A Domino Copper-Catalyzed C–N and C–O Cross-Coupling for the Conversion of Primary Amides into Oxazoles

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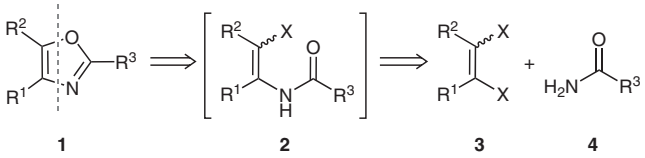
Dedicated to Professor Paul A. Wender on the occasion of this 60th birthday

Abstract: A variety of oxazoles can efficiently be prepared, in a single step and in good yield, from primary amides and 1,2-dihaloalkenes using copper-catalysis. This new method allows the regioselective formation of a range of substituted oxazoles. The required 1,2-dihaloalkenes can prepared by simple treatment of alkynes with elemental bromine or iodine.

Key words: oxazoles, C–N and C–O cross-coupling, copper, cyclization, domino reaction, heterocycles

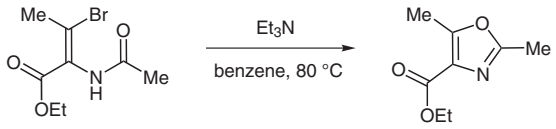
The oxazole ring is an important structural motif present in a vast number of natural and unnatural compounds.[1,2] Many different methods for the synthesis of this moiety have been developed, amongst which, cyclocondensation methods such as the Robinson–Gabriel cyclocondensation of α-acylamino ketones are the most popular. However, in many cases, rather harsh conditions for dehydration are required and, therefore, there is a constant need for additional methods for the synthesis of more sensitive oxazoles. Herein, we report an efficient copper-catalyzed formation of oxazoles from 1,2-dihaloalkenes and primary amides, based on cross-coupling reactions.

We aimed for a novel, one-pot synthesis of oxazoles **1**. Based on our experience with cross-coupling reactions, we planned to build up the oxazole ring with two successive C–N/C–O bond formations from an alkene component **3** and a primary carboxylic acid amide **4** (Scheme 1); ideally both steps being catalyzed by the same transition-metal catalyst. A related strategy has been successfully used by us[3a] and others[3b] in the synthesis of benzoxazoles from *ortho*-dihalobenzenes, thus complementing the traditional synthetic approaches to benzoxazoles. The copper-catalyzed amidation of aryl halides, developed by Buchwald et al., represents a powerful transformation and has found widespread applications.[4] Furthermore, the use of alkenyl halides as substrate was also reported.[4c,d] Consequently, our retrosynthetic analysis comprised of the copper-catalyzed formation and cyclization an halide-substituted enamide **2** (Scheme 1) and, ideally, two successive C–N/C–O bond formations incorporated in a domino process.



Scheme 1 Oxazole synthesis by successive C–N/C–O bond formations

The cyclization of halogen-substituted enamides has been previously employed in the synthesis of oxazoles. However, only activated substrates, namely those with the double bond being part of α,β-unsaturated carbonyl compounds, in which the addition of the amide carbonyl group can occur in a 1,4-fashion were suitable (Scheme 2).[5] We envisaged a related transformation of non-activated substrates by means of copper-catalyzed cross-coupling reactions.



Scheme 2 Uncatalyzed cyclization of activated enamides leading to the formation of oxazoles

1,2-Dihalogenated olefins **3** are the key synthetic intermediates of this new oxazole synthesis. Fortunately, these olefins can easily be prepared by the reaction of terminal or internal alkynes with bromine or iodine in dichloromethane at ambient temperature, resulting in 1,2-dihalogenated olefins in good yields (Table 1).[6] The stereochemistry of the products obtained were determined by comparison of the NMR data with literature values. In many cases, the *E*-product was formed predominantly, with the two iodinated olefins **3b** and **3d** being exclusively *E*-configured. In contrast, silylated olefin **3e** was obtained nearly exclusively as the *Z*-isomer (entry 6).

As a starting point for our investigation, 1,2-dibromophenylethylene (**3a**) was reacted with benzamide under copper catalysis. Copper(I) iodide, *N*,*N*′-dimethylethylenediamine (DMEDA), potassium carbonate, toluene and heating (110 °C), conditions previously employed in the synthesis of benzoxazoles by us,[3a] were found to be optimal.[7] It is important to note that it was beneficial to degas the solvent in order to avoid butadiyne products resulting from oxidative coupling. The highest yields were obtained

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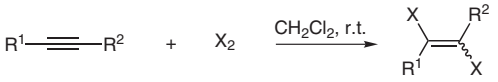
Table 1 Synthesis of 1,2-Dihalogenated Olefins



3

Entry	R^1	R^2	X	Olefin	*E*/*Z*[a]	Yield (%)[b]
1	Ph	H	Br	**3a**	63:37	88
2	Ph	H	I	**3b**	100:0	65
3	*n*-Hex	H	Br	**3c**	77:23	84
4	*n*-Hex	H	I	**3d**	100:0	91
5	Ph	$SiMe_3$	Br	**3e**	1:99	69
6	Ph	Ph	Br	**3f**	17:83	76
7	CO_2Me	CO_2Me	Br	**3g**	61:39	87
8	CH_2OH	H	Br	**3h**	44:56	72

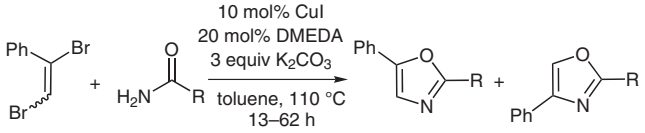
[a] Determinded by GC-MS.
[b] Isolated yield.

when 10 mol% of the copper catalyst were employed. Under these conditions, an 11:1 ratio of regioisomeric 2,5- and 2,4-diphenyloxazole was obtained in 70% yield (Table 2, entry 1). Using the diiodo- instead of the dibromo-substituted phenylethylene resulted in an equimolar mixture of the two regioisomeric products (entry 2).

A variety of different primary amides was reacted with 1,2-dibromophenylethylene (**3a**) under the same conditions (Table 2). With substituted aromatic amides, comparably good results were obtained (entries 3–5). Aliphatic amides reacted as well, although with somewhat lower yields (entries 6–12). In these cases, part of the reduced yield was due to the formation of diamidation side-products.

Again, using 1,2-diiodophenylethylene (**3b**) instead of the dibromo derivative **3a** (entry 7) led to a change in the ratio of regioisomeric products (entry 8). In the latter case, the temperature was gradually increased from 40 °C to 110 °C. Investigation by means of GC-MS revealed that the enamide corresponding to the 2,4-disubstituted oxazole was formed at 40 °C already, whereas the enamide of the 2,5-disubstituted oxazole needed increased temperatures and formed at 80 °C. In addition, the former enamide cyclized at a temperature of 80 °C, whereas the latter enamide cyclization required heating at 110 °C. This observation of enamide intermediates by GC-MS en route to the cyclization products was not observed in the case of benzoxazoles.[5a] Discontinuation of this reaction after 21 hours (instead of 45 h for complete conversion), allowed the isolation of 22% of the enamide intermediate product. This intermediate cyclized smoothly under standard conditions resulting in the desired product in 93% yield (Scheme 3). Interestingly, the reaction of acrylamide with 1,2-diiodo-1,2-diphenylethylene resulted in

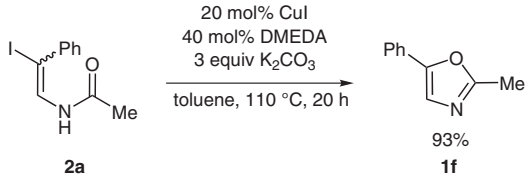
Table 2 Reaction of Primary Amides with 1,2-Dibromophenylethylene (**3a**)



3a **4** **1**

Entry	R	Product ratio[a,b]	Oxazole	Yield (%)[a,c]
1	Ph	11:1	**1a**	70
2	Ph	(1:1)	**1a**	(55)
3	4-$MeOC_6H_4$	6:1[d]	**1b**	72
4	CH=CHPh	6:1[d]	**1c**	71
5	4-BrC_6H_4	5:1[d]	**1d**	54
6[e]	H	10:1	**1e**	32
7[e]	Me	10:1	**1f**	48
8[f]	Me	(1:1)	**1f**	(34)
9[e]	*n*-Pr	8:1	**1g**	47
10	*t*-Bu	6:1[d]	**1h**	65
11[e]	$CH=CH_2$	10:1	**1i**	28
12	$CH=CH_2$	(1:4)	**1i**	(17)

[a] The results obtained with 1,2-diiodophenylethene (**3b**) are shown in brackets.
[b] Ratio of 2,5- to 2,4-oxazole determined by GC-MS.
[c] Isolated combined yield.
[d] Ratio of isolated isomers.
[e] CuI (20 mol%) and DMEDA (40 mol%) were used.
[f] Temperature was gradually increased from 40 °C to 110 °C.



Scheme 3 Cyclization of an intermediate enamide

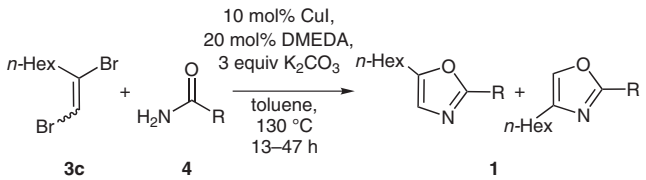
the predominant formation of the 2,4-disubstituted oxazole (entry 12).

Using dibromoalkenes as starting materials, a strong preference for the formation of the 2,5-disubstituted oxazoles was observed, whereas with diiodoalkenes greatly diminished selectivities were obtained. In the former case, the amide attacks the less sterically hindered position of the alkene. The more reactive diiodo-substituted olefins, however, react rather unselectively at both of the two alkene positions.

Intriguingly, *E*-, *Z*- or mixtures of *E*- and *Z*-configured dihalogenated olefins all reacted to form the desired oxazole products. In some cases, an isomerization of *E*- and *Z*-configured substrates was observed under the reaction conditions. However, no indication of isomerization of the *E*-configured diiodinated olefins was observed.[8] Thus, an isomerization prior to enamide formation does not seem to be a prerequisite for oxazole formation.

Dibromooctene (**3c**) has a much lower propensity to undergo oxidative homo-coupling. In addition, it is less reactive than the 1,2-dibromophenylethylene (**3a**) and therefore higher reaction temperatures (130 °C) were required for the enamide to cyclize (Table 3). Again, the formation of 2,5-disubstituted oxazoles was favored (entry 1). Use of the diiodo-substituted substrate still resulted in the predominant formation of the 2,5-disubstituted oxazole (entry 2).

Table 3 Reaction of Primary Amides with Dibromooctene (**3c**)



Entry	R	Product ratio[a,b]	Oxazole	Yield (%)[a,c]
1	Ph	8:1	**1j**	68
2	Ph	(3:1)	**1j**	(42)
3	4-$H_2NC_6H_4$	14:1	**1k**	50
4	*t*-Bu	9:1	**1l**	30

[a] Results obtained with 1,2-diiodo-*n*-hexylethene (**3d**) are shown in brackets.
[b] 2,5- to 2,4-Oxazole ratio determined by GC-MS.
[c] Isolated combined yield.

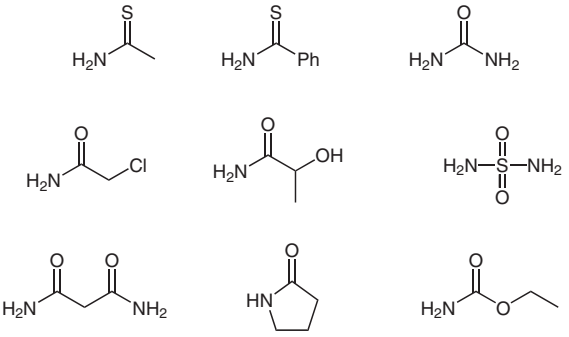
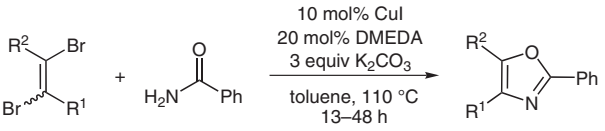


Figure 1 Amides and amide substitutes that did not lead to the desired products

A number of amides and amide derivatives, as well as 1,2-dihalogenated olefins did not provide oxazoles under these conditions (Figure 1); however, 1,2-dibrominated tetrasubstituted alkenes did undergo this transformation (Table 4). Since methods for the regioselective formation of 2,4,5-trisubstituted oxazoles are especially desirable, it was pleasing to find that 1,2-dibromo-1-trimethylsilyl-2-phenylethylene (**3e**) reacted highly regioselectively to give one oxazole only (entry 1); the other regioisomer could not be detected. Acid mediated cleavage of the trimethylsilyl group of this oxazole product (*p*-TsOH, MeOH, r.t.) allowed for the selective formation of 2,4-diphenyl oxazole in 91% yield. This route is complementary to the results reported in Table 2 and Table 3, since it provides ready access to the isomer previously formed as the minor isomer. 1,2-Dibromo-1,2-diphenylethylene can also react with benzamide to form the desired oxazole product, albeit with reduced yield (entry 2). Presumably, this is due to a reversal of the formation of the olefin substrate back to tolane and bromine. Hydroxy-substituted olefin **3h** did not provide any product.

In summary, we have developed a new copper-catalyzed method for the regioselective, single-step preparation of 2,5-disubstituted oxazoles from readily available 1,2-dihalogenated olefins and primary amides. Many functional groups such as halides, amino-, methoxy- and silyl groups

Table 4 Reaction of Benzamide with 1,2-Dibrominated Tetrasubstituted Alkenes



Entry	R^1	R^2	Oxazole	Yield (%)[a]
1	Ph	$SiMe_3$	**1m**	56
2	Ph	Ph	**1n**	24
3[b]	CO_2Me	CO_2Me	**1o**	12

[a] Isolated yield.
[b] K_3PO_4 (3 equiv) was used as base.

were tolerated. In addition, use of a silylated olefin allowed the selective preparation of 2,4-disubstituted oxazoles after acid mediated protodesilylation. The required dihalogenated olefins were easily prepared in high yields from the corresponding alkynes by treatment with bromine or iodine.

Chemicals were purchased in commercially available qualities (puriss., p.a. or purum) from Fluka, Aldrich, Acros, Lancaster and Merck and were used without further purification. Solvents toluene and CH_2Cl_2 were of technical quality and were distilled and dried over CaH_2. Solvents for extractions and column chromatography were of technical quality and were distilled prior to use. Molecular sieves (4 Å) were activated by microwave irradiation (3 × 3 min). For flash chromatography, Merck silica gel 60 (230–400 mesh) was used. NMR spectra were recorded on an ARX 300 or DRX 400 spectrometer (Bruker) in $CDCl_3$; chemical shifts (δ) are given in ppm relative to TMS, and coupling constants (*J*) are given in Hertz. For IR, a Bruker IFS 88 was used, with wavenumbers given in cm^{-1}. For MS (EI, 70 eV), a Varian CH7 was used and for HRMS, a Finnigan LTQ FT or TSQ 700 was used.

Synthesis of Oxazoles; General Procedure

K_2CO_3, CuI and amide were weighed into a vial under air. The vial was evacuated and filled with argon, followed by the addition of dihalogenated olefin, toluene (3 mL) and *N*,*N*′-dimethylethylenediamine (DMEDA). The vial was closed and the reaction mixture stirred at 110 °C for the given reaction time. After cooling to r.t., the reaction mixture was poured into aq NH_4OH (25%, 10 mL), extracted with EtOAc (3 × 20 mL), dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the products were purified by flash chromatography.

2,4-Diphenyloxazole and 2,5-Diphenyloxazole (1a)

Synthesis with dibromophenylethylene: The general procedure described above (reaction time: 13 h) was followed using 1,2-dibromophenylethylene (**3a**; 261 mg, 1.00 mmol, 1.00 equiv), benzamide (182 mg, 1.49 mmol, 1.49 equiv), K_2CO_3 (414 mg, 2.99 mmol, 2.99 equiv), CuI (19.8 mg, 0.10 mmol, 0.10 equiv) and DMEDA (23 μL, 0.21 mmol, 0.21 equiv). The products were obtained after purification by flash chromatography (pentane–EtOAc, 30:1) on Et_3N-impregnated silica to give 2,5-**1a** (137 mg, 62%) and 2,4-**1a** (17 mg, 8%) in a 11:1 ratio (GC-MS).

Synthesis with (E)-diiodophenylethylene: The general procedure described above (reaction time: 13 h) was followed using diiodophenylethylene (**3b**; 357 mg, 1.00 mmol, 1.00 equiv), benzamide (184 mg, 1.51 mmol, 1.51 equiv), K_2CO_3 (415 mg, 3.00 equiv, 3.00 mmol), CuI (19.1 mg, 0.10 mmol, 0.10 equiv) and DMEDA (22 μL, 0.20 mmol, 0.2 equiv). In contrast to the general procedure, the olefin was weighed into the vial together with the other solids. The products were obtained after purification by flash chromatography (pentane–EtOAc, 15:1) to give 2,5-**1a** and 2,4-**1a** in a 1:1 ratio (GC-MS).

2,5-Diphenyloxazole

Yield: 41 mg, 19%; pale-yellow solid; R_f = 0.19 (pentane–EtOAc, 15:1).

IR (KBr): 3059 (w), 1609 (w), 1567 (w), 1542 (w), 1481 (m), 1447 (m), 1348 (w), 1153 (w), 1132 (m), 1069 (w), 1057 (w), 1026 (w), 952 (w), 907 (w), 822 (w), 775 (m), 760 (m), 707 (s), 685 (s), 479 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.14–8.11 (m, 2 H, $HC_{Ar,2\text{-}Ph}$), 7.73–7.71 (m, 2 H, $HC_{Ar,5\text{-}Ph}$), 7.49–7.42 (m, 6 H, HC_{Ar}, HCN), 7.36 (t, *J* = 7.5 Hz, 1 H, $HC_{Ar,5\text{-}Ph}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.1 (OC=N), 151.2 (O*C*=C), 130.2 (HC_{Ar}), 128.8 (2 × HC_{Ar}), 128.7 (2 × HC_{Ar}), 128.3 (HC_{Ar}), 128.0 (C_q), 127.4 (C_q), 126.2 (2 × HC_{Ar}), 124.1 (2 × HC_{Ar}), 123.4 (HC_{Ar}).

MS (EI): *m*/*z* (%) = 221 (100) $[M]^+$, 193 (11), 165 (52), 116 (21), 89 (58), 77 (87), 63 (55), 39 (44), 28 (10).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}NO$: 221.0841; found: 221.0835.

2,4-Diphenyloxazole

Yield: 80 mg (36%); pale-yellow solid; R_f = 0.34 (pentane–EtOAc, 15:1).

IR (KBr): 2962 (w), 1670 (w), 1607 (w), 1586 (w), 1553 (s), 1488 (s), 1446 (s), 1339 (m), 1290 (w), 1262 (m), 1157 (w), 1123 (m), 1069 (s), 1022 (m), 929 (m), 782 (m), 755 (s), 718 (s), 705 (w), 691 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15–8.11 (m, 2 H, $HC_{Ar,2\text{-}Ph}$), 7.98 (s, 1 H, HCO), 7.85–7.82 (m, 2 H, $HC_{Ar,4\text{-}Ph}$), 7.51–7.41 (m, 5 H, HC_{Ar}), 7.34 (tt, *J* = 7.5, 1.2 Hz, 1 H, $HC_{Ar,4\text{-}Ph}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0 (OCH=N), 151.2 (C_q, OC=C), 133.4, 131.2, 130.4, 128.7, 128.1, 127.5, 126.5, 125.7 (all C_{Ar}).

MS (EI): *m*/*z* (%) = 221 (56) $[M]^+$, 193 (52), 165 (9), 105 (23), 89 (100), 77 (19), 63 (26), 51 (17), 39 (17), 28 (28).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}NO$: 221.0841; found: 221.0840.

2-(4-Methoxyphenyl)-4-phenyloxazole and 2-(4-Methoxyphenyl)-5-Phenyloxazole (1b)

The general procedure described above (reaction time: 24 h) was followed using dibromophenylethylene (**3a**; 259 mg, 0.99 mmol, 1.00 equiv), 4-methoxybenzamide (165 mg, 1.09 mmol, 1.10 equiv), K_2CO_3 (411 mg, 2.97 mmol, 3.00 equiv), CuI (18.8 mg, 0.10 mmol, 0.10 equiv) and DMEDA (21.5 μL, 0.20 mmol, 0.20 equiv). The products were obtained after purification by flash chromatography (pentane–EtOAc, 10:1) on Et_3N-impregnated silica to give 2,4-**1b** and 2,5-**1b** in a 1:21 ratio (GC-MS).

2-(4-Methoxyphenyl)-5-phenyloxazole

Yield: 153 mg (62%); pale-yellow solid; R_f = 0.16 (pentane–EtOAc, 10:1).

IR (KBr): 2968 (w), 2840 (w), 1610 (s), 1589 (w), 1469 (s), 1460 (w), 1442 (w), 1418 (w), 1350 (m), 1301 (m), 1251 (s), 1173 (m), 1154 (w), 1134 (w), 1107 (w), 1024 (s), 828 (m), 762 (m), 736 (m), 687 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06–8.03 (m, 2 H, $HC_{Ar,2\text{-}Ph}$), 7.71–7.68 (m, 2 H, HC_{Ar}), 7.45–7.40 (m, 3 H, HC_{Ar}, HCN), 7.31 (tt, *J* = 7.5, 1.6 Hz, 1 H, $HC_{Ar,5\text{-}Ph}$), 7.00–6.97 (m, 2 H, HC_{Ar}), 3.85 (s, 3 H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.3 (C_q), 161.2 (C_q), 150.6 (C_q), 128.8 (C_{Ar}), 128.1 (2 × C_{Ar}), 127.9 (C_{Ar}), 124.0 (C_{Ar}), 123.2 (C_{Ar}), 120.2 (C_q), 114.2 (C_{Ar}), 55.3 (OCH_3).

MS (EI): *m*/*z* (%) = 251 (100) $[M]^+$, 236 (5), 181 (5), 77 (6), 28 (27).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{14}NO_2$: 252.1019; found: 252.1016.

2-(4-Methoxyphenyl)-4-phenyloxazole

Yield: 26 mg (10%); pale-yellow solid; R_f = 0.40 (pentane–EtOAc, 10:1).

IR (KBr): 3446 (w), 2926 (w), 1699 (m), 1605 (s), 1501 (m), 1467 (m), 1412 (w), 1256 (s), 1173 (s), 1112 (m), 1076 (w), 1028 (m), 942 (w), 931 (w), 841 (m), 756 (s), 740 (m), 711 (w), 694 (m), 951 (w) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08–8.05 (m, 2 H, $HC_{Ar,2\text{-}Ph}$), 7.92 (s, 1 H, HCO) 7.83–7.81 (m, 2 H, HC_{Ar}), 7.45–7.39 (m, 2 H, HC_{Ar}), 7.33 (tt, *J* = 7.4, 1.2 Hz, 1 H, $HC_{Ar,5\text{-}Ph}$), 7.01–6.99 (m, 2 H, HC_{Ar}), 3.88 (s, 3 H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0 (C_q), 161.4 (C_q), 141.8 (C_q), 132.9 (C_{Ar}), 131.3 (C_{Ar}), 128.7 (C_{Ar}), 128.2 (C_{Ar}), 128.0 (C_{Ar}), 125.6 (C_q), 120.4 (C_{Ar}), 114.2 (C_{Ar}), 55.4 (OCH_3).

MS (EI): *m*/*z* (%) = 251 (100) [M$^+$], 223 (18), 208 (19), 152 (7), 135 (20), 120 (13), 105 (16), 90 (15), 77 (15), 51 (9), 28 (53).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}NO_2$: 251.0947; found: 251.0945.

2-Styryl-4-phenyloxazole and 2-Styryl-5-phenyloxazole (1c)

The general procedure described above (reaction time: 14 h) was followed using dibromophenylethylene (**3a**; 260 mg, 0.99 mmol, 1.00 equiv), cinnamide (220 mg, 1.49 mmol, 1.50 equiv), K_2CO_3 (415 mg, 3.00 mmol, 3.03 equiv), CuI (18.8 mg, 0.10 mmol, 0.10 equiv) and DMEDA (22 μL, 0.20 mmol, 0.20 equiv). The products were obtained after purification by flash chromatography (pentane–EtOAc, 30:1→10:1) to give 2,4-**1c** and 2,5-**1c** in a 1:20 ratio (GC-MS).

2-Styryl-5-phenyloxazole

Yield: 150 mg (61%); pale-yellow solid; R_f = 0.18 (pentane–EtOAc, 10:1).

IR (KBr): 3444 (br s), 3099 (w), 3053 (w), 2924 (w), 1644 (w), 1534 (w), 1484 (w), 1447 (m), 1342 (m), 1279 (w), 1261 (w), 1235 (w), 1109 (w), 1069 (m), 1024 (m), 965 (m), 943 (m), 751 (s), 691 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73–7.70 (m, 2 H, HC_{Ar}), 7.61–7.55 (m, 3 H, HC_{Ar}, HC_{vin}), 7.47–7.32 (m, 7 H, HC_{Ar}, HCN), 7.00 (d, *J* = 16.2 Hz, 1 H, HC_{vin}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.1 (OC=N), 150.9 (O*C*=C), 135.8, 135.6, 129.1, 128.9, 128.9, 128.4, 127.9, 127.2, 124.2, 123.7, 113.9 (C_{vin}).

MS (EI): *m*/*z* (%) = 246 (100) [M$^+$], 115 (23), 77 (18), 28 (59).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{12}NO$: 246.0919; found: 246.0920.

2-Styryl-4-phenyloxazole

Yield: 25 mg (10%); pale-yellow solid; R_f = 0.17 (pentane–EtOAc, 30:1).

IR (KBr): 3051 (w), 1659 (w), 1635 (w), 1605 (w), 1520 (s), 1479 (m), 1445 (m), 1357 (w), 1286 (w), 1161 (w), 1132 (w), 1074 (w), 1062 (w), 972 (s), 941 (m), 909 (w), 830 (m), 754 (s), 688 (s), 501 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90 (s, 1 H, HCO), 7.80–7.77 (m, 2 H, HC_{Ar}), 7.61–7.55 (m, 3 H, HC_{Ar}, HC_{vin}), 7.46–7.32 (m, 6 H, HC_{Ar}), 7.02 (d, *J* = 16.2 Hz, 1 H, HC_{vin}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.8 (OC=N), 142.1 (C_{vin}), 136.5 (O*C*H=C), 135.5, 133.1, 131.0, 129.2, 128.9, 128.8, 128.2, 127.2, 125.6 (all C_{Ar}), 113.9 (C_{vin}).

MS (EI): *m*/*z* (%) = 246 (49) [M$^+$], 218 (9), 115 (100), 104 (20), 89 (47), 77 (11), 63 (17), 51 (10), 39 (12).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{12}NO$: 246.0919; found: 246.0917.

2-(4-Bromophenyl)-4-phenyloxazole and 2-(4-Bromophenyl)-5-phenyloxazole (1d)

The general procedure described above (reaction time: 40 h) was followed using dibromophenylethylene (262 mg, 1.00 mmol, 1.00 equiv), 4-bromobenzamide (221 mg, 1.10 mmol, 1.10 equiv), CuI (19.5 mg, 0.10 mmol, 0.10 equiv), K_2CO_3 (414 mg, 3.00 mmol, 3.00 equiv) and DMEDA (22 μL, 0.20 mmol, 0.20 equiv). The products were obtained after purification by flash chromatography (pentane–EtOAc, 30:1→20:1) to give 2,4-**1d** and 2,5-**1d** in a 1:14 ratio (GC-MS).

2-(4-Bromophenyl)-5-phenyloxazole

Yield: 135 mg (45%); orange solid; R_f = 0.13 (pentane–EtOAc, 20:1).

IR (KBr): 1667 (w), 1598 (m), 1539 (w), 1473 (s), 1447 (m), 1398 (m), 1278 (w), 1135 (m), 1110 (w), 1073 (m), 1056 (w), 1007 (m), 950 (s), 932 (w), 914 (w), 828 (s), 763 (s), 729 (s), 692 (s), 489 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98–7.94 (m, 2 H, $HC_{Ar,2\text{-}Ph}$), 7.72–7.69 (m, 2 H, $HC_{Ar,5\text{-}Ph}$), 7.63–7.60 (m, 2 H, $HC_{Ar,2\text{-}Ph}$), 7.47–7.42 (m, 3 H, HCN, $HC_{Ar,5\text{-}Ph}$), 7.35 (tt, *J* = 7.4, 1.2 Hz, 1 H, $HC_{Ar,5\text{-}Ph}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.2 (OC=N), 161.2 (C_q), 151.5 (O*C*=C), 132.1 (2 × $C_{Ar,2\text{-}Ph}$), 128.9 (2 × $C_{Ar,5\text{-}Ph}$), 128.6 ($C_{Ar,5\text{-}Ph}$), 127.8 ($C_{Ar,5\text{-}Ph}$), 127.7 (2 × $C_{Ar,2\text{-}Ph}$), 126.3 ($C_{q,Ar\text{-}2\text{-}Ph}$), 124.7 (CBr), 124.2 (2 × $C_{Ar,5\text{-}Ph}$), 123.5 (HCN).

MS (EI): *m*/*z* (%) = 301 (18) [M$^+$], 299 (18) [M$^+$], 192 (5), 165 (62), 105 (19), 89 (35), 77 (100), 62 (30), 50 (32), 39 (14), 28 (14).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{10}NOBr$: 298.9946; found: 298.9947.

2-(4-Bromophenyl)-4-phenyloxazole

Yield: 26 mg (9%); colorless solid; R_f = 0.23 (pentane–EtOAc, 30:1).

IR (KBr): 2924 (w), 1719 (w), 1601 (m), 1475 (s), 1446 (m), 1399 (m), 1263 (m), 1232 (w), 1122 (w), 1075 (s), 1009 (m), 943 (w), 932 (m), 914 (w), 833 (s), 762 (s), 736 (s), 694 (s), 657 (w), 540 (w) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.97 (m, 3 H, $HC_{Ar,2\text{-}Ph}$, HCO), 8.84–8.01 (m, 2 H, $HC_{Ar,4\text{-}Ph}$), 7.63–7.60 (m, 2 H, $HC_{Ar,2\text{-}Ph}$), 7.46–7.41 (m, 2 H, $HC_{Ar,4\text{-}Ph}$), 7.34 (m, 1 H, $HC_{Ar,4\text{-}Ph}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.1 (OC=N), 142.2 (C_q), 133.6 (C_q, O*C*=C), 132.0, 128.8, 128.2, 128.0, 126.4, 124.7, 125.6, 124.9.

MS (EI): *m*/*z* (%) = 301 (54) [M$^+$], 299 (54) [M$^+$], 271 (14), 192 (60), 165 (18), 105 (13), 89 (100), 77 (9), 63 (24), 51 (9), 39 (10), 28 (70).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{10}NOBr$: 298.9946; found: 298.9958.

5-Phenyloxazole (1e)

The general procedure described above (reaction time: 13 h) was followed using dibromophenylethylene (**3a**; 263 mg, 1.00 mmol, 1.00 equiv), formamide (60 μL, 1.51 mmol, 1.51 equiv), K_2CO_3 (415 mg, 3.00 mmol, 3.00 equiv), CuI (38.9 mg, 0.20 mmol, 0.20 equiv) and DMEDA (44 μL, 0.40 mmol, 0.40 equiv). In contrast to the general procedure, formamide was added after the addition of toluene. The product was obtained after purification by flash chromatography (pentane–EtOAc, 10:1). 4-Phenyloxazole was not isolated. 2,4-**1e** and 2,5-**1e** were obtained as a mixture in a ratio of 1:10 (GC-MS).

Yield: 47 mg (32%); pale-yellow oil; R_f = 0.18 (pentane–EtOAc, 10:1).

IR (KBr): 3131 (w), 3062 (w), 2926 (w), 1703 (s), 1600 (w), 1506 (m), 1485 (m), 1449 (m), 1315 (w), 1273 (m), 1177 (w), 1105 (m), 1023 (w), 942 (m), 916 (w), 824 (w), 763 (s), 714 (m), 692 (s), 641 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (s, 1 H, OCH=N), 7.67–7.64 (m, 2 H, HC_{Ar}), 7.46–7.32 (m, 4 H, HC_{Ar}, C=HCN).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.7 (OHC=N), 150.5 (O*C*=C), 128.9 (2 × HC_{Ar}), 128.6 (HC_{Ar}), 127.8 ($C_{q,Ar}$), 124.4 (2 × HC_{Ar}), 121.5 (C=*C*HN).

MS (EI): *m*/*z* (%) = 145 (5) [M$^+$], 117 (5), 90 (5), 77 (5), 32 (21), 28 (100).

HRMS (EI): *m*/*z* calcd for C_9H_7NO: 145.0528; found: 145.0531.

2-Methyl-4-phenyloxazole and 2-Methyl-5-phenyloxazole (1f)

Synthesis with dibromophenylethylene: The general procedure described above (reaction time: 24 h) was followed using dibromophenylethylene (**3a**; 278 mg, 1.06 mmol, 1.00 equiv), acetamide (75.4 mg, 1.28 mmol, 1.21 equiv), K_2CO_3 (440 mg, 3.19 mmol, 3.01 equiv), CuI (41.6 mg, 0.22 mmol, 0.21 equiv) and DMEDA (48 μL, 0.44 mmol, 0.42 equiv). Purification by flash chromatography (pentane–EtOAc, 10:1) gave 2,4-**1f** and 2,5-**1f** in a 1:10 ratio (GC-MS). 2-Methyl-5-phenyloxazole (81 mg, 48%) was obtained as a colorless solid. 2-Methyl-4-phenyloxazole was not isolated.

Synthesis with diiodophenylethylene: The general procedure described above (reaction time: 45 h) was followed using diiodophenylethylene (**3a**; 357 mg, 1.00 mmol, 1.00 equiv), acetamide (66.1 mg, 1.12 mmol, 1.12 equiv), K_2CO_3 (415 mg, 3.01 mmol, 3.01 equiv), CuI (38.6 mg, 0.20 mmol, 0.20 equiv) and DMEDA (44 μL, 0.40 mmol, 0.40 equiv). In contrast to the general procedure, the olefin was weighed into the vial together with the other solids. The products 2,4-**1f** and 2,5-**1f** were obtained after purification by flash chromatography (pentane–EtOAc, 30:1) in a ratio of 1:1 (GC-MS).

2-Methyl-5-phenyloxazole

Yield: 33 mg (21%); pale-yellow solid; R_f = 0.12 (pentane–EtOAc, 10:1).

IR (KBr): 3120 (w), 3061 (w), 2926 (m), 2854 (w), 1689 (s), 1578 (m), 1560 (s), 1486 (m), 1451 (s), 1372 (w), 1337 (w), 1278 (m), 1217 (m), 1132 (m), 1061 (m), 942 (m), 765 (s), 694 (s), 674 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62–7.68 (m, 2 H, HC_{Ar}), 7.42–7.37 (m, 2 H, HC_{Ar}), 7.32–7.27 (m, 1 H, HC_{Ar}), 7.20 (s, 1 H, HCO), 2.52 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.0 (OC=N), 151.1 (O*C*=C), 128.8 (2 × HC_{Ar}), 128.1 ($C_{q,Ar}$), 128.1 (HC_{Ar}), 123.9 (2 × HC_{Ar}), 121.8 (HCN), 14.0 (CH_3).

MS (EI): *m*/*z* (%) = 159 (100) [M$^+$], 130 (25), 104 (49), 90 (17), 77 (24), 54 (8), 51 (16), 27 (7).

HRMS (EI): *m*/*z* calcd for $C_{10}H_9NO$: 159.0684; found: 159.0685.

2-Methyl-4-phenyloxazole

Yield: 21 mg (13%); pale-yellow solid; R_f = 0.28 (pentane–EtOAc, 10:1).

IR (KBr): 3059 (w), 1609 (w), 1587 (m), 1481 (s), 1445 (s), 1348 (m), 1153 (m), 1132 (s), 1100 (w), 1069 (m), 1058 (m), 1026 (m), 952 (m), 822 (m), 775 (m), 760 (s), 707 (s), 685 (s), 479 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81 (s, 1 H, HCO), 7.72–7.69 (m, 2 H, HC_{Ar}), 7.42–7.37 (m, 2 H, HC_{Ar}), 7.30 (tt, *J* = 7.4, 1.4 Hz, 1 H, HC_{Ar}), 2.52 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.9 (OC=N), 140.7 (C=*C*N), 133.1 (HCO), 131.2 ($C_{q,Ar}$), 128.7 (2 × HC_{Ar}), 127.9 (HC_{Ar}), 125.4 (2 × HC_{Ar}), 13.9 (CH_3).

MS (EI): *m*/*z* (%) = 159 (94) [M$^+$], 130 (32), 103 (14), 90 (84), 77 (23), 63 (15), 51 (17), 43 (9), 39 (17), 32 (11), 28 (100).

HRMS (EI): *m*/*z* calcd for $C_{10}H_9NO$: 159.0684; found: 159.0696.

2-Propyl-4-phenyloxazole and 2-Propyl-5-phenyloxazole (1g)

The general procedure described above (reaction time: 24 h) was followed using dibromophenylethylene (**3a**; 263 mg, 1.00 mmol, 1.00 equiv), butyramide (96.6 mg, 1.11 mmol, 1.11 equiv), K_2CO_3 (418 mg, 3.03 mmol, 3.03 equiv), CuI (38.3 mg, 0.20 mmol, 0.20 equiv) and DMEDA (44 μL, 0.40 mmol, 0.40 equiv). Purification by flash chromatography (pentane–EtOAc, 30:1→10:1) gave 2,4-**1g** and 2,5-**1g** in a ratio of 1:8 (GC-MS).

2-Propyl-5-phenyloxazole

Yield: 74.2 mg (40%); colorless oil; R_f = 0.21 (pentane–EtOAc, 10:1).

IR (film): 3061 (w), 2965 (s), 2934 (m), 2874 (w), 1697 (s), 1578 (w), 1557 (s), 1489 (m), 1449 (m), 1382 (w), 1274 (w), 1198 (w), 1134 (m), 1083 (m), 1054 (w), 1026 (w), 967 (w), 942 (w), 762 (s), 692 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62–7.59 (m, 2 H, HC_{Ar}), 7.42–7.37 (m, 2 H, HC_{Ar}), 7.31–7.26 (m, 1 H, HC_{Ar}), 7.22 (s, 1 H, HCN), 2.80 (t, *J* = 7.4 Hz, 2 H, CH_2CH_2CH_3), 1.85 (sext, *J* = 7.4 Hz, 2 H, CH_2CH_2CH_3), 1.03 (t, *J* = 7.4 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.5 (OC=N), 151.0 (O*C*=C), 128.8 (2 × H*C*$_{Ar}$), 128.2 ($C_{q,Ar}$), 128.0 (HC_{Ar}), 123.9 (2 × HC_{Ar}), 121.7 (HCN), 30.1 (*C*H_2CH_2CH_3), 20.5 (CH_2*C*H_2CH_3), 12.6 (CH_3).

MS (EI): *m*/*z* (%) = 187 (37) [M$^+$], 172 (10), 159 (100), 103 (77), 89 (9), 77 (45), 51 (8), 32 (16), 28 (100).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{13}NO$: 187.0991; found: 187.0994.

2-Propyl-4-phenyloxazole

Yield: 13 mg (7%); colorless oil; R_f = 0.44 (pentane–EtOAc, 10:1).

IR (film): 3100 (w), 2923 (w), 1717 (w), 1644 (w), 1577 (w), 1534 (w), 1484 (w), 1447 (m), 1342 (m), 1261 (w), 1235 (w), 1109 (w), 1069 (m), 1024 (w), 965 (m), 943 (m), 912 (w), 751 (s), 690 (s), 525 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.82 (s, 1 H, HCO), 7.73–7.71 (m, 2 H, HC_{Ar}), 7.42–7.37 (m, 2 H, HC_{Ar}), 7.32–7.26 (m, 1 H, HC_{Ar}), 2.80 (t, *J* = 7.5 Hz, CH_2CH_2CH_3), 1.84 (sext, *J* = 7.5 Hz, CH_2CH_2CH_3), 1.02 (t, *J* = 7.4 Hz, CH_2CH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3 (OC=N), 140.5 (C=*C*N), 133.0 (HCO), 131.3 ($C_{q,Ar}$), 128.7 (2 × HC_{Ar}), 127.8 (HC_{Ar}), 125.5 (2 × HC_{Ar}), 30.2 (*C*H_2CH_2CH_3), 20.6 (CH_2*C*H_2CH_3), 13.7 (CH_3).

MS (EI): *m*/*z* (%) = 187 (89) [M$^+$], 172 (20), 159 (100), 130 (85), 104 (29), 90 (53), 77 (18), 63 (18), 51 (9), 39 (21), 27(21).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{13}NO$: 187.0997; found: 187.0995.

2-*tert*-Butyl-4-phenyloxazole and 2-*tert*-Butyl-5-phenyloxazole (1h)

The general procedure described above (reaction time: 62 h) was followed using dibromophenylethylene (**3a**; 259 mg, 0.99 mmol, 1.00 equiv), pivalamide (116 mg, 1.14 mmol, 1.15 equiv), K_2CO_3 (411 mg, 2.97 mmol, 3.00 equiv), CuI (19.6 mg, 0.10 mmol, 0.10 equiv) and DMEDA (22 μL, 0.20 mmol, 0.20 equiv). The product was obtained after purification by flash chromatography (pentane–EtOAc, 30:1→10:1).

2-*tert*-Butyl-5-phenyloxazole

Yield: 112 mg (56%); colorless oil; R_f = 0.24 (pentane–EtOAc, 10:1).

IR (film): 3448 (w), 3061 (w), 2972 (s), 2932 (w), 1715 (w), 1590 (m), 1566 (m), 1478 (m), 1449 (m), 1396 (w), 1367 (w), 1294 (w), 1247 (w), 1140 (m), 1110 (m), 1071 (w), 942 (m), 743 (s), 693 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63–7.60 (m, 2 H, HC_{Ar}), 7.42–7.37 (m, 2 H, HC_{Ar}), 7.32–7.26 (tt, *J* = 7.5, 1.2 Hz, 1 H, HC_{Ar}), 7.21 (s, 1 H, HCN), 1.45 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7 (OC=N), 150.6 (O*C*=C), 128.7 (2 × HC_{Ar}), 128.4 ($C_{q,Ar}$), 128.0 (HC_{Ar}), 123.9 (2 × HC_{Ar}), 121.4 (HCN), 33.8 [$C(CH_3)_3$], 28.6 [$C(CH_3)_3$].

MS (EI): *m*/*z* (%) = 201 (41) [M$^+$], 186 (100), 105 (13), 96 (46), 77 (40), 69 (54), 57 (40), 51 (19), 41 (90), 29 (52).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{15}NO$: 201.1154; found: 201.1152.

2-*tert*-Butyl-4-phenyloxazole

Yield: 18 mg (9%); pale-yellow oil; R_f = 0.30 (pentane–EtOAc, 30:1).

IR (film): 3061 (w), 2972 (s), 2932 (m), 2905 (m), 2871 (w), 1550 (s), 1490 (m), 1448 (m), 1367 (m), 1244 (m), 1147 (s), 1121 (s), 1061 (m), 1027 (w), 962 (m), 945 (w), 824 (w), 764 (s), 749 (s), 691 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (s, 1 H, HCO), 7.75–7.72 (m, 2 H, HC_{Ar}), 7.41–7.36 (m, 2 H, HC_{Ar}), 7.31–7.26 (m, 1 H, HC_{Ar}), 1.43 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.5 (OC=N), 140.2 (C=*C*N), 132.7 (HCO), 131.5 ($C_{q,Ar}$), 128.6 (2 × HC_{Ar}), 127.7 (HC_{Ar}), 125.6 (2 × HC_{Ar}), 33.8 [$C(CH_3)_3$], 28.6 [$C(CH_3)_3$].

MS (EI): *m*/*z* (%) = 201 (89) [M$^+$], 186 (60), 172 (23), 158 (24), 145 (52), 117 (28), 105 (18), 90 (31), 77 (18), 69 (11), 57 (100), 51 (19), 41 (52), 29 (56).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{15}NO$: 201.1153; found: 201.1158.

2-Vinyl-5-phenyloxazole (1i)

The general procedure described above (reaction time: 14 h) was followed using dibromophenylethylene (**3a**; 85.1 mg, 0.32 mmol, 1.00 equiv), acrylamide (25.1 mg, 0.35 mmol, 1.09 equiv), K_2CO_3 (132 mg, 0.95 mmol, 2.98 equiv), CuI (13 mg, 0.07 mmol, 0.21 equiv) and DMEDA (15 μL, 0.14 mmol, 0.43 equiv) in toluene (1 mL). After addition of aq NH_4OH (25%, 5 mL) and extraction into EtOAc (3 × 10 mL), the product was purified by flash chromatography (pentane–EtOAc, 10:1) to give 2,4-**1i** and 2,5-**1i** in a ratio of 1:10 (GC-MS). 2-Vinyl-4-phenyloxazole was not isolated.

Yield: 15 mg (28%); colorless oil; R_f = 0.29 (pentane–EtOAc, 10:1).

IR (film): 3120 (w), 3062 (w), 2928 (w), 1701 (s), 1589 (w), 1551 (m), 1517 (m), 1488 (s), 1449 (s), 1315 (w), 1278 (m), 1178 (w), 1125 (s), 1061 (s), 1027 (s), 983 (w), 943 (s), 826 (m), 760 (s), 691 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.68–7.65 (m, 2 H, HC_{Ar}), 7.45–7.39 (m, 2 H, HC_{Ar}), 7.36–7.30 (m, 2 H, HC_{Ar}, HCN), 6.64 (dd, *J* = 18, 12 Hz, 1 H, *H*C=CHH), 6.25 (dd, *J* = 18, 0.9 Hz, 1 H, HC=C*H*H, *Z*), 5.65 (dd, *J* = 12, 1.1 Hz, 1 H, HC=CH*H*, *E*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.5 (OC=N), 150.9 (O*C*=C), 128.9 (2 × HC_{Ar}), 128.5 (C_{sp2}), 127.9 ($C_{q,Ar}$), 124.2 (2 × HC_{Ar}), 123.4 (C_{sp2}), 123.2 (C_{sp2}), 121.4 (C_{sp2}).

MS (EI): *m*/*z* (%) = 171 (90) [M$^+$], 143 (12), 116 (32), 105 (19), 90 (21), 77 (78), 63 (9), 51 (24), 39 (24), 32 (15), 28 (100).

HRMS (EI): *m*/*z* calcd for $C_{11}H_9NO$: 171.0685; found: 171.0686.

2-Vinyl-4-phenyloxazole (1i)

The general procedure described above (reaction time: 24 h) was followed using diiodophenylethylene (**3b**; 108 mg, 0.30 mmol, 1.00 equiv), acrylamide (25.6 mg, 0.36 mmol, 1.20 equiv), K_2CO_3 (124 mg, 0.90 mmol, 3.00 equiv), CuI (11.9 mg, 0.06 mmol, 0.21 equiv) and DMEDA (13 μL, 0.12 mmol, 0.40 equiv) in toluene (1 mL). In contrast to the general procedure, the olefin was weighed into the vial with the other solids. After addition of aq NH_4OH (25%, 5 mL) and extraction into EtOAc (3 × 10 mL), the product was purified by flash chromatography (pentane–EtOAc, 30:1) to give 2,4-**1i** and 2,5-**1i** in a ratio of 1:10 (GC-MS). 2-Vinyl-5-phenyloxazole was not isolated.

Yield: 9 mg (17%); reddish oil; R_f = 0.21 (pentane–EtOAc, 30:1).

IR (film): 3293 (br s), 3063 (w), 2960 (w), 2927 (m), 2856 (w), 1634 (s), 1598 (w), 1489 (w), 1449 (m), 1406 (w), 1261 (s), 1178 (w), 1072 (w), 1027 (w), 801 (w), 756 (s), 696 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.86 (s, 1 H, HCO), 7.76–7.73 (m, 2 H, HC_{Ar}), 7.44–7.39 (m, 2 H, HC_{Ar}), 7.32 (tt, *J* = 7.4, 1.2 Hz, 1 H, HC_{Ar}), 6.67 (dd, *J* = 18, 12 Hz, 1 H, *H*C=CHH), 6.24 (dd, *J* = 18, 0.9 Hz, 1 H, HC=C*H*H, *Z*), 5.65 (dd, *J* = 12, 0.9 Hz, 1 H, HC=CH*H*, *E*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2 (OC=N), 141.8 (C=*C*N), 133.1 (HCO), 130.9 ($C_{q,Ar}$), 128.7 (2 × HC_{Ar}), 128.1 (HC_{Ar}), 125.5 (2 × HC_{Ar}), 123.4 (H*C*=CH$_2$), 122.2 [HC=*C*H$_2$].

MS (EI): *m*/*z* (%) = 171 (69) [M$^+$], 143 (41), 115 (8), 105 (12), 90 (43), 77 (13), 63 (23), 51 (13), 39 (43), 32 (15), 28 (100).

HRMS (EI): *m*/*z* calcd for $C_{11}H_9NO$: 171.0682; found: 171.0683.

2-Phenyl-4-hexyloxazole and 2-Phenyl-5-hexyloxazole (1j) from Dibromo-1-octene

The general procedure described above (reaction time: 13 h) was followed using 1,2-dibromo-1-octene (**3c**; 266 mg, 0.99 mmol, 1.00 equiv), benzamide (132 mg, 1.08 mmol, 1.09 equiv), K_2CO_3 (408 mg, 2.95 mmol, 2.98 equiv), CuI (19.2 mg, 0.10 mmol, 0.10 equiv) and DMEDA (22 μL, 0.20 mmol, 0.20 equiv). In contrast to the general procedure, the reaction was performed at 130 °C. Purification by flash chromatography (hexane) on Et_3N-impregnated silica gave 2,4-**1j** (21 mg, 9%) and 2,5-**1j** (134 mg, 59%) as pale-yellow liquids in a 1:8 ratio (GC-MS).

2-Phenyl-4-hexyloxazole and 2-Phenyl-5-hexyloxazole (1j) from (*E*)-Diiodo-1-octene

The general procedure described above (reaction time: 24 h) was followed using 1,2-diiodo-1-octene (**3d**; 359 mg, 0.99 mmol, 1.00 equiv), benzamide (134 mg, 1.10 mmol, 1.11 equiv), K_2CO_3 (415 mg, 3.00 mmol, 3.04 equiv), CuI (20.1 mg, 0.11 mmol, 0.11 equiv) and DMEDA (24 μL, 0.22 mmol, 0.22 equiv). In contrast to the general procedure, the reaction was performed at 130 °C. Purification by flash chromatography (pentane–EtOAc, 30:1) gave 2,4-**1j** (26 mg, 11%) and 2,5-**1j** (68 mg, 31%) in a 1:3 ratio (GC-MS)

2-Phenyl-5-hexyloxazole

Pale-yellow liquid; R_f = 0.10 (pentane–EtOAc, 30:1).

IR (film): 3436 (w), 3064 (w), 2930 (s), 2858 (m), 1567 (m), 1550 (m), 1487 (m), 1467 (m), 1449 (m), 1378 (w), 1353 (w), 1122 (m), 1099 (w), 1065 (m), 1025 (w), 988 (m), 825 (m), 775 (m), 712 (s), 692 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02–7.99 (m, 2 H, HC_{Ar}), 7.46–7.40 (m, 3 H, HC_{Ar}), 6.84 (s, 1 H, HCN), 2.71 [t, *J* = 7.5 Hz, 2 H, $CH_2(CH_2)_4CH_3$], 1.70 [quint, *J* = 7.5 Hz, 2 H, $CH_2CH_2(CH_2)_3CH_3$], 1.42–1.29 [m, 6 H, $CH_2CH_2(CH_2)_3CH_3$], 0.92–0.88 (m, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.5 (OC=N), 153.2 (OC=C), 129.8 (HC_{Ar}), 128.6 (2 × HC_{Ar}), 127. 8 ($C_{q,Ar}$), 125.9 (2 × HC_{Ar}), 123.5 (HCN), 31.4, 28.7, 27.6, 25.6, 22.5 (all CH_2), 14.0 (CH_3).

MS (EI): *m*/*z* (%) = 229 (28) [M$^+$], 158 (100), 131 (9), 117 (20), 105 (20), 89 (11), 77 (11), 41 (7), 27 (6).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{19}NO$: 229.1473; found: 229.1470.

2-Phenyl-4-hexyloxazole

Pale-yellow liquid; R_f = 0.47 (hexane–EtOAc, 10:1).

IR (film): 3429 (w), 3064 (w), 2928 (s), 2857 (m), 1689 (w), 1590 (m), 1553 (m), 1486 (m), 1467 (m), 1450 (m), 1378 (w), 1345 (m), 1286 (w), 1103 (m), 1062 (m), 1023 (w), 934 (m), 778 (m), 713 (s), 691 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.04–8.01 (m, 2 H, HC_{Ar}), 7.47–7.41 (m, 4 H, HC_{Ar}, HCO), 2.60 [t, J = 7.7 Hz, 2 H, $CH_2(CH_2)_4CH_3$], 1.73–1.63 [m, 2 H, $CH_2CH_2(CH_2)_3CH_3$], 1.41–1.25 [m, 6 H, $CH_2CH_2(CH_2)_3CH_3$], 0.91–0.87 (m, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.3 (OC=N), 142.7 (C=*C*N), 133.8 (HCO), 130.0 (HC_{Ar}), 128. 7 (2 × HC_{Ar}), 127.8 ($C_{q,Ar}$), 126.3 (2 × HC_{Ar}), 31.6, 29.0, 28.4, 26.5, 22.6 (all CH_2), 14.0 (CH_3).

MS (EI): *m*/*z* (%) = 229 (18) [M^+], 200 (16), 186 (15), 172 (15), 159 (100), 130 (14), 105 (50), 77 (19), 41 (9), 28 (18).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{19}NO$: 229.1470; found: 229.1468.

2-(4-Aminophenyl)-4-hexyloxazole and 2-(4-Aminophenyl)-5-hexyloxazole (1k)

The general procedure described above (reaction time: 38 h) was followed using 1,2-dibromo-1-octene (**3c**; 271 mg, 1.00 mmol, 1.00 equiv), 4-aminobenzamide (150 mg, 1.00 mmol, 1.10 equiv), K_2CO_3 (414.2 mg, 3.00 mmol, 3.00 equiv), CuI (19.5 mg, 0.10 mmol, 0.10 equiv) and DMEDA (22 μL, 0.20 mmol, 0.20 equiv). In contrast to the general procedure, the reaction was performed at 130 °C. The products were obtained after purification by flash chromatography (pentane–EtOAc, 1:1) in a 2,4-**1k** to 2,5-**1k** ratio of 1:14 (GC-MS).

2-(4-Aminophenyl)-5-hexyloxazole

Yield: 107 mg (44%); brown solid; R_f = 0.22 (pentane–EtOAc, 1:1).

IR (KBr): 3474 (s), 3380 (s), 3316 (w), 3208 (m), 3108 (w), 2955 (s), 2929 (s), 2857 (m), 1608 (s), 1580 (w), 1500 (s), 1466 (w), 1437 (w), 1377 (w), 1306 (m), 1172 (m), 1116 (m), 833 (m), 742 (m), 707 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.80–7.77 (m, 2 H, HC_{Ar}), 6.74 (s, 1 H, *H*CN=C), 6.70–6.67 (m, 2 H, HC_{Ar}), 3.85 (br s, 2 H, NH_2), 2.66 [t, J = 7.5 Hz, 2 H, $CH_2(CH_2)_4CH_3$], 1.66 [quint, J = 7.4 Hz, 2 H, $CH_2CH_2(CH_2)_3CH_3$], 1.40–1.27 [m, 6 H, $CH_2CH_2(CH_2)_3CH_3$], 0.91–0.86 (m, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.1 (OC=N), 152.0 (O*C*=C), 148.1 (CNH_2), 127.5 (2 × HC_{Ar}), 122.9 (HCN), 118.3 (C_q), 114.7 (2 × HC_{Ar}), 31.4, 28.7, 27.6, 25.6, 22.5 (all CH_2), 13.9 (CH_3).

MS (EI): *m*/*z* (%) = 244 (43) [M^+], 173 (100), 145 (7), 120 (19), 104 (6), 27 (11).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{20}ON_2$: 244.1564; found: 244.1570.

2-(4-Aminophenyl)-4-hexyloxazole

Yield: 18 mg (6%); brown solid; R_f = 0.34 (pentane–EtOAc, 1:1).

IR (film): 3342 (br s), 3222 (br s), 2954 (m), 2928 (s), 2857 (m), 1611 (s), 1500 (s), 1439 (w), 1298 (w), 1177 (m), 1103 (w), 1068 (w), 934 (w), 835 (m), 729 (m), 616 (w), 519 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.83–7.80 (m, 2 H, HC_{Ar}), 7.32 (s, 1 H, HCO), 6.71–6.68 (m, 2 H, HC_{Ar}), 3.90 (br s, 2 H, NH_2), 2.54 [t, J = 7.5 Hz, 2 H, $CH_2(CH_2)_4CH_3$], 1.68–1.61 [m, 2 H, $CH_2CH_2(CH_2)_3CH_3$], 1.33–1.29 [m, 6 H, $CH_2CH_2(CH_2)_3CH_3$], 0.91–0.84 (m, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.9 (OC=N), 148.2 (CNH_2), 142.2 (C=*C*N), 132.7 (HCO), 127. 9 (2 × HC_{Ar}), 118.3 ($C_{q,Ar}$), 114.7 (2 × HC_{Ar}), 31.6, 29.0, 28.4, 26.6, 22.6 (all CH_2), 14.0 (CH_3).

MS (EI): *m*/*z* (%) = 244 (28) [M^+], 187 (24), 174 (86), 145 (12), 120 (100), 104 (9), 91 (11), 65 (8), 41 (11), 28 (10).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{20}ON_2$: 244.1576; found: 244.1578.

2-(*tert*-Butyl)-5-hexyloxazole (1l)

The general procedure described above (reaction time: 47 h) was followed using 1,2-dibromo-1-octene (**3c**; 270 mg, 1.00 mmol, 1.00 equiv), pivalamide (112 mg, 1.10 mmol, 1.10 equiv), K_2CO_3 (416 mg, 3.01 mmol, 3.01 equiv), CuI (38.4 mg, 0.20 mmol, 0.20 equiv) and DMEDA (54 μL, 0.50 mmol, 0.50 equiv). Purification by flash chromatography (pentane) on Et_3N-saturated silica gave 2,4-**1l** and 2,5-**1l** in a 1:9 ratio (GC-MS). 2-(*tert*-Butyl)-4-hexyloxazole (2,4-**1l**) was not isolated.

Yield: 62 mg (30%); colorless oil; R_f = 0.14 (pentane–EtOAc, 30:1).

IR (film): 3438 (w), 3118 (w), 2960 (s), 2931 (s), 2860 (m), 1693 (w), 1607 (w), 1563 (m), 1461 (m), 1395 (w), 1365 (m), 1262 (w), 1214 (w), 1142 (s), 1113 (m), 1030 (m), 975 (m), 820 (m), 751 (w), 728 (w) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.55 (s, 1 H, HCN), 2.57 [t, J = 7.5 Hz, 2 H, $CH_2(CH_2)_4CH_3$], 1.66 [quint, J = 7.5 Hz, 2 H, $CH_2CH_2(CH_2)_3CH_3$], 1.64–1.28 [m, 15 H, $CH_2CH_2(CH_2)_3CH_3$, $C(CH_3)_3$], 0.89–0.84 (m, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.9 (OC=N), 152.3 (O*C*=C), 121.3 (HCN), 33.5 [$C(CH_3)_3$], 31.4 (CH_2), 28.7 (CH_2), 28.5 [$C(CH_3)_3$], 27.5 (CH_2), 25.5 (CH_2), 22.5 (CH_2) 14.0 (CH_3).

MS (EI): *m*/*z* (%) = 209 (5) [M^+], 194 (29), 139 (8), 111 (11), 102 (28), 97 (16), 85 (11), 69 (21), 57 (100), 41 (49), 29 (27).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{23}NO$: 209.1779; found: 209.1778.

5-(Trimethylsilyl)-2,4-diphenyloxazole (1m)

The general procedure described above (reaction time: 21 h) was followed using 1,2-dibromo-1-(trimethylsilyl)-2-phenylethylene (**3e**; 295 mg, 0.88 mmol, 1.00 equiv, melted), benzamide (134 mg, 1.10 mmol, 1.25 equiv), K_2CO_3 (417 mg, 3.01 mmol, 3.43 equiv), CuI (19.8 mg, 0.10 mmol, 0.11 equiv) and DMEDA (22 μL, 0.20 mmol, 0.23 equiv). Purification by flash chromatography (pentane–EtOAc, 50:1) gave 2,4-**1m**. No 2,5-**1m** was detected (GC-MS).

Yield: 143 mg (56%); colorless solid; R_f = 0.19 (pentane–EtOAc, 50:1).

IR (KBr): 2924 (m), 1587 (w), 1554 (m), 1486 (m), 1446 (m), 1336 (m), 1253 (m), 1138 (w), 1082 (w), 1067 (w), 1025 (w), 976 (m), 919 (m), 845 (s), 779 (w), 761 (m), 720 (m), 700 (m), 687 (m), 634 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.17–8.13 (m, 2 H, HC_{Ar}), 7.70–7.67 (m, 2 H, HC_{Ar}), 7.52–7.35 (m, 6 H, HC_{Ar}), 0.37 [s, 9 H, $Si(CH_3)_3$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.2 (OC=N), 151.3 (O*C*=C), 149.8, 133.1, 130.2, 128.6, 128.2, 128.1, 127.8, 126.6, 29.7, –1.09 [$Si(CH_3)_3$].

MS (EI): *m*/*z* (%) = 293 (58) [M^+], 278 (31), 175 (54), 145 (8), 105 (20), 89 (27), 77 (14), 73 (100), 63 (10), 45 (30) cm^{-1}.

HRMS (EI): *m*/*z* calcd for $C_{18}H_{19}NOSi$: 293.1236; found: 293.1227.

2,4,5-Triphenyloxazole (1n)

The general procedure described above (reaction time: 44 h) was followed using 1,2-dibromo-1,2-diphenylethylene (**3f**; 340 mg, 1.01 mmol, 1.00 equiv), benzamide (136 mg, 1.11 mmol, 1.10 equiv), K_2CO_3 (422 mg, 3.05 mmol, 3.02 equiv), CuI (20.5 mg, 0.11 mmol, 0.10 equiv) and DMEDA (24 μL, 0.22 mmol, 0.22 equiv). In contrast to the general procedure, the olefin was weighed into the vial with the other solids. The product was obtained after purification by flash chromatography (pentane–EtOAc, 100:1).

Yield: 70 mg (24%); colorless solid; R_f = 0.20 (Pentane–EtOAc, 100:1).

IR (KBr): 3054 (w), 1704 (w), 1600 (w), 1552 (w), 1501 (w), 1486 (m), 1447 (m), 1365 (w), 1326 (w), 1244 (w), 1086 (w), 1069 (m), 1054 (w), 1023 (m), 965 (m), 769 (s), 728 (m), 714 (m), 693 (s), 607 (w) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.20–8.17 (m, 2 H, HC_{Ar}), 7.77–7.69 (m, 4 H, HC_{Ar}), 7.52–7.35 (m, 9 H, HC_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1 (OC=N), 145.6, 136.8, 132.6, 130.3, 129.0, 128.7, 128.7, 128.6, 128.5, 128.2, 128.1, 127.4, 126.6, 126.5 (all C_{Ar}).

MS (EI): *m/z* (%) = 297 (100) [M^+], 269 (11), 165 (88), 105 (10), 89 (20), 77 (16), 63 (8), 51 (6), 28 (27).

HRMS (EI): *m/z* calcd for $C_{21}H_{15}NO$: 297.1154; found: 297.1157.

Dimethyl 2-Phenyloxazole-4,5-dicarboxylate (1o)

The general procedure described above (reaction time: 48 h) was followed using 2,3-dibromobut-2-enedimethylester (**3g**; 477 mg, 1.58 mmol, 1.45 equiv), benzamide (133 mg, 1.09 mmol, 1.00 equiv), CuI (20.5 mg, 0.11 mmol, 0.10 equiv) and DMEDA (24 μL, 0.22 mmol, 0.20 equiv). In contrast to the general procedure, K_3PO_4 (694 mg, 3.27 mmol, 3.00 equiv) was used as base. The product was obtained after purification by flash chromatography (hexane–EtOAc, 5:1).

Yield: 33 mg (12%); pale-yellow solid; R_f = 0.09 (hexane–EtOAc, 5:1).

IR (KBr): 2955 (w), 1760 (s), 1606 (w), 1533 (m), 1481 (m), 1441 (m), 1349 (s), 1324 (m), 1301 (m), 1263 (m), 1225 (s), 1138 (m), 1091 (s), 1073 (s), 965 (w), 828 (m), 794 (m), 769 (m), 719 (s), 692 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.17–8.14 (m, 2 H, HC_{Ar}), 7.57–7.45 (m, 3 H, HC_{Ar}), 4.00 (s, 3 H, CH_3), 3.99 (s, 3 H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.5 (C=O), 161.0 (C=O), 157.2 (OC=N), 141.9 (O*C*=CN), 137.3 (OC=*C*N), 132.1 (HC_{Ar}), 128.9 ($2 \times HC_{Ar}$), 127.5 ($2 \times HC_{Ar}$), 125.4 ($C_{q,Ar}$), 52.9 (OCH_3), 52.8 (OCH_3).

MS (EI): *m/z* (%) = 261 (49) [M^+], 202 (100), 174 (34), 146 (14), 115 (6), 105 (14), 89 (6), 77 (19), 51 (6), 28 (11).

HRMS (EI): *m/z* calcd for $C_{13}H_{11}NO_5$: 261.0627; found: 261.0632.

1,2-Dibromophenylethylene (3a)[9]

To a solution of phenylacetylene (4.45 g, 43.6 mmol, 1.05 equiv) in CH_2Cl_2 (150 mL) was added a solution of Br_2 (6.55 g, 41.0 mmol, 1.00 equiv) in CH_2Cl_2 (250 mL). After stirring at r.t. for 2 h, aq $Na_2S_2O_3$ (10%, 300 mL) was added and the organic layer was separated, washed with H_2O (2×200 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash chromatography (pentane) gave the product **3a**.

Yield: 9.47 g (88%); pale-yellow liquid; R_f = 0.69 (*E*) and 0.62 (*Z*) (pentane); *E*/*Z* = 63:37 (GC-MS).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.50 (m, 5 H, HC_{Ar}, *Z*), 7.41–7.35 (m, 5 H, HC_{Ar}, *E*), 7.07 (s, 1 H, HC_{vin}, *Z*), 6.81 (s, 1 H, HC_{vin}, *E*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.1 ($C_{q,Ar}$, *Z*), 137.0 ($C_{q,Ar}$, *E*), 131.1 (HC_{Ar}, *Z*), 129.4 (HC_{Ar}, *E* + *Z*), 129.1 (HC_{Ar}, *E*), 128.5 (HC_{Ar}, *Z*), 128.2 (HC_{Ar}, *E*), 127.7 ($HC_{q,vin}$, *Z*), 121.3 ($HC_{q,vin}$, *E*), 108.8 (HC_{vin}, *Z*), 103.0 (HC_{vin}, *E*).

(*E*)-1,2-Diiodophenylethylene (3b)[9]

To a solution of phenylacetylene (5.16 g, 50.5 mmol, 1.00 equiv) in CH_2Cl_2 (150 mL) was added a solution of I_2 (12.8 g, 50.4 mmol, 1.00 equiv) in CH_2Cl_2 (350 mL), dropwise, over 1 h. After stirring at r.t. for 2.5 h, aq $Na_2S_2O_3$ (10%, 300 mL) was added and the organic layer was separated, washed with H_2O (200 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The product was recrystallized (MeOH) to give **3b**.

Yield: 11.7 g (65%); colorless product; R_f = 0.32 (pentane).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.27 (m, 5 H, HC_{Ar}), 7.19 (s, 1 H, HC_{vin}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.1 ($C_{q,Ar}$), 128.9 (C_{Ar}), 128.5 (C_{Ar}), 128.4 (C_{Ar}), 96.2 ($C_{q,vin}$), 80.7 (C_{vin}).

1,2-Dibromo-1-octene (3c)[9]

To a solution of 1-octyne (3.67 g, 33.4 mmol, 1.04 equiv) in CH_2Cl_2 (150 mL) was added a solution of Br_2 (5.12 g, 32.0 mmol, 1.00 equiv) in CH_2Cl_2 (150 mL). After stirring at r.t. for 16 h, the solution was concentrated under reduced pressure and purified by flash chromatography (pentane) to give **3c**.

Yield: 7.27 g (84%); colorless liquid; R_f = 0.58 (*E*) and 0.47 (*Z*) (pentane); *E*/*Z* = 77:23 (GC-MS).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.56 (s, 1 H, HC_{vin}, *E*), 6.40 (s, 1 H, HC_{vin}, *Z*), 2.59 [t, *J* = 7.2 Hz, 2 H, $CH_2(CH_2)_4CH_3$, *E*], 2.50 [t, *J* = 7.4 Hz, 2 H, $CH_2(CH_2)_4CH_3$, *Z*], 1.60–1.53 (m, 3 H, CH_2), 1.36–1.29 (m, 10 H, CH_2), 0.92–0.87 (m, 5 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.1 ($C_{q,vin}$, *Z*), 127.0 ($C_{q,vin}$, *E*), 105.2 (HC_{vin}, *Z*), 102.1 (HC_{vin}, *E*), 41.2, 36.9, 31.5, 28.0, 27.0, 22.5, 14.0 (all C_{alk}).

(*E*)-1,2-Diiodo-1-octene (3d)[10]

To a solution of I_2 (10.23 g, 40.3 mmol, 1.00 equiv) in CH_2Cl_2 (200 mL) was added a solution of 1-octyne (4.87 g, 44.2 mmol, 1.10 equiv) in CH_2Cl_2 (100 mL). After stirring at r.t. for 69 h, aq $Na_2S_2O_3$ (10%, 300 mL) was added and the organic layer was separated, washed with H_2O (2×200 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (hexane) gave the product **10**.

Yield: 13.4 g (91%); reddish liquid; R_f = 0.45 (hexane).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.80 (s, 1 H, HC_{vin}), 2.50 (t, *J* = 6.0 Hz, 2 H, CH_2C_{vin}), 1.54 (quint, *J* = 6.6 Hz, 2 H, $CH_2CH_2C_{vin}$), 1.36–1.29 (m, 6 H, $3 \times CH_2$), 0.93–0.88 (m, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 104.4 ($C_{q,vin}$), 78.9 (HC_{vin}), 44.7, 31.6, 28.1, 27.8, 22.5, 14.1 (all C_{alk}).

1,2-Dibromo-1-(trimethylsilyl)-2-phenylethylene (3e)[11]

A solution of 1-(trimethylsilyl)-2-phenylacetylene (1.70 g, 9.75 mmol, 1.00 equiv) in CH_2Cl_2 (20 mL) was cooled to –10 °C and a solution of Br_2 (9.3 mL, 9.77 mmol, 1.00 equiv) in CH_2Cl_2 (*c* = 1.05 mol/L) was added. The reaction mixture was stirred at –10 °C for 30 min then allowed to warm to r.t., concentrated under reduced pressure and the residue was purified by flash chromatography (pentane) to give **3e**.

Yield: 2.26 g (69%); colorless solid; R_f = 0.40 (pentane); *E*/*Z* = 1:99 (GC-MS).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.56–7.46 (m, 5 H, HC_{Ar}), 0.15 [s, 9 H, $(CH_3)_3Si$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.4 ($C_{q,Ar}$), 133.5 ($C_{q,vin}$), 131.4 ($C_{q,vin}$), 129.2 (HC_{Ar}), 128.9 (HC_{Ar}), 128.2 (HC_{Ar}), 0.12 [$Si(CH_3)_3$].

1,2-Dibromo-1,2-diphenylethylene (3f)[11]

Tolane (5.14 g, 28.8 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (60 mL) at –10 °C and a solution of Br_2 (5.59 g, 35.0 mmol, 1.21 equiv) in CH_2Cl_2 (40 mL) was added dropwise over 15 min. The reaction mixture stirred at –10 °C for a further 30 min then allowed to warm to r.t. and the precipitated product was filtrated. Aq $Na_2S_2O_3$ (10%, 100 mL) was added to the filtrate and the organic layer was separated. The aqueous layer was washed with pentane

(2 × 150 mL) and the combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the residue was recrystallized (EtOH) to give **3f**.

Yield: 7.36 g (76%); colorless solid; R_f = 0.18 (pentane); *E*/*Z* = 17:83 (GC-MS).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56–7.52 (m, 4 H, HC_{Ar}), 7.47–7.38 (m, 6 H, HC_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.8 ($C_{q,Ar}$), 129.1 (HC_{Ar}), 128.9 ($C_{q,Ar}$), 128.4 (HC_{Ar}), 118.1 ($C_{vin}Br$).

Dimethyl 2,3-Dibromobut-2-endicarboxylate (3g)[12]

To a solution of Br_2 (6.00 g, 37.5 mmol, 1.04 equiv) in CH_2Cl_2 (160 mL) was added a solution of dimethyl acetylenedicarboxylate (5.15 g, 36.2 mmol, 1.00 equiv) in CH_2Cl_2 (35 mL). After stirring at r.t. for 16 h, aq $Na_2S_2O_3$ (10%, 250 mL) was added and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 75 mL) and the combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and the residue was purified by flash chromatography (pentane–EtOAc, 10:1).

Yield: 9.55 g (87%); colorless solid; R_f = 0.43 (*E* + *Z*; pentane–EtOAc, 5:1); *E*/*Z* = 61:39 (GC-MS).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, CH_3, *E*), 3.83 (s, 3 H, CH_3, *Z*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.6 (C=O), 162.5 (C=O), 125.0 (C_{vin}, *Z*), 112.6 (C_{vin}, *E*), 53.8 (CH_3), 53.6 (CH_3).

2,3-Dibromoprop-2-en-1-ol (3h)[12]

To a solution of Br_2 (13.4 g, 83.1 mmol, 1.00 equiv) in CH_2Cl_2 (350 mL) was added a solution of propargyl alcohol (5.37 g, 95.8 mmol, 1.15 equiv) in CH_2Cl_2 (100 mL). After stirring at r.t. for 17 h, the solution was concentrated under reduced pressure and the residue was purified by flash chromatography (pentane–EtOAc, 5:1) to give **3h**.

Yield: 12.9 g (72%); colorless liquid; R_f = 0.28 and 0.36 (pentane–EtOAc, 5:1); *E*/*Z* = 44:56 (GC-MS).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.96 (s, 1 H, HC_{vin}, *Z*), 6.56 (s, 1 H, HC_{vin}, *E*), 4.42 (s, 2 H, CH_2, *E*), 4.26 (s, 2 H, CH_2, *Z*), 3.64–3.12 (m, 2 H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 131.7 (C_{vin}), 124.9 (C_{vin}), 108.6 (C_{vin}), 104.4 (C_{vin}), 67.4 (OCH_2), 63.6 (OCH_2).

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References

(1) (a) *Oxazoles: Synthesis, reactions, and spectroscopy*, Part B, Vol. 60; Palmer, D. C., Ed.; J. Wiley & Sons: Hoboken, **2004**. (b) *Oxazoles: Synthesis, reactions, and spectroscopy*, Part A, Vol. 60; Palmer, D. C., Ed.; J. Wiley & Sons: Hoboken, **2003**. (c) Boyd, G. V. In *Science of Synthesis*, Vol. 11; Schaumann, E., Ed.; Georg Thieme Verlag: Stuttgart, **2002**, 383. (d) Hartner, F. W. In *Comprehensive Heterocyclic Chemistry II*, Vol. 3; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Pergamon Press: Oxford, **1996**, 261. (e) Wipf, P. *Chem. Rev.* **1995**, *95*, 2115. (f) Turchi, I. J. *Oxazoles in Heterocyclic Compounds*, Vol. 45; Turchi, I. J., Ed.; Wiley: New York, **1986**. (g) Turchi, I. J.; Dewar, M. J. S. *Chem. Rev.* **1975**, *75*, 389.

(2) For recent reviews on the synthesis of oxazole containing natural products, see: (a) Jin, Z. *Nat. Prod. Rep.* **2006**, *23*, 464. (b) Yeh, V. S. C. *Tetrahedron* **2004**, *60*, 11995.

(3) (a) Altenhoff, G.; Glorius, F. *Adv. Synth. Catal.* **2004**, *346*, 1661. (b) Evindar, G.; Batey, R. A. *J. Org. Chem.* **2006**, *71*, 1802.

(4) (a) Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421. (b) Kwong, F. Y.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 581. (c) Jiang, L.; Job, G. E.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 3667. (d) Han, C.; Shen, R.; Su, S.; Porco, A. Jr. *Org. Lett.* **2003**, *6*, 27. For profound reviews on Cu-catalyzed C–N, C–O and C–S couplings, see: (e) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400. (f) Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, 2428.

(5) For example, see: (a) Shin, C.-G.; Sato, Y.; Sugiyama, H.; Nanjo, K.; Yoshumura, J. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1788. (b) Chattopadhyay, S. K.; Kempson, J.; McNeil, A.; Pattenden, G.; Reader, M.; Rippon, D. E.; Waite, D. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2415.

(6) For related syntheses and mechanistic investigations, see: (a) Uemura, S.; Okazaki, H.; Okano, M. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1278. (b) Bianchini, R.; Chiappe, C.; Lo Moro, G.; Lenoir, D.; Lemmen, P.; Goldberg, N. *Chem. Eur. J.* **1999**, *5*, 1570. (c) Selina, A. A.; Sergey, S. K.; Gauchenova, E. V.; Churakov, A. V.; Kuz'mina, L. G.; Howard, A. K.; Lorberth, J.; Zaitseva, G. S. *Heteroat. Chem.* **2004**, *15*, 43. (d) Barluenga, J.; Rodriuez, M. A.; Campos, P. J. *J. Org. Chem.* **1990**, *55*, 3104. (e) Kodomari, M.; Sakamoto, T.; Yoshitomi, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 4053. (f) Pagni, R. M.; Kabalka, G. W.; Boothe, R.; Gaetano, K.; Stewart, L. J.; Conaway, R.; Dial, C.; Gray, D.; Larson, S.; Luidhardt, T. *J. Org. Chem.* **1988**, *53*, 4477. (g) Al-Hassan, M. I. *J. Organomet. Chem.* **1989**, *372*, 183.

(7) Parameters screened: *Ligands*: DMEDA (optimal), *rac*-1,2-diaminocyclohexane (lower conversion, more side products), phenanthroline (no reaction); *bases*: K_2CO_3 (optimal), K_3PO_4 (lower conversion, more side products), Cs_2CO_3 (lower conversion), Et_3N and NaOAc (no reaction). *Reaction temperature*: <110 °C conversion was found to be incomplete; *solvents*: toluene (optimal), chlorobenzene (lower conversion), *t*-BuOH, dioxane (much lower conversion), DMF (no conversion).

(8) In a series of experiments, a range of olefins were heated at 110 °C with and without CuI and DMEDA. Whereas (*E*)-1,2-diiodophenylethylene did not isomerize to the *Z*-isomer, an isomerization of 1,2-dibromophenylethylene was obtained in cases of older substrates or if small amounts of bromine were added. Bromine-catalyzed isomerizations of dihaloalkenes have previously been described, see: Uemura, S.; Okazaki, H.; Okano, M. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1278.

(9) Barhate, N. B.; Gajare, A. S.; Wakharkar, R. D.; Bedekar, A. V. *Tetrahedron* **1999**, *55*, 11127.

(10) Pagni, R. M.; Kabalka, G. W.; Boothe, R.; Gaetano, K.; Stewart, L. J.; Conaway, R.; Dial, C.; Gray, D.; Larson, S.; Luidhardt, T. *J. Org. Chem.* **1988**, *53*, 4477.

(11) Al-Hassan, M. I. *J. Organomet. Chem.* **1989**, *372*, 183.

(12) Kodomari, M.; Sakamoto, T.; Yoshitomi, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 4053.