064 (w), 1660 (s), 1596 (w), 1496 (m), 1422 (m), 1402 (s), 1326 (w), 1274 (m), 1256 (m), 1232 (w), 1148 (w), 1074 (w), 1040 (w), 1016 (w), 988 (w), 932 (w), 836 (w), 796 (w), 754 (m), 696 (m) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{13}H_{13}ClNO$ [M + H]$^+$ 234.0686; found 234.0688.

Supporting Information (see footnote on the first page of this article): Experimental procedures, analysis data, and NMR spectra.

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