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Synthesis of 5-Acetyloxazoles and 1,2-Diketones from β-Alkoxy-β-ketoenamides and Their Subsequent Transformations

Tilman Lechel,[a] Markus Gerhard,[a] Daniel Trawny,[a] Boris Brusilowskij,[a] Luise Schefzig,[a] Reinhold Zimmer,[a] Jürgen P. Rabe,[b] Dieter Lentz,[a] Christoph A. Schalley,[a] and Hans-Ulrich Reissig*[a]

Dedicated to the memory of Ilya M. Lyapkalo

Abstract: Lithiated alkoxyallenes, nitriles, and carboxylic acids have been employed as precursors in a three-component reaction leading to highly substituted β-alkoxy-β-ketoenamides. Upon treatment with trifluoroacetic acid, these enamides could be easily cyclized to 5-acetyloxazole derivatives. The synthesis is very flexible with respect to the substitution pattern at C-2 and C-4 of the oxazole core. A mechanistic suggestion for the oxazole formation is presented on the basis of ^{18}O-labeled compounds and their mass spectrometric analysis. In several cases, 1,2-diketones are formed as side products or even as major components. The acetyl moiety at C-5 of the oxazole derivatives can efficiently be converted into alkenyl or alkynyl moieties, which allows a multitude of subsequent reactions. Condensation reactions of the acetyl group provided the expected oxime or hydrazone. By applying a Fischer reaction, the phenylhydrazone could be transferred into an indole, which emphasizes the potential of 5-acetyloxazoles for the preparation of highly substituted (poly)heterocyclic systems. The alkynyl group at C-2 is prone to addition reactions, providing an enamine with interesting photophysical properties. Sonogashira couplings were performed with 5-alkynyl-substituted oxazoles, furnishing the expected aryl-substituted products. This alkynyl unit was employed for the preparation of a new, star-shaped trisoxazole derivative. The ability of this multivalent compound to form self-assembled monolayers between the basal plane of highly oriented pyrolytic graphite and 1-phenyloctane was demonstrated by scanning tunneling microscopy (STM). The star-shaped compound seems to prefer the C_3-symmetric arrangement in this two-dimensional crystal. Two 1,2-diketones were smoothly converted into functionalized quinoxaline derivatives.

Keywords: allenes · cross-coupling · heterocycles · monolayers · scanning probe microscopy · self-assembly

Introduction

The oxazole unit plays a privileged role as a substructure in naturally occurring compounds with potent biological activities and, hence, represents a widely used building block in medicinal chemistry.[1] Furthermore, there are many oxazole derivatives with interesting photophysical properties, which is also of importance in the development of new functional compounds.[2] One of the traditional methods used to prepare oxazoles is the cyclodehydration of α-acylamino ketones, which can be conducted under conditions developed Robinson and Gabriel.[3a,b] This method often requires harsh dehydrating agents and the available substitution pattern is hence restricted to a fairly small number of functional groups. The development of milder and more flexible synthetic approaches is therefore highly desirable.[3] However, only a few reports deal with the synthesis of 2,4,5-trisubstituted oxazoles with a flexible substitution pattern at all positions and a direct introduction of functional groups.[4,5]

In previous studies, we reported on the synthetic use of alkoxyallenes, which have found numerous and versatile applications as C_3-building blocks in the synthesis of natural products or other interesting compounds.[6] We serendipitously discovered a novel access to β-alkoxy-β-ketoenamides **5** by a mechanistically intriguing, three-component reaction using lithiated alkoxyallenes **1**, nitriles **2**, and carboxylic acids **3** as precursors.[7,8] Enamides, in general, are interesting synthetic building blocks in organic chemistry.[9,10] We demonstrated that the functionalized enamides **5** represent

[a] Dr. T. Lechel, M. Gerhard, Dipl.-Chem. D. Trawny, Dr. B. Brusilowskij, L. Schefzig, Dr. R. Zimmer, Prof. Dr. D. Lentz, Prof. Dr. C. A. Schalley, Prof. Dr. H.-U. Reissig
Institut für Chemie und Biochemie
Freie Universität Berlin
Takustr. 3, 14195 Berlin (Germany)
Fax: (+49) 30-83855367
E-mail: hans.reissig@chemie.fu-berlin.de

[b] Prof. Dr. J. P. Rabe
Institut für Physik
Humboldt Universität zu Berlin
Newtonstraße 15, 12489 Berlin (Germany)

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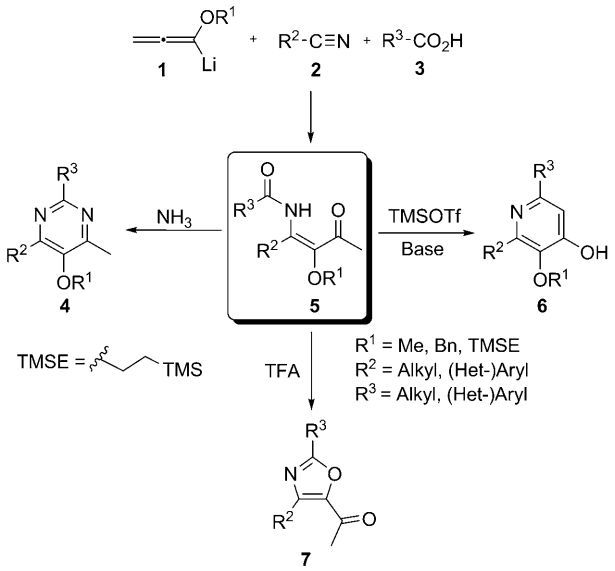
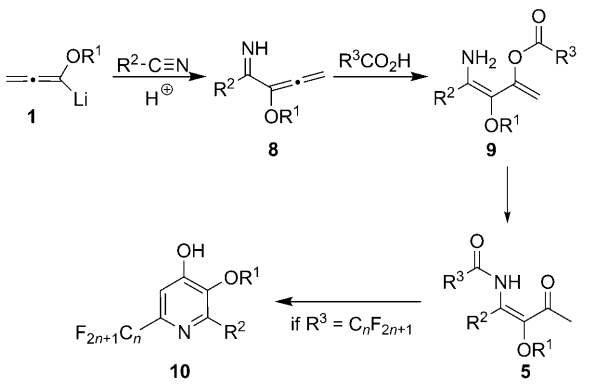
particularly flexible precursors for the cyclization to give interestingly substituted heteroaromatic compounds such as 5-alkoxypyrimidines **4** and 4-hydroxypyridines **6** (Scheme 1).[8] Previous results have also shown that treatment of **5** (R^1=2-(trimethylsilyl)ethyl=TMSE) with trifluoroacetic acid at elevated temperatures provided highly substituted 5-acetyloxazoles **7**.[11]



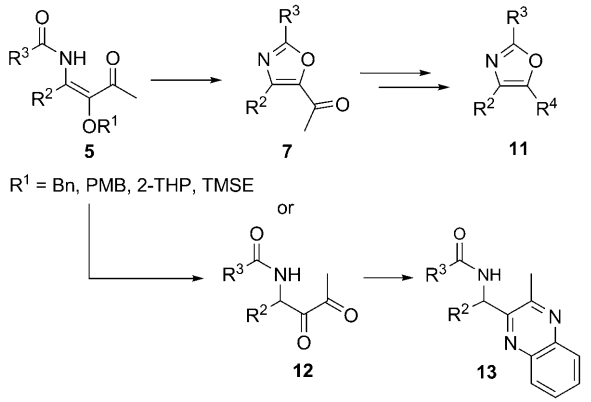
Scheme 1. General route to 5-alkoxypyrimidines **4**, 4-hydroxypyridines **6**, and 5-acetyl-oxazole derivatives **7** via β-alkoxy-β-ketoenamides **5** starting from lithiated alkoxyallenes **1**, nitriles **2**, and carboxylic acids **3**.

The mechanism of enamide synthesis is illustrated in Scheme 2 and has been described in earlier publications in more detail.[7] In the first step, lithiated alkoxyallene **1** attacks the nitrile to form an allenyl imine **8**. Treatment with an excess of carboxylic acid furnishes the protonated species of **8**, which, upon nucleophilic attack of the carboxylate anion at the central allene carbon, forms intermediate **9**. A subsequent intramolecular acyl transfer gives enamide **5**. When perfluorinated carboxylic acids, such as trifluoroacetic acid, are employed, a partial acid-catalyzed aldol-type condensation of enamides **5** to give perfluoroalkyl-substituted 4-hydroxpyridine derivatives **10** is observed under the reaction conditions. For compounds **5** with less electrophilic amide units, the reaction sequence generally stops at the enamide stage, which may then be used for the preparation of alternative heterocyclic systems.



Scheme 2. Proposed mechanism for the formation of β-alkoxy-β-ketoenamides **5** and perfluoroalkyl-substituted 4-hydroxypyridines **10**.

The transformation of enamides **5** into 5-acetyloxazoles **7** requires that R^1 groups undergo fast cleavage under acidic conditions (e.g., R^1=TMSE).[11] In this report, we increased the variety of substituents R^2 and R^3 and also studied the use of alternative protective groups R^1 (Scheme 3) to fully



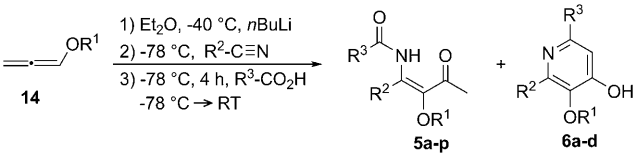
Scheme 3. Conversion of β-alkoxy-β-ketoenamides **5** into 5-acetyloxazoles **7**, their subsequent transformations into products **11**, and formation of 1,2-diketones **12** and quinoxaline derivatives **13**.

explore the scope and limitations of this route to highly substituted oxazoles. In several cases, 1,2-diketone amides **12** have been found as side (or even major) products. Their formation will be discussed in more detail and their conversion into quinoxaline amides **13** will also be reported. The mechanism of oxazole formation was not clear. Therefore, we performed ^{18}O-labeling experiments and, with the aid of mass spectrometry techniques, obtained a more profound insight into the mechanism. A series of subsequent reactions, mostly employing the C-5 acetyl group, was performed to demonstrate the utility of the prepared oxazole. The preparation of an interesting multivalent trisoxazole derivative is presented and its arrangement on highly oriented pyrolytic graphite (HOPG) was investigated by scanning tunneling microscopy (STM).

Results and Discussion

Synthesis of 5-acetyloxazoles—scope and limitations: The β-alkoxy-β-ketoenamides **5a–p** could be prepared by methods A or B by applying the reaction conditions summarized in Table 1. In Method A, alkoxyallene **14** (2.7 equiv) was lithiated by reaction with *n*-butyllithium and treated with 1.0 equivalent of the corresponding nitrile. In Method B, only 1.0 equivalent of lithiated alkoxyallene was used. In

Table 1. Three-component synthesis of β-alkoxy-β-ketoenamides **5** with 6-trifluoromethyl-substituted 4-hydroxypyridines **6** as side products.



	R^1	R^2	R^3	Method[a]		Yield of **5** [%]		Yield of **6** [%]
1	Bn	nC_9H_{19}	Ph[b]	A	**5a**	27	–	
2	Bn	*t*Bu	2-thienyl[c]	A	**5b**	52	–	
3	Bn	Ph	CF_3	A	**5c**	40	**6a**	36
4	Bn	Ph	Ph[b]	A	**5d**[8b]	54	–	
5	Bn	Ph	2-Py[c]	B	**5e**[8b]	27	–	
6	PMB	Ph	CF_3	A	**5f**	23	**6b**	10
7	2-THP	*c*Pr	*c*Pr	A	**5g**	24	–	
8	TMSE	*c*Pr	*c*Pr	A	**5h**	75	–	
9	TMSE	*t*Bu	Me	B	**5i**	52	–	
10	TMSE	*t*Bu	CF_3	B	**5j**[7e]	14	**6c**[7e]	28
11	TMSE	Ad	*c*Pr	A	**5k**	57	–	
12	TMSE	Ph	CF_3	A	**5l**	39	**6d**	24
13	TMSE	Ph	2-thienyl[b]	A	**5m**	75	–	
14	TMSE	Ph	2-Py[c]	B	**5n**	24	–	
15	TMSE	Ph	C≡CH	A	**5o**	21	–	
16	TMSE	Ph	Ac	A	**5p**	28	–	

[a] Method A: lithiated alkoxyallene (2.7 equiv), nitrile (1.0 equiv), carboxylic acid (5.4 equiv); Method B: lithiated alkoxyallene (1.0 equiv), nitrile (1.5–3.0 equiv), carboxylic acid (6.0 equiv); [b] Dissolved in either diethyl ether or THF; [c] Dissolved in DMF.

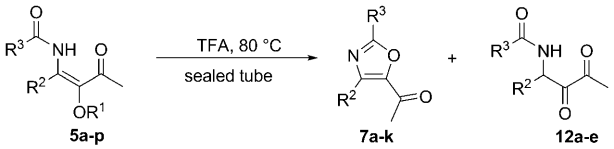
both cases, an excess of the corresponding carboxylic acid was necessary. Table 1 shows the high flexibility of this approach to β-alkoxy-β-ketoenamides with respect to R^2 and R^3. Aliphatic, aromatic, and heteroaromatic substituents were tolerated in both positions. Even an alkynyl or an acetyl group could be introduced through use of the corresponding carboxylic acid (Table 1, entries 15 and 16). When perfluorinated carboxylic acids such as trifluoroacetic acid (TFA) were employed, trifluoromethyl-substituted pyridinols **6** were obtained as side products in considerable quantities (Table 1, entries 3, 6, 10, and 12). Enamides with different O-substituents, such as benzyl-, *para*-methoxybenzyl-, 2-tetrahydropyranyl-, and (2-trimethylsilyl)ethoxyl, could be obtained in moderate to good yields. The efficacy often depends on the carboxylic acid employed. In particular, the solid aromatic and heteroaromatic carboxylic acids had to be dissolved in solvents such as tetrahydrofuran (THF) or *N*,*N*-dimethylformamide (DMF) prior to addition to the reaction mixture. This modification of the protocol could not inhibit in all cases a partial precipitation of the corresponding acid at −78 °C, which might have strongly contributed to the decreased yields. We did not optimize the preparation of the individual examples of β-alkoxy-β-ketoenamides **5** collected in Table 1, thus, the efficiency of this first step can probably be raised in many cases.

Following the previously described standard conditions, enamides **5a–p** were subsequently cyclized to give the corresponding oxazole derivatives **7a–k** (Table 2). The transformation was carried out in a sealed tube by using an excess of TFA and heating to 80 °C for 15–20 min, providing a single product in most cases in moderate to very good yields (39–99 %). The method allows the preparation of oxazoles with alkyl and aryl substituents at C-2 and C-4 in yields up to 98 %. With respect to R^3, the substitution pattern was then extended to hetaryl, alkynyl, and acetyl groups (Table 2, entries 2, 5, and 13–16). It should also be noted that only a few alternative synthetic methods are available for the direct introduction of perfluoroalkyl groups at C-2 of an oxazole derivative (Table 2, entries 3, 6, 10, and 12).[12]

The results given in Table 2 reveal that β-alkoxy-β-ketoenamides **5** with alkoxy groups that are less labile against acid (e.g., Bn), are also suitable substrates for the cyclization to 5-acetyloxazoles **7**. A comparison of the reactivity of benzyl-, *para*-methoxybenzyl-, and 2-(trimethylsilyl)ethyl-substituted enamides could be achieved by the preparation of enamides **5** with identical substituents R^2 and R^3 (compare Table 2, entries 3, 6, and 12, and entries 5 and 14). In both series, higher cyclization yields were obtained for oxazoles **7d** and **7b** starting from the TMSE-substituted enamides **5l** and **5n**, respectively.

If R^2 represents a moderately bulky substituent, such as a cyclopropyl group, the formation of 1,2-diketones **12** was ob-

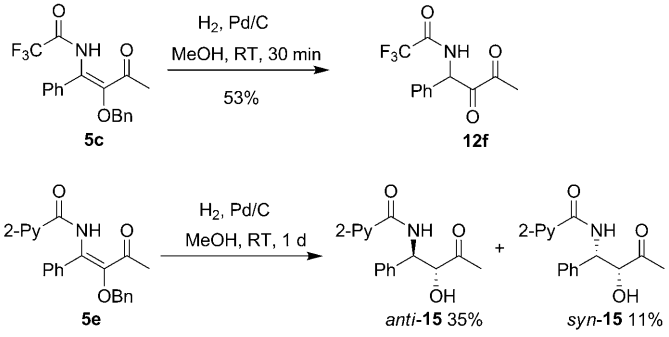
Table 2. Synthesis of 5-acetyloxazoles **7** and 1,2-diketones **12** starting from β-alkoxy-β-ketoenamides **5**.



	Enamide	R^1	R^2	R^3		Yield of **7** [%]		Yield of **12** [%]
1	**5a**	Bn	nC_9H_{19}	Ph	**7a**	51	–	–
2	**5b**	Bn	*t*Bu	2-thienyl	–	–	**12a**	83
3	**5c**	Bn	Ph	CF_3	**7b**	74	–	–
4	**5d**	Bn	Ph	Ph	**7c**	48	–	–
5	**5e**	Bn	Ph	2-Py	**7d**	64	–	–
6	**5f**	PMB	Ph	CF_3	**7b**	53	–	–
7	**5g**	2-THP	*c*Pr	*c*Pr	**7e**	51	**12b**	trace
8	**5h**	TMSE	*c*Pr	*c*Pr	**7e**	67	**12b**	trace
9	**5i**	TMSE	*t*Bu	Me	**7f**	24	**12c**	29
10	**5j**	TMSE	*t*Bu	CF_3	**7g**	60	**12d**	30
11	**5k**	TMSE	Ad	*c*Pr	**7h**	12	**12e**	65
12	**5l**	TMSE	Ph	CF_3	**7b**	98	–	–
13	**5m**	TMSE	Ph	2-thienyl	**7i**	68	–	–
14	**5n**	TMSE	Ph	2-Py	**7d**	99	–	–
15	**5o**	TMSE	Ph	C≡CH	**7j**	57	–	–
16	**5p**	TMSE	Ph	Ac	**7k**	39	–	–

served in trace amounts (Table 2, entries 7 and 8). Enamides **5** with very bulky groups (R^2 = *tert*-butyl or adamantyl, Table 2, entries 9, 10, and 11) furnished 1,2-diketones **12** in low to good yields as by-products. Enamide **5b** was the first example in which 1,2-diketone **12a** was obtained as the exclusive product (Table 2, entry 2). Attempts to convert these 1,2-diketones into oxazoles by applying longer reaction times or through the use of dehydrating reagents, such as phosphorous oxychloride or trifluoroacetic acid anhydride, failed. This was a first indication that 1,2-diketones are not intermediates in the formation of oxazoles.

An alternative pathway for the formation of 1,2-diketones was found during the hydrogenation of benzyl-protected enamides (Scheme 4). Enamide **5c** was reduced with catalytic



Scheme 4. Hydrogenation of enamides **5c** and **5e** to give 1,2-diketone **12f** and α-hydroxy β-amino ketones **15**.

amounts of palladium on charcoal in methanol to give **12f** in 53% yield after 30 min. When R^1 was a pyridinyl substituent, the corresponding enamide **5e** was completely hydrogenated after one day to give an approximate 1:3 mixture of *syn*- and *anti*-configured acylated α-hydroxy β-amino ketones **15**. The constitution and configuration of these diastereomeric compounds were confirmed by X-ray crystal structure analyses (Figures 1 and 2).[13]

We also looked for a method to prepare oxazoles with alternative substituents at C-5 (Scheme 5). The required γ-phenyl-substituted 2-(trimethylsilyl)ethoxyalkyne **16** was

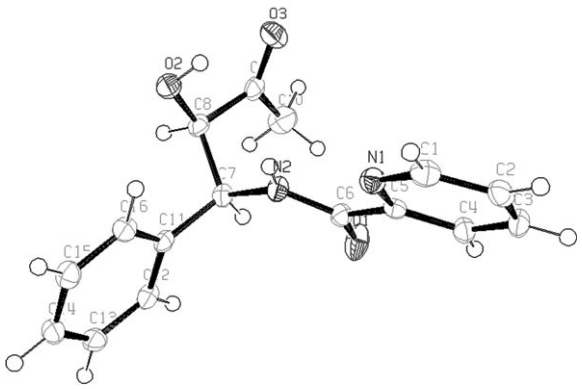


Figure 1. Solid-state structure of *syn*-**15** (ORTEP plot 50% probability level).

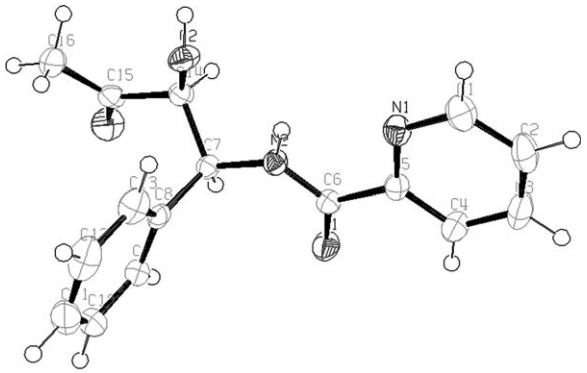
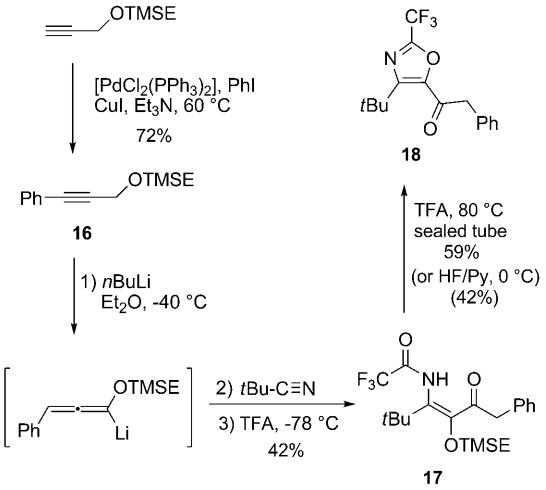


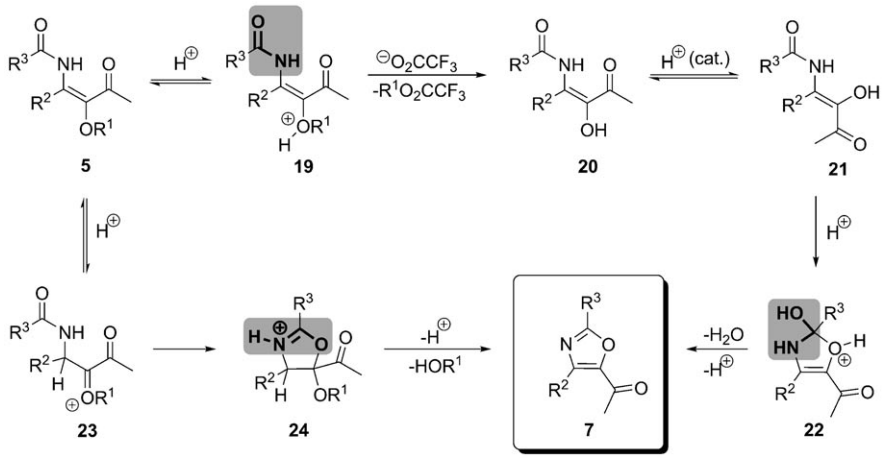
Figure 2. Solid-state structure of *anti*-**15** (ORTEP plot 50% probability level).



Scheme 5. Preparation of 2-phenylacetyl-substituted oxazole **18**.

synthesized by palladium-catalyzed coupling of iodobenzene with (2-trimethylsilyl)ethyl propargyl ether. According to the standard conditions for the enamide synthesis, the alkyne was isomerized in situ to an α-lithiated alkoxyallene,[14] and subsequent treatment with pivalonitrile and TFA generated enamide **17** in moderate yield. Cyclization mediated by TFA led to the formation of 2-phenylacetyl-substituted oxazole **18** (59%) as the sole product. A second method was tested that involved treatment of enamide **17** with HF in pyridine, which furnished **18** in 42% yield.

Mechanism of oxazole formation: Prior to this work, the detailed mechanism of oxazole formation was unclear. Scheme 6 represents the two most probable pathways starting from enamide **5**. The first route is based on the cyclodehydration mechanism of α-acylamino ketones (Robinson and Gabriel pathway).[3,15] Initially, enamide **5** will be protonated by TFA to form intermediate **23**; subsequent cyclization can then occur to afford **24** through nucleophilic attack of the amide oxygen atom. After elimination of the alcohol R^1OH and deprotonation, oxazole **7** is formed. The

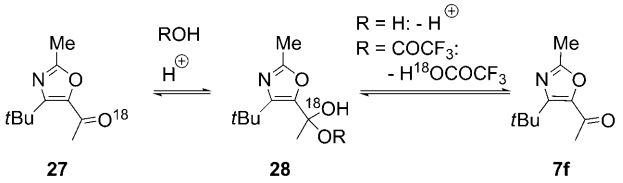


Scheme 6. Two likely reaction pathways to oxazole **7** starting from enamide **5**.

second possible route might proceed analogously to a mechanism suggested for the conversion of *ortho*-hydroxybenzene amides into benzoxazoles.[16] In this case, the protonation provides intermediate **19**, which will be rapidly cleaved by the trifluoroacetate anion to give (*E*)-configured enol intermediate **20**. After acid-catalyzed isomerization to the (*Z*)-configured enol **21**, the hydroxyl function is ready to attack the amide carbonyl carbon atom. Dehydration and deprotonation of intermediate **22** furnishes oxazole **7**.

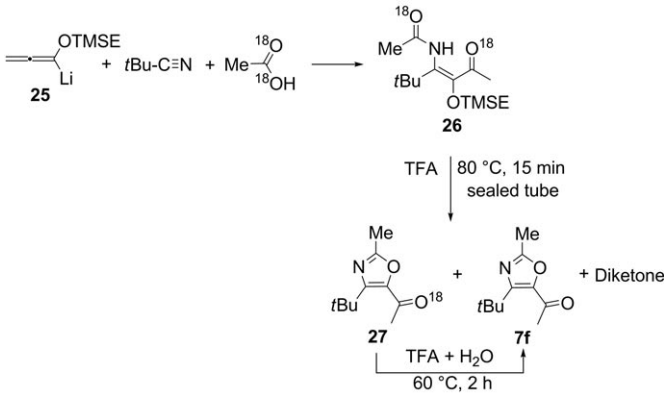
We assumed that the use of ^{18}O-labeled compounds combined with mass spectrometric analysis could provide a more profound insight into these pathways. Hence, an ^{18}O-labeled enamide was prepared by using our standard three-component protocol. Lithiated (2-trimethylsilyl)ethoxyallene **25** was reacted with pivalonitrile and ^{18}O-labeled acetic acid to give the expected enamide **26**. Mass spectrometric analyses of the crude product proved that only the desired enamide was formed with two labeled oxygen atoms incorporated into the scaffold (Scheme 7). This observation also supports the mechanism of enamide formation as proposed in Scheme 2.

Cyclization of **26** to the corresponding oxazole was achieved under the standard conditions. Mass spectrometry revealed that two oxazoles with different masses were formed in an approximate 1:1 ratio, together with the ^{18}O-labeled 1,2-diketone. Oxazole **7f** represents the unlabeled form, and **27** an oxazole with only one ^{18}O atom. To prove that the ^{18}O-labeled oxygen was not incorporated into the heterocyclic ring, this mixture of **27** and **7f** was treated with a mixture of TFA in water. Mass spectrometric analysis of the resulting product showed only one peak, which was assigned to the unlabeled oxazole **7f**. Apparently, the labeled oxygen was located exclusively in the acetyl moiety and was rapidly exchanged by formation of a carbonyl hydrate or hemiacylal **28** (Scheme 8). The very fast exchange of the oxygen isotopes of the carbonyl groups under acidic conditions is well-known.[17]

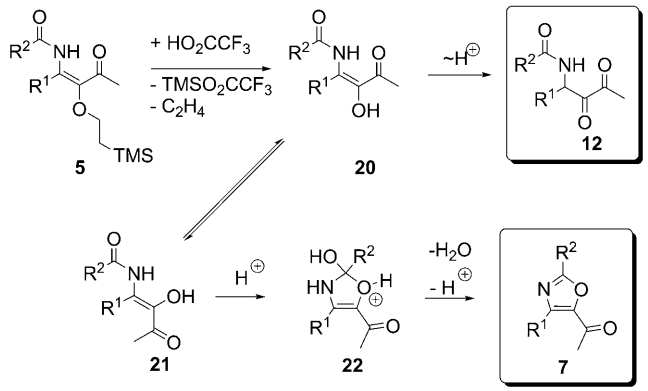


Scheme 8. Proposed mechanism of the ^{18}O–^{16}O-exchange in oxazole derivative **27** leading to **7f**.

Because no ^{18}O was incorporated into the oxazole ring, the second mechanistic option as discussed above seems to be most likely. This mechanism is illustrated in Scheme 9. Thus (2-trimethylsilyl)ethyl-substituted enamide **5** is protonated and attacked by the trifluoroacetate anion. Under fragmentation the TMS-ester, ethylene, and *E*-configured inter-



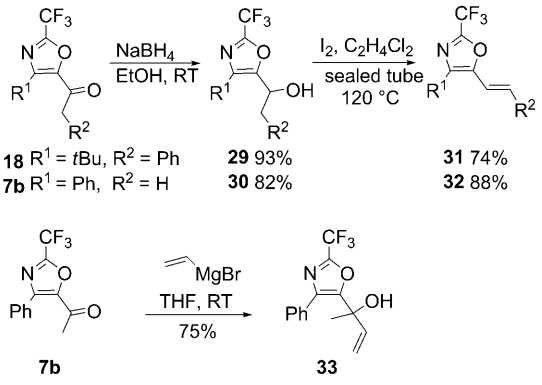
Scheme 7. Synthesis of ^{18}O-labeled enamide **26** and oxazoles **27** and **7f**.



Scheme 9. Final mechanistic scenario of oxazole formation.

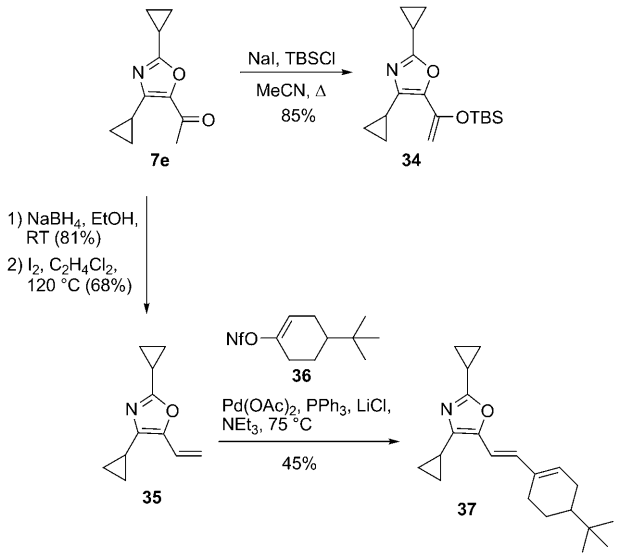
mediate **20** are formed. Its acid-catalyzed isomerization leads to either 1,2-diketone **12** or *Z*-configured enol **21**. The hydroxyl group of **21** can then undergo an intramolecular nucleophilic attack to the amide moiety, providing intermediate **22**. Finally, dehydration and deprotonation furnish oxazole **7**. It is noteworthy that the conversion of *E*-configured enol **20** into 1,2-diketone **12** seems to be essentially irreversible.

Transformations of 5-acetyloxazoles: It is not simple to introduce an acyl group at the C-5 position of oxazole derivatives by standard methods,[18] and only a few reports deal with the synthesis of related oxazol-5-yl ketones.[19] This functional group clearly allows the application of a series of useful functional group transformations. As first examples, oxazoles **7b** and **18** were reduced by sodium borohydride to the secondary alcohols **29** and **30** in very good yields (Scheme 10). Subsequent Hibbert dehydration reaction gave the corresponding alkenes **31** and **32** in 74–88% yield. NMR spectroscopic analysis clearly confirmed the assumed *trans*-configuration of compound **31**. Furthermore, Grignard reaction of oxazole **7b** with vinylmagnesium bromide furnished tertiary alcohol **33** in 75% yield.



Scheme 10. Addition of nucleophiles to 5-acyl-substituted oxazole derivatives leading to compounds **29**–**33**.

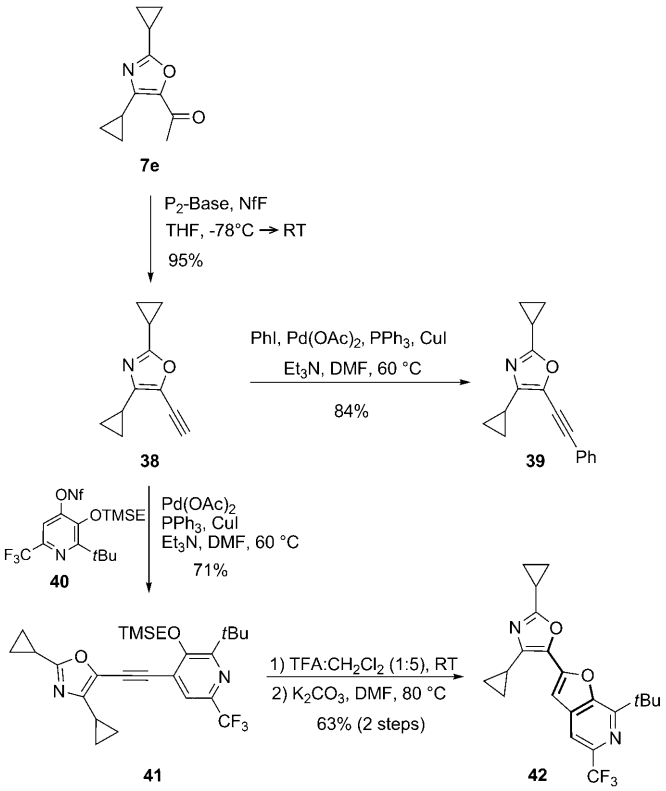
Because cyclopropyl-substituted heterocycles are of particular interest in medicinal chemistry,[20] we performed further model reactions with dicyclopropyl-substituted oxazole derivative **7e**. The conversion of the acetyl group into a silyl enol ether moiety was achieved in 85% yield by subjecting oxazole **7e** to a mixture of sodium iodide and *tert*-butyldimethylsilyl chloride in acetonitrile (Scheme 11). Product **34** should be a very useful precursor for a variety of subsequent reactions that are typical for silyl enol ethers. A smooth reduction of **7e** with sodium borohydride, followed by elimination, provided the vinyl-substituted oxazole derivative **35** in good overall yield. This was a suitable precursor for a Heck reaction employing cyclohexenyl nonaflate **36**,[21] and furnished the expected oxazol-5-yl-substituted 1,3-diene **37** in moderate yield.



Scheme 11. Conversion of 5-acetyloxazole **7e** into silyl enol ether **34**, alkene **35**, and Heck coupling product **37**.

By applying the elegant method developed by Lyapkalo and Vogel,[22] direct conversion of **7e** into alkyne **38** could be achieved in excellent yield. This one-pot reaction was carried out with a mixture of P_2-base[23] and nonafluorobutanesulfonyl fluoride (NfF), and proceeded via the corresponding alkenyl nonaflate, which suffered immediate elimination to the alkyne. The terminal alkyne **38** is an excellent precursor for a variety of other oxazole derivatives. Palladium-catalyzed coupling reaction[24] of **38** with iodobenzene under standard Sonogashira conditions furnished **39** in 84% yield. Coupling of the highly substituted pyridinyl nonaflate **40**[7e] afforded the desired product **41** in good yield.[25] Moreover, the disubstituted alkyne **41** is a precursor for the synthesis of the oxazol-5-yl-substituted furo[2,3-*c*]pyridine **42**.[26] In general, these compounds have interesting photophysical features[7d,8d] that might be useful for the development of novel organic light emitting materials or optoelectronics.[27] A two-step method[7d] was employed for the conversion of **41** into **42**. After removal of the 2-(trimethylsilyl)ethyl group by TFA, subsequent intramolecular cyclization reaction with potassium carbonate provided the expected product **42** in 63% yield over two steps. The preparation of compounds such as **42** demonstrates again the high versatility of alkoxyallenes as C_3-building blocks for the synthesis of functionalized heterocycles. Here, two alkoxyallene units are incorporated in the heterocyclic cores (in Scheme 12 the two allene units are highlighted for clarity). The UV/Vis and fluorescence spectra of compound **42** show an absorption at 320 nm and emission at 380 nm, resulting in a moderate Stokes shift of approximately 60 nm (Figure 3).

Treatment of oxazole **7b** with hydroxylammonium chloride led to the formation of oxime **43** as a single isomer in 64% yield (Scheme 13). Condensation of **7e** with phenylhydrazine provided hydrazone **44** almost quantitatively, again as single isomer. The anticipated Fischer indole synthesis to



Scheme 12. Conversion of 5-acetyloxazole **7e** into alkyne **38** according to Lyapkalo and Vogel followed by Sonogashira reactions to give **39** and **41** and cyclization to furopyridine derivative **42**.

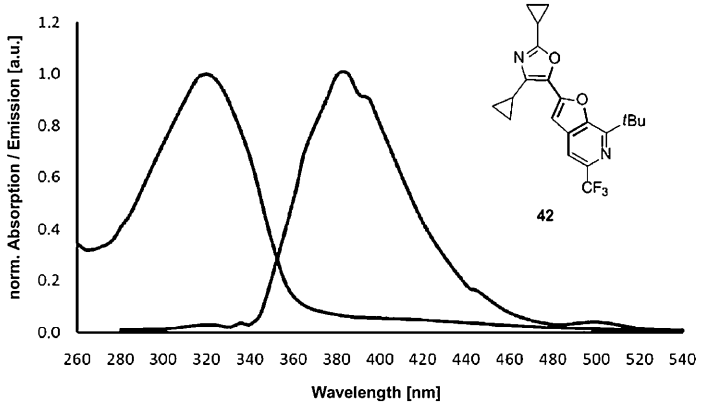
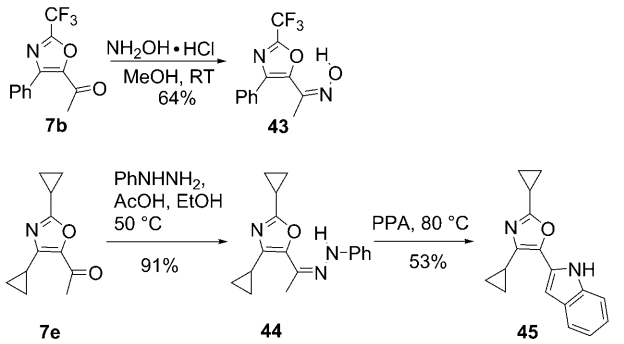


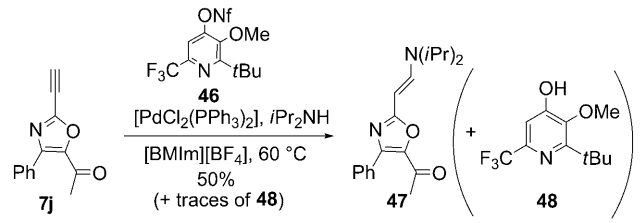
Figure 3. UV/Vis and fluorescence spectra of oxazol-5-yl substituted furopyridine derivative **42**.

generate **45** was accomplished by treatment with polyphosphoric acid at 80 °C. This example demonstrates the high potential of our approach to the preparation of oxazol-5-yl-substituted heterocycles of various types.[28]

The acetylene moiety at C-2 of oxazole **7j** should also be suitable for Sonogashira reactions with appropriate coupling partners. Interestingly, attempts to employ pyridinyl nonaflate **46**[7a] as a component in an ionic liquid, without use of a copper catalyst (which should minimize homo-coupling of the alkyne) led to an unexpected product (Scheme 14).[29]



Scheme 13. Conversion of 5-acetyloxazole **7b** into oxime **43** and of oxazoles derivative **7e** into hydrazone **44** and indole **45**.



Scheme 14. Addition of diisopropylamine to alkynyl-substituted oxazole **7j** to provide oxazol-5-yl-substituted enamine **47**.

Instead of the desired coupling reaction, diisopropylamine added to the activated triple bond to provide enamine **47** in 50 % yield together with traces of pyridinol **48**.[7a] Oxazole derivative **47**, containing a donor–acceptor-substituted double bond, was investigated by UV/Vis spectroscopy in more detail; Figure 4 depicts the absorption and emission data of **47**. Two absorption maxima at 292 and 378 nm were observed, while the emission maximum was strongly shifted to the visible region (482 nm), resulting in a high Stokes shift of approximately 100 nm.

Transformation of 1,2-diketones into quinoxalines: Functionalized 1,2-diketones, such as **12a** and **12e**, which were obtained during the preparation of oxazole derivatives **7**,

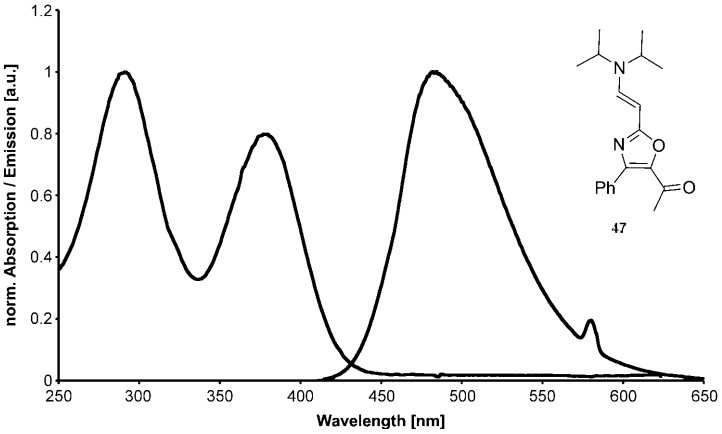
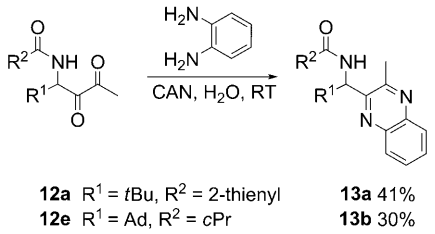


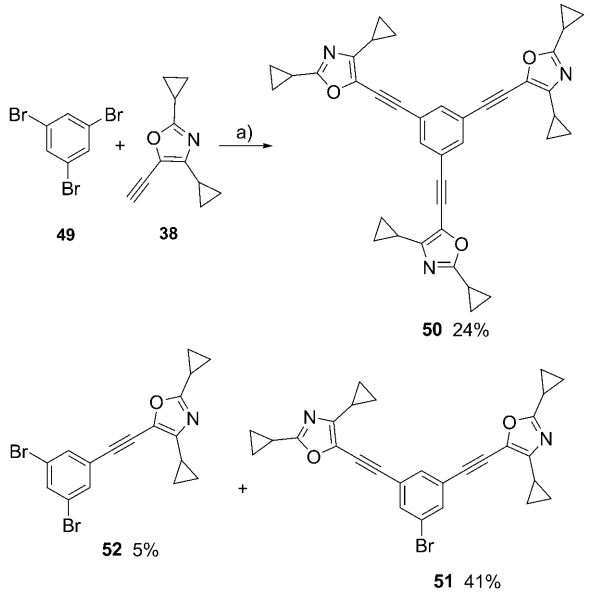
Figure 4. UV/Vis and fluorescence spectra of oxazole derivative **47**.



Scheme 15. Conversion of 1,2-diketones **12** into quinoxaline derivatives **13**.

are also precursors for the synthesis of other heterocyclic compounds (Scheme 15).[30] In the presence of catalytic amounts of cerium ammonium nitrate (CAN)[31] and *ortho*-phenylenediamine, the 1,2-diketone moiety was incorporated into the corresponding quinoxalines **13a** and **13b**, which were obtained in moderate yields.

Synthesis and self-assembly behavior of a star-shaped multivalent oxazole derivative: We also attempted to apply oxazol-5-yl-substituted alkyne **38** to a triple Sonogashira reaction employing 1,3,5-tribromobenzene **49** as the core element, to prepare a compound with C_3-symmetry (Scheme 16). This study formed part of our research on multivalent, star-shaped compounds containing heterocyclic ligands, which are promising objects for studying two-dimensional supramolecular chemistry at surfaces.[32] When an excess of alkyne **38** and 1,3,5-tribromobenzene **49** were treated under standard conditions for a Sonogashira reaction, a mixture was obtained that contained the desired trisubstituted benzene derivative **50** together with disubstituted product **51** as the major component and mono-coupling



Scheme 16. Synthesis of star-shaped molecule **50** by Sonogashira reaction of alkyne **38**. Reagents and conditions: a) $[PdCl_2(PPh_3)_2]$, CuI, Et_3N, 50 °C, sealed tube, overnight.

product **52**. No attempts to optimize this coupling process were undertaken. The three components could easily be separated by column chromatography.

The prepared star-shaped compound **50** (Scheme 16) was investigated with respect to its ability to form self-assembled monolayers at the interface between the basal plane of highly oriented pyrolytic graphite (HOPG) and a saturated solution in 1-phenyloctane. Scanning tunneling microscopy (STM) revealed that **50** self-assembles into long chains with two oppositely oriented molecules per unit cell, with the chains being packed parallel to each other without interdigitations (Figure 5). Bright areas in the STM image correspond to high tunneling current, indicating the positions of the π-systems,[33] whereas the dark areas indicate the cyclopropyl groups. The molecular orbitals were calculated with the DMol3 interface of Accelrys Materials Studio using the local-density approximation method and Perdew Wang correlation.[34] The implemented space-filling models are based on standard van-der-Waals parameters.

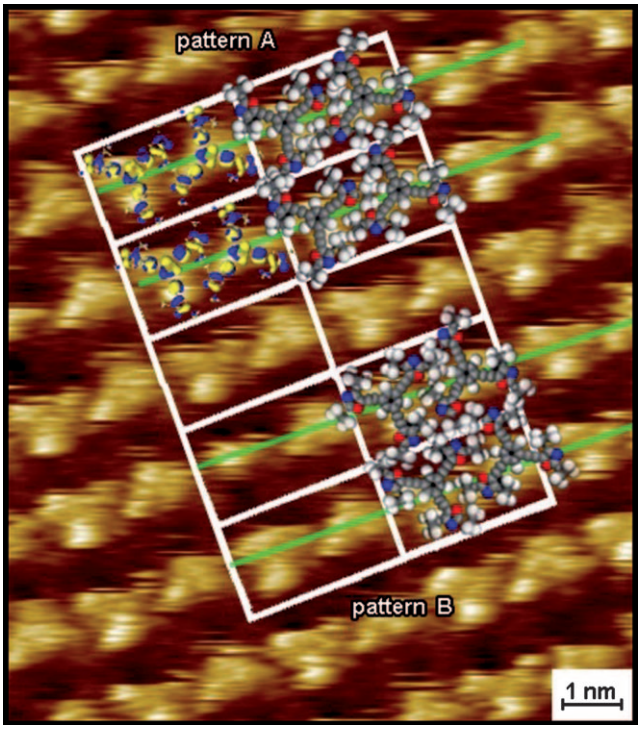


Figure 5. STM current image of C_3-symmetric compound **50** at the interface between a solution in 1-phenyloctane and the basal plane of HOPG. Unit cell size: $a = (2.65 \pm 0.05)$ nm, $b = (1.42 \pm 0.05)$ nm, $\alpha = (94 \pm 3)°$, $A = (3.74 \pm 0.17)$ nm^2.

In the resulting crystalline monolayers on HOPG, **50** may assume two different conformations, leading to two differing packing patterns. Pattern A, with a C_3-symmetric arrangement of the three oxazole rings, gives the best fit, with the experimentally determined centers of the molecules (green lines, Figure 5) matching exactly the centers of a close packing of flat-lying molecules. In contrast, in pattern B, the asymmetric conformer does not match as well as in patter-

n A because the chains are too close to prevent crowding in certain areas. Apparently the cyclopropyl groups need sufficient space to pack in the molecular chains.

Under similar conditions, compound **51** did not form related monolayers, indicating that a more extended π-system is present in **50** that favors the generation of two-dimensional crystals of flat-lying molecules on HOPG. The STM measurements show that C_3-symmetric multivalent components such as **50** are good candidates to achieve highly ordered two-dimensional arrangements on HOPG. The behavior of these ordered structures and structure–property relationships will be further investigated.

Conclusion

The treatment of (2-trimethylsilyl)ethyl or benzyl protected β-alkoxy-β-ketoenamides with trifluoroacetic acid allows quick and simple access to highly substituted 5-acetyloxazoles. This oxazole synthesis is very flexible with respect to the substitution pattern at all positions and even enables the introduction of different functional groups at the C-2 position. The reaction mechanism of this cyclization has been clarified in more detail by ^{18}O-labeling experiments combined with mass spectrometric analyses. The acetyl group of the prepared oxazoles enables the smooth preparation of a variety of different, interesting oxazole derivatives. A star-shaped compound with three oxazole ligands was investigated by STM measurements and showed a remarkable self-assembled monolayer on HOPG.

Experimental Section

General methods: see the Supporting Information.

Typical procedure for the preparation of enamides (Method A)

Preparation of *N*-{(1*E*)-1-cyclopropyl-3-oxo-2-[2-(trimethylsilyl)ethoxy]-but-1-enyl}-cyclopropanecarboxamide (5h): (2-Trimethylsilyl)ethoxyallene (4.00 g, 25.6 mmol) was dissolved in diethyl ether (52 mL) and *n*-butyllithium (9.73 mL, 24.3 mmol, 2.5 M in hexanes) was added at −40 °C. After 25 min at −50 to −40 °C, cyclopropane nitrile (0.95 mL, 12.8 mmol) was added. The solution was stirred at −40 °C for 30 min and then cooled to −78 °C. After stirring for 4 h at this temperature, cyclopropane carboxylic acid (4.06 mL, 51.2 mmol) was added and the mixture was warmed overnight to RT. The mixture was quenched with satd. aq. $NaHCO_3$ (40 mL) and extracted with Et_2O (2×40 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated. Column chromatography (silica gel; hexane/ethyl acetate, 10:1) provided **5h** (2.98 g, 75 %) as a colorless oil. ^1H NMR ($CDCl_3$, 500 MHz): $\delta = -0.01$ (s, 9H; TMS), 0.76–0.84 (m, 4H; *c*Pr), 0.90–0.98 (m, 4H; *c*Pr), 1.08 (m_c, 2H; CH_2Si), 1.51 (m_c, 1H; *c*Pr), 2.09 (m_c, 1H; *c*Pr), 2.22 (s, 3H; 4-H), 3.77 (m_c, 2H; OCH_2), 11.74 ppm (br s, 1H; NH); ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta = -1.6$ (q; TMS), 8.3, 8.7 (2×t; *c*Pr), 11.8, 16.5 (2×d; *c*Pr), 18.8 (t; CH_2Si), 27.2 (q; C-4), 72.1 (t; OCH_2), 139.0 (s; C-2), 146.4 (s; C-1), 172.6 (s; C-1′), 201.4 ppm (s; C-3); IR (neat): $\tilde{\nu} = 3290$–3210 (N-H), 3095–2870 (C−H), 1725–1640 cm^{-1} (C=O, C=C); elemental analysis calcd (%) for $C_{16}H_{27}NO_3Si$ (309.5): C 62.10, H 8.79, N 4.53; found: C 62.26, H 8.96, N 4.35.

Typical procedure for the preparation of oxazoles

Preparation of 1-(2,4-dicyclopropyl-1,3-oxazol-5-yl)ethanone (7e): Enamide **5h** (144 mg, 0.465 mmol) was added in an ACE sealed tube and dissolved in TFA (2 mL). The reaction mixture was placed in a preheated oil bath (80 °C). After stirring for 15 min at this temperature, water (4 mL) was slowly added and the reaction mixture was extracted with CH_2Cl_2 (3×4 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated. Column chromatography (silica gel; hexane/ethyl acetate = 10:1) provided **7e** (60 mg, 67 %) as a colorless solid and traces of 1,2-diketone **12b** (<1 %). M.p. 48 °C; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 0.95$–0.99 (m, 4H; *c*Pr), 1.04–1.11 (m, 4H; *c*Pr), 2.01 (m, 1H; *c*Pr), 2.56 (m, 1H; *c*Pr), 2.39 ppm (s, 3H; 2′-H); ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta = 8.4$, 9.2 (2×d; *c*Pr), 8.9, 9.1 (2×t; *c*Pr), 27.3 (q; C-2′), 144.9, 151.9 (2×s; C-4, C-5), 167.6 (s, C-2), 186.9 ppm (s, C-1′); IR (KBr): $\tilde{\nu} = 3015$–2850 (C−H), 1750–1585 cm^{-1} (C=O, C=C); elemental analysis calcd (%) for $C_{11}H_{13}NO_2$ (191.2): C 69.09, H 6.85, N 7.32; found: C 69.29, H 6.85, N 7.29.

Data for 1,2-diketone 12b: ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 0.98$–1.07 (m, 4H; *c*Pr), 1.10–1.18 (m, 4H; *c*Pr), 1.84 (m, 1H; *c*Pr), 2.33 (m, 1H; *c*Pr), 2.32 (s, 3H; Me), 5.65 ppm (s, 1H; CH).

Preparation of *N*-(2,3-dioxo-1-phenylbutyl)-2,2,2-trifluoroacetamide (12f): A mixture of enamide **5c** (210 mg, 0.578 mmol) and palladium on charcoal (10 %, 62 mg, 0.058 mmol) in MeOH (5 mL) was stirred for 30 min under an atmosphere of hydrogen. Filtration of the reaction mixture through Celite with MeOH, and column chromatography (silica gel; hexane/ethyl acetate = 5:1) afforded **12f** (84 mg, 53 %) as a yellow solid. M.p. 77–78 °C; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 2.29$ (s, 3H; 4-H), 6.33 (d, $J = 6.5$ Hz, 1H; 1-H), 7.29–7.40 ppm (m, 6H; Ph, NH); ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta = 24.4$ (q; C-4), 57.5 (d; C-1), 115.5 (q, $^1J(C,F) = 288$ Hz; CF_3), 128.4, 129.62, 129.63, 131.9 (3×d, s; Ph), 156.4 (q, $^2J(C,F) = 38.1$ Hz; C-1′), 190.7, 195.0 ppm (2×s; C-2, C-3); ^{19}F NMR ($CDCl_3$, 470 MHz): $\delta = -75.5$ ppm (s; CF_3); IR (KBr): $\tilde{\nu} = 3350$ (N-H), 3095–3030 (=C−H), 2985–2850 (C−H), 1730–1670 cm^{-1} (C=O); UV/Vis (MeCN): $\lambda_{max} =$ 275 nm (shoulder); elemental analysis calcd (%) for $C_{12}H_{10}F_3NO_3$ (273.2): C 52.75, H 3.69, N 5.13; found: C 53.12, H 3.64, N 5.08.

Preparation of 1-[4-phenyl-2-(trifluoromethyl)-1,3-oxazol-5-yl]ethanol (30): Oxazole **7b** (129 mg, 0.505 mmol) and $NaBH_4$ (38 mg, 1.01 mmol) were dissolved in EtOH (5 mL). After stirring for 10 min at RT, the reaction was quenched with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated. Column chromatography (silica gel; hexane/ethyl acetate = 10:1) provided **30** (107 mg, 82 %) as a colorless oil. ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 1.66$ (d, $J = 6.6$ Hz, 3H; 2′-H), 2.35 (br s, 1H; OH), 5.18 (q, $J = 6.6$ Hz, 1H; 1′-H), 7.36–7.46, 7.65–7.68 ppm (2×m, 5H; Ph); ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta = 21.3$ (q; C-2′), 61.5 (d; C-1′), 116.5 (q, $^1J(C,F) = 275$ Hz; CF_3), 127.7, 128.8, 128.9, 129.7 (3×d, s; Ph), 137.1 (s; C-4), 149.2 (q, $^2J(C,F) = 44.0$ Hz; C-2), 150.6 ppm (q, $^4J(C,F) = 1.2$ Hz; C-5); ^{19}F NMR ($CDCl_3$, 470 MHz): $\delta = -65.6$ ppm (s; CF_3); IR (neat): $\tilde{\nu} = 3390$ (O-H), 3085–3035 (=C−H), 2990–2835 (C−H), 1675–1575 cm^{-1} (C=C); HRMS (ESI-TOF): *m/z*: calcd for $C_{12}H_{11}F_3NO_2$: 258.0736 $[M+H]^+$; found: 258.0765.

Preparation of 4-phenyl-2-(trifluoromethyl)-5-vinyl-1,3-oxazole (32): Oxazole **30** (66 mg, 0.257 mmol) was placed in an ACE sealed tube and dissolved in 1,2-dichloroethane (3 mL). Two crystals of I_2 were added and the solution was heated for 1 d at 120 °C. After cooling to RT, the mixture was quenched with satd. aq. $Na_2S_2O_3$ (5 mL) and extracted with CH_2Cl_2 (2×5 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated. Column chromatography (silica gel; hexane/ethyl acetate = 20:1) provided **32** (54 mg, 88 %) as a colorless oil. ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 5.55$ (d, $J = 11.7$ Hz, 1H; =CH_2), 5.99 (d, $J = 17.7$ Hz, 1H; =CH_2), 6.84 (dd, $J = 17.7$, 11.7 Hz, 1H; HC=), 7.36–7.47, 7.65–7.66 ppm (2×m, 5H; Ph); ^{13}C NMR ($CDCl_3$, 101 MHz): $\delta = 116.6$ (q, $^1J(C,F) = 267$ Hz; CF_3), 119.1 (t; =CH_2), 121.2 (d; HC=), 127.7, 128.9, 130.2 (2×d, s; overlapping Ph), 137.0 (s; C-4), 149.1 (q, $^2J(C,F) = 43.9$ Hz; C-2), 146.8 ppm (q, $^4J(C,F) = 1.3$ Hz; C-5); ^{19}F NMR ($CDCl_3$, 470 MHz): $\delta = -65.7$ ppm (s; CF_3); IR (neat): $\tilde{\nu} = 3070$–2935 (=C−H, C−H), 1740–1580 cm^{-1} (C=C); HRMS (ESI-TOF): *m/z* calcd for $C_{12}H_9F_3NO$: 240.0631 $[M+H]^+$; found: 240.0630.

Preparation of 2,4-dicyclopropyl-5-ethynyl-1,3-oxazole (38): Oxazole **7e** (287 mg, 1.50 mmol) was dissolved in THF (4 mL) under an argon atmosphere, the solution was cooled to −78 °C, and NfF (500 mg, 1.65 mmol)

was added. The phosphazene P_2-base (2.0 M in THF, 1.65 mL, 3.30 mmol) was added dropwise to the solution at the same temperature and the mixture was slowly warmed to RT overnight. Purification of the mixture directly on column chromatography (silica gel; hexane/ethyl acetate = 20:1) gave **38** (244 mg, 95%) as a colorless solid. M.p. 36–39 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.88–0.93 (m, 4H; *c*Pr), 0.98–1.06 (m, 4H; *c*Pr), 1.85 (m_c, 1H; *c*Pr), 1.98 (m_c, 1H; *c*Pr), 3.70 ppm (s, 1H; C≡CH); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 7.0, 8.4 (2×t; *c*Pr), 7.6, 9.3 (2×d; *c*Pr), 71.6, 87.0 (s, d; C≡CH), 128.1 (s, C-4), 148.1 (s, C-5), 165.8 ppm (s, C-2); IR (ATR): $\tilde{\nu}$ = 3190 (≡C−H), 2970–2865 (C−H), 1570–1600 cm^{-1} (C=N, C=C); HRMS (ESI-TOF): *m*/*z* calcd for $C_{11}H_{12}O$: 174.0913 $[M+H]^+$; found: 174.0926.

Preparation of 2,4-dicyclopropyl-5-(phenylethynyl)-1,3-oxazole (39): A mixture of iodobenzene (196 mg, 0.960 mmol), **38** (200 mg, 1.15 mmol), $Pd(OAc)_2$ (15 mg, 0.067 mmol), PPh_3 (63 mg, 0.240 mmol), and CuI (9.1 mg, 0.050 mmol) in DMF (4.8 mL) and triethylamine (2.4 mL) was heated to 60 °C for 3 h under an argon atmosphere. The mixture was allowed to cool to RT, diluted with brine (10 mL), and extracted with diethyl ether (3×10 mL). The combined organic phase was dried with Na_2SO_4 and concentrated to dryness. The residue was purified by chromatography on silica gel (hexane/ethyl acetate = 20:1) to give **39** (201 mg, 84%) as a colorless solid. M.p. 38 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.96–0.99 (m, 4H; *c*Pr), 1.03–1.09 (m, 4H; *c*Pr), 1.93 (m_c, 1H; *c*Pr), 2.02 (m_c, 1H; *c*Pr), 7.26–7.36, 7.49–7.52 ppm (2×m, 3H, 2H; Ph); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 7.1, 8.4 (2×t; *c*Pr), 7.9, 9.4 (2×d; *c*Pr), 76.7 (s; C-1′), 98.4 (s; C-2′), 122.4, 128.4, 128.6, 131.1 (3×d, s; Ph), 128.7 (s; C-4), 147.0 (s; C-5), 165.7 ppm (s; C-2); IR (ATR): $\tilde{\nu}$ = 3085–3010 (=C−H), 2205 (C≡C), 1570 cm^{-1} (C=C); UV/Vis (MeCN): λ (log ε) = 302 nm (4.36); Fluorescence (MeCN): λ = 376 nm; HRMS (ESI-TOF): *m*/*z* calcd for $C_{17}H_{16}NO$: 250.1154 $[M+H]^+$; found: 250.1219; elemental analysis calcd (%) for $C_{17}H_{15}NO$ (249.1): C 81.90, H 6.06, N 5.62; found: C 82.01, H 5.86, N 5.67.

Preparation of 7-*tert*-butyl-2-(2′,4′-dicyclopropyl-1,3-oxazol-5′-yl)-5-(trifluoromethyl)furo[2,3-*c*]pyridine (42): Pyridine **41** (329 mg, 0.671 mmol) was dissolved in a 1:5 mixture of trifluoroacetic acid and CH_2Cl_2 (4 mL). After stirring for 2 h at RT, the reaction mixture was quenched with H_2O (5 mL) and extracted with CH_2Cl_2 (3×5 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The resulting crude product was dissolved in DMF (3.5 mL) and K_2CO_3 (278 mg, 0.671 mmol) was added. After heating for 3 h at 80 °C, the mixture was quenched at RT with H_2O (10 mL) and extracted with Et_2O (3×10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. Column chromatography on silica gel (hexane/ethyl acetate = 20:1) afforded **42** (165 mg, 63%) as a colorless solid. M.p. 117–119 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.01–1.16 (m, 8H; *c*Pr), 1.56 (s, 9H; *t*Bu), 2.08 (tt, *J* = 8.2, 5.2 Hz, 1H; 1″-H), 2.39 (tt, *J* = 8.1, 5.3 Hz, 1H; 1‴-H), 6.82 (s, 1H; 3-H), 7.74 ppm (s, 1H; 4-H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 7.6, 8.8 (2×t; *c*Pr), 7.8, 9.1 (2×d; C-1″, C-1‴), 28.8, 37.4 (q, s; *t*Bu), 100.1 (d; C-3), 111.4 (dq, ^3J(C,F) = 3.0 Hz; C-4), 122.2 (q, ^1J = 275 Hz; CF_3), 128.9 (s; C-3a), 135.8 (s; C-4′), 136.3 (s; C-5′), 140.4 (q, ^2J(C,F) = 33.9 Hz; C-5), 143.1 (s; C-7a), 149.9 (s; C-2), 153.2 (s; C-7), 166.6 ppm (s; C-2′); ^{19}F NMR ($CDCl_3$, 470 MHz): δ = −66.5 ppm (s; CF_3); IR (ATR): $\tilde{\nu}$ = 3105–3040 (=C−H), 2960–2870 (C−H), 1645–1575 (C=N, C=C), 1150–1130 cm^{-1} (C-F); UV/Vis (MeCN): λ (log ε) = 328 nm (4.48); fluorescence (MeCN): λ = 385 nm; HRMS (ESI-TOF): *m*/*z* calcd for $C_{21}H_{22}N_2O_2$: 391.1633 $[M+H]^+$; found: 391.1637.

Preparation of 1-(2,4-dicyclopropyl-1,3-oxazol-5-yl)ethanone phenylhydrazone (44): Phenylhydrazine (158 mg, 1.45 mmol) dissolved in EtOH (2.5 mL) and acetic acid (43 μL, 0.75 mmol) were successively added to a solution of oxazole **7e** (287 mg, 1.50 mmol) dissolved in EtOH (2.5 mL). After stirring for 30 min at 50 °C, the mixture was quenched with water (1 mL) and the volume of the mixture was reduced to half. After storing the solution for 6 d at 4 °C, the resulting precipitate was recrystallized (EtOH/water = 5:1). Drying in vacuo provided **44** (384 mg, 91%) as a light-yellow solid. M.p. 81–84 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.93–1.04 (m, 8H; *c*Pr), 2.00 (tt, *J* = 5.2, 8.2 Hz, 1H; *c*Pr), 2.18 (s, 3H; 2′-H), 2.55 (tt, *J* = 5.5, 8.0 Hz, 1H; *c*Pr), 6.86 (m_c, 1H; Ph), 7.07 (m_c, 2 H; Ph), 7.27 (m_c, 2 H; Ph), 7.29 ppm (s, 1H; NH); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 7.2, 8.1 (2×t; *c*Pr), 8.0, 9.0 (2×d; *c*Pr), 11.9 (q; C-2′), 112.9, 120.1, 129.3 (3×d; Ph), 134.5 (s; C-4), 139.0 (s; C-5), 144.9 (s; C-1′), 163.3 ppm (s; C-2); IR (ATR): $\tilde{\nu}$ = 3200 (N-H), 3080–3025 (=C−H), 2980–2860 (C−H), 1695–1635 cm^{-1} (C=C, C=N); HRMS (ESI-TOF): *m*/*z* calcd for $C_{11}H_{19}N_3ONa$: 304.1420 $[M+Na]^+$; found: 304.1454.

Preparation of 2,4-dicyclopropyl-5-(1*H*-indol-2-yl)oxazole (45): A mixture of **44** (700 mg, 0.533 mmol) and polyphosphoric acid (700 mg) was heated at 80 °C for 1 h. Further polyphosphoric acid (700 mg) was added and the mixture was heated for an additional 30 min. The mixture was slowly diluted with ice water (10 mL) and extracted with $CHCl_3$ (2×10 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 4:1 to 1:1) to give **45** (75 mg, 53%) as a colorless solid. M.p. 115–119 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.94–1.02 (m, 4H; *c*Pr), 1.04 (m_c, 2H; *c*Pr), 1.11 (m_c, 2H; *c*Pr), 1.98–2.11 (m, 2H; *c*Pr), 6.76 (s, 1H; 3′-H), 7.13 (m, 1H; 8′-H), 7.20 (m, 1H; 7′-H), 7.39 (d, *J* = 8.1 Hz, 2H; 6′-H), 7.62 (d, *J* = 7.8 Hz, 2H; 9′-H), 8.47 ppm (br. s, 1H; NH); ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 6.8, 8.2 (2×t; *c*Pr), 7.6, 9.0 (2×d; *c*Pr), 99.6 (d; C-3′), 110.7 (d; C-6′), 120.3 (d; C-9′), 120.4 (d; C-7′), 122.4 (d; C-8′), 127.0 (s; C-4′), 128.8 (s; C-2′), 135.9 (s; C-5′), 137.5 (s; C-4), 139.1 (s; C-5), 163.8 ppm (s; C-2); IR (ATR): $\tilde{\nu}$ = 3420 (NH), 3090, 3050, 3005 (=CH), 2920, 2850 (C−H), 1635, 1580 cm^{-1} (C=C); HRMS (ESI-TOF): *m*/*z* calcd for $C_{17}H_{17}N_2O$: 265.1341 $[M+H]^+$; found: 265.1342.

Preparation of 1-{2-[(*E*)-2-(diisopropylamino)ethenyl]-4-phenyl-1,3-oxazol-5-yl}ethanone (47): A mixture of **46** (91 mg, 0.170 mmol), $PdCl_2(PPh_3)_2$ (5.0 mg, 0.007 mmol), and **7j** (30 mg, 0.142 mmol) in [BMIm][BF_4] (0.5 mL) and diisopropylamine (90 μL) was heated to 60 °C for 3 h under an argon atmosphere. The mixture was allowed to cool to RT, diluted with brine (3 mL), and extracted with diethyl ether (3×3 mL). The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1) to give **47** (22 mg, 50%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.41 (s, 3H; 2′-H), 1.26 (d, *J* = 6.8 Hz, 12H; *i*Pr), 3.68–3.78 (hept, *J* = 6.8 Hz, 2H; *i*Pr), 5.20 (d, *J* = 13.3 Hz, 1H; =CH), 7.37–7.44, 8.06–8.09 (2 m, 3H, 2H; Ph), 7.64 ppm (d, *J* = 13.3 Hz, 1H; =CH); ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 21.6, 48.2 (q, d; *i*Pr), 27.9 (q; C-2′), 80.5 (d; =CH), 128.0, 129.3, 129.5, 131.6 (3×d, s; Ph), 143.4 (d; =CH), 142.0, 148.3, 166.5 (3×s; C-4, C-5, C-2), 185.4 ppm (s; C-1′); IR (neat): $\tilde{\nu}$ = 3070–3030 (=C−H), 2975–2870 (C−H), 1670–1580 cm^{-1} (C=O, C=C); UV/Vis (MeCN): λ (log ε) = 292 (4.35), 378 nm (4.19); fluorescence (MeCN): λ = 482 nm; HRMS (ESI-TOF): *m*/*z* calcd for $C_{19}H_{25}N_2O_2$: 313.1911 $[M+H]^+$; found: 313.1918.

Preparation of star-shaped compound 50: 1,3,5-Tribromobenzene **49** (75 mg, 0.250 mmol) and alkyne **38** (216 mg, 1.25 mmol) were dissolved in Et_3N (4 mL) and $[PdCl_2(PPh_3)_2]$ (44 mg, 0.0625 mmol) was added. After stirring for 5 min, CuI (6 mg, 0.0312 mmol) was added and the mixture was heated at 50 °C overnight. The solution was filtered and concentrated in vacuo. The residue was taken up in diethyl ether (15 mL) and washed with water (5 mL). The organic layer was dried with $MgSO_4$, filtered, and concentrated. Column chromatography (silica gel; hexane/ethyl acetate = 10:1, 4:1 to 1:1) provided **52** (12 mg, 3%) as a yellow oil, **51** (51 mg, 41%) and **50** (35 mg, 24%) both as pale-yellow solids.

Data for compound 50: M.p. 120–122 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.90–1.10 (m, 24H; *c*Pr), 1.90 (tt, *J* = 5.4, 7.9 Hz, 3H; *c*Pr), 2.01 (tt, *J* = 5.1, 8.4 Hz, 3H; *c*Pr), 7.55 ppm (s, 3H; Ar); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 7.3, 8.5 (2×t; *c*Pr), 8.0, 9.4 (2×d; *c*Pr), 78.4, 96.7 (2×s; C≡C), 123.5, 128.3, 132.8, 148.2, 166.2 ppm (2×s, d, 2×s; oxazole, Ar); IR (ATR): $\tilde{\nu}$ = 3090–2850 (=C−H, C−H), 2205 cm^{-1} (C≡C); HRMS (ESI-TOF): *m*/*z* calcd for $C_{39}H_{34}N_3O_3$: 592.2600 $[M+H]^+$; found: 592.2606.

Data for compound 51: M.p. 118–120 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.95–1.10 (m, 16H; *c*Pr), 1.86–1.94 (m, 2H; *c*Pr), 1.96–2.05 (m, 2H; *c*Pr), 7.52 (t, *J* = 1.4 Hz, 1H; Ar), 7.57 ppm (d, *J* = 1.4 Hz, 2H; Ar); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 7.4, 8.6 (2×t; *c*Pr), 8.0, 9.4 (2×d; *c*Pr), 79.0, 96.3 (2×s; C≡C), 122.1, 124.6, 128.2, 131.7, 133.3, 148.5, 166.2 ppm (3×s, 2×d, 2×s; oxazole, Ar); IR (ATR): $\tilde{\nu}$ = 3090–2850 (=C−H, C−H), 2200 cm^{-1} (C≡C); HRMS (ESI-TOF): *m*/*z* calcd for $C_{28}H_{24}BrN_2O_2$: 499.0943 $[M+H]^+$; found: 499.1035.

Data for compound 52: ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 0.89$–1.10 (m, 8H; *c*Pr), 1.85–2.05 (m, 2H; *c*Pr), 7.55 (d, $J = 1.6$ Hz, 2H; Ar), 7.62 ppm (t, $J = 1.6$ Hz, 1H; Ar); HRMS (ESI-TOF): *m*/*z* calcd for $C_{17}H_{14}Br_2NO$: 407.9422 $[M]^+$; found: 407.9448.

Scanning tunneling microscopy: STM imaging was carried out at RT at the interface between freshly cleaved HOPG substrate and a saturated solution in 1-phenyloctane (Aldrich)[35] by employing a home-made set-up at a scan speed between 10 and 50 lines/s. After visualization of the HOPG lattice, a drop of the saturated solution was applied to the basal plane of HOPG. The STM images were corrected with respect to the hexagonal HOPG lattice underneath by exploiting SPIP software.[36] In this way, the unit cell of the crystalline adsorbate could be determined with a high degree of precision.

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