Preparation of New Polyfunctional Magnesiated Heterocycles Using a Chlorine−, Bromine−, or Iodine−Magnesium Exchange

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The reaction of heteroaryl iodides with *i*-PrMgBr (ca. 1.0 equiv) in THF provides the corresponding magnesiated heterocycles. Functional groups such as an ester, cyano, or chloride functions are tolerated in these new Grignard reagents if the exchange can be performed below −20 °C. This is the case for all heterocycles bearing electron-withdrawing groups or chelating functions facilitating the iodine−magnesium exchange. In many cases, the exchange can be extended to heteroaryl bromides, and a case of a chlorine−magnesium exchange is described with tetrachlorothiophene. This new preparation of functionalized heteroarylmagnesium compounds provides after reaction with various electrophiles a new entry to a broad range of polyfunctional pyridines, imidazoles, furanes, thiophenes, pyrroles, antipyrines, and uracil derivatives. The application of the halogen−magnesium exchange in the solid phase allows the performance of solid-phase synthesis, with potential applications for combinatorial chemistry.

Introduction

The preparation of polyfunctional heterocyclic compounds is of interest in many research fields: natural product synthesis,[1] drug design,[2] molecular recognition,[3] and preparation of new materials with defined properties.[4] Although directed metalation[5] or selective bromine−lithium exchange[6] has provided a very selective way to a range of lithiated heterocycles, the high polarity of the carbon−lithium bond precludes the presence of sensitive functional groups such as esters and cyano groups in these lithium organometallics due to their too high reactivity. On the other hand, the more covalent character of the carbon−magnesium bond tolerates the presence of more functional groups. The synthesis of these polyfunctional Grignard reagents is however a problem since the insertion of magnesium metal to aryl (or heteroaryl) halides bearing electron-withdrawing groups is inhibited by the presence of these functions.[7] Recently, we have shown that the iodine−magnesium exchange reaction is a unique method for preparing a range of new functionalized aryl,[8] alkenyl,[9] and heteroaryl[10] magnesium compounds as well as magnesium carbenoids.[11] Herein, we wish to report our full results demonstrating that iodine−, bromine−, or chlorine−magnesium exchange reactions provide an entry to numerous polyfunctional heterocycles otherwise difficult to prepare.

Results and Discussion

Iodine−Magnesium Exchange. Although, the iodine−magnesium exchange has been known for several years,[12] its use for the preparation of polyfunctional organomagnesium derivatives besides some magnesium carbenoids[13] has not been reported. It was found that aryl iodides bearing electron-withdrawing groups undergo an iodine−magnesium exchange between −30 and −20 °C within a few hours,[8] and this exchange was applicable to a wide range of heteroaryl iodides. At first, we found that electron-poor heterocycles such as iodopyridines[10a,14,12f] undergo in THF under previously developed reaction conditions[8] a smooth iodine−magnesium exchange within a few minutes at −40 °C (Scheme 1 and Table 1). Thus, the treatment of 2-chloro-4-iodopyridine (**1a**) with *i*-

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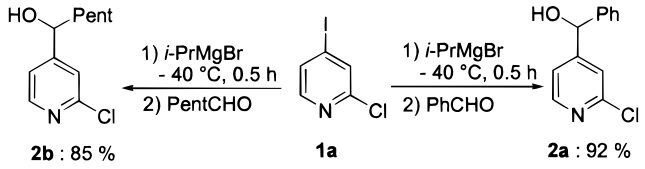
Scheme 1

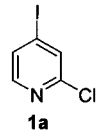
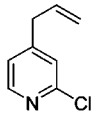
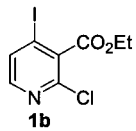
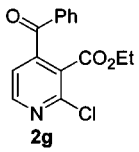
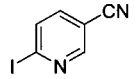
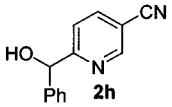
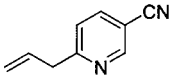
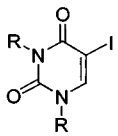
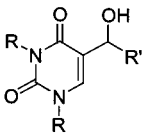


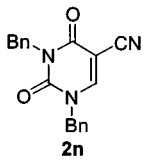
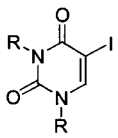
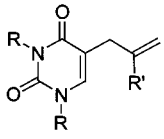
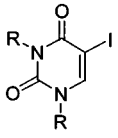
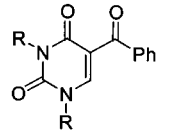
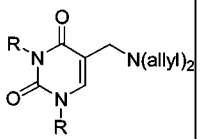
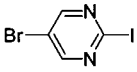
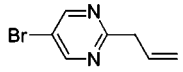
PrMgBr in THF at −40 °C leads to a smooth iodine−magnesium exchange within 0.5 h, affording an intermediate organomagnesium derivative, which reacts with benzaldehyde or aliphatic aldehydes such as hexanal leading to the corresponding alcohols **2a** and **2b** respectively with 92% and 85% yield. Allylation with allyl bromide in the presence of a catalytic amount of CuCN·2LiCl affords the allylated product **2c** in 85% yield (entry 1 of Table 1).

Ester functions such as a carboethoxy group are tolerated under these conditions, and the polyfunctional pyridine **1b** reacts well with *i*-PrMgBr, leading to the desired organomagnesium derivative. Its reaction with benzaldehyde furnishes after lactonization the product **2d** in 56% yield, whereas its copper-catalyzed allylation[15] affords the allylated product **2e** in 82% yield (Scheme 2). The cyanation of this organomagnesium compound can be accomplished with tosyl cyanide, leading to pyridine **2f** (55%, 0 °C, 10 h); see entry 2 of Table 1.

In the case of 2-iodo-5-cyanopyridine (**1c**), the iodine−magnesium exchange must be performed at −78 °C using an inverse addition in order to avoid a competitive homocoupling reaction (see entries 4 and 5 of Table 1). Uracils are important heterocyclic building blocks. The magnesiation of 5-iodouracils **1d**−**f** with *i*-PrMgBr in THF proceeds smoothly at −40 °C within 30 min. The reaction of these organomagnesium derivatives with various electrophiles affords the desired products **2j**−**r** in good to excellent yield.

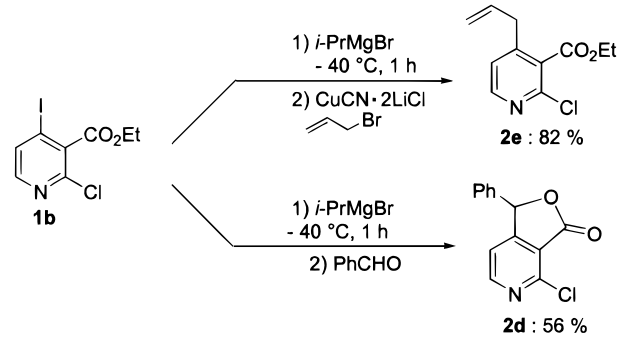
Table 1. Products of Type 2 Obtained by an Iodine−Magnesium Exchange Reaction Starting from the Heteroaryl Iodides 1a−g

Entry	Heteroaryl	Electrophile	Product of type 2	yield (%)[a]
1	 **1a**	allyl bromide	 **2c**	85[b]
2	 **1b**	TosCN	 **2f**	55
3	**1b**	PhCOCl	 **2g**	84[b]
4	 **1c**	PhCHO	 **2h**	67
5	**1c**	allyl bromide	 **2i**	50[b]
				
6	**1d** : R=Bn	PhCHO	**2j** : R=Bn ; R′=Ph	80
7	**1d** : R=Bn	n-HexCHO	**2k** : R=Bn ; R′=n-Hex	77
8	**1e** : R=3,5-diMeO$C_6H_3CH_2$	PhCHO	**2l** : R′=Ph	83
9	**1f** : R=CH_2OEt	n-HexCHO	**2m** : R′=n-Hex	74

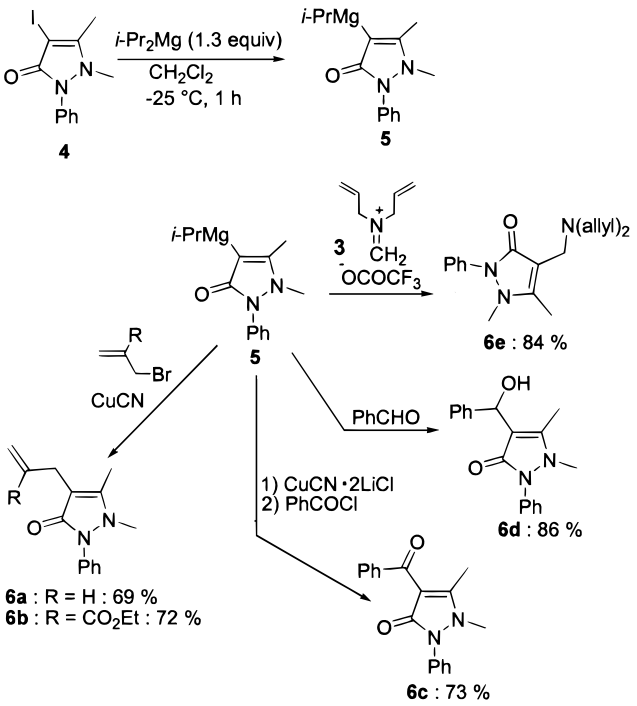
Entry	Heteroaryl	Electrophile	Product of type 2	yield (%)[a]
10	 **1d**	TosCN	 **2n**	47
				
11	**1d** : R=Bn		**2o** : R′=H	81[b]
12	**1d** : R=Bn		**2p** : R′=CO_2Et	76[b]
13	**1e** : R=3,5-diMeOC_6H_3		**2q** : R′=H	81[b]
14	**1f** : R=CH_2OEt		**2r** : R′=CO_2Et	83[b]
				
15	**1d** R=Bn	PhCOCl	**2s** : R=Bn	73[b]
16	**1f** R=CH_2OEt	PhCOCl	**2t** : R=CH_2OEt	75[b]
				
17	**1d**	$H_2C{=}\overset{+}{N}(allyl)_2$ $CF_3CO_2^-$ **3**	**2u** : R=Bn	85
18	**1e**		**2v** : R=CH_2OEt	82
19	 **1g**	allyl bromide	 **2w**	81[b]

[a] Isolated yield of analytically pure products. [b] The reaction with the electrophile is performed in the presence of a copper salt.

Scheme 2



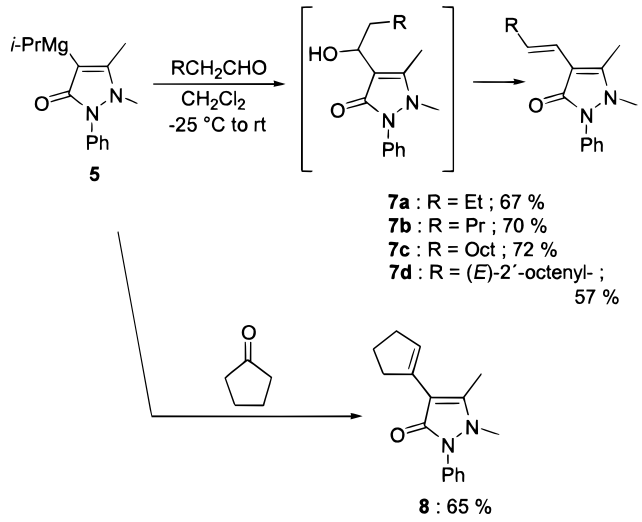
Scheme 3



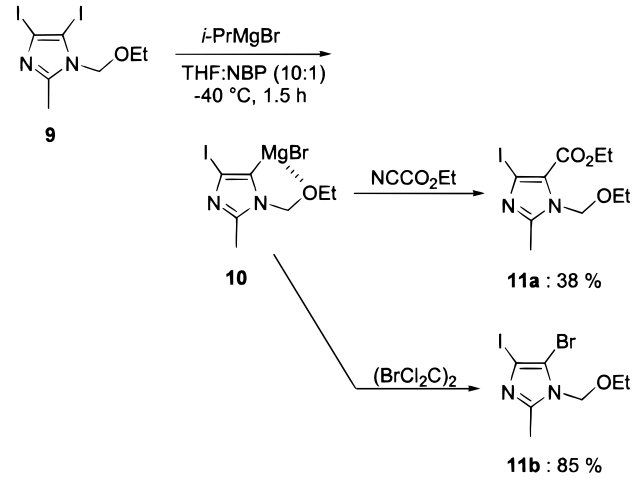
Especially interesting is aminomethylation using the new immonium trifluoroacetate **3** ($CH_2{=}N(allyl)_2^+$, $CF_3CO_2^-$),[16] leading to 5-aminomethyl uracil derivatives such as **2u**,**v** in 82−85% yield (entries 17 and 18 of Table 1). 5-Bromo-2-iodopyrimidine (**1g**)[17] reacts very rapidly with *i*-PrMgBr (−80 °C, 10 min), affording the desired organomagnesium reagent, which is allylated in the presence of CuCN·2LiCl leading to the product **2w** in 81% yield (entry 19 of Table 1). Unfortunately, the reaction with other typical electrophiles used in this work failed. A smooth iodine−magnesium exchange proceeds with a 4-iodo-3-pyrazolin-5-one derivative such as **4** by performing the reaction in CH_2Cl_2 and using *i*-Pr_2Mg (prepared in *tert*-butylmethyl ether (TBME); 1.3 equiv). The exchange reaction is complete at −25 °C within 1 h, leading to the Grignard reagent **5**, which is efficiently trapped by various electrophiles (Scheme 3). Allylation in the presence of a catalytic amount of CuCN affords the antipyrines **6a**,**b** (69−72%).

After transmetalation of **5** with CuCN·2LiCl (1.0 equiv), leading presumably to the corresponding copper species,[18] treatment with PhCOCl results in the formation of **6c** in 73% yield. The direct reaction of **5** with benzaldehyde or the immonium salt **3** affords the addition products **6d** (86%) and **6e** (84%). Interestingly, the treatment of **5** with various aliphatic aldehydes RCH_2CHO provides after workup pyrazolinone derivatives **7a**−**d** (Scheme 4). The stereochemistry of the newly formed double bond is *E* (>99% *E*), Scheme 4. The reaction of **5** with cyclopentanone furnishes after elimination the cyclopentenyl pyrazolinone **8** (65%).

Scheme 4



Scheme 5



The rate of the iodine−magnesium exchange is generally accelerated by the presence of electron-withdrawing groups attached to the heterocyclic ring. Thus, the 4,5-diiodoimidazole derivative **9**[19] undergoes a regioselective iodine−magnesium exchange with *i*-PrMgBr in THF/*N*-butylpyrrolidinone (NBP) (10:1) at −40 °C within 1.5 h, leading to the chelate-stabilized magnesiated imidazole **10**, which can be trapped with several electrophiles such as ethyl cyanoformate[20] (−40 to 0 °C, 16 h), leading to the substituted ester imidazole **11a** (38% yield). The reaction of **10** with 1,2-dibromo-1,1,2,2-tetrachloroethane[21] (−40 °C, 1.5 h) gives the 4-iodo-5-bromoimidazole **11b** in 85% yield (Scheme 5).

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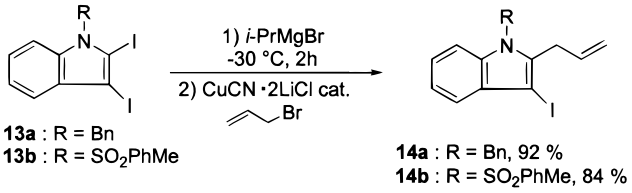
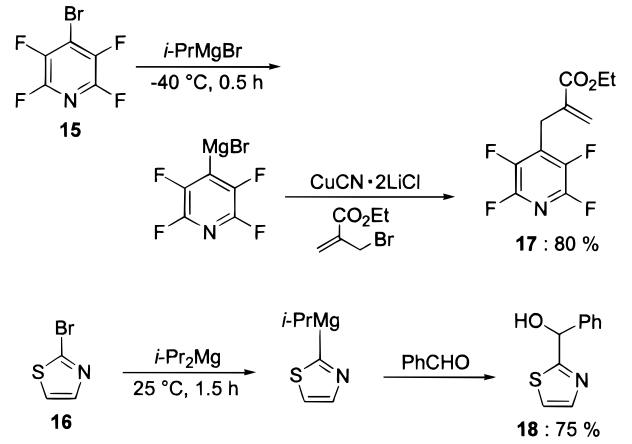
(20) Rho, T.; Abuh, Y. F. *Synth. Commun.* **1994**, *24*, 253.

Scheme 6



Scheme 7

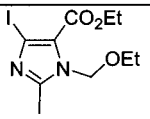
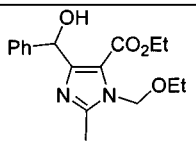
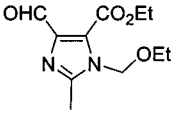
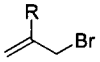
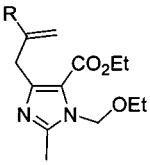
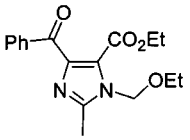
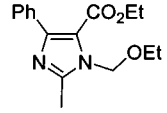
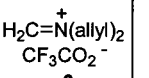
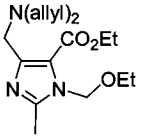
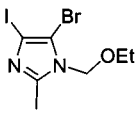
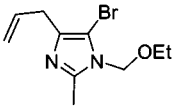


The imidazoles **11a** and **11b** undergo readily an iodine−magnesium exchange (*i*-PrMgBr, THF, − 40 °C, 0.5−1 h) leading to the corresponding functionalized magnesiated imidazoles, which react smoothly with typical electrophiles such as benzaldehyde (**12a**, 66%; entry 1 of Table 2), DMF (**12b**, 59%, entry 2), allylic bromides (**12c** (91%); **12d** (62%); entries 3 and 4), and benzoyl chloride (**12e**, 67%, entry 5). A Pd(0)-catalyzed coupling reaction with iodobenzene can be realized after transmetalating the intermediate Grignard reagent with $ZnBr_2$, furnishing the phenylated imidazole **12f** in 63% yield. The reaction with the immonium salt **3** gives the aminomethyl derivative **12g** in 60% yield. The 4-iodo-5-bromoimidazole derivative **11b** undergoes a selective iodine−magnesium exchange, resulting after allylation in the formation of imidazole **12h** in 83% yield (entry 8 of Table 2). A selective iodine−magnesium exchange can also be performed with 2,3-diiodoindoles[22] **13a** and **13b**. Only the iodine atom at position 2 undergoes the exchange reaction, leading after allylation to the products **14a** (92%) and **14b** (84%; Scheme 6). The exchange of the remaining iodine in position 3 is considerably more difficult.

Bromine−Magnesium Exchange. The bromine−magnesium exchange although less general[8b,14] can be applied to various heterocycles substituted with electron-withdrawing groups. Whereas the perfluorinated 4-bromopyridine **15** undergoes a bromine−magnesium exchange at −40 °C within 0.5 h, the unfunctionalized 2-bromothiazole **16** undergoes the exchange reaction only at room temperature and requires the use of *i*-Pr_2Mg (1.1 equiv). In both cases, the corresponding allylation product **17** and addition product **18** to benzaldehyde are obtained in satisfactory yields (Scheme 7).

A range of functionalized bromo-heterocycles bearing electron-withdrawing groups such as an ester function (**19a**,**b**,**e**,**f**,**h**), a cyano group (**12i**), or halide (**19c**−**h**) undergo a selective bromine−magnesium exchange reaction when treated with *i*-PrMgBr or *i*-Pr_2Mg (see Experimental Section). Thus, the bromofuran **19a** or bromothiophene **19b** undergoes the exchange reaction at − 30 °C, whereas the dibromothiophenes **19e** and **19f**

Table 2. Polyfuctional Imidazoles 12a−i Prepared from 11a and 11b via an Iodine−Magnesium Exchange Followed by the Reaction with an Electrophile

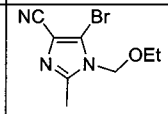
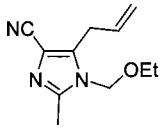
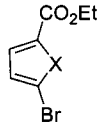
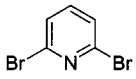
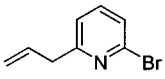
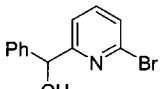
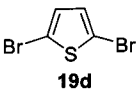
Entry	Heteroaryl	Electrophile	Product of type 2	yield (%)[a]
1	 **11a**	PhCHO	 **12a**	66
2	**11a**	DMF	 **12b**	59
3	**11a**		 **12c** : R=H	91[b]
4	**11a**		**12d** : R=CO_2Et	62[b]
5	**11a**	PhCOCl	 **12e**	67[b]
6	**11a**	PhI	 **12f**	63[c]
7	**11a**	 **3**	 **12g**	60
8	 **11b**	allyl bromide	 **12h**	83[b]

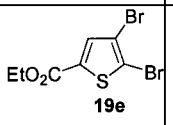
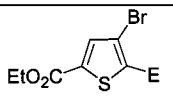
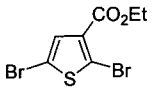
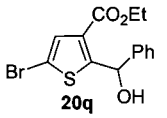
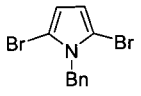
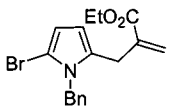
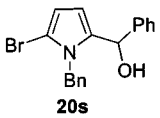
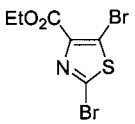
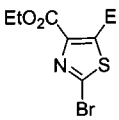
[a] Isolated yield of analytically pure products. [b] The reaction with the electrophile is performed in the presence of a copper salt. [c] A Pd(0) catalysis is used ($Pd(dba)_2$ and dppf (10%)).

(21) Almena, J. J. P.; Börner, A.; Knochel, P. *Tetrahedron Lett.* **1998**, *39*, 8073.

(22) Bergman, J.; Venemalm, L. *J. Org. Chem.* **1992**, *57*, 2495.

Table 3. Polyfuctional Heterocycles 20a−y Obtained from the Functionalized Heterocyclic Bromides 12h and 19a−i via a Bromine−Magnesium Exchange Followed by a Reaction with an Electrophile

Entry	Heteroaryl	Electrophile	Product of type **2**	yield (%)[a]
1	 **12i**	allyl bromide	 **20a**	65[b]
2	 **19a** : X=O	allyl bromide	**20b** : X=O ; E=allyl	80[b]
3	**19a** : X=O	PhCHO	**20c** : X=O ; E=HC(OH)Ph	73
4	**19b** : X=S	PhCHO	**20d** : X=S ; E=HC(OH)Ph	72
5	 **19c**	allyl bromide	 **20e**	68[b]
6	**19c**	PhCHO	 **20f**	63
7	 **19d**	allyl bromide	**20g** : E=allyl	86[b]
8	**19d**	PhCHO	**20h** : E=HC(OH)Ph	74
9	**19d**	$NCCO_2Et$	**19b** : $E=CO_2Et$	72
10	**19d**		**20i** : $E=CH_2C(CO_2Et)=CH_2$	78[b]

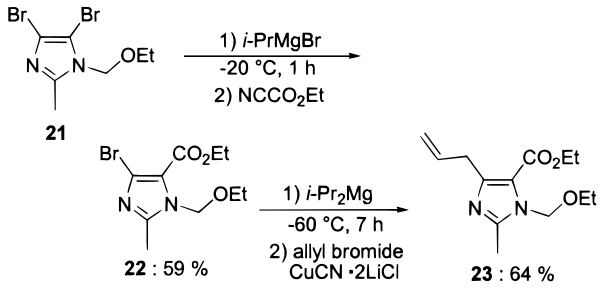
Entry	Heteroaryl	Electrophile	Product of type **2**	yield (%)[a]
	 **19e**			
11	**19e**	H_2O	**20j** : E=H	90
12	**19e**	PhCHO	**20k** :E=HC(OH)Ph	83
13	**19e**	allyl bromide	**20l** : E=allyl	68[b]
14	**19e**	Me_3SiCl	**20m**: $E=SiMe_3$	88
15	**19e**	Bu_3SnCl	**20n** : $E=SnBu_3$	76
16	**19e**	$NCCO_2Et$	**20o** : $E=CO_2Et$	82
17	**19e**		**20p** : $E=CH_2C(CO_2Et)=CH_2$	78[b]
18	 **19f**	PhCHO	 **20q**	76
19	 **19g**		 **20r**	72[b]
20	**19g**	PhCHO	 **20s**	73
	 **19h**			
21	**19h**	Me_3SiCl	**20t** : $E=SiMe_3$	67
22	**19h**	allyl bromide	**20u** : E=allyl	81[b]
23	**19h**	PhCHO	**20v** : E=CH(OH)Ph	58
24	**19h**	$NCCO_2Et$	**20w** : $E=CO_2Et$	67

[a] Isolated yield of analytically pure products. [b] The reaction with the electrophile is performed in the presence of a copper salt.

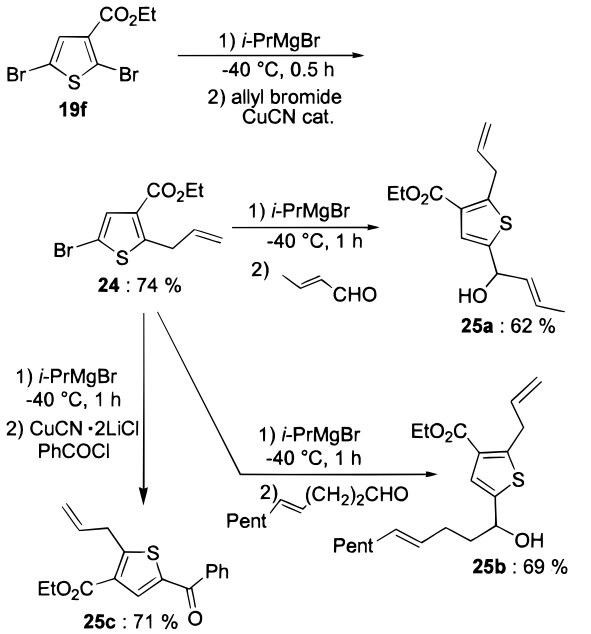
undergo the bromine−magnesium exchange already at −40 °C within 1 h. In all cases, the expected products of type **20** are obtained in satisfactory yields after quenching with an electrophile (Table 3). The presence of the ester function leads to a fast exchange reaction. Remarkably, a highly selective monoexchange reaction is observed for all the dibromides used. Thus, the 2,6-dibromopyridine **19c** furnishes after exchange (*i*-Pr_2Mg, 25 °C, 4 h) only the products **20e** and **20f** derived from a monoexchange (entries 5 and 6 of Table 3). In the case of the 4,5-dibromoester **19e**, only an exchange reaction at position 5 is observed, leading to a variety of polyfunctional thiophenes (**20j**−**p**; entries 11−17 of Table 3). A similar behavior is observed for the 2,5-dibromoester **19f**. An exchange at position 2, which leads to an organomagnesium compound stabilized by chelation, is observed accompanied by minor amounts (10%) of the regioisomeric magnesium reagents (entry 18). The 4,5-dibromoimidazole **21** undergoes an exchange only at position 5 due to the stabilization by chelation of the resulting organomagnesium derivative, leading after the reaction with ethyl cyanoformate[20] to the bromoimidazole **22** in 59% yield. This substituted ester bromoimidazole undergoes a second fast bromine−magnesium exchange (−60 °C, 7 h), furnishing after allylation the imidazole **23** in 64% yield (Scheme 8).

The 2,5-dibromothiophene **19f** undergoes two selective bromine−magnesium exchanges. Thus, the reaction of **19f** with *i*-PrMgBr at −40 °C (30 min) followed by a copper(I)-catalyzed allylation furnishes the monobromothiophene **24** in 74% yield. The reaction of **24** with a further equivalent of *i*-PrMgBr (−40 °C, 1 h) leads to a functionalized organomagnesium reagent which reacts with aldehydes, providing the polyfunctional thiophenes **25a**,**b** (Scheme 9). A double regioselective bromine−magnesium exchange reaction is also possible starting

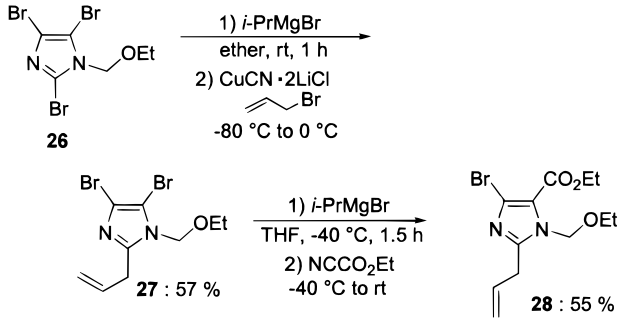
Scheme 8



Scheme 9



Scheme 10

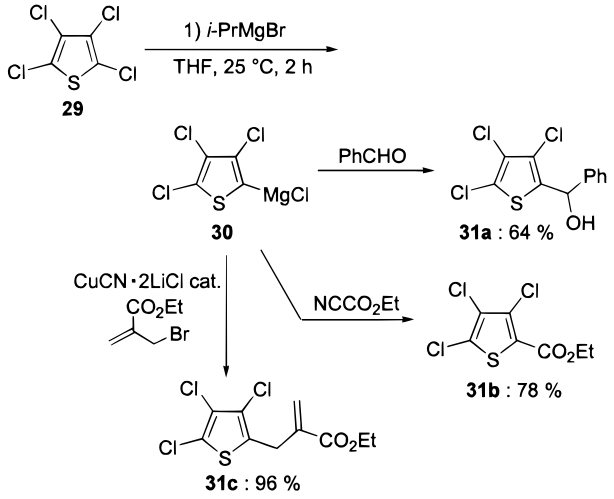


from the tribromoimidazole **26**. First, the bromine atom at position 2 undergoes exchange affording the 4,5-dibromoimidazole **27** in 57% yield. It is essential to perform the exchange reaction in diethyl ether in order to get this high selectivity.[23] As expected, the second exchange is regioselective, leading after reaction with ethyl cyanoformate to product **28** in 55% yield (Scheme 10).

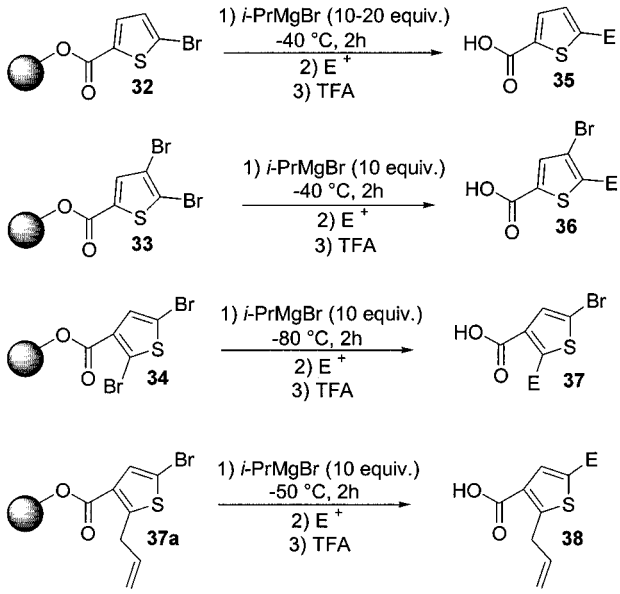
Chlorine−Magnesium Exchange. Finally, the presence of several electron-withdrawing groups such as tetrachlorothiophene allows the performance of a chlorine−magnesium exchange. Thus, the reaction of **29** with *i*-PrMgBr (1.1 equiv) in THF at 25 °C for 2 h leads to the

(23) (a) Hartly, D. J.; Iddon, B. *Tetrahedron Lett.* **1997**, *38*, 4667; (b) O'Connell, J. F.; Parquette, J.; Yelle, W. E.; Wang, W.; Rapoport, H. *Synthesis* **1988**, 767.

Scheme 11



Scheme 12



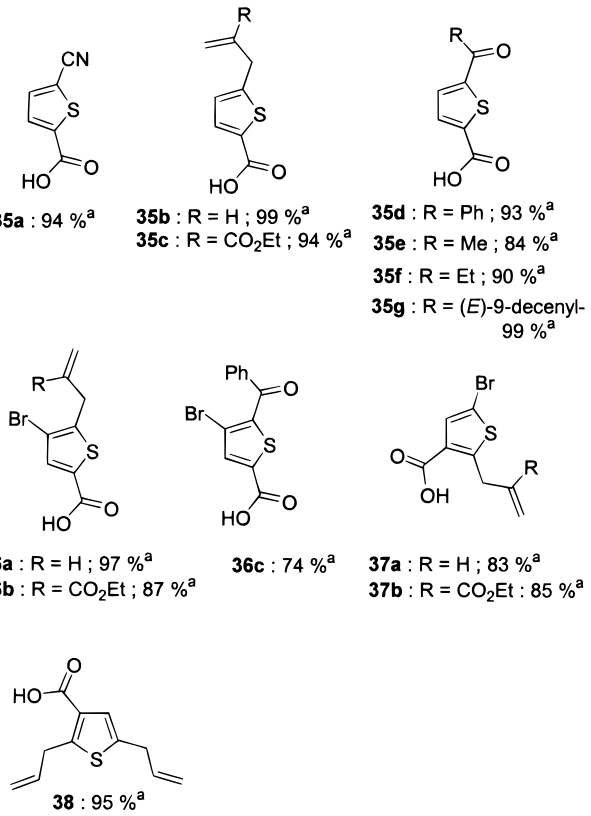
desired organomagnesium compound **30**, which reacts with typical electrophiles such as benzaldehyde, ethyl (2-bromomethyl)acrylate, and ethyl cyanoformate, leading to the products **31a**−**c** in 64−96% yield (Scheme 11).

Several of these exchange reactions can be performed in the solid phase using a heterocyclic bromide attached to the resin. Thus, various functionalized thiophenes have been attached to Wang resin leading to the substrates **32**, **33**, and **34**. Their treatment with an excess of *i*-PrMgBr at low temperature followed by the reaction of various electrophiles (Scheme 12) affords after cleavage from the resin a range of polyfunctional thiophenes with satisfactory purity (determined by HPLC at 254 nm). Using this method the products in Chart 1 have been obtained.

Conclusion

The halogen−magnesium exchange reaction is an excellent method for preparing new magnesiated polyfunctional building blocks. Whereas the rate of the exchange reaction strongly depends on the presence of electron-withdrawing functional groups, the iodine−magnesium exchange is always faster than the corre-

Chart 1 [a]



[a]Purity determined by HPLC (254 nm).

sponding bromine−magnesium exchange. These exchange reactions have been used to prepare a range of polyfunctional pyridines, uracils, imidazoles, antipyrines, thiophenes, and furans. The resulting heterocyclic organomagnesium compounds display the typical reactivity of a Grignard reagent and react with a variety of electrophiles in satisfactory yield.

Experimental Section

General Methods. Unless otherwise indicated, all reactions were carried out under an argon atmosphere. THF, Et_2O, and *tert*-butylmethyl ether (TBME) were distilled from sodium/benzophenone; CH_2Cl_2 and DMF, from CaH_2. Reactions were monitored by gas chromatography (GC) analysis of worked-up reaction aliquots. Analytical thin-layer chromatography (TLC) was performed using Merck silica gel (60 F-254) plates (0.25 mm) precoated with a fluorescent indicator. Column chromatography was carried out on silica gel 60 (70−230 mesh). NMR data were recorded on a 200, 300, and 400 MHz NMR spectrometer. The ionization method used was electron impact ionization (EI, 70 eV). Melting points are uncorrected. Elemental analyses were performed by the Microanalytical Service Laboratory of Universität München.

Starting Materials. Wang resin (copolystyrene-2% DVB matrix, 100−200 mesh, loading 0.75 mmol/g) was purchased from Novabiochem. The following starting materials were prepared according to literature procedures: **1a**,**b**,[24] **1c**,[25] **1d**−**f**,[26] **1g**,[17] **9**,[28] **13a**,**b**,[22] **19f**,[28] **19g**,[29] **19h**,[30] **21**,[27] and **26**.[27]

Typical Procedure A: 4-Bromo-5-(hydroxyphenylmethyl)thiophene-2-carboxylic Acid Ethyl Ester (20k). A solution of *i*-PrMgBr (1.05 mmol) in THF (0.8 M, 1.31 mL) was added dropwise over 5 min to a stirred solution of **19e** (314 mg, 1 mmol) in THF (10 mL) at −40 °C under argon. The resulting solution was then stirred for 30 min, and benzaldehyde (122 μL, 1.20 mmol) was added. The reaction mixture was allowed to warm to room temperature, brine (20 mL) was added, and the reaction was worked up as usual. The crude residue was purified by column chromatography on silica (pentane/Et_2O, 4:1) to give the alcohol **20k** (283 mg, 83%) as a colorless oil. IR (neat): 3443 (vs), 3090 (w), 3063 (w), 3031 (w), 1710 (vs), 1251 (vs), 1146 (vs), 1074 (s), (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.43 (s, 1H), 7.35−7.31 (m, 2H), 7.26−7.19 (m, 3H), 5.92 (s, 1H), 4.17 (q, J = 7.2 Hz, 2H), 3.34 (bs, 1H), 1.22 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.9, 150.8, 141.4, 136.1, 132.8, 129.1, 128.7, 127.0, 108.4, 72.3, 62.1, 14.7. *m*/*z* (EI-MS): 341 (15), 340 (50), 237 (86), 235 (100), 105 (78). HRMS: calcd for $C_{14}H_{13}BrO_3S$ 339.9769, found 339.9768.

(2-Chloropyridin-4-yl)-1-phenylmethanol (2a). The reaction was carried out according to typical procedure A using **1a** (718 mg, 3.0 mmol), *i*-PrMgBr (4.74 mL, 3.6 mmol, 0.76 M in THF, exchange at −40 °C, 30 min), and benzaldehyde (413 mg, 3.9 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 1:1) affording the product **2a** (606 mg, 92%) as a colorless oil. IR (neat): 3236 (vs), 1593 (m), 1457 (m), 1384 (m), 1081 (w), 1053 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.02 (d, J = 5.1 Hz, 1H), 7.37−7.01 (m, 2H), 5.69 (s, 1H), 4.55 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.7, 151.4, 149.1, 142.1, 128.8, 128.5, 127.0, 121.8, 120.3, 74.3. *m*/*z* (EI-MS): 221 (30), 220 (17), 219 (98), 218 (15), 140 (20), 107 (70). Anal. Calcd for $C_{12}H_{10}ClNO$: C, 65.61; H, 4.58; N, 6.38. Found: C, 65.74; H, 4.71; N, 6.25.

1-(2-Chloropyridin-4-yl)-hexan-1-ol (2b). The reaction was carried out according to typical procedure A using **1a** (718 mg, 3.0 mmol), *i*-PrMgBr (4.74 mL, 3.6 mmol, 0.76 M in THF, exchange at −40 °C, 30 min), and hexanal (390 mg, 3.9 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 1:1) affording the product **2b** (544 mg, 85%) as a yellow oil. IR (neat): 3370 (vs), 2955 (s), 2932 (s), 1596 (s), 1549 (m), 1466 (m), cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.18 (d, J = 4.8 Hz, 1H), 7.32−7.34 (m, 1H), 7.19 (dd, J = 4.8 Hz, J = 1 Hz, 1H), 4.69 (m, 1H), 4.25 (bs, 1H), 1.73−1.62 (m, 2H), 1.37−1.25 (6H), 0.87 (t, J = 7.0 Hz, 3H).^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.4, 151.4, 149.1, 121.6, 119.9, 72.2, 38.8, 31.6, 25.1, 22.5, 14.0. *m*/*z* (EI-MS): 213 (6), 144 (26), 143 (27), 142 (100), 78 (25). Anal. Calcd for $C_{11}H_{16}ClNO$: C, 61.82; H, 7.55; N, 6.55. Found: C, 61.63; H, 7.58; N, 6.68.

4-Allyl-2-chloropyridine (2c). The reaction was carried out according to typical procedure A using **1a** (718 mg, 3.0 mmol), *i*-PrMgBr (4.74 mL, 3.6 mmol, 0.76 M in THF, exchange at −40 °C, 30 min), CuCN (10% mol, 27 mg), and allyl bromide (472 mg, 3.9 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 9:1) affording the product **2c** (391 mg, 85%) as an orange oil. IR (neat): 1592 (m), 1458 (w), 1382 (m), 1087 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.26 (d, J = 5.0 Hz, 1H), 7.15 (s, 1H), 7.05 (d, J = 5.0 Hz), 5.94−5.91 (m, 1H), 5.19−4.97 (m, 2H), 3.36 (d, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 152.5, 151.6, 149.5, 134.3, 124.2, 122.8, 118.1, 38.9. *m*/*z* (EI-MS): 153 (37), 152 (30), 118 (100), 91 (47), 39 (20). Anal. Calcd for C_8H_8ClN: C, 62.55; H, 5.25; N, 9.12. Found: C, 62.78; H, 5.45; N, 8.98.

4-Chloro-1-phenyl-1*H*-furo[3,4-*c*]pyridin-3-one (2d). The reaction was carried out according to typical procedure A using **1b** (467 mg, 1.50 mmol), *i*-PrMgBr (2.0 mL, 1.50 mmol, 0.76 M in THF, exchange at −40 °C, 1 h), and benzaldehyde (240 mg, 2.25 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 1:1) affording the product **2d** (206 mg, 56%) as an orange oil. IR (neat): 1756

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(s), 1660 (w), 1592 (w), 1405 (w), 1254 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 8.58 (s, 1H), 7.53−7.25 (m, 6H), 6.42 (s, 1H). ^{13}C NMR (D_2O, 400 MHz): δ 165.7, 161.1, 153.5, 149.3, 134.0, 129.8, 129.5, 126.6, 119.1, 117.2, 80.8. *m/z* (EI-MS): 245 (100), 167 (36), 166 (22), 139 (88), 105 (49). HRMS: calcd for $C_{13}H_8ClNO_2$ 245.0244, found 245.0245.

4-Allyl-2-chloronicotinic Acid Ethyl Ester (2e). The reaction was carried out according to typical procedure A using **1b** (467 mg, 1.50 mmol), *i*-PrMgBr (1.74 mL, 1.50 mmol, 0.86 M in THF, exchange at −40 °C, 1 h), CuCN·2LiCl (1.70 mL, 1.70 mmol, 1 M in THF), and allyl bromide (273 mg, 2.25 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 1:1) affording the product **2e** (278 mg, 82%) as an orange oil. IR (neat): 1735 (s), 1582 (m), 1382 (w), 1278 (m), 1123 (w), 1061 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 8.33 (d, J = 5.0 Hz, 1H), 7.16 (d, J = 5.0 Hz, 1H), 5.88−5.80 (m, 1H), 5.20−5.09 (m, 2H), 4.44 (q, J = 7.0 Hz, 2H), 3.41 (d, J = 6.6 Hz, 2H), 1.41 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.6, 149.8, 149.5, 147.7, 133.6, 130.0, 123.3, 118.4, 62.2, 37.2, 14.0. *m/z* (EI-MS): 225 (46), 197 (19), 182 (100), 180 (89), 116 (30). HRMS: calcd for $C_{11}H_{12}ClNO_2$ 225.0557, found 225.0555.

2-Chloro-4-cyanonicotinic Acid Ethyl Ester (2f). The reaction was carried out according to typical procedure A using **1b** (467 mg, 1.5 mmol), *i*-PrMgBr (1.94 mL, 1.65 mmol, 0.86 M in THF, exchange at −40 °C, 45 min), and *p*-toluenesulfonyl cyanide (353 mg, 1.95 mmol, 0 °C, 10 h) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 9:1) affording the product **2f** (173 mg, 55%) as a colorless oil. IR (neat): 1740 (s), 1573 (m), 1384 (m), 1273 (s), 1124 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.17 (d, J = 5.0 Hz, 1H), 7.61 (d, J = 5.0 Hz, 1H), 4.55 (q, J = 7.1 Hz, 2H), 1.45 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.5, 151.3, 149.6, 130.6, 124.6, 121.7, 113.8, 63.5, 13.8. *m/z* (EI-MS): 210 (30), 184 (21), 182 (65), 167 (38), 165 (100), 140 (19), 138 (34), 137 (29), 76 (24). Anal. Calcd for $C_9H_7ClN_2O_2$: C, 51.32; H, 3.35; N, 13.30. Found: C, 51.05; H, 3.52; N, 12.80.

4-Benzoyl-2-chloronicotinic Acid Ethyl Ester (2g). The reaction was carried out according to typical procedure A using **1b** (467 mg, 1.5 mmol), *i*-PrMgBr (1.94 mL, 1.65 mmol, 0.86 M in THF, exchange at −40 °C, 30 min), CuCN·2LiCl (1.65 mL, 1.65 mmol, 1 M in THF), and benzoyl chloride (274 mg, 1.95 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 7:3) affording the product **2g** (364 mg, 84%) as a yellow oil. IR (neat): 1742 (s), 1675 (s), 1450 (w), 1382 (w), 1282 (s), 1174 (w), 1121 (w), 1063 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.45 (d, J = 5.0 Hz, 1H), 7.71−7.41 (m, 5H), 7.24 (d, J = 5.0 Hz, 1H), 4.05 (q, J = 7.1 Hz, 2H), 1.04 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 192.9, 164.0, 150.5, 149.3, 148.5, 134.9, 134.2, 129.8, 128.7, 127.4, 120.9, 62.3, 13.3. *m/z* (EI-MS): 289 (5), 105 (100), 77 (33). Anal. Calcd for $C_{15}H_{12}ClNO_3$: C, 62.18; H, 4.18; N, 4.84. Found: C, 62.11; H, 4.33; N, 4.94.

6-(Hydroxyphenylmethyl)nicotinonitrile (2h). The reaction was carried out using an inverse addition. A solution of **1c** (230 mg, 1 mmol) in THF (2 mL) was added over 1 min to a stirred solution of *i*-PrMgBr (1.16 mL, 1.1 mmol, 0.87 M in THF) at −78 °C under argon. The resulting solution was then stirred for 5 min, and benzaldehyde (159 mg, 1.5 mmol) was added. The reaction mixture was then quenched with brine and the reaction worked up as usual. The crude residue was purified by column chromatography on silica (pentane/Et_2O, 2:1) affording the alcohol **2h** (141 mg, 67%) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.71 (d, J = 2.1 Hz, 1H), 7.80 (dd, J = 8.2 Hz, J = 2.1 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.7, 151.2, 141.8, 139.9, 128.8, 128.4, 126.9, 121.2, 116.4, 108.6, 75.6. *m/z* (EI-MS): 210 (47), 107 (29), 105 (29), 104 (31), 86 (69), 84 (100), 79 (23), 77 (40). HRMS: calcd for $C_{13}H_{20}N_2O_2$ 210.0793, found 210.0790.

6-Allylnicotinonitrile (2i). The reaction was carried out using an inverse addition. A solution of **1c** (230 mg, 1 mmol) in THF (2 mL) was added over 1 min to a stirred solution of *i*-PrMgBr (1.16 mL, 1.1 mmol, 0.87 M in THF) at −78 °C under argon. The resulting solution was then stirred for 5 min, and CuCN (10% mol, 9 mg) and allyl bromide (181 mg, 1.5 mmol) were added. The crude residue was purified by column chromatography on silica (pentane/Et_2O, 5:1) to give the product **2i** (71 mg, 50%) as a colorless oil. ^1H NMR ($CDCl_3$, 200 MHz): δ 8.82 (d, J = 3.0 Hz, 1H), 7.90 (dd, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 6.10−5.96 (m, 1H), 5.26−5.16 (m, 2H), 3.67 (d, J = 7.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 165.1, 152.6, 139.9, 134.4, 123.2, 118.6, 117.2, 107.9, 43.3. *m/z* (EI-MS): 144 (39), 143 (100), 142 (20), 118 (16). HRMS: calcd for $C_9H_8N_2$ 144.0687, found 144.0682.

1,3-Dibenzyl-5-(hydroxyphenylmethyl)-1*H*-pyrimidine-2,4-dione (2j). The reaction was carried out according to typical procedure A using **1d** (700 mg, 1.67 mmol), *i*-PrMgBr (2.51 mL, 2.01 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), and benzaldehyde (424 μL, 2.34 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 1:1) affording the product **2j** (531 mg, 80%) as a colorless oil. IR (neat): 3468 (s), 3088 (s), 1701 (s), 1655 (s), 1606 (m), 1586 (m), 1078 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.4−6.99 (m, 15H), 6.77 (s, 1H), 5.57 (s, 1H), 4.98 (s, 2H), 4.67 (s, 2H), 3.72 (bs, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163, 151.1, 140.5, 139.4, 136.5, 135, 129, 128.9, 128.2, 128.1, 128, 127.9, 127.6, 126.5, 116.6, 70, 52.5, 44.6. *m/z* (EI-MS): 398 (11), 397 (2), 380 (21), 105 (19), 91 (100). HMRS: calcd for $C_{25}H_{22}N_2O_3$ 398.1630, found 398.1634.

1,3-Dibenzyl-5-(1-hydroxyheptyl)-1*H*-pyrimidine-2,4-dione (2k). The reaction was carried out according to typical procedure A using **1d** (700 mg, 1.67 mmol), *i*-PrMgBr (2.51 mL, 2.01 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), and heptanal (293 μL, 2.17 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 3:2) affording the product **2k** (523 mg, 77%) as a colorless oil. IR (neat): 3470 (s), 3087 (s), 1703 (s), 1660 (s), 1603 (m), 1588 (m), 1067 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.4−7.18 (m, 10H), 7.04 (s, 1H), 5.07 (s, 2H), 4.86 (s, 1H), 4.84 (s, 1H), 4.38 (t, J = 6.4 Hz, 1H), 2.87 (bs, 1H), 1.6 (dt, J = 6.5 Hz, J = 6.4 Hz, 2H), 1.33−1.11 (m, 8H), 0.79 (t, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163, 151.3, 138, 136.6, 135.5, 129, 128.9, 128.5, 128.4, 127.9, 127.6, 116.2, 69, 52.4, 44.5, 35.9, 31.7, 29, 25.7, 22.5, 14. *m/z* (EI-MS): 388 (4), 322 (23), 321 (95), 92 (15), 91 (100). HRMS: calcd for $C_{25}H_{30}O_3N_2$ 406.2256, found 406.2272.

1,3-Bis-(3,5-dimethoxybenzyl)-5-(hydroxyphenylmethyl)-1*H*-pyrimidine-2,4-dione (2l). The reaction was carried out according to typical procedure **A** using **1e** (700 mg, 1.30 mmol), *i*-PrMgBr (2.11 mL, 1.69 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), and benzaldehyde (179 μL, 1.69 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 1:4) affording the product **2l** (559 mg, 83%) as a colorless oil. IR (neat): 3486 (s), 3055 (s), 2988 (s), 1705 (s), 1663 (m), 1640 (s), 1599 (s), 1159 (s), 1068 (s), 1026 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.39−7.29 (s, 5H), 6.81 (d, J = 1 Hz, 1H), 6.58 (s, 1H), 6.57 (s, 1H), 6.39−6.28 (m, 4H), 5.7 (dd, J = 4 Hz, J = 1 Hz, 1H), 5.07 (s, 2H), 4.76 (s, 2H), 3.73 (s, 12H), 3.61 (d, J = 4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.2, 160.6, 151, 140.2, 139.2, 138.6, 137.1, 128.4, 127.9, 126.4, 116.4, 106.4, 105.7, 100.2, 99.7, 70.3, 55.2, 55.1, 52.5, 44.5. *m/z* (EI-MS): 518 (46), 501 (27), 500 (84), 152 (63), 151 (100). HRMS: calcd for $C_{29}H_{30}N_2O_7$ 518.2052, found 518.2060.

1,3-Bisethoxymethyl-5-(1-hydroxyheptyl)-1*H*-pyrimidine-2,4-dione (2m). The reaction was carried out according to typical procedure A using **1f** (500 mg, 1.41 mmol), *i*-PrMgBr (2.29 mL, 1.83 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), and heptanal (265 μL, 1.97 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 7:3) affording the product **2m** (357 mg, 74%) as a colorless oil. IR (neat): 3489 (s), 2975 (s), 1703 (s), 1652 (s), 1134 (s), 1062 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.25 (s, 1H), 5.35 (s, 2H), 5.1 (s, 2H), 4.46 (t, J = 6.4 Hz, 1H), 3.63−3.49 (m, 4H), 1.67−1.1 (m, 6H), 0.8 (t, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.9, 151.3, 137.8, 116.7, 77.4, 70.5, 68.6, 65.9, 65.2, 35.7, 31.7, 28.9, 25.7, 22.5, 15, 14.8, 13.9. *m/z* (EI-MS): 297 (3), 257 (95), 211 (46), 59 (100). HMRS: calcd for $C_{17}H_{30}N_2O_5$ 342.2155, found 342.2171.

1,3-Dibenzyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (2n). The reaction was carried out according to typical procedure A using **1d** (700 mg, 1.67 mmol), *i*-PrMgBr (2.51 mL, 2.01 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), and *p*-toluenesulfonyl cyanide (424 mg, 2.34 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 3:2) affording the product **2n** (250 mg, 47%) as a white solid, mp 130°C. IR (KBr): 2232 (s), 1722 (s), 1671 (s), 1629 (m), 1584 (m), 1336 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.68 (s, 1H), 7.39−7.17 (m, 10H), 5.03 (s, 2H), 4.87 (s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.9, 149.9, 149.4, 135.3, 133.3, 129.3, 129.2, 128.4, 128, 112.9, 89.7, 53.3, 45.2. *m*/*z* (EI-MS): 317 (59), 226 (56), 121 (47), 91 (100). HRMS: calcd for $C_{19}H_{15}O_2N_3$ 317.1164, found 317.1164.

5-Allyl-1,3-dibenzyl-1*H*-pyrimidine-2,4-dione (2o). The reaction was carried out according to typical procedure A using **1d** (700 mg, 1.67 mmol), *i*-PrMgBr (2.51 mL, 2.01 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), CuCN (10% mol, 20 mg), and allyl bromide (203 μL, 2.34 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 7:3) affording the product **2o** (450 mg, 81%) as a white solid, mp 100 °C. IR (KBr): 1695 (s), 1653 (s), 1638 (s), 1602 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.39−7.15 (s, 10H), 6.83 (s, 1H), 5.68 (m, 1H), 5.05 (s, 2H), 4.98 (d, J = 14.7 Hz, 1H), 4.96 (d, J = 9 Hz, 1H), 4.77 (s, 2H), 2.95 (d, J = 5.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163, 151.7, 138.7, 137, 135.7, 134.5, 129, 128.9, 128.5, 128.4, 127.8, 127.6, 117.5, 112.9, 52.3, 44.8, 31.3. *m*/*z* (EI-MS): 332 (15), 241 (14), 91 (100). HRMS: calcd for $C_{21}H_{20}N_2O_2$ 332.1525, found 332.1521.

2-(1,3-Dibenzyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-ylmethyl)acrylic Ethyl Ester (2p). The reaction was carried out according to typical procedure A using **1d** (700 mg, 1.67 mmol), *i*-PrMgBr (2.51 mL, 2.01 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), CuCN·2LiCl (2.17 mL, 2.17 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate (324 μL, 2.34 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 1:1) affording the product **2p** (514 mg, 76%) as a colorless oil. IR (neat): 1712 (s), 1661 (s), 1651 (m), 1607 (s), 1586 (s), 1209 (s), 1147 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.4−7.14 (m, 10H), 7.08 (s, 1H), 6.14 (d, J = 1.1 Hz, 1H), 5.67 (s, J = 1.1 Hz, 1H), 5.06 (s, 2H), 4.82 (s, 2H), 4.04 (q, J = 7.1 Hz, 2H), 3.23 (s, 2H), 1.14 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 166.6, 162.9, 151.6, 140.3, 137.1, 137, 135.7, 129, 128.2, 128.1, 127.6, 127.5, 126.9, 112.2, 60.8, 52.3, 44.8, 29.7, 14.2. *m*/*z* (EI-MS): 404 (17), 359 (10), 358 (30), 267 (55), 91 (100). HRMS: calcd for $C_{24}H_{24}N_2O_4$ 404.1736, found 404.1737.

5-Allyl-1,3-(3,5-dimethoxybenzyl)-1*H*-pyrimidine-2,4-dione (2q). The reaction was carried out according to typical procedure A using **1e** (700 mg, 1.30 mmol), *i*-PrMgBr (2.11 mL, 1.69 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), CuCN (10% mol, 12 mg), and allyl bromide (169 μL, 1.95 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 3:7) affording the product **2q** (476 mg, 81%) as a white solid, mp 62 °C. IR (KBr): 3062 (s), 2963 (s), 1704 (s), 1664 (m), 1655 (s), 1642 (s), 1596 (s), 1160 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.86 (t, J = 1.1 Hz, 1H), 6.53 (s, 1H), 6.52 (s, 1H), 6.30−6.26 (m, 4H), 5.8−5.67 (m, 1H), 5.03 (s, 2H), 5.05−4.99 (m, 2H), 4.76 (s, 2H), 3.67 (s, 12H), 2.99 (dd, J = 6.6 Hz, J = 1.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.8, 161.3, 160.7, 151.6, 139.2, 138.5, 138, 134.4, 117.4, 112.9, 106.6, 105.7, 99.9, 99.7, 55.3, 55.2, 52.2, 44.7, 31.2. *m*/*z* (EI-MS): 452 (99), 299 (40), 298 (12), 256 (38), 152 (57), 151 (100). HRMS: calcd for $C_{25}H_{28}N_2O_6$ 452.1947, found 452.1940.

2-(1,3-Bisethoxymethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-ylmethyl)acrylic Acid Ethyl Ester (2r). The reaction was carried out according to typical procedure A using **1f** (500 mg, 1.41 mmol), *i*-PrMgBr (2.29 mL, 1.83 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), CuCN·2LiCl (1.97 mL, 1.97 mmol, 1 M in THF), and ethyl (2-bromomethyl)-acrylate (273 μL, 1.97 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 3:7) affording the product **2r** (398 mg, 83%) as a white solid, mp 60 °C. IR (KBr): 1707 (s), 1668 (s), 1653 (s), 1336 (s), 1289 (s), 1146 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.27 (s, 1H), 6.28 (s, 1H), 5.8 (s, 1H), 5.41 (s, 2H), 5.15 (s, 2H), 4.2 (q, J = 7 Hz, 2H), 3.66 (q, J = 7 Hz, 2H), 3.59 (q, J = 6.8 Hz, 2H), 3.36 (s, 2H), 1.29 (t, J = 7 Hz, 3H), 1.20 (t, J = 6.8 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.1, 162.7, 151.1, 139.4, 136.6, 127.6, 111.6, 77.2, 70.6, 65.7, 65, 60.6, 29.3, 15, 14.7, 14. *m*/*z* (EI-MS): 340 (5), 296 (6), 295 (25), 294 (66), 237 (13), 208 (10), 207 (13), 59 (100). HRMS: calcd for $C_{16}H_{24}N_2O_6$ 340.1634, found 340.1636.

5-Benzoyl-1,3-dibenzyl-1*H*-pyrimidine-2,4-dione (2s). The reaction was carried out according to typical procedure A using **1d** (700 mg, 1.67 mmol), *i*-PrMgBr (2.51 mL, 2.01 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), CuCN·2LiCl (2.17 mL, 2.17 mmol, 1 M in THF), and benzoyl chloride (272 μL, 2.34 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 2:3) affording the product **2s** (484 mg, 73%) as a white solid, mp 118 °C. IR (KBr): 1716 (s), 1658 (s), 1645 (m), 1601 (s), 1450 (s), 1382 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.8 (s, 1H), 7.8 (d, J = 7.2 Hz, 2H), 7.36−7.1 (m, 13H), 5.0 (s, 2H), 4.81 (s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.7, 160.1, 150,9, 147.9, 137.5, 136.3, 134.6, 132.9, 129.3, 129.2, 129.1, 128.7, 128.4, 128.3, 128, 127.8, 113.3, 53, 44.7. *m*/*z* (EI-MS): 396 (62), 200 (37), 105 (100). HRMS: calcd for $C_{25}H_{20}N_2O_3$ 396.1474, found 396.1479.

5-Benzoyl-1,3-bisethoxymethyl-1*H*-pyrimidine-2,4-dione (2t). The reaction was carried out according to typical procedure A using **1f** (500 mg, 1.41 mmol), *i*-PrMgBr (2.29 mL, 1.83 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), CuCN·2LiCl (1.97 mL, 1.97 mmol, 1 M in THF), and benzoyl chloride (229 μL, 1.97 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O/MeOH, 8:2:1) affording the product **2t** (351 mg, 75%) as a colorless oil. IR (neat): 3055 (s), 2932 (s), 1728 (s), 1682 (s), 1615 (s), 1582 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.94 (s, 1H), 7.69−7.35 (m, 5H), 5.36 (s, 2H), 5.19 (s, 2H), 3.59 (q, J = 7 Hz, 4H), 1.17 (t, J = 7 Hz, 3H), 1.12 (t, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.5, 160.1, 151, 147.3, 137.3, 133, 129.2, 128.2, 113.9, 78, 70.8, 66, 65.8, 15, 14.8. *m*/*z* (EI-MS): 332 (3), 288 (60), 275 (57), 229 (31), 200 (20). HRMS calcd for $C_{17}H_{20}N_2O_5$ 332.1372, found 332.1371.

1,3-Dibenzyl-5-diallylaminomethyl-1*H*-pyrimidine-2,4-dione (2u). The reaction was carried out according to typical procedure A using **1d** (700 mg, 1.67 mmol), *i*-PrMgBr (2.51 mL, 2.01 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), and *N*,*N*-diallylmethyleniminium salt (2.18 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 1:1) affording the product **2u** (517 mg, 85%) as a colorless oil. IR (neat): 3055 (m), 2986 (s), 1701 (s), 1662 (s), 1643 (s), 1586 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.42−7.14 (m, 10H), 7.15 (s, 1H), 5.65 (qt, J = 17 Hz, J = 10.3 Hz, J = 6.2 Hz, 2H), 5.06 (s, 2H), 5.05−4.97 (m, 4H), 4.84 (s, 2H), 3.27 (s, 2H), 2.94 (d, J = 6.2 Hz, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.9, 151.5, 139.6, 136.9, 135.6, 135.3, 129, 128.9, 128.3, 128.2, 128, 127.5, 117.3, 111.6, 56.8, 52.2, 49.2, 44.5. *m*/*z* (EI-MS): 401 (3), 361 (8), 360 (29), 110 (74), 96 (100). HRMS: calcd. for $C_{25}H_{27}O_2N_3$ 401.2103, found 401.2097.

5-Diallylaminomethyl-1,3-bisethoxymethyl-1*H*-pyrimidine-2,4-dione (2v). The reaction was carried out according typical procedure A using **1e** (500 mg, 1.41 mmol), *i*-PrMgBr (2.29 mL, 1.83 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), and *N*,*N*-diallylmethyleniminium (1.83 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O/MeOH, 5:5:1) affording the product **2v** (390 mg, 82%) as a colorless oil. IR (neat): 2930 (s), 2816 (s), 1713 (s), 1667 (s), 1153 (s), 1055 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37 (s, 1H), 5.82 (qt, J = 15 Hz, J = 8.5 Hz, J = 7.6 Hz, 2H), 5.4 (s, 2H), 5.17 (d, J = 15 Hz, 2H), 5.16 (s, 2H), 5.15 (d, J = 8.5 Hz, 2H), 3.64 (q, J = 7 Hz, 2H), 3.57 (q, J = 7 Hz, 2H), 3.38 (s, 2H), 2.95 (d, J = 7.6 Hz, 4H), 1.20 (t, J = 7 Hz, 3H), 1.18 (t, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ 163, 151.6, 139.6, 135.2, 117.7, 112, 76.7, 70.6,

65.8, 65, 56.9, 49, 15.1, 14.9. *m*/*z* (EI-MS): 337 (1), 296 (7), 192 (11), 137 (11), 110 (22), 96 (100). HMRS: calcd for $C_{17}H_{27}N_3O_4$ 337.2001, found 337.2007.

2-Allyl-5-bromopyrimidine (2w). The reaction was carried out according to typical procedure A using **1g** (285 mg, 1.00 mmol), *i*-PrMgBr (1.53 mL, 1.50 mmol, 0.98 M in THF, exchange at −80 °C, 10 mn), CuCN·2LiCl (1.10 mL, 1.10 mmol, 1.0 M in THF, −80 °C), and allyl bromide (130 μL, 1.50 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 9:1) affording the product **2w** (162 mg, 81%) as a colorless oil. IR (neat): 3082 (m), 3034 (m), 2982 (m), 2238 (w), 1641 (m), 1552 (s), 1539 (vs), 1423 (vs), 1116 (s), 1012 (vs) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 8.67 (s, 2H), 6.06 (ddt, J = 17.1 Hz, J = 12.2 Hz, J = 6.8 Hz, 1H), 5.17 (dd, J = 17.1 Hz, J = 1.5 Hz, 1H), 5.14 (dd, J = 12.2 Hz, J = 1.5 Hz, 1H), 3.66 (d, J = 6.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.6, 157.7, 133.7, 117.8, 117.5, 43.1. *m*/*z* (EI-MS): 199 (35), 198 (100), 118 (30), 41 (94). HRMS: calcd for $C_7H_7BrN_2$ 197.9793, found 197.9797.

4-Allyl-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one (6a). The reaction was carried out according to typical procedure A using **4** (1 g, 3.18 mmol) in CH_2Cl_2 (10 mL), *i*-Pr_2-Mg (3.5 mL, 1.95 mmol, 0.5 M in TBME, exchange at −25 °C, 1 h), CuCN (10% mol, 28 mg), and allyl bromide (386 μL, 4.46 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 1:9) affording the product **6a** (501 mg, 69%) as a colorless oil. IR (neat): 3050 (s), 2980 (s), 1667 (s), 1595 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.43−7.13 (m, 5H), 5.87−5.76 (m, 1H), 5 (dd, J = 17 Hz, J = 1.6 Hz, 1H), 4.94 (dd, J = 8.3 Hz, J = 1.6 Hz, 1H), 3.0 (d, J = 6.3 Hz, 2H), 2.92 (s, 3H), 2.1 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166, 154, 135.7, 129, 126, 123.4, 115, 109, 36.5, 26.7, 11.2. *m*/*z* (EI-MS): 228 (100), 227 (28), 201 (11). HRMS: calcd for $C_{14}H_{16}N_2O$ 228.1263, found 228.1271.

2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-ylmethyl)acrylic Acid Ethyl Ester (6b). The reaction was carried out according to typical procedure A using **4** (1 g, 3.18 mmol) in CH_2Cl_2 (10 mL), *i*-Pr_2Mg (3.5 mL, 1.75 mmol, 0.5 M in TBME, exchange at −25 °C, 1 h), CuCN·2LiCl (3.82 mL, 3.82 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 1:9) affording the product **6b** (688 mg, 72%) as a colorless oil. IR (neat): 3053 (s), 2986 (s), 1713 (s), 1663 (s), 1595 (s), 1200 (s), 1150 (s) cm^{-1}. ^{1}HNMR ($CDCl_3$, 200 MHz): δ 7.35−7.14 (m, 5H), 6.16 (d, J = 1.5 Hz, 1H), 5.65 (d, J = 1.5 Hz, 1H), 4.13 (q, J = 7 Hz, 2H), 3.23 (s, 2H), 2.95 (s, 3H), 2.16 (s, 3H), 1.22 (t, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 167.4, 166.3, 154.7, 137.7, 135.8, 129.4, 126.6, 126.4, 123.8, 108, 61, 36.7, 25, 14.6, 11.7. *m*/*z* (EI-MS): 300 (21), 299 (24), 271 (14), 228 (15), 227 (65), 226 (15). HRMS: calcd for $C_{17}H_{20}N_2O_3$ 300.1474, found 300.1478.

4-Benzoyl-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one (6c). The reaction was carried out according to typical procedure A using **4** (1 g, 3.18 mmol) in CH_2Cl_2 (10 mL), *i*-Pr_2-Mg (3.5 mL, 1.75 mmol, 0.5 M in TBME, exchange at −25 °C, 1 h), CuCN·2LiCl (3.82 mL, 3.82 mmol, 1 M in THF), and benzoyl chloride (443 μL, 3.82 mmol) to give a crude residue, which was then purified by column chromatography on silica (Et_2O/AcOEt, 9:1) affording the product **6c** (679 mg, 73%) as a white solid, mp 149 °C. IR (KBr): 3061 (s), 1668 (s), 1626 (s), 1600 (s), 1579 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 7.91−7.86 (m, 2H), 7.51−7.26 (m, 8H), 3.33 (s, 3H), 2.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 190.7, 163.3, 157.5, 138.7, 134.5, 132.4, 129.8, 128.7, 128.1, 126.7, 107.2, 34.4, 12.8. *m*/*z* (EI-MS): 292 (100), 291 (86), 215 (13). HRMS: calcd for $C_{18}H_{16}N_2O_2$ 292.1212, found 292.1208.

4-(Hydroxyphenylmethyl)-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one (6d). The reaction was carried out according to typical procedure A using **4** (1 g, 3.18 mmol) in CH_2Cl_2 (10 mL), *i*-Pr_2Mg (3.5 mL, 1.95 mmol, 0.5 M in TBME, exchange at −25 °C, 1 h), and benzaldehyde (388 μL, 3.82 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 3:7) affording the product **6d** (805 mg, 86%) as a white solid, mp 140°C. IR (KBr): 3325 (s), 3063 (m), 1636 (s), 1606 (m), 1341 (s), 1026 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.45−7.22 (m, 10H), 5.60 (d, J = 7.5 Hz, 1H), 4.94 (d, J = 7.5 Hz, 1H), 2.98 (s, 3H), 2 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166, 151.3, 143.5, 135, 129, 128.3, 127.2, 126.7, 126, 124, 112, 69, 35.4, 11. *m*/*z* (EI-MS): 294 (36), 217 (64), 202 (20), 105 (37), 77 (33), 56 (100). HRMS: calcd for $C_{18}H_{18}O_2N_2$ 294.1368, found 294.1379.

4-Diallylaminomethyl-1,5-dimethyl-1,2-dihydropyrazol-3-one (6e). The reaction was carried out according to typical procedure A using **4** (1 g, 3.18 mmol) in CH_2Cl_2 (10 mL), *i*-Pr_2-Mg (3.5 mL, 1.75 mmol, 0.5 M in TBME, exchange at −25 °C, 1 h), and *N*,*N*-diallylmethyleniminium salt (4.47 mmol) to give a crude residue, which was then purified by column chromatography on silica (Et_2O/MeOH, 95:5) affording the product **6e** (794 mg, 84%) as a colorless oil. IR (neat): 3051 (s), 2980 (s), 2924 (s), 2808 (s), 1661 (s), 1595 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 7.2−7.12 (m, 5H), 5.89−5.73 (m, 2H), 5.17−5.02 (m, 4H), 3.24 (s, 2H), 3.04 (d, J = 6.3 Hz, 4H), 2.95 (s, 3H), 2.19 (s, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 166.8, 156, 136.4, 135.8, 129.4, 126.5, 124, 117.8, 107.7, 57.1, 45.7, 36.3, 11.8. *m*/*z* (EI-MS): 297 (97), 201 (100), 110 (21), 96 (52). HRMS: calcd for $C_{18}H_{23}N_3O$ 297.1841, found 297.1836.

4-But-1-enyl-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one (7a). The reaction was carried out according to typical procedure A using **4** (500 mg, 1.6 mmol, 6 mL of CH_2Cl_2), *i*-Pr_2-Mg (1.75 mL, 0.87 mmol, 0.5 M in TBME, exchange −25 °C, 1 h), and *n*-butyraldehyde (186 μL, 2 mmol) to give a crude residue, which was then purified by column chromatography on silica (Et_2O/MeOH, 95:5) affording the product **7a** (258 mg, 67%) as colorless crystals, mp 83 °C. IR (KBr): 2956 (m), 2929 (m), 2870 (w), 1667 (s), 1595 (m), 1496 (m), 1456 (m), 1343 (m), 1075 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.35−7.20 (m, 5H), 6.72 (dt, J = 15.5 Hz, J = 7.5 Hz, 1H), 5.98 (dt, J = 15.5 Hz, J = 1.3 Hz, 1H), 2.94 (s, 3H), 2.16 (s, 3H), 2.11 (m, 2H), 0.98 (t, J = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.0, 151.5, 135.6, 133.9, 129.4, 126.7, 124.3, 117.0, 108.5, 42.7, 36.4, 27.3, 19.5, 14.2, 11.3. *m*/*z* (EI-MS): 242 (43), 241 (19), 228 (14), 227 (100), 217 (29), 150 (27). HRMS: calcd for $C_{15}H_{18}N_2O$ 242.1419, found 242.1414.

4-Pent-1-enyl-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one (7b). The reaction was carried out according to typical procedure A using **4** (500 mg, 1.6 mmol, CH_2Cl_2 (6 mL)), *i*-Pr_2Mg (1.75 mL, 0.87 mmol, 0.5 M in TBME, exchange: −25 °C, 1 h), and *n*-valeraldehyde (200 μL, 2 mmol) to give a crude residue, which was then purified by column chromatography on silica (Et_2O/MeOH, 9.5:0.5) affording the product **7b** (285 mg, 70%) as colorless crystals, mp 93−94 °C. IR (KBr): 2947 (s), 2929 (s), 2865 (s), 1634 (s), 1634 (s), 1616 (s), 1592 (s), 1486 (m), 1312 (m), 1256 (m), 1080 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.18−7.03 (m, 5H), 6.49 (dt, J = 15.5 Hz, J = 7.2 Hz, 1H), 5.80 (dt, J = 15.5 Hz, J = 1.2 Hz, 1H), 2.76 (s, 3H), 1.97 (s, 3H), 1.89 (m, 2H), 1.21 (m, 2H), 0.67 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.0, 151.6, 135.6, 132.2, 129.4, 126.7, 124.3, 118.1, 108.5, 36.5, 23.1, 14.2, 11.3. *m*/*z* (EI-MS): 256 (26), 228 (13), 227 (100), 217 (66), 164 (14). HRMS: calcd for $C_{15}H_{20}N_2O$ 256.1576, found 256.1563.

4-Dec-1-enyl-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one (7c). The reaction was carried out according to typical procedure A using **4** (500 mg, 1.6 mmol, CH_2Cl_2 (6 mL)), *i*-Pr_2-Mg (1.75 mL, 0.87 mmol, 0.5 M in TBME, exchange: −25 °C, 1 h), and *n*-decanal (345 μL, 1.83 mmol) to give a crude residue, which was then purified by column chromatography on silica (Et_2O/MeOH, 9.5:0.5) affording the product **7d** (374 mg, 72%) as a colorless oil. IR (neat): 2925 (vs), 2854 (m), 1646 (s), 1665 (s), 1594 (m), 1496 (m), 1456 (m), 1340 (w), 1077 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.32−7.09 (m, 5H), 6.68 (dt, J = 15.9 Hz, J = 6.9 Hz, 1H), 5.94 (dt, J = 15.9 Hz, J = 1.5 Hz, 1H), 2.86 (s, 3H), 2.09 (s, 3H), 2.05 (m, 2H), 1.38−1.10 (m, 12H), 0.77 (t, J = 7.20 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.6, 151.7, 135.9, 132.1, 129.2, 126.2, 124.2, 117.9, 108.2, 36.4, 34.4, 31.9, 29.9, 29.8, 23.0, 14.4, 10.9. *m*/*z* (EI-MS): 326 (18), 241 (12), 234 (15), 228 (14), 227 (100). HRMS: calcd for $C_{21}H_{30}N_2O$ 326.2358, found 326.2339.

4-Deca-1,4-dienyl-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one (7d). The reaction was carried out according to typical procedure A using **4** (500 mg, 1.6 mmol, CH_2Cl_2 (6

mL)), *i*-Pr_2Mg (1.75 mL, 0.87 mmol, 0.5 M in TBME, exchange: −25 °C, 1 h), and *trans*-4-decen-1-al (335 μL, 1.83 mmol) to give a crude residue, which was then purified by column chromatography on silica (Et_2O/MeOH, 9.5:0.5) affording the product **7d** (294 mg, 57%) as colorless crystals, mp 38 °C. IR (KBr): 2955 (s), 2927 (s), 2856 (m), 1659 (vs), 1592 (s), 1496 (s), 1456 (m), 1366 (w), 1311 (w), 1136 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.34−7.15 (m, 5H), 6.69 (dt, *J* = 15.7 Hz, *J* = 6.6 Hz, 1H), 5.98 (dt, *J* = 15.7 Hz, *J* = 1.6 Hz, 1H), 5.46−5.32 (m, 2H), 2.94 (s, 3H), 2.79 (m, 2H), 2.15 (s, 3H), 1.91 (m, 2H), 1.30−1.16 (m, 6H), 0.81 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.4, 151.1, 135.2, 131.5, 130, 128.9, 127.7, 126.2, 123.7, 117.8, 108.1, 36.6, 35.9, 32.5, 31.9, 29.1, 22.4, 13.9, 10.8. *m*/*z* (EI-MS): 324 (29), 267 (21), 232 (19), 227 (29), 201 (100). HRMS: calcd for $C_{21}H_{28}N_2O$ 324.2202, found 324.2177.

4-Cyclopent-1-enyl-1,5-dimethyl-2-phenyl-1,2dihydropyrazol-3-one (8). The reaction was carried out according to typical procedure A using **4** (500 mg, 1.6 mmol, CH_2Cl_2 (6 mL)), *i*-Pr_2Mg (1.75 mL, 0.87 mmol, 0.5 M in TBME, exchange: −25 °C, 1 h), and cyclopentanone (162 μL, 1.83 mmol) to give a crude residue, which was then purified by column chromatography on silica (Et_2O/MeOH, 9.5:0.5) affording the product **8** (263 mg, 65%) as colorless crystals, mp 102 °C. IR (KBr): 2947 (w), 2839 (w), 1653 (s), 1596 (w), 1557 (w), 1455 (w), 1302 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.34−7.15 (m, 5H), 6.26 (m, 1H), 2.95 (s, 3H), 2.68 (m, 2H), 2.37 (m, 2H), 2.24 (s, 3H), 1.83 (s, *J* = 6.9 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.0, 151.4, 135.7, 133.8, 129.4, 128.2, 127.1, 124.0, 108.2, 36.4, 35.7, 33.1, 24.9, 12.2. *m*/*z* (EI-MS): 255 (15), 254 (100), 253 (29), 162 (51). HRMS: calcd for $C_{16}H_{18}N_2O$ 254.1419, found 254.1421.

3-Ethoxymethyl-5-iodo-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (11a). The reaction was carried out according to typical procedure A using **9** (2.74 g, 7.00 mmol), in THF/NBP (10:1, 22 mL), *i*-PrMgBr (8.60 mL, 7.70 mmol, 0.90 M in THF, exchange −40 °C, 1.5 h), and ethyl cyanoformate (760 μL, 7.70 mmol, 0°C, 16 h) to give a crude residue, which was then purified by column chromatography on silica (pentane/AcOEt, 7:3) affording the product **11a** (900 mg, 38%) as a colorless oil. IR (neat): 2967 (vs), 2910 (m), 1705 (vs), 1483 (m), 1246 (s), 1211 (s), 1105 (s), 1020 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.65 (s, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.46 (q, *J* = 7.0 Hz, 2H), 2.44 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.3, 152.4, 124.3, 93.0, 73.7, 64.0, 60.7, 14.6, 13.8, 13.3. *m*/*z* (EI-MS): 338 (31), 294 (18), 235 (11), 59 (100). HRMS: calcd for $C_{10}H_{15}IN_2O_3$ 338.0127, found 338.0131.

5-Bromo-1-ethoxymethyl-4-iodo-2-methyl-1*H*-imidazole (11b). The reaction was carried out according to typical procedure A using **9** (1.567 g, 4.00 mmol), in THF/NBP (10:1, 9.5 mL), *i*-PrMgBr (4.30 mL, 4.20 mmol, 0.98 M in THF, exchange −40 °C, 1.5 h), and 1,2-dibromo-1,1,2,2-tetrachloroethane (1.68 g, 5.00 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/AcOEt, 4:1) affording the product **11b** (1.167 g, 85%) as colorless crystals, mp 53 °C. IR (KBr): 2980 (m), 1516 (m), 1388 (m), 1339 (vs), 1261 (m), 1178 (s), 1127 (m), 1099 (vs), 1056 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.20 (s, 2H), 3.41 (q, *J* = 7.0 Hz, 2H), 2.39 (s, 3H), 1.15 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 148.6, 109.6, 85.3, 74.6, 64.3, 14.7, 13.9. *m*/*z* (EI-MS): 345 (20), 221 (5), 59 (100). HRMS: calcd for $C_7H_{10}BrIN_2O$ 343.9021, found 343.9019.

3-Ethoxymethyl-5-(hydroxyphenylmethyl)-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (12a). The reaction was carried out according to typical procedure A using **11a** (350 mg, 1.00 mmol), *i*-PrMgBr (1.22 mL, 1.10 mmol, 0.9 M in THF, exchange at −40 °C, 30 min), and benzaldehyde (150 μL, 1.50 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 1:1) affording the product **12a** (209 mg, 66%) as a white solid, mp 112−113 °C. IR (KBr): 3232 (br), 2926 (s), 1698 (s), 1376 (m), 1261 (m), 1174 (m), 1097 (vs) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.35−7.33 (m, 2H), 7.25−7.15 (m, 3H), 6.17 (s, 1H), 5.65 (d, *J* = 10.7 Hz, 1H), 5.57 (d, *J* = 10.7 Hz, 1H), 4.24−4.17 (m, 2H), 3.45 (q, *J* = 7.0 Hz, 2H), 2.42 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.5, 151.2, 150.4, 143.5, 128.2, 127.3, 126.6, 117.8, 73.7, 70.2, 64.2, 60.8, 15.0, 14.2, 13.7. *m*/*z* (EI-MS): 318 (3), 259 (10), 213 (13), 183 (25), 168 (29), 59 (100). HRMS: calcd for $C_{17}H_{22}N_2O_4$ 318.1580, found 318.1577.

3-Ethoxymethyl-5-formyl-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (12b). The reaction was carried out according to typical procedure A using **11a** (94 mg, 0.28 mmol), *i*-PrMgBr (0.31 mL, 0.30 mmol, 0.98 M in THF, exchange at −40 °C, 30 min), and DMF (0.08 mL, 1.00 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 1:3) affording the product **12b** (40 mg, 59%) as a colorless oil. IR (neat): 2980 (s), 2930 (s), 1714 (vs), 1690 (vs), 1520 (s), 1246 (s), 1179 (s), 1105 (vs), 1016 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 10.31 (s, 1H), 5.68 (s, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 3.47 (q, *J* = 7.0 Hz, 2H), 2.49 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 185.3, 159.2, 151.8, 142.8, 128.6, 73.8, 64.5, 61.9, 14.8, 14.1, 13.5. *m*/*z* (EI-MS): 240 (4), 211 (5), 194 (24), 122 (18), 59 (100). HRMS calcd for $C_{11}H_{16}N_2O_4$ 240.1110, found 240.1112.

5-Allyl-3-ethoxymethyl-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (12c). The reaction was carried out according to typical procedure A using **11a** (276 mg, 0.70 mmol), *i*-PrMgBr (1.00 mL, 0.74 mmol, 0.73 M in THF, exchange at −40 °C, 30 min), CuCN·2LiCl (0.74 mL, 0.74 mmol, 1.0 M in THF), and allyl bromide (90 μL, 1.00 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 1:1) affording the product **12c** (160 mg, 91%) as a colorless oil. IR (neat): 3079 (w), 2980 (s), 1701 (vs), 1676 (vs), 1479 (s), 1387 (vs), 1302 (vs), 1255 (vs), 1172 (vs), 1099 (vs), 1020 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.92 (ddt, J = 17.0, *J* = 10.0, *J* = 6.6 Hz, 1H), 5.61 (s, 2H), 5.04 (ddt, J = 17.0 Hz, *J* = 1.7 Hz, *J* = 1.4 Hz, 1H), 4.97 (ddt, *J* = 10.0 Hz, *J* = 1.7 Hz, *J* = 1.4 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.55 (dt, *J* = 6.6 Hz, *J* = 1.4 Hz, 2H), 3.44 (q, *J* = 7.0 Hz, 2H), 2.40 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.9, 150.2, 148.5, 135.6, 118.3, 115.7, 73.4, 63.8, 60.2, 34.0, 14.8, 14.2, 13.5. *m*/*z* (EI-MS): 252 (53), 206 (36), 147 (53), 134 (48), 59 (100). HRMS: calcd for $C_{13}H_{20}N_2O_3$ 252.1474, found 252.1476.

5-(2-Ethoxycarbonylallyl)-3-ethoxymethyl-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (12d). The reaction was carried out according to typical procedure A using **11a** (200 mg, 0.59 mmol), *i*-PrMgBr (0.85 mL, 0.62 mmol, 0.73 M in THF, exchange at −40 °C, 30 min), CuCN·2LiCl (0.62 mL, 0.62 mmol, 1.0 M in THF), and ethyl (2-bromomethyl)-acrylate (0.143 g, 0.74 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 1:3) affording the product **12d** (118 mg, 62%) as a colorless oil. IR (neat): 3108 (w), 2980 (s), 1707 (vs), 1676 (vs), 1512 (s), 1479 (m), 1300 (s), 1255 (vs), 1172 (vs), 1099 (vs) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 6.14 (d, J = 1.3 Hz, 1H), 5.63 (s, 2H), 5.25 (d, *J* = 1.3 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.80 (s, 2H), 3.45 (q, *J* = 7.0 Hz, 2H), 2.40 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.15 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.8, 160.8, 150.2, 147.1, 138.6, 125.0, 119.2, 73.4, 63.9, 60.5, 60.2, 31.5, 14.8, 14.1, 14.0, 13.5. *m*/*z* (EI-MS): 325 (19), 324 (84), 265 (44), 175 (24), 59 (100). HRMS: calcd. for $C_{16}H_{24}N_2O_5$ 324.1685, found 324.1685.

5-Benzoyl-3-ethoxymethyl-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (12e). The reaction was carried out according to typical procedure A using **11a** (249 mg, 0.74 mmol), *i*-PrMgBr (1.11 mL, 0.81 mmol, 0.73 M in THF, exchange at −40 °C, 30 mn), CuCN·2LiCl (0.81 mL, 0.81 mmol, 1.0 M in THF), and benzoyl chloride (230 μL, 2.00 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 1:1) affording the product **12e** (156 mg, 67%) as a colorless oil. IR (neat): 3061 (w), 2980 (s), 1716 (vs), 1676 (vs), 1512 (s), 1448 (s), 1373 (s), 1215 (vs), 1178 (vs), 1105 (vs) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.87−7.84 (m, 2H), 7.53−7.37 (m, 3H), 5.68 (s, 2H), 3.97 (q, *J* = 7.1 Hz, 2H), 3.53 (q, *J* = 7.0 Hz, 2H), 2.52 (s, 3H),

1.15 (t, J = 7.0 Hz, 3H), 0.85 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.8, 159.8, 150.2, 144.1, 137.2, 133.0, 129.6, 128.2, 122.4, 73.5, 64.3, 61.0, 14.8, 13.4, 13.2. *m/z* (EI-MS): 316 (18), 259 (20), 212 (60), 105 (41), 59 (100). HRMS: calcd for $C_{17}H_{20}N_2O_4$ 316.1423, found 316.1421.

3-Ethoxymethyl-2-methyl-5-phenyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (12f). **11a** (344 mg, 1.00 mmol) in THF (2 mL) was cooled to −40 °C, and *i*-PrMgBr (2.89 mL, 1.10 mmol, 0.38 M in THF) was added dropwise. The reaction mixture was stirred for 45 min, $ZnBr_2$ (0.80 mL, 1.20 mmol, 1.5 M in THF) was added, and the reaction mixture was allowed to reach room temperature. Iodobenzene (312 mg, 1.50 mmol), $Pd(dba)_2$ (53 mg, 0.10 mmol), dppf (55 mg, 0.10 mmol), and NBP (2 mL) were added. The reaction mixture was stirred for 20 h at 90 °C, quenched with brine, and worked up as usual. The crude residue was purified by column chromatography on silica (pentane/EtOAc, 3:2) to give as a brown oil **12f** (181 mg, 63%). IR (neat): 3057 (w), 3033 (w), 2980 (m), 1701 (vs), 1483 (s), 1385 (s), 1246 (vs), 1176 (vs), 1101 (vs), 1074 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.60−7.57 (m, 2H), 7.36−7.30 (m, 3H), 5.69 (s, 2H), 4.17 (q, J = 7.1 Hz, 2H), 3.54 (q, J = 7.0 Hz, 2H), 2.52 (s, 3H), 1.16 (t, J = 7.0 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.1, 150.1, 148.2, 134.5, 129.6, 128.0, 127.5, 118.4, 73.8, 64.1, 60.5, 15.0, 13.8, 13.6. *m/z* (EI-MS): 288 (66), 244 (50), 213 (41), 185 (38), 59 (100). HRMS: calcd for $C_{16}H_{20}N_2O_3$ 288.1474, found 288.1473.

4-Diallylaminomethyl-3-ethoxymethyl-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (12g). The reaction was carried out according to typical procedure A using **11a** (348 mg, 1.03 mmol), *i*-PrMgBr (1.44 mL, 1.05 mmol, 0.73 M in THF, exchange at −35 °C, 45 min), and *N*,*N*-diallylmethyleniminium salt (1.51 mmol) giving a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 1:1) affording the product **12g** (200 mg, 60%) as a colorless oil. IR (neat): 3077 (m), 2980 (vs), 1701 (s), 1421 (m), 1174 (m), 1018 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.86 (ddt, J = 17.2 Hz, J = 10.2 Hz, J = 6.6 Hz, 2H), 5.60 (s, 2H), 5.09 (dd, J = 17.2 Hz, J = 2.0 Hz, 2H), 5.04 (dd, J = 10.2 Hz, J = 2.0 Hz, 2H), 4.26 (q, J = 7.1 Hz, 2H), 3.74 (s, 2H), 3.42 (q, J = 7.0 Hz, 2H), 3.12 (d, J = 6.6 Hz, 4H), 2.40 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.07 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.9, 150.2, 147.3, 135.8, 120.0, 117.2, 73.4, 63.8, 60.3, 56.9, 50.4, 14.8, 14.2, 13.5. *m/z* (EI-MS): 322 (5), 321 (30), 226 (100), 167 (46), 96 (52), 59 (60). HRMS: calcd for $C_{17}H_{27}N_3O_3$ 321.2052, found 321.2045.

4-Allyl-5-bromo-1-ethoxymethyl-2-methyl-1*H*-imidazole (12h). The reaction was carried out according to typical procedure A using **11b** (345 mg, 1.00 mmol), *i*-PrMgBr (1.12 mL, 1.10 mmol, 0.98 M in THF, exchange at −50 °C, 10 min), CuCN·2LiCl (1.20 mL, 1.20 mmol, 1.0 M in THF), and allyl bromide (170 μL, 2.00 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 4:1) affording the product **12h** (216 mg, 83%) as a colorless oil. IR (neat): 3079 (m), 2978 (vs), 1516 (m), 1404 (s), 1385 (vs), 1352 (s), 1101 (vs), 1063 (s), 1026 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.87 (ddt, J = 16.6 Hz, J = 10.0 Hz, J = 6.5 Hz, 1H), 5.17 (s, 2H), 5.08 (ddt, J = 16.6 Hz, J = 1.6 Hz, 1.5 Hz, 1H), 4.98 (ddt, J = 10.0 Hz, J = 1.6 Hz, J = 1.5 Hz, 1H), 3.43 (q, J = 7.0 Hz, 2H), 3.20 (dt, J = 6.5 Hz, J = 1.5 Hz, 2H), 2.38 (s, 3H), 1.11 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 146.1, 136.6, 135.0, 115.7, 99.6, 73.4, 63.9, 31.6, 14.7, 13.8. *m/z* (EI-MS): 259 (6), 200 (3), 80 (10), 59 (100). HRMS: calcd for $C_{10}H_{15}BrN_2O$ 258.0368, found 258.0377.

2-Allyl-1-benzyl-3-iodo-1*H*-indole (14a). The reaction was carried out according to typical procedure A using **13a** (367 mg, 0.8 mmol), *i*-PrMgBr (1.15 mL, 0.84 mmol, 0.73 M in THF, exchange at −30 °C, 2 h), CuCN·2LiCl (80 μL, 0.08 mmol, 1 M in THF), and allyl bromide (145 mg, 1.2 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 95:5) affording the product **14a** (275 mg, 92%) as a colorless liquid. IR (neat): 1495 (s), 1183 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71−7.66 (m, 1H), 7.45−7.37 (m, 6H), 7.16−7.14 (m, 2H), 6.09−6.00 (m, 1H), 5.55 (s, 2H), 5.31−5.18 (m, 2H), 3.79−3.77 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.4, 137.4, 133.5, 130.1, 128.8, 127.4, 125.8, 122.5, 121.1, 120.5, 116.8, 109.8, 60.1, 47.5, 31.5. *m/z* (EI-MS): 374 (23), 373 (100), 246 (14), 155 (11), 154 (15), 92 (11), 91 (76). HRMS: calcd for $C_{18}H_{16}IN$ 373.0328, found 373.0323.

2-Allyl-3-iodo-1-(toluene-4-sulfonyl)-1*H*-indole (14b). The reaction was carried out according to typical procedure A using **13b** (262 mg, 0.5 mmol), *i*-PrMgBr (0.72 mL, 0.53 mmol, 0.73 M in THF, exchange at −30 °C, 2 h), CuCN·2LiCl (50 μL, 0.05 mmol, 1 M in THF), and allyl bromide (189 mg, 1.5 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/Et_2O, 98:2) affording the product **14b** (184 mg, 84%) as colorless liquid. IR (neat): 1434 (s), 1396 (m), 1221 (s), 1176 (m) cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.06−8.01 (m, 1H), 7.57−7.53 (m, 2H), 7.24−7.04 (m, 5H), 6.01−5.80 (m, 1H), 5.09−4.97 (m, 2H), 3.86 (dt, J = 6, J = 1.5 Hz, 2H), 2.20 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.5, 139.2, 136.9, 136.1, 134.1, 132.1, 130.3, 127.0, 125.9, 124.6, 122.0, 117.5, 115.4, 74.8, 33.76, 22.0. *m/z* (EI-MS): 437 (16), 437 (50), 282 (14), 156 (14), 155 (100), 154 (66), 91 (42), 84 (23). HRMS: calcd for $C_{18}H_{16}INO_2S$ 436.9947, found 436.9941.

2-(2,3,5,6-Tetrafluoropyridin-4-ylmethyl)acrylic Acid Ethyl Ester (17). The reaction was carried out according to typical procedure A using **15** (300 mg, 1.30 mmol), *i*-PrMgBr (2.12 mL, 1.69 mmol, 0.8 M in THF, exchange at −40 °C, 30 min), CuCN·2LiCl (1.82 mL, 1.82 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate (376 mg, 1.95 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 94:6) affording the product **17** (274 mg, 80%) as a colorless oil. IR (neat): 3111 (s), 3063 (s), 2986 (s), 2941 (s), 1717 (s), 1649 (s), 1215 (s), 1142 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.3 (s, 1H), 5.53 (s, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.75 (s, 2H), 1.23 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.5, 145, 138.8, 135, 132, 128, 61.5, 26.4, 14. *m/z* (EI-MS): 263 (18), 235 (36), 218 (24), 215 (27), 190 (19), 189 (12), 187 (15), 186 (22), 171 (13), 170 (60), 164 (19), 29 (100). HRMS calcd for $C_{11}H_9F_4NO_2$ 263.0569, found 263.0575.

Phenylthiazol-2-yl-methanol (18). The reaction was carried out according to typical procedure A using **16** (500 mg, 3.05 mmol), *i*-Pr_2Mg (6.7 mL, 3.35 mmol, 0.5 M in TBME, exchange at room temperature, 1.5 h), and benzaldehyde (620 μL, 6.09 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 5:5) affording the product **18** (437 mg, 75%) as colorless crystals, mp 106 °C. IR (KBr): 3122 (s), 2851 (s), 1597 (s), 1584 (m), 1141 (s), 1087 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.58 (d, J = 3.2 Hz, 1H), 7.39−7.23 (m, 5H), 7.19 (d, J = 3.2 Hz, 1H), 5.96 (s, 1H), 4.2 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 174.6, 142.2, 141.5, 128.7, 128.4, 126.6, 119.5, 73.7. *m/z* (EI-MS): 191(100), 190 (20), 162 (29), 114 (23). HRMS: calcd for $C_{10}H_9NOS$ 191.0405, found 191.0409.

5-Bromothiophen-2-carboxylic Acid Ethyl Ester (19b). The reaction was carried out according to typical procedure A using **19d** (520 mg, 2.15 mmol), *i*-PrMgBr (2.85 mL, 2.25 mmol, 0.8 M in THF, exchange: −20 °C, 15 min), and ethyl cyanoformate (0.36 mL, 3.65 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 95:5) affording the product **19b** (363 mg, 72%) as a colorless oil. IR (neat): 3101 (s), 2984 (s), 2938 (s), 2873 (s), 1713 (s), 1209 (s), 1173 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.43 (d, J = 3.7 Hz, 1H), 6.96 (d, J = 3.7 Hz, 1H), 4.77 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161, 135.3, 133.5, 131, 120, 61.4, 14.3. *m/z* (EI-MS): 236 (40), 234 (39), 208 (20), 206 (45), 191 (54), 190 (18), 189 (100). HRMS: calcd for $C_7H_7BrSO_2$ 234.9350, found 234.9387.

5-Allyl-1-ethoxymethyl-2-methyl-1*H*-imidazole-4-carbonitrile (20a). The reaction was carried out according to typical procedure A using **12i** (111 mg, 0.45 mmol), *i*-PrMgBr (0.51 mL, 0.50 mmol, 0.98 M in THF, exchange at −50 °C, 10 mn), CuCN·2LiCl (0.51 mL, 0.51 mmol, 1.0 M in THF), and allyl bromide (70 μL, 0.80 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 1:1) affording the product **20a** (60 mg, 65%) as a

colorless oil. IR (neat): 3084 (m), 2980 (vs), 2931 (m), 2901 (m), 2228 (vs), 1641 (m), 1537 (vs), 1424 (vs), 1387 (s), 1356 (s), 1109 (vs) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.82 (ddt, J = 16.8 Hz, J = 10.1 Hz, J = 6.0 Hz, 1H), 5.15 (d, J = 10.1 Hz, 1H), 5.14 (s, 2H), 5.06 (d, J = 16.8 Hz, 1H), 3.51 (t, J = 6.0 Hz, 2H), 3.43 (q, J = 7.0 Hz, 2H), 2.40 (s, 3H), 1.11 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.3, 139.6, 132.4, 128.3, 118.9, 114.7, 73.3, 64.4, 28.2, 14.7, 13.4. *m/z* (EI-MS): 205 (5), 159 (3), 121 (7), 59 (100). HRMS: calcd for $C_{11}H_{15}N_3O$ 205.1215, found 205.1218.

5-Allylfuran-2-carboxylic Acid Ethyl Ester (20b). The reaction was carried out according to typical procedure A using **19a** (750 mg, 3.42 mmol), *i*-PrMgBr (5.14 mL, 4.11 mmol, 0.8 M in THF, exchange at −30 °C, 1 h), CuCN (10% mol, 31 mg), and allyl bromide (593 μL, 6.85 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 9:1) affording the product **20b** (492 mg, 80%) as a colorless oil. IR (neat): 3084 (s), 2982 (s), 2937 (s), 1717 (s), 1643 (s), 1595 (s), 1206 (s), 1174 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.1 (d, J = 3.4 Hz, 1H), 6.15 (d, J = 3.4 Hz, 1H), 6−5.86 (m, 1H), 5.22−5.11 (m, 2H), 4.36 (q, J = 7 Hz, 2H), 3.35 (d, J = 6.2 Hz, 2H), 1.35 (t, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.8, 158.7, 143.6, 132.5, 119, 118, 108, 60.7, 32.8, 14.3. *m/z* (EI-MS): 181 (24), 180 (100), 179 (23), 167 (12), 152 (23), 135 (75). HRMS: calcd for $C_{10}H_{12}O_3$ 180.0786, found 180.0779.

5-(Hydroxyphenylmethyl)-furan-2-carboxylic Acid Ethyl Ester (20c). The reaction was carried out according to typical procedure A using **19a** (750 mg, 3.42 mmol), *i*-PrMgBr (5.14 mL, 4.11 mmol, 0.8 M in THF, exchange at −30 °C, 1 h), and benzaldehyde (452 μL, 4.45 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 7:3) affording the product **20c** (615 mg, 73%) as a colorless oil. IR (neat): 3435 (s), 3088 (s), 3063 (s), 2876 (s), 1713 (s), 1643 (s), 1213 (s), 1093 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.43−7.07 (m, 5H), 7.08 (d, J = 3.7 Hz, 1H), 6.21 (d, J = 3.7 Hz, 1H), 5.86 (s, 1H), 4.33 (q, J = 7 Hz, 2H), 2.88 (bs, 1H), 1.34 (t, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.5, 158.9, 144.5, 140, 128.7, 128.5, 127, 118.6, 109.2, 70.2, 61, 14.4. *m/z* (EI-MS): 246 (19), 217 (11), 201 (14), 174 (11), 173 (100). HRMS: calcd for $C_{14}H_{14}O_4$ 246.0892, found 246.0911.

2-Ethoxycarbonyl-5-(1-hydroxybenzyl)thiophene (20d). The reaction was carried out according to typical procedure A using **19b** (560 mg, 2.38 mmol), *i*-PrMgBr (3.57 mL, 2.86 mmol, 0.8 M in THF, exchange: −40 °C, 1 h), and benzaldehyde (315 μL, 3.10 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 7:3) affording the product **20d** (450 mg, 72%) as a colorless oil. IR (neat): 3468 (s), 3055 (s), 2687 (s), 1709 (s), 1601 (s), 1581 (s), 1265 (s), 1155 (s), 1041 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.52 (d, J = 3.6 Hz, 1H), 7.35−7.17 (m, 5H), 6.77 (d, J = 3.6 Hz, 1H), 5.9 (s, 1H), 4.2 (q, J = 7 Hz, 2H), 2.6 (bs, 1H), 1.25 (t, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.5, 155.7, 142.6, 133.3, 129, 128.8, 128.5, 126.5, 125, 72.7, 61.2, 14.4. *m/z* (EI-MS): 262 (25), 261 (11), 245 (15), 217 (13), 189 (23), 157 (100). HRMS: calcd for $C_{14}H_{14}SO_3$ 262.0664, found 262.0672.

2-Bromo-6-(2-propenyl)pyridin (20e). The reaction was carried out according to typical procedure A using **19c** (600 mg, 2.53 mmol) in CH_2Cl_2 (5 mL), *i*-Pr_2Mg (5.57 mL, 2.78 mmol, 0.5 M in TBME, exchange at room temperature, 4 h), CuCN (10% mol, 23 mg), and allyl bromide (460 μL, 5.31 mmol, 2 h at room temperature) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 97:3) affording the product **20e** (320 mg, 68%) as a colorless oil. IR (neat): 3055 (s), 2687 (s), 1667 (s), 1584 (s), 1557 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.42−7.35 (m, 1H), 7.25−7.20 (m, 1H), 7.07−7.03 (m, 1H), 6.04−5.83 (m, 1H), 5.13−5.03 (m, 2H), 3.47 (dt, J = 6.8 Hz, J = 2.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.6, 141.3, 138.6, 134.7, 125.4, 121.3, 117.3, 42. *m/z* (EI-MS): 199 (18), 198 (100), 197 (20), 196 (98), 117 (30). HRMS: calcd for C_8H_8NBr 196.9840, found 196.9816.

(6-Bromopyridin-2-yl)phenylmethanol (20f). The reaction was carried out according to typical procedure A using **19c** (600 mg, 2.53 mmol) in CH_2Cl_2 (5 mL), *i*-Pr_2Mg (5.57 mL, 2.78 mmol, 0.5 M in TBME, exchange at room temperature, 4 h), and benzaldehyde (309 μL, 3.04 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 85:15) affording the product **20f** (421 mg, 63%) as a colorless oil. IR (neat): 3432 (s), 3055 (s), 2986 (s), 1584 (s), 1557 (s), 1086 (s), 1049 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.48−7.11 (m, 8H), 5.74 (d, J = 4 Hz, 1H), 4.44 (d, J = 4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163, 142.3, 140.9, 139.2, 128.7, 128.2, 127, 126.8, 120, 75. *m/z* (EI-MS): 265 (9), 86 (45), 84 (100), 79 (14), 78 (14), 77 (10), 49 (20), 47 (26). HRMS: calcd for $C_{12}H_{10}NBrO$ 262.9946, found 262.9939.

2-Allyl-5-bromothiophene (20g). The reaction was carried out according to typical procedure A using **19d** (520 mg, 2.15 mmol), *i*-PrMgBr (2.85 mL, 2.25 mmol, 0.8 M in THF, exchange −20 °C, 15 min), CuCN (10% mol, 19 mg), and allyl bromide (262 μL, 2.58 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 98:2) affording the product **20g** (377 mg, 86%) as a colorless oil. IR (neat): 3054 (s), 2986 (s), 2831 (s), 1641 (s), 1603 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 6.78 (d, J = 3.6 Hz, 1H), 6.47 (d, J = 3.6 Hz, 1H), 5.91−5.80 (m, 1H), 5.07 (d, J = 15.8 Hz, 1H), 5.07 (d, J = 9.5 Hz, 1H), 3.4 (d, J = 6.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 144.7, 135.8, 129.7, 125, 117, 109.7, 34.6. *m/z* (EI-MS): 204 (80), 203 (17), 202 (77), 177 (47), 175 (27). HRMS: calcd for C_7H_7BrS 201.9452, found 201.9463.

(5-Bromothiophen-2-yl)phenylmethanol (20h). The reaction was carried out according to typical procedure A using **19d** (520 mg, 2.15 mmol), *i*-PrMgBr (2.85 mL, 2.25 mmol, 0.8 M in THF, exchange −20 °C, 15 min), and benzaldehyde (262 μL, 2.58 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 7:3) affording the product **20h** (427 mg, 74%) as a colorless oil. IR (neat): 3125 (s), 2852 (s), 1597 (s), 1584 (m), cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.32−7.17 (m, 5H), 6.79 (d, J = 3.7 Hz, 1H), 6.53 (d, J = 3.7 Hz, 1H), 5.85 (s, 1H), 2.42 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.5, 142.3, 129.3, 128.6, 128.2, 126.1, 125, 112.3, 72.4. *m/z* (EI-MS): 270 (46), 269 (13), 268 (46), 253 (10), 251 (11), 193 (19), 191 (39), 190 (32), 189 (100). HRMS: calcd for $C_{11}H_9BrSO$ 268.9557, found 268.9588.

2-(5-Bromothiophen-2-ylmethyl)acrylic Acid Ethyl Ester (20i). The reaction was carried out according to typical procedure A using **19d** (520 mg, 2.15 mmol), *i*-PrMgBr (2.85 mL, 2.25 mmol, 0.8 M in THF, exchange −20 °C, 15 min), CuCN·2LiCl (2.58 mL, 2.58 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate (368 μL, 2.79 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 95:5) affording the product **20i** (461 mg, 78%) as a colorless oil. IR (neat): 3085 (s), 3062 (s), 2982 (s), 1713 (s), 1633 (s), 1256 (s), 1196 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ 6.78 (d, J = 4 Hz, 1H), 6.51 (d, J = 4 Hz, J = 1 Hz, 1H), 6.17 (s, 1H), 5.55−5.52 (m, 1H), 4.13 (q, J = 7 Hz, 2H), 3.66 (bs, 2H), 1.2 (t, J = 7 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.4, 143.2, 139.2, 129.7, 126.5, 126.2, 110.2, 61, 32.7, 14.2. *m/z* (EI-MS): 276 (62), 275 (6), 274 (47), 247 (28), 231 (16), 229 (15), 202 (73), 200 (54), 196 (11), 195 (70), 167 (38), 166 (100). HRMS: calcd for $C_{10}H_{11}BrO_2S$ 275.9663, found 275.9662.

4-Bromothiophene-2-carboxylic Acid Ethyl Ester (20j). The reaction was carried out according to typical procedure A using **19e** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.05 mmol, 0.8 M in THF, exchange −40 °C, 30 min), and H_2O (5 mL) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 95:5) affording the product **20j** (211 mg, 90%) as a colorless oil. IR (neat): 3105 (m), 2982 (m), 1714 (vs), 1517 (m), 1464 (w), 1445 (w), 1407 (s), 1281 (vs), 1249 (vs), 1182 (s), 1099 (s), 1064 (m), 1011 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.56 (d, J = 1.9 Hz, 1H), 7.33 (d, J = 1.9 Hz, 1H), 4.24 (q, J = 7.2 Hz, 2H), 1.27 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.6, 134.9, 134.7, 129.1, 110.2, 61.3, 14.0. *m/z* (EI-MS): 236 (46), 234 (45), 208 (54), 206 (53), 192 (17), 191 (100), 190 (17), 189 (99). HRMS: calcd for $C_7H_7BrO_2S$ 233.9350, found 233.9346.

20k. See typical procedure A above.

5-Allyl-4-bromothiophene-2-carboxylic Acid Ethyl Ester (20l). The reaction was carried out according to typical procedure A using **19e** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.05 mmol, 0.8 M in THF, exchange: −40 °C, 30 min), CuCN (10% mol, 9 mg), and allyl bromide (173 μL, 2 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 95:5) affording the product **20l** (187 mg, 68%) as a colorless oil. IR (neat): 3085 (w), 2981 (m), 1714 (vs), 1640 (w), 1528 (w), 1454 (s), 1336 (m), 1279 (vs), 1248 (vs), 1149 (m), 1068 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.52 (s, 1H), 5.78 (ddt, J = 16.3 Hz, J = 11.5 Hz, J = 6.6 Hz, 1H), 5.12 (m, 1H), 5.07 (m, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.43 (dt, J = 6.6 Hz, J = 1.3 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.5, 145.4, 136.0, 134.0, 131.8, 118.4, 110.9, 61.7, 34.4, 14.7. *m*/*z* (EI-MS): 269 (100), 274 (96), 248 (12), 246 (11), 231 (57), 229 (54). HRMS: calcd for $C_{10}H_{11}BrO_2S$ 273.9663, found 273.9678.

4-Bromo-5-trimethylsilanylthiophene-2-carboxylic Acid Ethyl Ester (20m). The reaction was carried out according to typical procedure A using **19e** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.05 mmol, 0.8 M in THF, exchange −40 °C, 30 min), and chlorotrimethylsilane (254 μL, 2 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 99:1) affording the product **20m** (270 mg, 88%) as a colorless oil. IR (neat): 3097 (w), 2980 (m), 2959 (m), 1717 (vs), 1511 (s), 1403 (m), 1316 (vs), 1275 (vs), 1251 (vs), 1134 (s), 1074 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.48 (s, 1H), 4.10 (q, J = 7.2 Hz, 2H), 1.13 (t, J = 7.2 Hz, 3H), 0.18 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.0, 144.3, 139.2, 138.4, 118.2, 62.5, 15.3, 0.2. *m*/*z* (EI-MS): 308 (32), 306 (30), 295 (10), 294 (18), 293 (100), 292 (18), 291 (98). HRMS: calcd for $C_{10}H_{15}BrO_2SSi$ 305.9745, found 305.9748.

4-Bromo-5-tributylstannanylthiophene-2-carboxylic Acid Ethyl Ester (20n). The reaction was carried out according to typical procedure A using **19e** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.05 mmol, 0.8 M in THF, exchange −40 °C, 30 min), and tributyltin chloride (325 μL, 1.2 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O/Et_2N, 98:1:1) affording the product **20n** (396 mg, 76%) as a colorless oil. IR (neat): 2957 (vs), 2926 (vs), 2872 (s), 2853 (s), 1715 (vs), 1510 (m), 1463 (m), 1384 (m), 1311 (s), 1271 (vs), 1243 (s), 1127 (m), 1070 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.66 (s, 1H), 4.26 (q, J = 6.9 Hz, 2H), 1.53−1.46 (m, 6H), 1.31−1.13 (m, 15H), 0.82 (t, J = 7.2 Hz, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.3, 145.4, 140.3, 136.5 (J_{Sn-C} = 29 Hz), 119.2, 61.6, 29.2 (J_{Sn-C} = 22.5 Hz), 27.7 (J_{Sn-C} = 29 Hz), 14.7, 14, 11.7 (J_{Sn-C} = 347−363 Hz). *m*/*z* (EI-MS): 469 (61), 467 (100), 413 (22), 411 (34), 355 (43), 353 (39), 199 (7). HRMS: calcd for $C_{19}H_{33}BrO_2SSn$ 522.0407, found. 522.0433.

4-Bromothiophene-2,5-dicarboxylic Acid Diethyl Ester (20o). The reaction was carried out according to typical procedure A using **19e** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.05 mmol, 0.8 M in THF, exchange −40 °C, 30 min), and ethyl cyanoformate (128 μL, 1.3 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 99:1) affording the product **20o** (251 mg, 82%) as a white solid, mp 83 °C. IR (KBr): 3088 (m), 2984 (w), 2940 (w), 1725 (vs), 1638 (w), 1522 (w), 1450 (m), 1366 (w), 1335 (s), 1259 (vs), 1238 (vs), 1091 (m), 1017 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.62 (s, 1H), 4.32 (q, J = 7.2 Hz, 2H), 4.29 (q, J = 7.2 Hz, 2H), 1.33 (t, J = 7.2 Hz, 3H), 1.30 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.6, 160.6, 137.9, 137.6, 133.0, 116.5, 62.5, 62.3, 14.6. *m*/*z* (EI-MS): 308 (47), 306 (47), 280 (27), 278 (26), 264 (18), 263 (100), 262 (17), 261 (94), 236 (24), 235 (81), 234 (24), 233 (78). HRMS: calcd for $C_{10}H_{11}BrO_4S$ 305.9561, found 305.9573. Anal. Calcd C, 39.10; H, 3.61; S, 10.44; Br, 26.01. Found: C, 39.30; H, 3.66; S, 10.29; Br, 26.09.

4-Bromo-5-(2-ethoxycarbonylallyl)thiophene-2-carboxylic Acid Ethyl Ester (20p). The reaction was carried out according to typical procedure A using **19e** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.05 mmol, 0.8 M in THF, exchange −40 °C, 30 min), CuCN·2LiCl (1.2 mL, 1.2 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate (251 mg, 1.3 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 9:1) affording the product **20p** (270 mg, 78%) as a colorless oil. IR (neat): 3100 (w), 2982 (m), 1715 (vs), 1632 (w), 1529 (w), 1453 (m), 1368 (m), 1336 (m), 1281 (vs), 1251 (vs), 1146 (s), 1070 (m), 1024 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.53 (s, 1H), 6.25 (s, 1H), 5.54 (s, 1H), 4.24 (q, J = 7.2 Hz, 2H), 4.15 (q, J = 7.2 Hz, 2H), 3.73 (s, 2H), 1.29 (t, J = 7.2 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.3, 161.5, 143.8, 137.4, 135.9, 132.4, 127.8, 111.0, 61.8, 61.5, 32.4, 14.6, 14.5. *m*/*z* (EI-MS): 348 (2), 346 (2), 319 (12), 317 (11), 303 (20), 301 (19), 274 (17), 272 (16), 268 (16), 267 (100). HRMS: calcd for $C_{13}H_{15}BrO_4S$ 345.9874, found 345.9878.

5-Bromo-2-(hydroxyphenylmethyl)-thiophene-3-carboxylic Acid Ethyl Ester (20q). The reaction was carried out according to typical procedure **A** using **19f** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.05 mmol, 0.8 M in THF, exchange −40°C, 1 h), and benzaldehyde (122 μL, 1.2 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 7:3) affording the product **20q** (259 mg, 76%) as a colorless oil. IR (neat): 3474 (vs), 3060 (w), 2994 (w), 1688 (vs), 1537 (m), 1454 (m), 1369 (m), 1343 (m), 1266 (vs), 1235 (s), 1154 (m) 1025 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.37−7.34 (m, 2H), 7.28−7.21 (m, 4H), 6.28 (s, 1H), 4.45 (bs, 1H), 4.19 (q, J = 6.9 Hz, 2H), 1.23 (t, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.3, 160.0, 141.6, 132.0, 129.0, 128.9, 128.8, 127.2, 121.4, 70.7, 61.8, 14.6. *m*/*z* (EI-MS): 342 (8), 340 (8), 313 (20), 311 (19), 296 (14), 295 (100), 294 (13), 293 (84). HRMS: calcd for $C_{14}H_{13}BrO_3S$ 339.9769, found 339.9769.

2-(1-Benzyl-5-bromo-1*H*-pyrrol-2-ylmethyl)acrylic Acid Ethyl Ester (20r). The reaction was carried out according to typical procedure A using **19g** (650 mg, 2.06 mmol), *i*-PrMgBr (3.1 mL, 2.47 mmol, 0.8 M in THF, exchange at −5 °C, 30 min), CuCN·2LiCl (2.47 mL, 2.47 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate (477 mg, 2.47 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 95:5) affording the product **20r** (517 mg, 72%) as a colorless oil. IR (neat): 3065 (s), 3033 (s), 2982 (s), 1713 (s), 1634 (s), 1605 (s), 1588 (s), 1196 (s), 1138 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.52−6.86 (m, 6H), 6.61 (s, 1H), 6.11−6.07 (m, 1H), 5.15−5.2 (m, 1H), 4.88 (s, 2H), 4.18 (q, J = 7 Hz, 1H), 3.48 (s, 2H), 1.21 (t, J = 7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.4, 136.7, 136.5, 128.8, 128.7, 128.6, 127.5, 126, 112.4, 102, 97.5, 60.8, 49.4, 27.6, 14. *m*/*z* (EI-MS): 348 (14), 267 (22), 92 (31), 91 (100). HRMS: calcd for $C_{17}H_{18}BrNO_2$ 347.0521, found 347.0524.

(1-Benzyl-5-bromo-1*H*-pyrrol-2-yl)phenylmethanol (20s). The reaction was carried out according to typical procedure A using **19g** (650 mg, 2.06 mmol), *i*-PrMgBr (3.1 mL, 2.47 mmol, 0.8 M in THF, exchange at −20 °C, 30 min), and benzaldehyde (293 μL, 2.88 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 9:1) affording the product **20s** (515 mg, 73%) as colorless crystals, mp 92 °C. IR (KBr): 3535 (s), 3057 (s), 2926 (s), 1597 (s), 1037 (s), 1024 (s) cm^{-1}. ^1H NMR (benzene-d_6, 300 MHz): δ 7.26−7.14 (m, 5H), 7−6.87 (m, 4H), 6.52−6.49 (m, 2H), 6.23 (s, 1H), 6 (d, J = 4.3 Hz, 1H), 4.82 (s, 1H), 4.81 (s, 1H), 1.34 (d, J = 4.3 Hz, 1H). ^{13}C NMR (benzene-d_6, 75 MHz): δ 141, 137.6, 133.4, 128.4, 128.3, 127.9, 127.6, 125.8, 125.6, 113, 105, 97.7, 67.6, 50. HRMS: calcd for $C_{18}H_{16}NOBr$ 341.0415, found 341.0409.

Bromotrimethylsilanylthiazole-4-carboxylic Acid Ethyl Ester (20t). The reaction was carried out according to typical procedure A using **19h** (810 mg, 2.57 mmol), *i*-PrMgBr (4.75 mL, 3.1 mmol, 0.65 M in THF, exchange at −80 °C, 10 min), and trimethylsilyl chloride (0.65 mL, 5.14 mmol, −40 °C, 1 h) to give a crude residue, which was purified by column chromatography on silica (pentane/EtOAc, 9:1) affording the product **20t** (531 mg, 67%) as a yellow oil. IR (neat): 1714 (s), 1423 (s), 1303 (s), 1250 (w), 1200 (s), 1008 (s), 846 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 4.43 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 161.9, 151.5, 149.8, 139.6, 62.3, 14.9. *m*/*z* (EI-MS): 310 (21), 308 (19), 305

(20), 291 (25), 230 (100). HRMS: calcd for $C_8H_{11}BrNO_2SSi$ (M − CH_3) 291.9464, found 291.9455.

5-Allyl-2-bromothiazole-4-carboxylic Acid Ethyl Ester (20u). The reaction was carried out according to typical procedure A using **19h** (473 mg, 1.5 mmol), *i*-PrMgBr (2.74 mL, 1.8 mmol, 0.65 M in THF, exchange at −80 °C, 10 min), and allyl bromide (290 mg, 2.4 mmol, −40 °C, 1 h) to give a crude residue, which was purified by column chromatography on silica (pentane/EtOAc, 95:5) affording the product **20u** (335 mg, 81%) as a yellow oil. IR (neat): 1714 (vs), 1442 (s), 1318 (s), 1195 (s), 1031 (s), 1013 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.88−5.83 (m, 1H), 5.16−5.08 (m, 2H), 4.32 (q, J = 7.2 Hz, 2H), 3.87 (d, J = 6.6 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.0, 151.1, 139.9, 134.7, 133.1, 131.9, 117.4, 60.5, 30.8, 13.3. *m/z* (EI-MS): 277 (15), 275 (14), 231 (100), 229 (97), 150 (24), 122 (26). HRMS: calcd for $C_9H_{10}BrNO_2S$ 274.9650, found 274.9652.

2-Bromo-5-(hydroxyphenylmethyl)thiazole-4-carboxylic Acid Ethyl Ester (20v). The reaction was carried out according to typical procedure A using **19h** (240 mg, 0.79 mmol), *i*-PrMgBr (1.22 mL, 0.79 mmol, 0.65 M in THF, exchange at −80 °C, 10 min), and benzaldehyde (134 mg, 1.26 mmol, −40 °C, 1 h) to give a crude residue, which was purified by column chromatography on silica (pentane/EtOAc, 8:2) affording the product **20v** (150 mg, 58%) as a slightly yellow oil. IR (neat): 3409 (vs), 1714 (vs), 1441 (s), 1314 (s), 1199 (s), 1031 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.39−7.19 (m, 5H), 6.34 (m, 1H), 4.32 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.1, 158.7, 141.5, 140.9, 135.4, 129.1, 126.8, 69.5, 62.6, 14.6. *m/z* (EI-MS): 341 (2), 296 (100), 294 (98), 216 (13), 188 (19), 162 (16). HRMS: calcd for $C_{13}H_{12}BrNO_3S$ 340.9765, found 340.9761.

2-Bromothiazole-4,5-dicarboxylic Acid Diethyl Ester (20w). The reaction was carried out according to typical procedure A using **19h** (250 mg, 0.79 mmol), *i*-PrMgBr (1.34 mL, 0.87 mmol, 0.65 M in THF, exchange at −80 °C, 10 min), and ethyl cyanoformate (126 mg, 1.27 mmol, −20 °C, 3 h) to give a crude residue, which was purified by column chromatography on silica (pentane/EtOAc, 95:5) affording the product **20w** (165 mg, 67%) as a yellow oil. IR (neat): 1744 (vs), 1731 (vs), 1526 (w), 1401 (m), 1386 (m), 1323 (m), 1272 (s), 1200 (s), 1090 (s), 1040 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 4.36 (q, J = 7.1 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.6, 159.2, 149.6, 140.6, 133.4, 63.0, 14.4. *m/z* (EI-MS): 309 (23), 307 (22), 264 (33), 262 (31), 236 (100), 234 (96), 193 (26), 191 (28). HRMS: calcd for $C_9H_{10}BrNO_4S$ 306.9514, found 306.9510.

5-Bromo-3-ethoxymethyl-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (22). The reaction was carried out according to typical procedure A using **21** (503 mg, 1.69 mmol), *i*-PrMgBr (1.81 mL, 1.77 mmol, 0.98 M in THF, exchange at −20 °C, 1 h), and ethyl cyanoformate (250 μL, 2.50 mmol, 0 °C, 18 h) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 4:1) affording the product **22** (288 mg, 59%) as a colorless oil. IR (neat): 2980 (s), 2932 (m), 1705 (vs), 1491 (s), 1383 (s), 1294 (s), 1250 (s), 1233 (vs), 1175 (s), 1103 (vs), 1020 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.62 (s, 2H), 4.27 (q, J = 7.1 Hz, 2H), 3.44 (q, J = 7.0 Hz, 2H), 2.40 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H), 1.07 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.5, 150.6, 123.6, 120.1, 73.9, 64.2, 60.8, 14.7, 14.0, 13.4. *m/z* (EI-MS): 291 (5), 262 (4), 247 (5). HRMS: calcd for $C_{10}H_{15}BrN_2O_3$ 290.0266, found 290.0257.

5-Allyl-3-ethoxymethyl-2-methyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (23). The reaction was carried out according to typical procedure A using **22** (275 mg, 0.94 mmol), *i*-Pr_2Mg (1.47 mL, 0.94 mmol, 0.64 M in THF, exchange −60 °C, 7 h), CuCN·2LiCl (1.00 mL, 1.00 mmol, 1 M in THF, −78 °C, 5 min), and allyl bromide (170 μL, 2.00 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/AcOEt, 7:3) affording the product **23** (152 mg, 64%) as a colorless oil. IR (neat): 3079 (w), 2980 (s), 1701 (vs), 1676 (vs), 1479 (s), 1387 (vs), 1302 (vs), 1255 (vs), 1172 (vs), 1099 (vs), 1020 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.92 (ddt, J = 17 Hz, J = 10 Hz, J = 6.6 Hz, 1H), 5.61 (s, 2H), 5.04 (ddt, J = 17 Hz, J = 1.7 Hz, J = 1.4 Hz, 1H), 4.97 (ddt, J = 10 Hz, J = 1.7 Hz, J = 1.4 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.55 (dt, J = 6.6 Hz, J = 1.4 Hz, 2H), 3.44 (q, J = 7.0 Hz, 2H), 2.40 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H), 1.08 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.9, 150.2, 148.5, 135.6, 118.3, 115.7, 73.4, 63.8, 60.2, 34.0, 14.8, 13.5. *m/z* (EI-MS): 252 (53), 206 (36), 147 (53), 134 (48), 59 (100). HRMS: calcd for $C_{13}H_{20}N_2O_3$ 252.1474, found 252.1476.

2-Allyl-5-bromothiophene-3-carboxylic Acid Ethyl Ester (24). The reaction was carried out according to typical procedure A using **19f** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.05 mmol, 0.8 M in THF, exchange −40 °C, 30 mn), CuCN (10% mol, 9 mg), and allyl bromide (173 μL, 2 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 97:3) affording the product **24** (203 mg, 74%) as a colorless oil. IR (neat): 3082 (w), 2981 (m), 2936 (w), 2905 (w), 1715 (vs), 1639 (w), 1537 (m), 1454 (s), 1370 (m), 1226 (vs), 1146 (m), 1097 (m), 1028 (s), 993 (m), 921 (m), 776 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.27 (s, 1H), 5.87 (ddt, J = 17.1 Hz, J = 10.5 Hz, J = 6.6 Hz, 1H), 5.09 (dt, J = 17.1 Hz, J = 1.5 Hz, 1H), 5.05 (dt, J = 10.5 Hz, J = 1.5 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.80 (dt, J = 6.6 Hz, J = 1.5 Hz, 2H), 1.27 (t, J = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.5, 154.3, 135.3, 132.1, 128.8, 118.0, 108.9, 61.0, 34.1, 14.7. *m/z* (EI-MS): 276 (29), 274 (28), 261 (13), 259 (11), 122 (100). HRMS: calcd for $C_{10}H_{11}BrO_2S$ 273.9663, found 273.9662.

2-Allyl-5-(1-hydroxy-but-2-enyl)-thiophene-3-carboxylic Acid Ethyl Ester (25a). The reaction was carried out according to typical procedure A using **24** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.20 mmol, 0.8 M in THF, exchange −40 °C, 1 h), and crotonaldehyde (126 μL, 1.53 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 3:2) affording the product **25a** (180 mg, 62%) as a colorless oil. IR (neat): 3428 (vs), 3080 (w), 2980 (m), 2938 (m), 1711 (vs), 1639 (m), 1552 (m), 1487 (m), 1376 (m), 1282 (s), 1219 (vs), 1173 (s), 1076 (m), 1029 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.15 (s, 1H), 5.91 (ddt, J = 10.2 Hz, J = 17 Hz, J = 6.6 Hz, 1H), 5.75−5.61 (m, 2H), 5.18 (d, J = 6.3 Hz, 1H), 5.10−5.00 (m, 2H), 4.20 (q, J = 7.2 Hz, 2H), 3.82 (dt, J = 6.6 Hz, J = 1.2 Hz, 2H), 2.47 (bs, 1H), 1.67 (dd, J = 5.4 Hz, J = 1.2 Hz, 3H), 1.27 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.8, 152.5, 144.3, 136.0, 132.7, 128.8, 127.7, 126.0, 117.4, 71.3, 60.7, 34.3, 18.0, 14.7. *m/z* (EI-MS): 267 (14), 266 (100), 251 (26), 249 (11), 197 (63). HRMS: calcd for $C_{14}H_{18}O_3S$ 266.0977, found 266.0942.

2-Allyl-5-(1-hydroxy-dec-4-enyl)thiophene-3-carboxylic Acid Ethyl Ester (25b). The reaction was carried out according to typical procedure A using **24** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.20 mmol, 0.8 M in THF, exchange −40 °C, 1 h), and *trans*-4-decen-1-al (238 μL, 1.3 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 3:2) affording the product **25b** (241 mg, 69%) as a colorless oil. IR (neat): 3435 (vs), 2956 (s), 2926 (s), 2855 (m), 1713 (vs), 1640 (w), 1553 (w), 1489 (w), 1377 (m), 1225 (s), 1028 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.16 (s, 1H), 5.93 (ddt, J = 10.2 Hz, J = 17.1 Hz, J = 6.6 Hz, 1H), 5.37−5.33 (m, 2H), 5.10−5.01 (m, 2H), 4.74 (t, J = 6.9 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.82 (dt, J = 6.6 Hz, J = 0.9 Hz, 2H), 2.25 (bs, 1H), 2.05−1.70 (m, 6H), 1.29−1.17 (m, 9H), 0.81 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.8, 152.1, 145.3, 136.0, 132.1, 129.4, 127.6, 125.8, 117.3, 70.0, 60.7, 39, 34.3, 32.9, 31.8, 29.7, 29.1, 22.9, 14.7, 14.4. *m/z* (EI-MS): 350 (24), 261 (11), 251 (33), 238 (70), 226 (16), 225 (100). HRMS: calcd for $C_{20}H_{30}O_3S$ 350.1916, found 350.1894.

2-Allyl-5-benzoylthiophene-3-carboxylic Acid Ethyl Ester (25c). The reaction was carried out according to typical procedure A using **24** (314 mg, 1 mmol), *i*-PrMgBr (1.31 mL, 1.20 mmol, 0.8 M in THF, exchange −40 °C, 1 h), CuCN·2LiCl (1.30 mL, 1.30 mmol, 1.0 M in THF), and benzoyl chloride (157 μL, 1.35 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/Et_2O, 1:1) affording the product **25c** (213 mg, 71%) as a colorless oil. IR (neat): 3082 (w), 2981 (m), 1714 (vs), 1640 (v), 1598

(m), 1578 (m), 1534 (v), 1455 (v), 1374 (m), 1291 (v), 1228 (v), 1150 (m), 1028 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.62 (s, 1H), 7.53 (d, J = 7.5 Hz, 2H), 7.28−7.14 (m, 3H), 5.72 (m, 1H), 4.94−4.86 (m, 2H), 3.99 (q, J = 7.2 Hz, 2H), 3.68 (d, J = 6.6 Hz, 2H), 1.03 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 187.6, 162.9, 161.0, 139.9, 137.7, 136.7, 134.8, 132.8, 129.5, 128.9, 118.5, 61.1, 34.8, 14.7. *m*/*z* (EI-MS): 301 (15), 300 (74), 285 (11), 227 (23), 195 (12), 105 (100). HRMS: calcd for $C_{17}H_{16}O_3S$ 300.0820, found 300.0792.

2-Allyl-4,5-dibromo-1-ethoxymethyl-1*H*-imidazole (27). The reaction was carried out according to typical procedure A using **26** (392 mg, 1.08 mmol), *i*-PrMgBr (1.20 mL, 1.19 mmol, 0.98 M in THF, exchange at room temperature, 1 h), CuCN·2LiCl (1.20 mL, 1.20 mmol, 1.0 M in THF, −78 °C, 5 min), and allyl bromide (170 μL, 2.00 mmol, 0 °C, 1 h) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 9:1) affording the product **27** (200 mg, 57%) as a colorless oil. IR (neat): 3082 (w), 2978 (vs), 2902 (s), 1509 (m), 1379 (m), 1216 (s), 1102 (vs), 1056 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 5.90 (ddt, J = 16.5 Hz, J = 10.0 Hz, J = 6.5 Hz, 1H), 5.23 (s, 2H), 5.16 (dd, J = 16.5 Hz, J = 1.5 Hz, 1H), 5.09 (dd, J = 10.0 Hz, J = 1.5 Hz, 1H), 3.48 (q, J = 7.0 Hz, 2H), 3.51 (d, J = 6.5 Hz, 2H), 1.14 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 148.0, 132.1, 117.8, 116.0, 103.3, 74.1, 64.4, 32.5, 14.7. *m*/*z* (EI-MS): 324 (7), 265 (2), 59 (100). HRMS: calcd for $C_9H_{12}Br_2N_2O$ 321.9316, found 321.9306.

2-Allyl-5-bromo-3-ethoxymethyl-3*H*-imidazole-4-carboxylic Acid Ethyl Ester (28). The reaction was carried out according to typical procedure A using **27** (170 mg, 0.52 mmol), *i*-PrMgBr (0.56 mL, 0.55 mmol, 0.98 M in THF, exchange at −40 °C, 1.5 h), and ethyl cyanoformate (129 μL, 1.30 mmol) to give a crude residue, which was then purified by column chromatography on silica (pentane/EtOAc, 4:1) affording the product **28** (90 mg, 55%) as a colorless oil. IR (neat): 3082 (m), 2980 (s), 1712 (vs), 1530 (s), 1483 (s), 1379 (s), 1294 (s), 1233 (vs), 1198 (vs), 1157 (s), 1101 (vs), 1022 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 5.92 (ddt, J = 16.7 Hz, J = 10.2 Hz, J = 6.5 Hz, 1H), 5.67 (s, 2H), 5.13 (dd, J = 16.7 Hz, J = 1.3 Hz, 1H), 5.04 (dd, J = 10.2 Hz, J = 1.3 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 3.55 (d, J = 6.5 Hz, 2H), 3.47 (q, J = 7.0 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 159.6, 151.7, 131.8, 123.9, 120.3, 118.1, 73.6, 64.3, 61.0, 31.8, 14.8, 14.0. *m*/*z* (EI-MS): 317 (4), 186 (3), 59 (100), 31 (54). HRMS: calcd for $C_{12}H_{17}BrN_2O_3$ 316.0423, found 316.0420.

Phenyl-(3,4,5-trichlorothiophen-2-yl)methanol (31a). The reaction was carried out according to typical procedure A using **29** (222 mg, 1 mmol), *i*-PrMgBr (1.51 mL, 1.1 mmol, 0.73 M in THF, exchange at room temperature, 2 h), and benzaldehyde (159 mg, 1.5 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/EtOAc, 96:4) affording the product **31a** (188 mg, 64%) as a colorless oil. IR (neat): 3306 (vs), 1454 (m), 1326 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.33−7.23 (m, 5H), 5.97 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 141.0, 139.1, 129.2, 126.7, 124.7, 123.3, 120.2, 71.2. *m*/*z* (EI-MS): 296 (31), 294 (100), 292 (97), 259 (47), 257 (68), 217 (37), 215 (51), 105 (99). HRMS: calcd for $C_{11}H_7Cl_3OS$ 291.9250, found 291.9252.

(3,4,5-Trichlorothiophen-2-yl)acetic Acid Ethyl Ester (31b). The reaction was carried out according to typical procedure A using **29** (222 mg, 1 mmol), *i*-PrMgBr (1.51 mL, 1.1 mmol, 0.73 M in THF, exchange at room temperature, 2 h), and ethyl cyanoformate (0.18 mL, 1.8 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/EtOAc, 99:1) affording the product **31b** (202 mg, 78%) as colorless needles, mp 53 °C. IR (KBr): 1722 (s), 1437 (s), 1325 (m), 1240 (s), 1094 (m), 1020 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 4.34 (q, J = 7.1 Hz, 2H), 1.35 (tr, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.4, 131.0, 129.9, 126.2, 124.1, 62.4, 14.6. *m*/*z* (EI-MS): 262 (14), 260 (40), 258 (39), 232 (43), 230 (41), 217 (33), 215 (100), 213 (99). HRMS: calcd for $C_7H_5Cl_3O_2S$ 257.9042, found 257.9054.

2-(3,4,5-Trichlorothiophen-2-ylmethyl)acrylic Acid Ethyl Ester (31c). The reaction was carried out according to typical procedure A using **29** (222 mg, 1 mmol), *i*-PrMgBr (1.51 mL, 1.1 mmol, 0.73 M in THF), CuCN·2LiCl (0.15 mL, 0.15 mmol, 1 M in THF, exchange at room temperature, 2 h), and ethyl (2-bromomethyl)acrylate (348 mg, 1.8 mmol) to give a crude residue, which was purified by column chromatography on silica (pentane/EtOAc, 99:1) affording the product **31c** (287 mg, 96%) as a colorless oil. IR (neat): 1715 (vs), 1324 (m), 1157 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 6.22 (s, 1H), 5.58 (s, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.67 (s, 2H), 1.22 (tr, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.2, 137.0, 132.2, 127.8, 123.1, 122.8, 122.0, 61.6, 31.3, 14.5. *m*/*z* (EI-MS): 302 (16), 300 (47), 298 (46), 271 (47), 269 (47), 265 (58), 263 (88), 237 (65), 236 (33), 235 (100), 234 (38). HRMS: calcd for $C_{10}H_9Cl_3O_2S$ 297.9419, found 297.9424.

Typical Procedure for Coupling to the Resin. Polymer-bound 5-bromothiophene-2-carboxylic acid **32**. Wang resin (copolystyrene − 2% DVB) matrix, 100−200 mesh, loading 0.75 mmol/g, 2 g, 1.5 mmol), 5-bromothiophene-2-carboxylic acid (3.10 g, 15 mmmol), DMAP (183 mg, 1.5 mmol), and DIC (947 mg, 7.5 mmol) were dissolved in DMF (20 mL), and the resulting mixture was stirred at room temperature overnight. The resin was filtrated and washed with DMF (5 mL) first and then sequentially with MeOH (5 mL) and CH_2Cl_2 (5 mL). The resin was dried in a vacuum and the loading determined by cleaving 100 mg of resin: 0.72 mmol/g. Polymer-bound 4,5-dibromothiophene-2-carboxylic acid **33** (loading 0.70 mmol/g) and polymer-bound 2,5-dibromothiophene-3-carboxylic acid **34** (loading 0.73 mmol/g) were obtained using the same procedure.

Typical Procedure B for Br−Mg Exchange on the Solid Phase. Preparation of 5-Allylthiophene-2-carboxylic Acid (35b). A suspension of the resin-bound 5-bromothiophene-2-carboxylic acid (**32**) (100 mg, 72 μmol) in THF (2 mL) was cooled to −40 °C, treated with *i*-PrMgBr (1.03 mL, 0.75 mmol, 0.73 M in THF), and stirred for 2 h. A solution of CuCN·2LiCl (0.90 mL, 0.9 mmol, 1.0 M in THF) and allyl bromide (182 mg, 1.50 mmol) was added. The reaction mixture was stirred at −40 °C for 1 h and then quenched with MeOH. The resin was filtrated and washed with DMF (5 mL) first and then sequentially with MeOH (5 mL) and CH_2Cl_2 (5 mL). The resulting resin was cleaved with 90% TFA in CH_2Cl_2 (5 mL) at room temperature for 15 min. After concentration in vacuum, product **35b** was obtained as a colorless solid (12 mg, 99% based on the loading level of **32**; 99% HPLC purity, UV 254 nm). ^1H NMR (acetone, 300 MHz): δ 7.64 (d, J = 3.5 Hz, 1H), 6.95 (s, 1H), 6.08−5.95 (m, 1H), 5.24−5.11 (m, 2H), 3.64 (d, J = 6.6 Hz, 2H). *m*/*z* (EI-MS): 168 (100), 141 (19), 123 (70). HRMS: calcd for $C_8H_8O_2S$ 168.0245, found 168.0247.

5-Cyanothiophene-2-carboxylic Acid (35a). The reaction was carried out according to typical procedure B using resin **32** (100 mg, 78 μmol), *i*-PrMgBr (1.03 mL, 0.75 mmol, 0.73 M in THF, exchange at −40 °C, 2 h), and *p*-toluenesulfonyl cyanide (156 mg, 0.75 mmol) to give product **35a** as a colorless solid (10.1 mg, 93%; 94% HPLC purity, UV 254 nm). ^1H NMR (acetone, 300 MHz): δ 7.72 (d, J = 3.8 Hz, 1H), 6.87 (d, J = 3.8 Hz, 1H), 6.30 (s, 1H), 5.64 (s, 1H), 4.20 (q, J = 7.2 Hz, 2H), 3.84 (s, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.3, 166.1, 151.4, 138.6, 135.3, 131.1, 127.0, 126.9, 61.1, 32.9, 14.1. *m*/*z* (EI-MS): 240 (68), 166 (100), 121 (37). HRMS: calcd for $C_{11}H_{12}O_4S$ 240.0456, found 240.0460.

35b. See typical procedure B.

5-(2-Ethoxycarbonylallyl)-thiophene-2-carboxylic Acid (35c). The reaction was carried out according to typical procedure B using resin **32** (100 mg, 78 μmol), *i*-PrMgBr (1.03 mL, 0.75 mmol, 0.73 M in THF, exchange at −40 °C, 2 h), CuCN·2LiCl (0.90 mL, 0.9 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate (338 mg, 1.75 mmol, 1 h at −40 °C) to give product **35c** as a colorless solid (15.9 mg, 92%; 94% HPLC purity, UV 254 nm). ^1H NMR (DMSO, 300 MHz): δ 8.00 (d, J = 4.0 Hz, 1H), 7.78 (d, J = 3.9 Hz, 1H). *m*/*z* (EI-MS): 153 (77), 136 (100). HRMS: calcd for $C_6H_3NO_2S$ 152.9884, found 152.9882.

5-Benzoylthiophene-2-carboxylic Acid (35d). The reaction was carried out according to typical procedure B using resin **32** (90 mg, 65 μmol), *i*-PrMgBr (2.6 mL, 1.69 mmol, 0.65 M in THF, exchange at −40 °C, 2 h), CuCN·2LiCl (1.7 mL, 1.7 mmol, 1 M in THF), and benzoyl chloride (0.4 mL, 3.38

mmol, 10 h at −10 °C) to give product **35d** (14 mg, 93%) as a colorless solid (93% HPLC purity, UV 254 nm). ^{1}H NMR (DMSO, 400 MHz): δ 7.94−7.52 (m, 7H). ^{13}C NMR (DMSO, 100 MHz): δ 187.5, 146.4, 136.7, 135.2, 133.0, 129.0, 128.8. *m*/*z* (EI-MS): 232 (91), 187 (36), 155 (92), 105 (100). HRMS: calcd for $C_{12}H_8O_3S$ 232.0194, found 232.0187.

5-Acetylthiophene-2-carboxylic Acid (35e). The reaction was carried out according to typical procedure B using resin **32** (125 mg, 90 μmol), *i*-PrMgBr (3.0 mL, 1.95 mmol, 0.65 M in THF, exchange at −40 °C, 2 h), CuCN·2LiCl (1.95 mL, 1.95 mmol, 1 M in THF), and acetyl chloride (0.33 mL, 4.7 mmol, 10 h at −10 °C) to give product **35e** (14 mg, 90%) as a colorless solid (84% HPLC purity, UV 254 nm). ^{1}H NMR (DMSO, 400 MHz): δ 7.92 (d, J = 4.0 Hz, 1H), 7.74 (d, J = 4.0 Hz, 1H), 2.60 (s, 3H). *m*/*z* (EI-MS): 170 (41), 155 (100), 111 (15). HRMS: calcd for $C_7H_6O_3S$ 170.0004, found 170.0019.

5-Propionylthiophene-2-carboxylic acid (35f). The reaction was carried out according to typical procedure B using resin **32** (90 mg, 65 μmol), *i*-PrMgBr (1.9 mL, 1.7 mmol, 0.9 M in THF, exchange at −40 °C, 2 h), CuCN·2LiCl (1.7 mL, 1.7 mmol, 1 M in THF), and propionyl chloride (0.29 mL, 3.4 mmol, 10 h at −10 °C) to give product **35f** (12 mg, 95%) as a colorless solid (90% HPLC purity, UV 254 nm). ^{1}H NMR (DMSO, 400 MHz): δ 7.91 (d, J = 4.0 Hz, 1H), 7.74 (d, J = 4.0 Hz, 1H), 3.02 (q, J = 7.1 Hz, 2H), 1.07 (t, J = 7.1 Hz, 3H). *m*/*z* (EI-MS): 184 (20), 155 (100). HRMS: calcd for $C_8H_8O_3S$ 184.0194, found 184.0188.

5-Benzoylthiophene-2-carboxylic Acid (35 g). The reaction was carried out according to typical procedure B using resin **32** (125 mg, 90 μmol), *i*-PrMgBr (3.0 mL, 1.95 mmol, 0.65 M in THF, exchange at −40 °C, 2 h), CuCN·2LiCl (1.95 mL, 1.95 mmol, 1 M in THF), and 5-undec-10-enoyl chloride (1.0 mL, 4.7 mmol, 10 h at −10 °C) to give product **35g** (14 mg, 90%) as a colorless solid (99% HPLC purity, UV 254 nm). ^{1}H NMR (DMSO, 400 MHz): δ 7.91 (d, J = 4.0 Hz, 1H), 7.75 (d, J = 4.0 Hz, 1H), 5.82−5.68 (m, 1H), 5.05−4.88 (m, 2H), 2.92 (t, J = 7.1 Hz, 2H), 1.98 (m, 2H), 1.20 (m, 12H). ^{13}C NMR (DMSO, 100 MHz): δ 194.4, 174.9, 162.9, 148.4, 139.3, 133.9, 133.3, 108.6, 38.8, 33.6, 29.2, 29.0, 28.9, 28.7, 24.4. *m*/*z* (EI-MS): 294 (3), 183 (33), 170 (100), 155 (63). HRMS: calcd for $C_{16}H_{22}O_3S$ 294.1290, found 294.1292.

5-Allyl-4-bromothiophene-2-carboxylic Acid (36a). The reaction was carried out according to typical procedure B using resin **33** (90 mg, 65 μmol), *i*-PrMgBr (1.23 mL, 0.75 mmol, 0.61 M in THF, exchange at −40 °C, 2 h), CuCN·2LiCl (0.9 mL, 0.9 mmol, 1 M in THF), and allyl bromide (136 mg, 1.12 mmol, 1 h at −40 °C) to give product **36a** (18 mg, 80%) as a colorless solid (97% HPLC purity, UV 254 nm). ^{1}H NMR (CD_3CN, 300 MHz): δ 7.66 (s, 1H), 6.09−5.93 (m, 1H), 5.24−5.18 (m, 2H), 3.59 (dd, J = 6.5 Hz, J = 1.2 Hz, 2H). *m*/*z* (EI-MS): 248 (66), 246 (64), 123 (100). HRMS: calcd for $C_8H_7BrO_2S$ 245.9350, found 245.9342.

3-Bromo-5-(2-ethoxycarbonylallyl)thiophene-2-carboxylic Acid (36b). The reaction was carried out according to typical procedure B using resin **33** (100 mg, 70 μmol), *i*-PrMgBr (1.23 mL, 0.75 mmol, 0.61 M in THF, exchange at −40 °C, 2 h), CuCN·2LiCl (0.9 mL, 0.9 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate (217 mg, 1.12 mmol, 90 min at −40 °C) to give product **36b** (20 mg, 90%) as a colorless solid (87% HPLC purity, UV 254 nm). ^{1}H NMR (CD_3CN, 400 MHz): δ 7.61 (s, 1H), 6.26 (s, 1H), 5.67 (s, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.79 (s, 2H), 1.24 (t, J = 7.1 Hz, 3H). *m*/*z* (EI-MS): 319 (10), 317 (10), 303 (20), 301 (19), 267 (100), 239 (60). HRMS: calcd for $C_{11}H_{11}BrO_4S$ 317.9528, found 317.9543.

5-Benzoyl-4-bromothiophene-2-carboxylic Acid (36c). The reaction was carried out according to typical procedure B using resin **33** (100 mg, 70 μmol), *i*-PrMgBr (1.23 mL, 0.75 mmol, 0.61 M in THF, exchange at −40 °C, 2 h), $ZnBr_2$ (0.64 mL, 0.9 mmol, 1 M in THF), $Pd(PPh_3)_4$ (9.7 mg, 7.5 μmol), and benzoyl chloride (0.13 mL, 1.12 mmol, 2 h at 0 °C) to give product **36c** (17 mg, 80%) as a colorless solid (74% HPLC purity, UV 254 nm). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.02−7.49 (m, 6H). *m*/*z* (EI-MS): 312 (55), 310 (53), 235 (24), 233 (26), 231 (25), 122 (37), 105 (100). HRMS: calcd for $C_{12}H_7BrO_3S$ 309.9299, found 309.9299.

2-Allyl-5-bromothiophene-3-carboxylic Acid (37a). The reaction was carried out according to typical procedure B using resin **34** (80 mg, 58 μmol), *i*-PrMgBr (1.1 mL, 0.6 mmol, 0.55 M in THF, exchange at −80 °C, 2 h), CuCN·2LiCl (0.72 mL, 0.72 mmol, 1 M in THF), and allyl bromide (109 mg, 0.9 mmol, 2 h at −40 °C) to give product **37a** (11 mg, 80%) as a colorless solid (83% HPLC purity, UV 254 nm). ^{1}H NMR (CD_3CN, 300 MHz): δ 7.40 (s, 1H), 6.09−5.96 (m, 2H), 5.22−5.13 (m, 2H), 3.91 (d, J = 6.6 Hz, 2H). *m*/*z* (EI-MS): 248 (100), 246 (98), 233 (97), 231 (98), 168 (21), 149 (34), 123 (33), 122 (95), 121 (85). HRMS: calcd for $C_8H_7BrO_2S$ 245.9350, found 245.9347.

2-Allyl-5-(2-ethoxycarbonylallyl)thiophene-3-carboxylic Ethyl Ester (37b). The reaction was carried out according to typical procedure B using resin **34** (80 mg, 58 μmol), *i*-PrMgBr (1.1 mL, 0.6 mmol, 0.55 M in THF, exchange at −80 °C, 2 h), CuCN·2LiCl (0.72 mL, 0.72 mmol, 1 M in THF), and ethyl (2-bromomethyl)acrylate (174 mg, 0.9 mmol, 2 h at −40 °C) to give product **37b** (17 mg, 90%) as a colorless solid (85% HPLC purity, UV 254 nm). ^{1}H NMR (CD_3CN, 300 MHz): δ 7.40 (s, 1H), 6.25 (s, 1H), 5.68 (s, 1H), 4.23−4.16 (m, 4H), 1.27 (t, J = 7.2 Hz, 3H). *m*/*z* (EI-MS): 320 (21), 318 (21), 274 (68), 272 (63), 247 (60), 246 (100), 245 (64), 244 (92). HRMS: calcd for $C_{11}H_{11}BrO_4S$ 317.9562, found 317.9566.

2,5-Diallylthiophene-3-carboxylic Acid (38). The reaction was carried out according to typical procedure B using resin **37a** (80 mg, 58 μmol), *i*-PrMgBr (0.83 mL, 0.6 mmol, 0.72 M in THF, exchange at −50 °C, 2 h), CuCN·2LiCl (0.72 mL, 0.72 mmol, 1 M in THF), and allyl bromide (80 μL, 0.9 mmol, 2 h at −40 °C) to give product **38** (10 mg, 91%) as a colorless solid (95% HPLC purity, UV 254 nm). ^{1}H NMR (CD_3CN, 300 MHz): δ 7.09 (s, 1H), 6.09−5.94 (m, 2H), 5.21−5.08 (m, 2H), 3.90 (d, J = 6.6 Hz, 2H), 3.52 (d, J = 6.6 Hz, 2H). *m*/*z* (EI-MS): 208 (100), 193 (30), 181 (17), 163 (31). HRMS: calcd for $C_{11}H_{12}O_2S$ 208.0558, found 208.0554.

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra for all products are available free of charge via the Internet at http://pubs.acs.org.

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