JOC The Journal of Organic Chemistry

ARTICLE

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Synthesis of Functionalized Pyridazin-3(2*H*)-ones via Selective Bromine−Magnesium Exchange and Lactam Directed Ortho C−H Magnesiation

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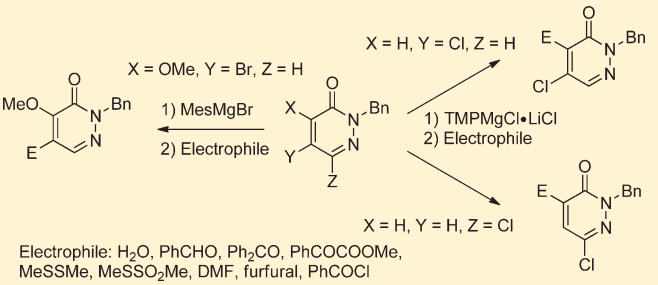
Supporting Information

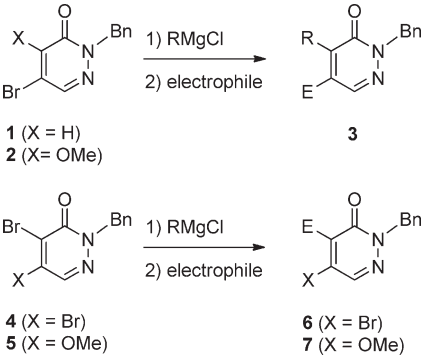
ABSTRACT: Selective bromine−magnesium exchange on 2-benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one could be achieved when MesMgBr was used as reagent. With more nucleophilic RMgCl species (R = Bu, *i*-Pr, Ph) both nucleophilic addition−elimination at C-4 and bromine−magnesium exchange at C-5 occurred. In 2-benzyl-5-bromopyridazin-3(2*H*)-one, which does not contain a substituent at C-4, addition could not be suppressed. Less nucleophilic Mg amides (TMPMgCl·LiCl) allowed regioselective C−H magnesiation at the C-4 position in such substrates, as exemplified for 2-benzyl-5-chloro- and 2-benzyl-6-chloropyridazin-3(2*H*)-one. Quenching of the magnesiated pyridazinones with electrophiles gives access to a variety of hitherto unknown pyridazin-3(2*H*)-one derivatives.



INTRODUCTION

The pyridazin-3(2*H*)-one nucleus can be considered as a privileged scaffold in agrochemistry. The available synthetic methods to selectively C-functionalize this core are limited, however.[1] Therefore, our group has an ongoing research program in which we aim to develop new functionalization methods via the reaction of halopyridazin-3(2*H*)-ones with organomagnesium species. In our previous reports we disclosed that RMgCl (R = alkyl, phenyl) species preferentially behave as nucleophiles rather than as halogen−magnesium exchange reagents when added to 5-bromopyridazin-3(2*H*)-one substrates (2-benzyl-5-bromopyridazin-3(2*H*)-one (**1**) and 2-benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one (**2**)).[2,3] The nucleophilic attack occurred regioselectively at C-4, which can be rationalized by taking into account a precoordination of the Grignard reagent to the oxygen atom of the lactam moiety of the pyridazinone, favoring an intramolecular reaction.[4] In addition this coordination increases both the nucleophilicity of the magnesium reagent and the electrophilicity of C-4 of the substrate. Thus, for 2-benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one (**2**) substitution of the methoxy group via S_NAE (nucleophilic substitution via addition elimination) preferentially occurred (Scheme 1).[2] Even in the case of 2-benzyl-5-bromopyridazin-3(2*H*)-one (**1**), in which no formal leaving group is present at C-4, nucleophilic addition still took place at this position (Scheme 1).[3] Subsequent quenching with electrophiles followed by HBr elimination (cine substitution) allowed for double functionalizations (C-4 and C-5) starting from **1** (Scheme 1). Only when a bromine atom was present at C-4, as in 2-benzyl-4,5-dibromopyridazin-3(2*H*)-one (**4**) and 2-benzyl-4-bromo-5-methoxypyridazin-3(2*H*)-one (**5**), can bromine−magnesium exchange be selectively achieved with the same RMgCl species (Scheme 1).[2] In these brominated substrates bromine−magnesium exchange at C-4 is faster than the competitive nucleophilic addition.

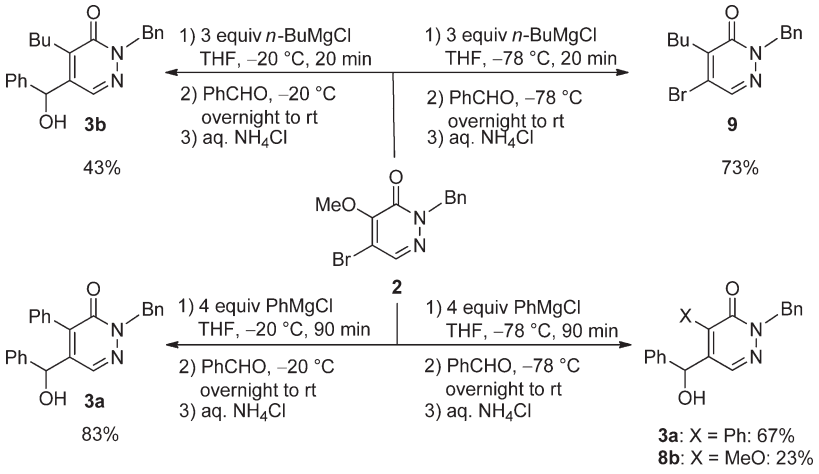
Scheme 1. Summary of Previous Research of the Reaction of Bromopyridazin-3(2*H*)-ones with RMgCl Species (R = Bu, *i*-Pr, Ph)



As a natural progression in this research area, we postulated whether less nucleophilic magnesium species would circumvent nucleophilic addition at C-4 in 5-bromopyridazin-3(2*H*)-ones. If this addition reaction could be suppressed, a hitherto unknown selective bromine−magnesium exchange at the C-5 position of

Received: May 18, 2011
Published: July 06, 2011

Scheme 2. Temperature Dependence (−20 °C versus −78 °C) of the S_NAE at C-4 and the Bromine−Magnesium Exchange at C-5 of 2-Benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one (2) in the Reaction with RMgCl Reagents (R = Bu versus R = Ph)



the scaffold that does not affect C-4 becomes feasible. In addition, this could open new ways of functionalizing the pyridazin-3(2*H*)-one core via a direct magnesiation at C-4 without preactivation with bromine atoms. This is unprecedented in the pyridazine series. In this paper we disclose our results dealing with the selectivity of the reaction of magnesium compounds with pyridazin-3(2*H*)-ones by varying the type of magnesium reagent.

RESULTS AND DISCUSSION

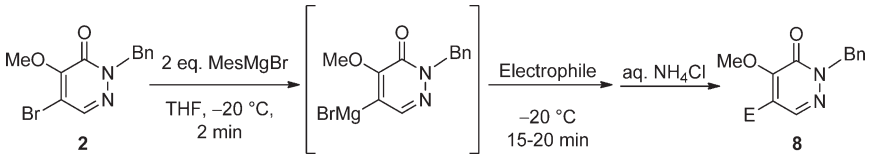
As mentioned in the Introduction, we previously reported that 2-benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one (**2**) undergoes an unusual double reaction with RMgCl reagents (R = *n*-Bu, *i*-Pr, Ph). The first step is a nucleophilic substitution of the C-4 methoxy group via an addition−elimination reaction for the R group of the Grignard reagent, followed by a bromine−magnesium exchange at C-5.[2] When this magnesium salt is quenched with an electrophile, this protocol smoothly allows double functionalizations of the pyridazin-3(2*H*)-one core to be performed with a variety of Grignard reagents and electrophiles in a one-pot approach (see Scheme 2 for two examples with benzaldehyde as electrophile). When the least nucleophilic Grignard reagent of the set (PhMgCl) was used, we observed that at a lower reaction temperature the nucleophilic substitution could be slowed down while bromine−magnesium exchange still occurred, as exemplified by reaction of **2** with PhMgCl at −78 °C, followed by quenching with benzaldehyde, which yielded a mixture of 2-benzyl-5-[hydroxy(phenyl)methyl]-4-phenylpyridazin-3(2*H*)-one (**3a**; 67%) and 2-benzyl-5-[hydroxy(phenyl)methyl]-4-methoxypyridazin-3(2*H*)-one (**8b**; 23%) (Scheme 2). In contrast, with more nucleophilic aliphatic RMgCl reagents, such as *n*-BuMgCl, only substitution of the methoxy group was observed at −78 °C, yielding 2-benzyl-5-bromo-4-butylpyridazin-3(2*H*)-one (**9**) (Scheme 2). On this basis, we proposed that the use of a more sterically hindered aryl Grignard reagent would allow a complete suppression of the S_NAE reaction at C-4, which would give access to a variety of novel 5-substituted 2-benzyl-4-methoxypyridazin-3(2*H*)-ones. These compounds are interesting building blocks, as we have previously shown that a methoxy group is an example of a PMF (provisionally masked functionality).[5] The regioselective introduction of a methoxy group, which can be easily achieved in dioxane as solvent,[2] temporarily protects C-4 of **4** for bromine−magnesium exchange and thereby allows a regioselective reaction at C-5 (rather than at C-4 as observed in 2-benzyl-4,5-dibromopyridazin-3(2*H*)-one (**4**))[2] but afterward still permits further functionalization at C-4 by direct substitution or by an initial chemical transformation of the methoxy group into a better leaving group (e.g., triflate).[5]

Commercially available MesMgBr (mesitylmagnesium bromide), which possesses a nucleophilic character lower than that of PhMgCl, seemed to be a suitable candidate to meet our requirements. This reagent has hitherto been used as a non-nucleophilic carbon-centered base, as an organometallic coupling partner in Kumada reactions and in halogen−metal exchange reactions.[6] Gratifyingly, when substrate **2** was used with MesMgBr, only bromine−magnesium exchange was observed, as desired. Remarkably, even at −20 °C, which is the temperature previously applied for the tandem protocol, only exchange occurred, as judged by quenching with water (Table 1, entry 1). The use of MesMgBr allows us for the first time to selectively magnesiate the C-5 position of a pyridazin-3(2*H*)-one without additional nucleophilic attack at C-4. Optimal reaction conditions at −20 °C involve the addition of 2.0 equiv of MesMgBr and an exchange reaction time of 2 min before the electrophile was added. The in situ generated (1-benzyl-5-methoxy-6-oxo-1,6-dihydropyridazin-4-yl)magnesium bromide could be reacted smoothly with a variety of electrophiles, benzaldehyde, benzophenone, methyl oxo(phenyl)acetate, and Me_2S_2, giving the corresponding 5-substituted 2-benzyl-4-methoxypyridazin-3(2*H*)-ones (**8**) in excellent yields (Table 1, entries 2−5). Addition of dimethyl sulfate as the electrophile gave a moderate yield of 2-benzyl-5-methoxy-4-methylpyridazin-3(2*H*)-one (**8f**) (Table 1, entry 6).

We have previously described that regioisomeric (2-benzyl-5-methoxy-3-oxo-2,3-dihydropyridin-4-yl)magnesium halide gave two different reaction products when using DMF as the electrophile, depending on the workup procedure applied.[2,7] When aqueous NH_4Cl was added, the expected 2-benzyl-5-methoxy-3-oxo-2,3-dihydropyridazine-4-carbaldehyde was isolated. Upon use of methanol to quench the reaction mixture, however, 2-benzyl-5-(dimethylamino)-3-oxo-2,3-dihydropyridazine-4-carbaldehyde was formed. When this methodology was applied

dx.doi.org/10.1021/jo201009m |*J. Org. Chem.* 2011, 76, 6670–6677

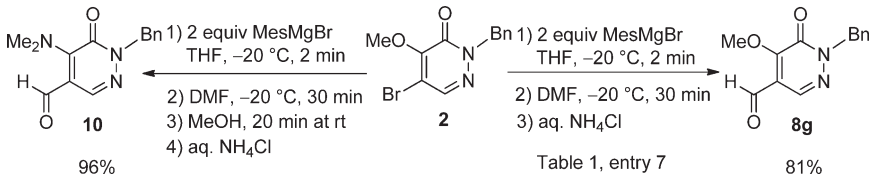
Table 1. Functionalization of 2-Benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one (2) via Bromine−Magnesium Exchange with MesMgBr[a]



entry	electrophile	E	8	yield (%)
1	H_2O	H	**8a**	99
2	PhCHO	PhCH(OH)	**8b**	90
3	Ph_2CO	$Ph_2C(OH)$	**8c**	95
4	PhCOCOOMe	PhC(OH)COOMe	**8d**	91
5	MeSSMe	SMe	**8e**	82
6	Me_2SO_4	Me	**8f**	49
7	DMF	CHO	**8g**	81

[a] Conditions: **2** (1 mmol), 2.0 mL of 1 M MesMgCl (2 equiv), THF (4 mL), −20 °C, 2 min; electrophile (3.0 equiv), −20 °C, 15−20 min; aqueous NH_4Cl.

Scheme 3. Dependence of the Reaction Product Formation on the Workup Procedure after Quenching of (1-Benzyl-5-methoxy-6-oxo-1,6-dihydropyridazin-4-yl)magnesium Bromide with DMF



to (1-benzyl-5-methoxy-6-oxo-1,6-dihydropyridin-4-yl)magnesium bromide, a similar reactivity was observed (Table 1, entry 7, and Scheme 3). The formation of reaction products **8g** and **10** can be rationalized on the basis of the different decomposition pathways of the deprotonated hemiaminal, generated by quenching (1-benzyl-5-methoxy-6-oxo-1,6-dihydropyridazin-4-yl)magnesium bromide with DMF, upon addition of aqueous NH_4Cl or MeOH as a proton source.

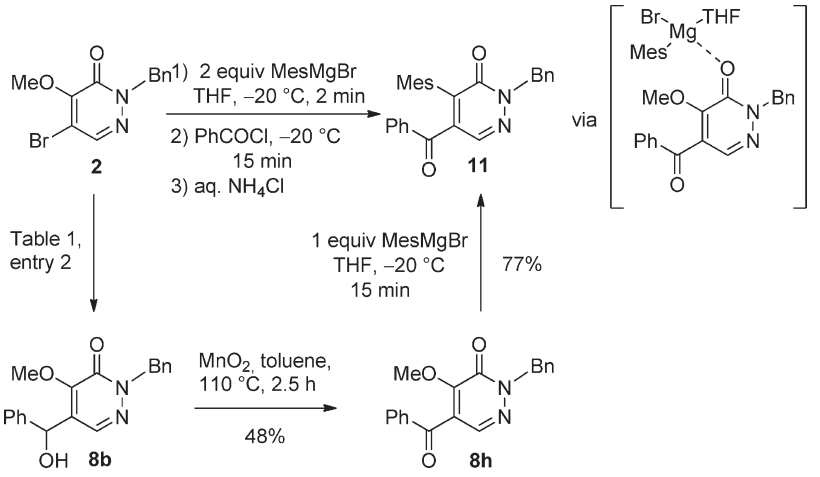
When benzoyl chloride was applied as the electrophile, 5-benzoyl-2-benzyl-4-mesitylpyridazin-3(2*H*)-one (**11**) was isolated as the sole reaction product (Scheme 4). This can be rationalized by considering that the reaction of (1-benzyl-5-methoxy-6-oxo-1,6-dihydropyridazin-4-yl)magnesium bromide with benzoyl chloride initially yields 5-benzoyl-2-benzyl-4-methoxypyridazin-3(2*H*)-one (**8h**) (Scheme 4). The α,β-unsaturated ketone functionality in **8h** subsequently reacts with MesMgBr at C-4 of the pyridazinone (1,4-addition). Although a preferential 1,2-addition is expected for hard nucleophiles in reaction with α,β-unsaturated ketones, the precomplexation of MesMgBr to the lactam oxygen explains the selective and preferential formation of **11**. The reaction of independently synthesized 5-benzoyl-2-benzyl-4-methoxypyridazin-3(2*H*)-one (**8h**) with MesMgBr supports this interpretation (Scheme 4).

Interestingly, the substituent present in C-4 seems to be crucial to suppress nucleophilic addition. When MesMgBr was used to magnesiate C-4 in 2-benzyl-5-bromopyridazin-3(2*H*)-one (**1**) substrate, no bromine−magnesium exchange was observed, only nucleophilic attack at C-4 by the Grignard reagent (even up to −78 °C), resulting in a double functionalization of the pyridazin-3(2*H*)-one upon quenching with electrophiles (Scheme 5).[3] As the use of MesMgBr did not suppress the nucleophilic addition at C-4 in **1**, it was proposed that even less nucleophilic magnesium reagents could be compatible with the electrophilic pyridazin-3(2*H*)-one scaffold and potentially allow a magnesiation via deprotonation in this position. TMPMgCl·LiCl is an example of such a reagent with a low nucleophilic character known to allow direct magnesiation of (hetero)arenes.[8] On the basis of the assumed precomplexation of magnesium species to the lactam moiety of pyridazin-3(2*H*)-ones it was hypothesized that a regioselective directed ortho C-4 magnesiation could be achieved on our scaffold. The easily accessible 5-chloro- (**13**)[9] and 6-chloro-2-benzylpyridazin-3(2*H*)-one (**15**)[3,10] were chosen as the substrates, since the chlorine atom permits further functionalization of the pyridazinone core via S_NAE and Pd-catalyzed cross-coupling reactions.[1,11,12] Moreover, chloro derivatives are cheaper than their corresponding bromo analogues.

The directed ortho magnesiation of **13** was found to proceed optimally when the pyridazinone solution was added rapidly to a cooled TMPMgCl·LiCl solution, followed by stirring the mixture for 30 s at −20 °C prior to addition of the electrophile. It was determined that 2.0 equiv of TMPMgCl·LiCl was necessary to push the metalation of **13** to completion. The same optimized protocol was applied to **15**, but in this case a much shorter metalation time was required. Instantly after adding **15** to TMPMgCl·LiCl at −20 °C, electrophile was added. Longer metalation reaction times were, for both substrates **13** and **15**, found to be ineffective; no desired reaction product could be isolated, pointing to a rapid decomposition of the magnesiated

dx.doi.org/10.1021/jo201009m |*J. Org. Chem.* 2011, 76, 6670–6677

Scheme 4. Formation of 5-Benzoyl-2-benzyl-4-mesitylpyridazin-3(2*H*)-one (11) via Quenching of (1-Benzyl-5-methoxy-6-oxo-1,6-dihydropyridazin-4-yl)magnesium Bromide, Synthesized from 2 via Reaction with MesMgBr, with Benzoyl Chloride



Scheme 5. Effect of the Substituent Present in C-4 on the Reaction of 5-Bromopyridazin-3(2*H*)-ones with MesMgBr: Nucleophilic Addition versus Bromine−Magnesium Exchange

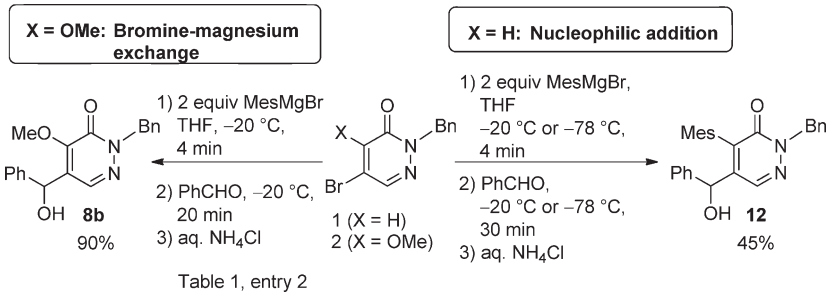
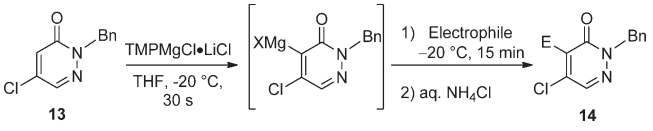


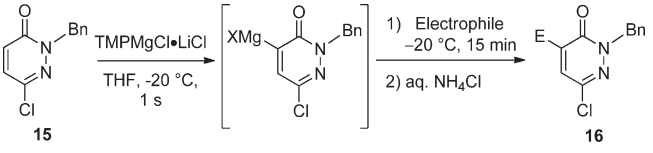
Table 2. Directed Ortho C−H Magnesiation in 2-Benzyl-5-chloropyridazin-3(2*H*)-one (13) with TMPMgCl·LiCl[a]



entry	electrophile	E	14	yield (%)
1	$MeSSO_2Me$	SMe	**14a**	44
2	PhCHO	PhCH(OH)	**14b**	52
3	furfural	$(C_4H_3O)CH(OH)$	**14c**	48
4	PhCOCOOMe	PhC(OH)COOMe	**14d**	37
5	PhCOCl	PhCO	**14e**	42[b]

[a] Conditions: **13** (1 mmol), 2.0 mL of 1 M TMPMgCl·LiCl (2 equiv), THF (4 mL), −20 °C, 30 s; electrophile (3.0−8.6 equiv), −20 °C, 15 min; aqueous NH_4Cl. [b] 10.0 equiv.

Table 3. Directed Ortho C−H Magnesiation in 2-Benzyl-6-chloropyridazin-3(2*H*)-one (15) with TMPMgCl·LiCl[a]



entry	electrophile	E	16	yield (%)
1	$MeSSO_2Me$	SMe	**16a**	66
2	PhCHO	PhCH(OH)	**16b**	54
3	furfural	$(C_4H_3O)CH(OH)$	**16c**	61
4	PhCOCOOMe	PhC(OH)COOMe	**16d**	58
5	PhCOCl	PhCO	**16e**	49[b]

[a] Conditions: **15** (1 mmol), 2.0 mL of 1 M TMPMgCl·LiCl (2 equiv), THF (4 mL), −20 °C, 1 s; electrophile (3.0−8.6 equiv), −20 °C, 15 min; aqueous NH_4Cl. [b] 10.0 equiv.

pyridazinones. A range of electrophiles (*S*-methyl methanesulfonothioate, benzaldehyde, furfural, methyl oxo(phenyl)acetate, and benzoyl chloride) were tested under these optimized reaction conditions, giving the corresponding 4-substituted 5- and 6-chloropyridazin-3(2*H*)-ones **14** and **16** in moderate to good yields (Tables 2 and 3, entries 1−5). It is important to note that *S*-methyl methanesulfonothioate has to be selected as an electrophile to introduce a methylthio group, and not dimethyl disulfide,

dx.doi.org/10.1021/jo201009m |*J. Org. Chem.* 2011, 76, 6670–6677

since upon addition of the latter a nucleophile (thiomethoxide) will be created in situ which will substitute the chlorine atom in the desired reaction product, giving rise to undesired 2-benzyl-4,5-bis(methylthio)- and 2-benzyl-4,6-bis(methylthio)pyridazin-3(2*H*)-one. The regioselectivity of the direct functionalization process was unambiguously proven by hydrogenolysis of the chlorine atom in the reaction products **14** and **16** (H_2, Pd/C). After all, in ^{1}H NMR J_{4-5}, J_{4-6}, and J_{5-6} have very typical values, in the 8−10, 1−3, and 3−6 Hz regions, respectively.[1,13]

CONCLUSION

Our results show that selective bromine−magnesium exchange in 2-benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one (**6**) is possible with the bulky arylmagnesium reagent MesMgBr. With more nucleophilic RMgCl reagents (R = alkyl, phenyl) nucleophilic addition at C-4 cannot be avoided. In addition, we have shown that precoordination of Grignard reagents to the lactam moiety of pyridazin-3(2*H*)-ones can be exploited to achieve regioselective directed C−H magnesiation at the C-4 position of C-5 and C-6 substituted pyridazin-3(2*H*)-ones **13** and **15**, when using TMPMgCl·LiCl as base. The presented synthetic methods further expand the limited functionalization procedures of the pyridazin-3(2*H*)-one scaffold hitherto available.

EXPERIMENTAL SECTION

General Considerations. All melting points reported were determined on a melting point apparatus and are uncorrected. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer in the solvent indicated with TMS as the internal standard. *J* values are given in hertz, and the chemical shifts are given in ppm. For high-resolution mass-spectrometric analysis, samples were dissolved in CH_3OH/CH_3CN (50/50) containing 0.1% formic acid and diluted to a concentration of approximately 10^{-5} mol/L. A 2 μL portion was injected using the CapLC system and electrosprayed through the nanoelectrospray source. The nanoelectrospray source was operated in positive ion mode at an electrospray potential of 1.7 kV. The eluents used were 30% A (H_2O with 0.1% formic acid) and 70% B (ACN/H_2O (95/5) with 0.1% formic acid) at a flow rate of 6 μL/min. Samples were injected at an interval of 3 min. Before analysis and after each seventh sample a 2 μL volume of a 0.025% H_3PO_4 solution (50/50 MeOH/H_2O) was injected that could be used as a lock mass. The MS was calibrated prior to use with a 0.015% H_3PO_4 solution. The spectra were lock mass corrected using the known mass of the nearest H_3PO_4 cluster. Flash column chromatography was performed on Kieselgel 60 or using an automated chromatography system with silica flash cartridges. Benzaldehyde and furfural were freshly distilled before use, and benzophenone was recrystallized from isopropyl alcohol. Dry THF on molecular sieves was obtained from a commercial source. The Grignard reagents *n*-BuMgCl, mesitylmagnesium bromide, and TMPMgCl·LiCl were obtained from a commercial source as solutions in THF. Crystallographic data for structures **14c** and **16a** have been deposited with the Cambridge Crystallographic Data Centre.

General Procedure 1 for Functionalization of 2-Benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one (2). 2-Benzyl-5-bromo-4-methoxypyridazin-3(2*H*)-one (**2**; 0.295 g, 1.0 mmol) was brought into a dry 25 mL double-necked flask and placed under an argon atmosphere using a Schlenk apparatus. Subsequently THF (4 mL) was added and the solution was cooled to −20 °C (ice−salt bath). Mesitylmagnesium bromide (2.00 mL, 1 M solution) was quickly added via a syringe. The mixture was stirred for 2 min, after which electrophile (3.00 mmol) was added. The reaction mixture was subsequently stirred at −20 °C until reaction was completed. The resulting mixture was quenched with aqueous NH_4Cl, extracted with EtOAc (3 × 50 mL), and subsequently dried over $MgSO_4$. The organic phase was evaporated to dryness under reduced pressure and the residue separated with an automated chromatography system using silica flash cartridges applying a heptane/ethyl acetate gradient (from 100% heptane to 100% ethyl acetate in 25 min, 25 mL/min).

2-Benzyl-4-methoxypyridazin-3(2*H*)-one (8a). General procedure 1 was followed using water (0.054 mL, 3.00 mmol) as the electrophile. The reaction time was 30 min. Compound **8a** was obtained in 99% (0.214 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.62 (d, 1H, *J* = 4.8 Hz), 7.40 (d, 2H, *J* = 7.9 Hz), 7.31−7.20 (m, 3H), 6.32 (d, 1H, *J* = 4.8 Hz), 5.32 (s, 2H), 3.80 (s, 3H). Mp: 75−76 °C. HRMS (ESI) for $C_{12}H_{12}N_2O_2$ $[M + H]^+$: *m*/*z* calcd 217.0972, found 217.0977. ^{13}C NMR ($CDCl_3$): δ 156.9, 156.1, 136.8, 136.3, 128.7, 128.5, 127.8, 104.1, 56.2, 55.0.

2-Benzyl-5-[hydroxy(phenyl)methyl]-4-methoxypyridazin-3(2*H*)-one (8b).[2] General procedure 1 was followed using benzaldehyde (0.318 mL, 3.00 mmol) as the electrophile. The reaction time was 30 min. Compound **8b** was obtained in 90% (0.290 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.92 (s, 1H), 7.37 (m, 2H), 7.38−7.19 (m, 8H), 5.88 (s, 1H), 5.23 (d, 1H, *J* = 13.7 Hz), 5.15 (d, 1H, *J* = 13.7 Hz), 3.93 (s, 3H), 3.68 (bs, 1H). Mp: 96−97 °C. HRMS (ESI) for $C_{19}H_{18}N_2O_3$ $[M + H]^+$: *m*/*z* calcd 323.1390, found 323.1396. ^{13}C NMR ($CDCl_3$): δ 157.6, 150.6, 141.7, 136.7, 136.0, 132.6, 128.7, 128.6, 128.5, 128.0, 127.9, 126.0, 67.9, 59.7, 55.3.

2-Benzyl-5-[hydroxy(diphenyl)methyl]-4-methoxypyridazin-3(2*H*)-one (8c). General procedure 1 was followed using benzophenone (0.547 g, 3.00 mmol) as the electrophile. The reaction time was 30 min. Compound **8c** was obtained in 81% (0.323 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.42 (m, 2H), 7.30 (m, 13H), 7.18 (s, 1H), 5.27 (s, 2H), 4.56 (s, 1H), 3.70 (s, 3H). Mp: 107−108 °C. HRMS (ESI) for $C_{25}H_{22}N_2O_3$ $[M + H]^+$: *m*/*z* calcd 399.1703, found 399.1698. ^{13}C NMR ($CDCl_3$): δ 157.6, 152.3, 144.2, 137.5, 136.3, 135.9, 128.9, 128.6, 128.2, 128.0, 127.9, 127.3, 79.6, 59.5, 55.3.

Methyl (1-Benzyl-5-methoxy-6-oxo-1,6-dihydropyridazin-4-yl)(hydroxy)phenylacetate (8d). General procedure 1 was followed using methyl 2-oxo-2-phenylacetate (0.225 mL, 3.00 mmol) as the electrophile. The reaction time was 30 min. Compound **8d** was obtained in 91% (0.346 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.59 (m, 2H), 7.33 (m, 8H), 7.20 (s, 1H), 5.26 (s, 2H), 4.42 (s, 1H), 4.12 (s, 3H), 3.80 (s, 3H). Mp: 108−109 °C. HRMS (ESI) for $C_{21}H_{20}N_2O_5$ $[M + H]^+$: *m*/*z* calcd 381.1445, found 381.1442. ^{13}C NMR ($CDCl_3$): δ 173.5, 157.6, 152.6, 137.6, 137.1, 135.9, 131.4, 131.1, 128.9, 128.6, 128.5, 128.0, 126.7, 76.4, 60.1, 55.3, 53.7.

2-Benzyl-4-methoxy-5-(methylthio)pyridazin-3(2*H*)-one (8e). General procedure 1 was followed using 1,2-dimethyl disulfide (0.227 mL, 3.00 mmol) as the electrophile. The reaction time was 30 min. Compound **8e** was obtained in 82% (0.215 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.61 (s, 1H), 7.42 (dd, 2H, *J* = 7.7, 1.6 Hz), 7.30 (m, 3H), 5.25 (s, 2H), 2.63 (s, 3H), 2.51 (s, 3H). Mp: 142−143 °C. HRMS (ESI) for $C_{13}H_{14}N_2O_2S$ $[M + H]^+$: *m*/*z* calcd 263.0849, found 263.0860. ^{13}C NMR ($CDCl_3$): δ 157.3, 145.4, 136.2, 131.8, 131.3, 128.7, 128.6, 127.9, 55.4, 16.0, 15.1.

2-Benzyl-4-methoxy-5-methylpyridazin-3(2*H*)-one (8f).[14] General procedure 1 was followed using dimethyl sulfate (0.285 mL, 3.00 mmol) as the electrophile. The reaction time was 30 min. Compound **8f** was obtained in 81% (0.186 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.54 (s, 1H), 7.40 (m, 2H), 7.32−7.21 (m, 3H), 5.28 (s, 2H), 4.12 (s, 3H), 2.05 (s, 3H). Mp: 40−41 °C. HRMS (ESI) for $C_{13}H_{14}N_2O_2$ $[M + H]^+$: *m*/*z* calcd 231.1128, found 231.1139. ^{13}C NMR ($CDCl_3$): δ 157.7, 152.6, 140.0, 136.5, 128.6, 128.5, 127.8, 126.9, 59.7, 55.0, 12.4.

1-Benzyl-5-methoxy-6-oxo-1,6-dihydropyridazine-4-carbaldehyde (8g). General procedure 1 was followed using *N*,*N*-dimethylformamide (0.219 mL, 3.00 mmol) as the electrophile.

The reaction time was 30 min. Compound **8g** was obtained in 91% (0.222 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 10.31 (s, 1H), 7.99 (s, 1H), 7.41 (m, 2H), 7.33−7.24 (m, 3H), 5.26 (s, 2H), 4.43 (s, 3H). Mp: 99−100 °C. HRMS (ESI) for $C_{13}H_{12}N_2O_3$ $[M + H]^+$: m/z calcd 245.0921, found 245.0920. ^{13}C NMR ($CDCl_3$): δ 187.9, 157.9, 157.9, 135.7, 133.6, 128.7, 128.6, 128.1, 120.3, 61.7, 55.7.

1-Benzyl-5-(dimethylamino)-6-oxo-1,6-dihydropyridazine-4-carbaldehyde (10). General procedure 1 was followed using *N*,*N*-dimethylformamide (0.219 mL, 3.00 mmol) as the electrophile. After 30 min prior to quenching with aqueous NH_4Cl, methanol (10 mL) was added and stirring was continued for another 20 min and then the reaction mixture was quenched with aqueous NH_4Cl. Compound **10** was obtained in 96% (0.247 g) yield. Yellow oil. ^{1}H NMR ($CDCl_3$): δ 9.80 (s, 1H), 7.88 (s, 1H), 7.41 (m, 2H), 7.33−7.23 (m, 3H), 5.21 (s, 2H), 3.35 (s, 6H). HRMS (ESI) for $C_{14}H_{15}N_3O_2$ $[M + H]^+$: m/z calcd 258.1237, found 258.1185. ^{13}C NMR ($CDCl_3$): δ 186.4, 158.2, 147.6, 138.8, 136.4, 128.5, 128.5, 127.8, 113.3, 55.6, 46.1.

5-Benzoyl-2-benzyl-4-methoxypyridazin-3(2*H*)-one (8h). A 0.289 g portion (0.897 mmol) of 2-benzyl-5-[hydroxy(diphenyl)-methyl]-4-methoxypyridazin-3(2*H*)-one (**8b**) was dissolved in dry toluene (10 mL), and MnO_2 (0.26 g) was added to this solution. The reaction mixture was refluxed for 2.5 h using a Dean−Stark apparatus. After the reaction mixture was cooled to room temperature, it was filtered and evaporated to dryness under reduced pressure; the residue was separated with an automated chromatography system using silica flash cartridges applying a heptane/ethyl acetate gradient (from 100% heptane to 100% ether in 25 min, 25 mL/min). The yield of the benzoyl derivative **8h** was 0.138 g (48%). Colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.87−7.83 (m, 2H), 7.69 (s, 1H), 7.67−7.62 (m, 1H), 7.53−7.47 (m, 4H), 7.40−7.30 (m, 3H), 5.37 (s, 2H), 4.04 (s, 3H). HRMS (ESI) for $C_{19}H_{16}N_2O_3$ $[M + H]^+$: m/z calcd 321.1234, found 321.1237. ^{13}C NMR ($CDCl_3$): δ 191.8, 157.6, 152.7, 136.1, 135.9, 135.6, 134.4, 129.6, 128.9, 128.8, 128.7, 128.1, 124.6, 60.7, 55.6.

5-Benzoyl-2-benzyl-4-mesitylpyridazin-3(2*H*)-one (11). (a) General procedure 1 was followed using benzoyl chloride (0.219 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **11** was obtained in 71% (0.290 g) yield.

(b) 5-Benzoyl-2-benzyl-4-methoxypyridazin-3(2*H*)-one (0.138 g, 0.431 mmol) was dissolved in 2 mL of THF and the solution cooled to −20 °C. A 0.52 mL portion (1 M solution in THF) of mesitylmagnesium bromide was added via a syringe. The reaction mixture was stirred for 15 min. The resulting mixture was quenched with aqueous NH_4Cl. The aqueous phase was then extracted with EtOAc (3 × 50 mL) and subsequently dried over $MgSO_4$. The organic phase was evaporated to dryness under reduced pressure and the residue separated with an automated chromatography system using silica flash cartridges applying a heptane/ethyl acetate gradient (from 100% heptane to 100% ethyl acetate in 25 min, 25 mL/min). Compound **11** was obtained in 77% (0.136 g) yield. Yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.82 (s, 1H), 7.66−7.61 (m, 2H), 7.55−7.47 (m, 3H), 7.40−7.29 (m, 5H), 6.69 (s, 2H), 5.44 (s, 2H), 2.14 (s, 3H), 1.98 (s, 6H). HRMS (ESI) for $C_{27}H_{24}N_2O_2$ $[M + H]^+$: m/z calcd 409.1911, found 409.1889. ^{13}C NMR ($CDCl_3$): δ 192.4, 171.6, 159.6, 140.2, 138.3, 136.2, 135.8, 135.2, 134.1, 133.6, 130.2, 129.2, 128.9, 128.7, 128.5, 128.4, 128.2, 128.0, 21.0, 20.1.

2-Benzyl-5-[hydroxy(phenyl)methyl]-4-mesitylpyridazin-3(2*H*)-one (12). 2-Benzyl-5-bromopyridazin-3(2*H*)-one (**5**; 0.265 g, 1.0 mmol) was brought into a dry 25 mL double-necked flask and placed under an argon atmosphere using a Schlenk apparatus. Subsequently THF (4 mL) was added and the solution was cooled to −78 °C (acetone-dry ice bath). Mesitylmagnesium bromide (2.00 mL, 1 M solution) was quickly added via a syringe. The mixture was stirred for 4 min, after which benzaldehyde (0.30 mL, 3.0 mmol) was added. The reaction mixture was subsequently stirred at −78 °C for 30 min. The resulting mixture was quenched with aqueous NH_4Cl, extracted with EtOAc (3 × 50 mL), and subsequently dried over $MgSO_4$. The organic phase was evaporated to dryness under reduced pressure and the residue separated with an automated chromatography system using silica flash cartridges applying a heptane/ethyl acetate gradient (from 100% heptane to 100% ethyl acetate in 25 min, 25 mL/min). Compound **12** was obtained in 45% (0.185 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 8.16 (s, 1H), 7.36−7.32 (m, 2H), 7.28−7.21 (m, 3H), 7.19−7.14 (m, 3H), 6.90−6.84 (m, 3H), 6.75 (bs, 1H), 5.27 (d, 1H, J = 13.7 Hz), 5.23 (d, 1H, J = 13.7 Hz), 5.15 (s, 1H), 3.09 (bs, 1H), 2.27 (s, 3H), 1.98 (s, 3H), 1.40 (s, 3H). Mp: 121−122 °C. HRMS (ESI) for $C_{27}H_{26}N_2O_2$ $[M + H]^+$: m/z calcd 411.2067, found 411.2065. ^{13}C NMR ($CDCl_3$): δ 159.3, 143.8, 140.8, 138.0, 137.7, 136.7, 136.6, 135.6, 134.4, 126.7, 128.5, 128.5, 128.5, 128.2, 127.7, 126.5, 71.5, 55.5, 21.1, 22.0, 19.1.

General Procedure 2 for Functionalization of 2-Benzyl-5-chloropyridazin-3(2*H*)-one (13). A dry 50 mL double-necked flask placed under an argon atmosphere using a Schlenk apparatus was charged with TMPMgCl·LiCl (2.00 mL, 1 M solution in THF) and cooled to −20 °C. 2-Benzyl-5-chloropyridazin-3(2*H*)-one (**13**; 0.221 g, 1.0 mmol) was brought into a second dry 25 mL double-necked flask and placed under an argon atmosphere using a Schlenk apparatus. Subsequently THF (2.00 mL) was added. The pyridazin-3(2*H*)-one solution was quickly added to the TMP solution (1 s), after which it was stirred for 30 s; subsequently the electrophile (3−8.6 mmol) was quickly added to this solution. The reaction mixture was stirred at room temperature until the reaction was complete. The resulting mixture was quenched with aqueous NH_4Cl. The aqueous phase was then extracted with EtOAc (3 × 50 mL) and subsequently dried over $MgSO_4$. The organic phase was evaporated to dryness under reduced pressure and the residue separated with an automated chromatography system using silica flash cartridges applying a heptane/ethyl acetate gradient (from 100% heptane to 100% ethyl acetate in 25 min, 25 mL/min).

2-Benzyl-5-chloro-4-(methylthio)pyridazin-3(2*H*)-one (14a). General procedure 2 was followed using *S*-methyl methanesulfonothioate (0.308 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **14a** was obtained in 45% (0.118 g) yield. Yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.66 (s, 1H), 7.43−7.39 (m, 2H), 7.35−7.27 (m, 3H), 5.27 (s, 2H), 2.74 (s, 3H). HRMS (ESI) for $C_{12}H_{11}ClN_2OS$ $[M + H]^+$: m/z calcd 289.0178, found 289.0178. ^{13}C NMR ($CDCl_3$): δ 158.2, 138.7, 136.0, 135.8, 135.2, 128.8, 128.7, 128.1, 55.7, 16.2.

2-Benzyl-5-chloro-4-[hydroxy(phenyl)methyl]pyridazin-3(2*H*)-one (14b). General procedure 2 was followed using benzaldehyde (0.304 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **14b** was obtained in 52% (0.170 g) yield. Orange oil. ^{1}H NMR ($CDCl_3$): δ 7.75 (s, 1H), 7.50−7.44 (m, 2H), 7.35−7.18 (m, 8H), 6.00 (d, 1H, J = 11.2 Hz), 5.86 (d, 1H, J = 11.2 Hz), 5.32 (d, 1H, J = 13.8 Hz), 5.10 (d, 1H, J = 13.8 Hz). HRMS (ESI) for $C_{18}H_{15}ClN_2O_2$ $[M + H]^+$: m/z calcd 349.0719, found 349.0720. ^{13}C NMR ($CDCl_3$): δ 159.8, 140.9, 138.4, 137.5, 135.4, 135.3, 128.8, 128.8, 128.7, 128.3, 128.2, 125.8, 72.2, 55.3.

2-Benzyl-5-chloro-4-[2-furyl(hydroxy)methyl]pyridazin-3(2*H*)-one (14c). General procedure 2 was followed using 2-furaldehyde (0.351 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **14c** was obtained in 48% (0.151 g) yield. Orange solid. ^{1}H NMR ($CDCl_3$): δ 7.77 (s, 1H), 7.40−7.34 (m, 2H), 7.33−7.23 (m, 4H), 6.34 (d, 1H, J = 3.3 Hz), 6.29 (dd, 1H, J = 3.3, 1.8 Hz), 5.99 (d, 1H, J = 11.2 Hz), 5.88 (d, 1H, J = 11.2 Hz), 5.36 (d, 1H, J = 13.7 Hz), 5.19 (d, 1H, J = 13.7 Hz). Mp: 98−99 °C. HRMS (ESI) for $C_{16}H_{13}ClN_2O_3$ $[M + H]^+$: m/z calcd 339.0500, found 339.0512. ^{13}C NMR ($CDCl_3$): δ 159.8, 152.9, 142.6, 137.4, 135.8, 135.8, 135.3, 128.8, 128.8, 128.3, 110.6, 107.4, 66.6, 55.3. The structure was unambiguously confirmed by single-crystal XRD analysis; see the Supporting Information and CCDC 832476.

Methyl (2-Benzyl-5-chloro-3-oxo-2,3-dihydropyridazin-4-yl)(hydroxy)phenylacetate (14d). General procedure 2 was followed using methyl 2-oxo-2-phenylacetate (0.428 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **14d** was obtained in 37% (0.141 g) yield. Yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.64 (s, 1H), 7.60−7.55 (m, 2H), 7.47−7.37 (m, 2H), 7.35−7.28 (m, 6H), 5.49 (bs, 1H), 5.31 (d, 1H, J = 13.4 Hz), 5.25 (d, 1H, J = 13.4 Hz), 3.74 (s, 3H). HRMS (ESI) for $C_{20}H_{17}ClN_2O_4$ $[M + H]^+$: m/z calcd 407.0778, found 407.0775. ^{13}C NMR ($CDCl_3$): δ 172.2, 159.8, 138.7, 138.4, 138.0, 137.5, 135.4, 128.9, 128.7, 128.6, 128.3, 128.3, 126.7, 78.3, 55.7, 53.5.

4-Benzoyl-2-benzyl-5-chloropyridazin-3(2*H*)-one (14e). General procedure 2 was followed using benzoyl chloride (1.00 mL, 8.61 mmol) as the electrophile. The reaction time was 15 min. Compound **14e** was obtained in 59% (0.190 g) yield. Colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.98−7.84 (m, 3H), 7.68−7.63 (tt, 1H, J = 7.2, 1.2 Hz), 7.53−7.43 (m, 4H), 7.39−7.31 (m, 3H), 5.33 (s, 2H). HRMS (ESI) for $C_{18}H_{13}ClN_2O_2$ $[M + H]^+$: m/z calcd 347.0556, found 347.0563. ^{13}C NMR ($CDCl_3$): δ 189.4, 157.0, 137.0, 136.5, 135.6, 135.2, 134.8, 134.7, 129.3, 129.1, 129.1, 128.8, 128.4, 55.5.

General Procedure 3 for Functionalization of 2-Benzyl-6-chloropyridazin-3(2*H*)-one (15). A dry 50 mL double-necked flask placed under an argon atmosphere using a Schlenk apparatus was charged with TMPMgCl·LiCl (2.00 mL, 1 M solution in THF) and cooled to −20 °C. 2-Benzyl-6-chloropyridazin-3(2*H*)-one (**15**; 0.221 g, 1.0 mmol) was brought into a second dry 25 mL double-necked flask and placed under an argon atmosphere using a Schlenk apparatus. Subsequently THF (2.00 mL) was added. The pyridazin-3(2*H*)-one solution was quickly added to the TMP solution; subsequently electrophile (3−8.6 mmol) was immediately added to this solution. The reaction mixture was stirred at room temperature until the reaction was complete. The resulting mixture was quenched with aqueous NH_4Cl. The aqueous phase was then extracted with EtOAc (3 × 50 mL) and subsequently dried over $MgSO_4$. The organic phase was evaporated to dryness under reduced pressure and the residue separated with an automated chromatography system using silica flash cartridges applying a heptane/ethyl acetate gradient (from 100% heptane to 100% ethyl acetate in 25 min, 25 mL/min).

2-Benzyl-6-chloro-4-(methylthio)pyridazin-3(2*H*)-one (16a). General procedure 3 was followed using *S*-methyl methanesulfonothioate (0.308 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **16a** was obtained in 66% (0.177 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.43−7.38 (m, 2H), 7.31−7.20 (m, 3H), 6.65 (s, 1H), 5.22 (s, 2H), 2.26 (s, 3H). Mp: 102−103 °C. HRMS (ESI) for $C_{12}H_{11}ClN_2OS$ $[M + H]^+$: m/z calcd 289.0178, found 289.0178. ^{13}C NMR ($CDCl_3$): δ 156.9, 149.3, 137.5, 135.6, 128.9, 128.6, 128.1, 121.6, 55.5, 13.9. The structure was unambiguously confirmed by single-crystal XRD analysis, see the Supporting Information and CCDC 832475.

2-Benzyl-6-chloro-4-[hydroxy(phenyl)methyl]pyridazin-3(2*H*)-one (16b). General procedure 3 was followed using benzaldehyde (0.304 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **16b** was obtained in 54% (0.176 g) yield. Yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.43−7.21 (m, 10H), 7.07 (d, 1H, J = 0.9 Hz), 5.76 (bs, 1H), 5.25 (d, 1H, J = 13.8 Hz), 5.11 (d, 1H, J = 13.8 Hz), 4.00 (bs, 1H). HRMS (ESI) for $C_{18}H_{15}ClN_2O_2$ $[M + H]^+$: m/z calcd 349.0719, found 349.0721. ^{13}C NMR ($CDCl_3$): δ 158.6, 146.5, 139.4, 138.3, 135.4, 128.9, 128.8, 128.8, 128.7, 128.5, 128.3, 126.9, 71.6, 55.5.

2-Benzyl-6-chloro-4-[2-furyl(hydroxy)methyl]pyridazin-3(2*H*)-one (16c). General procedure 3 was followed using 2-furaldehyde (0.351 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **16c** was obtained in 61% (0.194 g) yield. Yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.41 (d, 1H, J = 1.8 Hz), 7.39 (d, 1H, J = 1.2 Hz), 7.36 (d, 1H, J = 0.8 Hz), 7.34−7.27 (m, 3H), 7.19 (d, 1H, J = 0.7 Hz), 6.35 (m, 2H), 5.28 (d, 1H, J = 13.7 Hz), 5.19 (d, 1H, J = 13.7 Hz), 4.10 (bs, 1H). Mp: 87−88 °C. HRMS (ESI) for $C_{16}H_{13}ClN_2O_3$ $[M + H]^+$: m/z calcd 339.0510, found 339.0512. ^{13}C NMR ($CDCl_3$): δ 158.7, 151.8, 143.4, 142.9, 138.2, 135.3, 129.6, 128.9, 128.7, 128.3, 110.7, 108.6, 65.8, 55.5.

Methyl (2-Benzyl-6-chloro-3-oxo-2,3-dihydropyridazin-4-yl)(hydroxy)phenylacetate (16d). General procedure 3 was followed using methyl 2-oxo-2-phenylacetate (0.428 mL, 3.00 mmol) as the electrophile. The reaction time was 15 min. Compound **16d** was obtained in 58% (0.222 g) yield. Colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.64−7.59 (m, 2H), 7.50−7.41 (m, 5H), 7.40−7.32 (m, 3H), 6.61 (s, 1H), 5.36 (s, 1H, J = 13.6), 5.27 (s, 1H, J = 13.6), 5.21 (s, 1H), 3.83 (s, 3H). HRMS (ESI) for $C_{20}H_{17}ClN_2O_4$ $[M + H]^+$: m/z calcd 407.0786, found 407.0775. ^{13}C NMR ($CDCl_3$): δ 172.3, 159.3, 146.3, 138.2, 135.3, 135.2, 130.8, 129.2, 128.8, 128.8, 128.7, 128.3, 126.5, 78.3, 55.6, 53.5.

4-Benzoyl-2-benzyl-6-chloropyridazin-3(2*H*)-one (16e). General procedure 3 was followed using benzoyl chloride (1.00 mL, 8.61 mmol) as the electrophile. The reaction time was 15 min. Compound **16e** was obtained in 49% (0.158 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.79 (m, 2H), 7.60 (t, 1H, J = 7.5 Hz), 7.47−7.42 (m, 4H), 7.34−7.29 (m, 3H), 7.27 (s, 1H), 5.28 (s, 2H). Mp: 125−126 °C. HRMS (ESI) $C_{18}H_{13}ClN_2O_2$ $[M + H]^+$: m/z calcd 347.0556, found 347.0564. ^{13}C NMR ($CDCl_3$): δ 190.6, 156.6, 141.4, 137.2, 135.1, 135.0, 134.5, 132.4, 129.6, 129.1, 128.8, 128.7, 128.4, 55.9.

2-Benzyl-4-[hydroxy(phenyl)methyl]pyridazin-3(2*H*)-one (17). (a) 2-Benzyl-5-chloro-4-[hydroxy(phenyl)methyl]pyridazin-3(2*H*)-one (**14b**; 0.16 g, 0.50 mmol) was weighed into a Pyrex Parr flask and dissolved in EtOAc (6 mL); palladium on carbon (0.05 g, 10%) and potassium carbonate (0.14 g, 1.00 mmol) were added to this solution under an argon flow. The reaction mixture was placed under 25 psi of hydrogen gas and stirred for 2.5 h at room temperature. The resulting mixture was filtered through Celite and concentrated under vacuum. The residue was separated with an automated chromatography system using silica flash cartridges applying a heptane/ethyl acetate gradient (from 100% heptane to 100% ethyl acetate in 25 min, 25 mL/min). Compound **17** was obtained in 41% (0.06 g) yield.

(b) 2-Benzyl-6-chloro-4-[hydroxy(phenyl)methyl]pyridazin-3(2*H*)-one (**16b**; 0.16 g, 0.50 mmol) was weighed into a Pyrex Parr flask and dissolved in 6 mL of EtOAc; palladium on carbon (0.05 g, 10%) and potassium carbonate (0.14 g, 1.00 mmol) were added to this solution under an argon flow. The reaction mixture was placed under 35 psi of hydrogen gas and stirred for 3 h at room temperature. The resulting mixture was filtered through Celite and concentrated under vacuum. The residue was separated with an automated chromatography system using silica flash cartridges applying a heptane/ethyl acetate gradient (from 100% heptane to 100% ethyl acetate in 25 min, 25 mL/min). Compound **17** was obtained in 32% (0.05 g) yield. White solid. ^{1}H NMR ($CDCl_3$): δ 7.77 (d, 1H, J = 4.1 Hz), 7.47−7.30 (m, 10H), 6.94 (dd, 1H, J = 4.1, 1.1 Hz), 5.86 (d, 1H, J = 4.4 Hz), 5.39 (d, 1H, J = 13.8 Hz), 5.31 (d, 1H, J = 13.8 Hz), 4.38 (d, 1H, J = 4.4 Hz). Mp: 115−116 °C. HRMS (ESI) for $C_{18}H_{16}N_2O_2$ $[M + H]^+$: m/z calcd 313.0946, found 313.0944. ^{13}C NMR ($CDCl_3$): δ 160.6, 144.1, 139.8, 136.7, 135.9, 128.7, 128.7, 128.6, 128.3, 128.1, 126.9, 126.8, 72.2, 55.3.

■ ASSOCIATED CONTENT

Supporting Information. CIF files giving crystallographic data for **14c** and **16a** and figures giving characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

This work was supported by the Fund for Scientific Research-Flanders (FWO-Vlaanderen), the Agency for Innovation by Science and Technology in Flanders (IWT-Vlaanderen) (Ph.D. scholarship for T.V.), the Hercules foundation, and E. I. du Pont de Nemours and Co. We thank Prof. Matthias Zeller of Youngstown State University and Dr. Christophe Vande Velde of Karel de Grote University College for the collection of X-ray data sets. The diffractometer was funded by NSF Grant No. 0087210, Ohio Board of Regents Grant No. CAP-491, and YSU.

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