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C–H Bond Activation

Dimethylzinc-Initiated Radical Coupling of β-Bromostyrenes with Ethers and Amines

Amanda Sølvhøj, Andreas Ahlburg, and Robert Madsen*[a]

Abstract: A new coupling reaction has been developed in which β-bromostyrenes react with ethers and tertiary amines to introduce the styryl group in the α-position. The transformation is mediated by Me_2Zn/O_2 with 10% $MnCl_2$ and is believed to proceed by a radical addition–elimination mechanism. The ether and the amine are employed as solvent and the coupling takes place through the most stable α radical for unsymmetrical substrates. The products are obtained in moderate to good yields as the pure *E* isomers. The coupling can be achieved with a range of smaller cyclic and acyclic ethers/amines as well as various substituted β-bromostyrenes.

Introduction

α-Alkoxy alkyl and α-amino alkyl radicals are unique intermediates in organic synthesis and they can react with unsaturated acceptors to form carbon–carbon bonds under relatively mild conditions.[1] The carbon-centered radicals are nucleophilic and are typically formed by abstraction of the α-hydrogen from ethers and tertiary amines. α-Alkoxy alkyl radicals are rather versatile species and the addition of ethers (and especially tetrahydrofuran) to C=C,[2] C≡C,[3] C=N,[4] and C=O[5] bonds has been achieved under different conditions. Typically, the ether is used as the solvent and the radical is generated with either Me_2Zn/O_2, Et_3B/O_2, or peroxides as the initiator.[2–5] α-Amino alkyl radicals, on the other hand, have found fewer synthetic applications, which is mainly due to difficulties associated with their generation from tertiary amines because further oxidation to iminium cations takes place easily. However, the addition of tertiary amines to aldehydes[6] and electron-deficient C=C bonds[7] have been described with either Et_3B/O_2 or visible light photoredox catalysis.

Besides addition reactions, addition–elimination reactions can also be carried out with these radicals, although this scenario is relatively rare. The further development of this transformation is highly attractive because a new functional group (alkene or alkyne) is installed in the ether/amine to furnish the corresponding allyl/propargyl species. Under photoirradiation conditions, alkenyl and alkynyl sulfones have been coupled with ethers and amines to install the alkene/alkyne in the α-position.[8] Phenylethynyl bromide/benziodoxolone have been converted with ethers to introduce the alkynyl moiety in the same position.[9] β-Nitrostyrenes have been reacted with THF in the presence of dibenzoyl peroxide to afford styryl tetrahydrofurans.[10] Recently, a copper-catalyzed oxidative coupling between olefins and ethers to form α-alkenyl ethers was presented, although the mechanism is not known.[11] In most cases, the substrate scope of these radical addition–elimination reactions is rather narrow and there is clearly room for further development of these procedures to install olefins in the α-position of ethers and amines.

Herein, we describe a novel radical coupling between β-bromostyrenes and ethers/amines mediated by Me_2Zn and a catalytic amount of $MnCl_2$.

Results and Discussion

The radical coupling was discovered by serendipity when attempting a cross-coupling reaction between β-bromostyrene and *p*-tolylzinc iodide in THF. The Negishi coupling has had a significant impact on organic synthesis, but the reaction requires the use of expensive and toxic metal palladium as the catalyst.[12] It has, however, been shown that the cross coupling between vinyl halides and Grignard reagents can be catalyzed by the much less expensive and more benign catalyst $MnCl_2$.[13] The mechanism for this manganese-catalyzed coupling reaction is not known, but it seemed reasonable to attempt a similar coupling with an organozinc species. β-Bromostyrene was selected because it had served as a successful substrate for coupling with aryl Grignard reagents.[13] However, unexpectedly, the coupling did not occur with the organozinc reagent, but instead with the solvent THF.

The reaction was very clean and gave 2-styryltetrahydrofuran in 55% GC yield with the rest being unreacted β-bromostyrene (Table 1, entry 1). In the absence of $MnCl_2$ the yield dropped to 13%, which underlines the importance of manganese in combination with the zinc reagent (entry 2). No reaction occurred when the organozinc halide was replaced with $ZnCl_2$, whereas a low yield was obtained with *n*-propylzinc bromide (entries 3

[a] Dr. A. Sølvhøj, A. Ahlburg, Prof. Dr. R. Madsen
Department of Chemistry
Technical University of Denmark
2800 Kgs. Lyngby (Denmark)
E-mail: rm@kemi.dtu.dk

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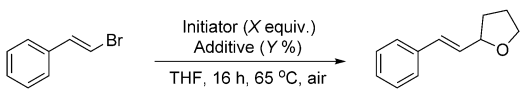
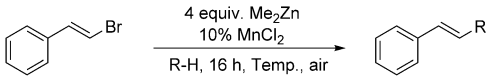
Table 1. Radical initiators and additives for the coupling between β-bromostyrene and THF.

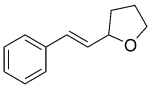
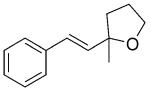
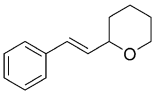
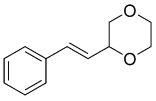
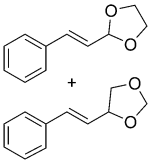
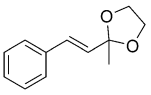
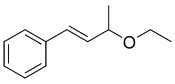
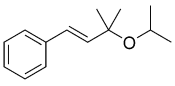
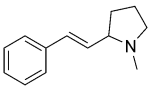


Entry	Initiator	X	Additive	Y [%]	Yield [%][a]
1[b]	*p*-MePhZnI	2	$MnCl_2$	30	55
2[b]	*p*-MePhZnI	2	none	–	13
3[b]	$ZnCl_2$	2	$MnCl_2$	25	0
4[b]	*n*-PrZnBr	2	$MnCl_2$	30	11
5	Me_2Zn	3	$MnCl_2$	30	67
6	Bz_2O_2	3	$MnCl_2$	12	35
7[b]	Bz_2O_2	3	None	–	6
8	Et_2Zn	3	$MnCl_2$	30	5[c]
9	Et_3B	3	None	–	12[c]
10[b]	AIBN	3	$MnCl_2$	30	<1
11[b]	AIBN	3	None	–	<1
12	Me_2Zn	2	$MnCl_2$	40	56
13	Me_2Zn	1	$MnCl_2$	35	31
14	**Me_2Zn**	**3**	**$MnCl_2$**	**10**	**75**
15	Me_2Zn	3	None	–	45
16	Me_2Zn	3	$MnBr_2$	10	62
17	Me_2Zn	3	$Mn(OAc)_2$	10	43
18	Me_2Zn	3	$Mn(OAc)_3$	10	75
19	Me_2Zn	3	$MnBr(CO)_5$	10	58
20	Me_2Zn	3	$Mn_2(CO)_{10}$	10	60
21	Me_2Zn	3	$FeCl_2{\cdot}H_2O$	30	21
22	Me_2Zn	3	$FeCl_3$	30	28
23	Me_2Zn	3	$CuCl_2$	10	49
24	Me_2Zn	3	$CoCl_2$	10	73
25	Me_2Zn	3	$CrCl_2$	20	62
26	Me_2Zn	3	NaCl	20	28

[a] GC yield. [b] Performed under an argon atmosphere. [c] 1-Phenylbut-1-ene was formed as a major byproduct.

Table 2. Coupling of β-bromostyrene with different substrates.



Entry	R–H	Temp. [°C]	Product	Yield [%][a]
1		65		47
2[b]		78		65
3		88		40
4		100		44
5		74		31 + 16
6[b]		82		34
7		35		67
8		68		12
9		80		71

[a] Isolated yield. [b] Me_2Zn (3 equiv) was employed.

and 4). Although organozinc halides are known to form carbon-centered radicals,[14] the corresponding diorganozinc reagents have found much wider applications as radical initiators in the presence of air.[15] Indeed, when Me_2Zn was employed as the zinc reagent, the yield of the coupling product increased to 67% (entry 5). Several other radical initiators were also investigated, but the results were poor. The use of Bz_2O_2, Et_2Zn, and Et_3B all led to low yields of the coupling product, and only traces were observed with AIBN (entries 6–11). Therefore, Me_2Zn was selected for general use as the initiator. Several experiments were performed with different amounts of Me_2Zn and $MnCl_2$, and 3 equiv of the zinc reagent and 10% of the manganese salt seemed to give the best results (entries 12–15). A number of other salts were also investigated (entries 16–26); however, although comparable results were obtained with both $Mn(OAc)_3$ and $CoCl_2$, $MnCl_2$ was subsequently employed for general use.

Thus, the optimized conditions employ Me_2Zn and 10% $MnCl_2$ in the ether as solvent at reflux under air. The conversion of β-bromostyrene was approximately 90% in THF, but upon scale up the isolated yield of 2-styryltetrahydrofuran was only 33%. Consequently, it was decided to increase the amount of Me_2Zn to 4 equiv, which gave full conversion of β-bromostyrene and an isolated yield of 47% (Table 2, entry 1). No byproducts could be detected by GC analysis and the fate of the remaining starting material is not known. β-Bromostyrene is employed as a 6:1 mixture of the *E* and the *Z* isomer, but only (*E*)-2-styryltetrahydrofuran was isolated as the product and none of the *Z* compound was detected. At lower temperature, the yield was reduced, but the *E* isomer was still the only product observed. At 0 °C, the GC yield was 42%, compared with 75% at reflux (Table 1, entry 14); no conversion occurred at −18 °C.

Full conversion was achieved with 2-methyltetrahydrofuran at reflux with 3 equiv of Me_2Zn, and 2-methyl-2-styryltetrahydrofuran was isolated in 65% yield (Table 2, entry 2). A small amount of the isomeric 2-methyl-5-styryl compound was also detected (as two diastereomers), but these were not isolated. The ratio between the 2-styryl and the 5-styryl compound was 6.3:1, as determined by GC analysis. This shows that the coupling mainly proceeds through the most stable α-alkoxy alkyl radical. In the absence of $MnCl_2$, the conversion of β-bromo-

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styrene was only around 50% and the ratio between the two isomeric products dropped to 2.7:1. A similar reactivity was observed with tetrahydropyran (THP), for which 2-styryltetrahydropyran was isolated as the main product in 40% yield (entry 3). Small amounts of two isomers resulting from reaction in the 3- and 4-position of THP were also observed, but these were not isolated. 1,4-Dioxane gave the 2-styryl derivative (entry 4), whereas 1,3-dioxolane afforded a mixture of the 2- and 4-styryl compound (entry 5). A mixture of the 2- and 4-derivative was also observed with 2-methyl-1,3-dioxolane in a 2.9:1 ratio, for which the former was isolated in 34% yield (entry 6). When $MnCl_2$ was omitted, the conversion of β-bromostyrene dropped to below 5% and it was no longer possible to determine the ratio between the product isomers.

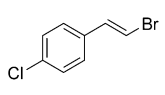
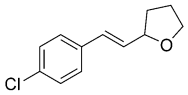
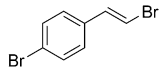
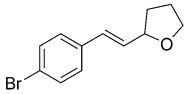
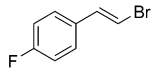
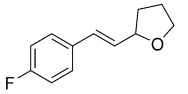
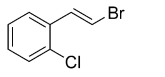
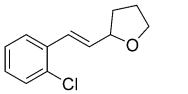
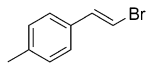
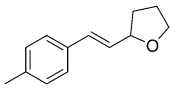
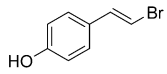
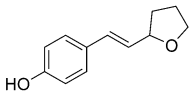
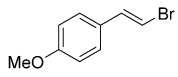
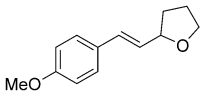
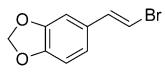
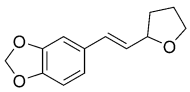
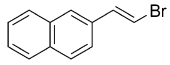
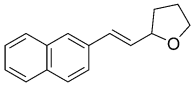
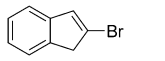
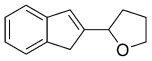
Full conversion of β-bromostyrene was not observed in the reactions with 1,4-dioxane, 1,3-dioxolane, or 2-methyl-1,3-dioxolane (Table 2, entries 5–7). The variations in the reactivity and selectivity correlate reasonably well with the differences between the calculated C–H dissociation energies for the cyclic ethers: THF 89.8 kcal mol^{-1} (H-2), THP 92.1 kcal mol^{-1} (H-2), 1,4-dioxane 93.2 kcal mol^{-1} (H-2), 1,3-dioxolane 90.0 kcal mol^{-1} (H-2), and 91.5 kcal mol^{-1} (H-4).[16] As a result, hydrogen abstraction from THP and 1,3-dioxolane is expected to occur both from the α-position and (to a lesser degree) from the other positions.[16]

Acyclic ethers could also be employed in the coupling, as shown with diethyl ether, which gave the α-styryl product in 67% yield (Table 2, entry 7). The reaction did not go to completion because similar conversion was observed for the starting β-bromostyrene. Diisopropyl ether, on the other hand, was a poor substrate and only gave 12% isolated yield of the product with approximately 30% conversion of β-bromostyrene (entry 8). Interestingly, the conditions were also amenable to a tertiary amine because *N*-methylpyrrolidine gave full conversion of β-bromostyrene and 71% isolated yield of the 2-styryl product (entry 9).

A range of substituted β-bromostyrenes were then investigated as substrates in the reaction with THF (Table 3). The starting materials were prepared from the corresponding carboxylic acids by a $Mn(OAc)_2$-catalyzed Hunsdiecker reaction with *N*-bromosuccinimide (NBS).[17] Interestingly, chloro, bromo, fluoro, methyl, hydroxyl, and ether substituents all gave higher yields of the coupling products than obtained with the parent β-bromostyrene under the same conditions (entries 1–8). This may be due to the enhanced ability of these substituents to stabilize a benzylic radical compared with a hydrogen atom.[18] In contrast, bicyclic substrates 2-(2-bromovinyl)naphthalene and 2-bromoindene reacted very slowly and the coupling products were only isolated in low yield even after addition of additional reagent (entries 9 and 10). Notably, all the products presented in Table 2 and Table 3 were isolated as the *E* isomers; the corresponding *Z* compounds were not detected.

The reaction with a tertiary amine (Table 2, entry 9) deserves further comment because the use of Me_2Zn and air has very seldom been employed for generating α-amino alkyl radicals.[19] As a result, it was decided to investigate the scope of the coupling with amines and amine derivatives in further

Table 3. Coupling of substituted β-bromostyrenes with THF.[a]

Entry	Substrate	Product	Yield [%][b]
1			48
2			48
3			40
4[c]			54
5			39
6[d]			39
7[d]			37
8[c]			54
9[e]			21
10[c,e]			18

[a] Reaction conditions: Me_2Zn (3 equiv), 10% $MnCl_2$, THF, 16 h, 65 °C, air. [b] Isolated yield. [c] Reaction time 3 d. [d] Reaction time 2 d. [e] Additional Me_2Zn (3 equiv) and 10% $MnCl_2$ were added followed by heating to reflux for another 16 h.

detail. β-Bromo-3,4-methylenedioxystyrene was selected for these studies because this substrate previously gave the highest yield (Table 3). First, the reaction with *N*-methylpiperidine was performed at different temperatures, which proved to have a considerable influence on the outcome. The best result was obtained when the reaction was performed at 65 °C; under these conditions, the 2-piperidyl compound was isolated in 83% yield and the corresponding *N*-methyl coupling product was obtained in 8% yield (Table 4, entry 1). Decreasing the temperature gave lower yields (entries 2–4), and almost no conversion occurred at −20 °C. The ratio between the two products was slightly different at lower temperature, but both compounds were only detected as the *E* isomers. Increasing the temperature had a detrimental effect and only 15% yield of the main product was obtained at 85 °C (entries 5 and 6). Attempts to use a co-solvent were unsuccessful; performing the coupling in benzene, heptane, and pyridine only produced

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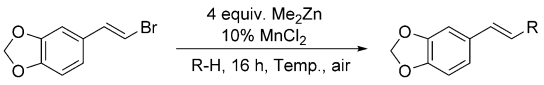
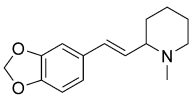
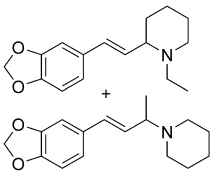
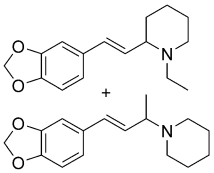
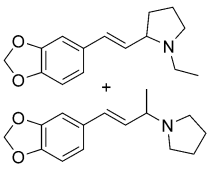
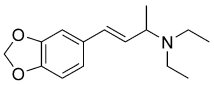
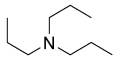
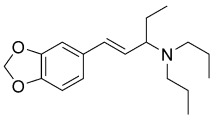
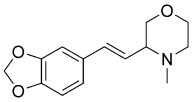
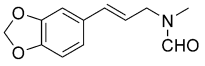
Table 4. Coupling of β-bromo-3,4-methylenedioxystyrene with tertiary amines and DMF.



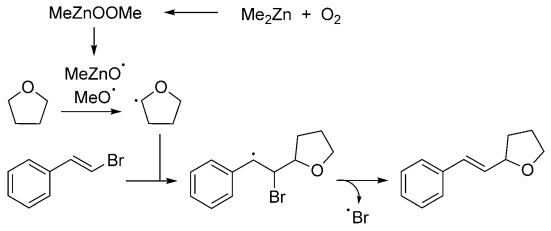
Entry	R–H	Temp. [°C]	Product	Yield [%][a]
1		65		83[b]
2		55		77
3		20		67[c]
4		0		51[b]
5		75		66
6		85		15
7		65		58 + 26
8		85		22 + 31
9		95		62 + 23
10		95		95
11		65		21
12		95		4
13		65		25
14		65		19
15		85		22
16		95		15

[a] Isolated yield. [b] *N*-(3,4-Methylenedioxycinnamyl)piperidine was also isolated in 8% yield. [c] *N*-(3,4-Methylenedioxycinnamyl)piperidine was also isolated in 18% yield.

approximately 20% yield at 65 °C (results not shown). Consequently, the coupling reactions with tertiary amines were performed under the same conditions developed for ethers.

N-Ethylpiperidine also gave a good yield at 65 °C, but the ratio between the two coupling products was now about 2:1, which reflects the similar stability of the two α-amino alkyl radicals (Table 4, entry 7). No improvement was observed by increasing the temperature to 85 °C (entry 8). The reaction with *N*-ethylpyrrolidine gave a similar result at 65 °C, whereby the two coupling products were isolated in 85% overall yield (entry 9). Triethylamine afforded one product in 95% yield at 95 °C (entry 10) and no further experiments were performed to investigate the influence of the temperature. Tri-*n*-propylamine, on the other hand, gave a disappointing 21% yield at 65 °C and a mere 4% at 95 °C (entries 11 and 12). Most likely, the increased steric hindrance in this substrate compared with that of triethylamine accounts for the significant difference in yield between the two acyclic amines. This is consistent with the observation that diethyl ether gave a much higher yield than diisopropyl ether (Table 2, entries 7 and 8). The reaction with *N*-methylmorpholine gave approximately 50% conversion of β-bromostyrene and afforded a 4:1 mixture of the α-amino and the α-alkoxy coupling product, from which the former could be isolated in 25% yield (Table 4, entry 13). In the absence of $MnCl_2$, the same experiment gave 34% conversion of β-bromostyrene and the two products were formed in a slightly lower ratio (3:1). *N*,*N*-Dimethylformamide (DMF) was a poor substrate and only furnished about 20% yield, depending on the temperature (entries 14–16). Heterocyclic amines such as pyridine, *N*-methylpyrrole, and *N*-methylindole did not react in the coupling and the same was observed with the secondary amine pyrrolidine. As observed in the ether coupling, all the products presented in Table 4 were obtained as the pure *E* isomers.

The mechanism for these coupling reactions has not been investigated in detail, but all indications are that they proceed by a radical pathway. Studies have shown that Me_2Zn reacts with O_2 to form a zinc methylperoxide, which is able to break down by homolysis to give the oxygen-centered radicals $MeZnO^{\cdot}$ and $MeO^{\cdot}$.[20] These may react with the ether or the tertiary amine to generate the α-alkoxy or α-amino alkyl radical, which, upon addition to β-bromostyrene, forms the benzylic radical (Scheme 1). Final elimination of a bromine radical then



Scheme 1. Proposed mechanism for radical addition–elimination with THF.

produces the addition–elimination product. The addition of a stoichiometric amount of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) completely blocks the reaction shown in Table 2, entry 1, which is presumably due to the formation of the complex MeZn(TEMPO) with the release of a $Me^{\cdot}$ radical,[21] which would inhibit the formation of the zinc methylperoxide. The coupling also did not progress when it was run under completely air-free conditions (and in the absence of $MnCl_2$). The exact role of the added $MnCl_2$ is not clear. However, it has previously been demonstrated that $MnCl_2$, $FeCl_3$, and $CrCl_3$ accelerate the conjugate addition of ethers to benzylidenemalonates in the presence of Me_2Zn/O_2, although the precise behavior of the added salts was not investigated.[19]

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Conclusion

A new procedure has been developed for introducing a styryl group at the α-position of ethers and tertiary amines. The conditions have been optimized and the reaction has been applied to a variety of substrates. The coupling is believed to proceed by a radical pathway and takes place through the most stable α radical in unsymmetrical ethers and amines. The transformation constitutes a new application of Me_2Zn and highlights the versatile nature of this reagent in organic synthesis.

Experimental Section

General methods: Gas chromatography was performed with a Shimadzu GCMS-QP2010S instrument fitted with an Equity 5, 30 m×0.25 mm×0.25 μm column. Flash column chromatography separations were performed on silica gel 60 (40–63 μm). Dry column vacuum chromatography (DCVC)[22] was carried out with silica gel 60 (15–40 μm). NMR spectra were recorded with a Bruker Ascend 400 spectrometer. Chemical shifts were measured relative to the signals of residual $CHCl_3$ (δ_H=7.26 ppm) and $CDCl_3$ (δ_C=77.16 ppm). HRMS measurements were made with ESI and TOF detection.

General procedure for ether coupling (procedure A): To a 50 mL round-bottomed flask equipped with a stir bar and a condenser, was added $MnCl_2$ (12.6 mg, 0.1 mmol), β-bromostyrene (1.0 mmol), and the ether (25 mL) as solvent. Me_2Zn (1.0 M in heptanes, 3–4 mL, 3–4 mmol) was then added and the mixture was heated to the indicated temperature for 16 h. The reaction was quenched with 1.0 M HCl (10 mL) and the mixture was stirred until both phases were clear. The phases were separated and the aqueous layer was extracted with Et_2O (2×20 mL). The combined organic phases were washed with water (20 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product, which was purified by DCVC.

General procedure for amine coupling (procedure B): To a 25 mL round-bottomed flask equipped with a stir bar and a condenser, was added $MnCl_2$ (12.6 mg, 0.1 mmol), β-bromo-3,4-methylenedioxystyrene (227 mg, 1.0 mmol) and the tertiary amine (10 mL) as solvent. Me_2Zn (1.0 M in heptanes, 4 mL, 4 mmol) was added and the mixture was heated to the indicated temperature for 16 h. The reaction was quenched with saturated sodium hydroxide (10 mL) and the mixture was extracted with CH_2Cl_2 (2×20 mL). The combined organic phases were concentrated in vacuo to give the crude product, which was purified by flash chromatography.

(*E*)-2-Styryltetrahydrofuran: Table 2, entry 1. Prepared by using procedure A, from β-bromostyrene and THF with Me_2Zn (4 equiv). DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.38 (d, J=7.2 Hz, 2H), 7.30 (t, J=7.5 Hz, 2H), 7.22 (t, J=7.3 Hz, 1H), 6.59 (d, J=15.8 Hz, 1H), 6.21 (dd, J=15.8, 6.6 Hz, 1H), 4.47 (td, J=7.5, 1.0 Hz, 1H), 3.97 (dd, J=14.2, 7.7 Hz, 1H), 3.84 (td, J=7.9, 6.2 Hz, 1H), 2.19–2.05 (m, 1H), 2.04–1.85 (m, 2H), 1.77–1.64 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ=136.9, 130.6, 130.5, 128.6, 127.5, 126.5, 79.7, 68.2, 32.5, 26.0 ppm; MS: *m/z*: 174 $[M]^+$; NMR data are in accordance with the reported values.[3d]

(*E*)-2-Methyl-2-styryltetrahydrofuran: Table 2, entry 2. Prepared by using procedure A, from β-bromostyrene and 2-methyltetrahydrofuran with Me_2Zn (3 equiv) and a reaction time of two days. DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.40 (d, J=7.2 Hz, 2H), 7.32 (t, J=7.6 Hz, 2H), 7.22 (t, J=7.3 Hz, 1H), 6.57 (d, J=16.0 Hz, 1H), 6.26 (d, J=16.0 Hz, 1H), 3.96 (t, J=6.8 Hz, 2H), 2.04–1.90 (m, 3H), 1.85–1.76 (m, 1H), 1.43 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ=137.2, 135.5, 128.5, 127.2, 126.8, 126.4, 82.4, 67.7, 37.9, 26.8, 25.8 ppm; MS: *m/z*: 188 $[M]^+$; HRMS: *m/z* calcd for $C_{13}H_{17}O$: 189.1279 $[M+H]^+$; found: 189.1290.

(*E*)-2-Styryltetrahydropyran: Table 2, entry 3. Prepared by using procedure A, from β-bromostyrene and THP with Me_2Zn (4 equiv). DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.39 (d, J=7.2 Hz, 2H), 7.31 (t, J=7.5 Hz, 2H), 7.23 (t, J=7.3 Hz, 1H), 6.60 (d, J=16.1 Hz, 1H), 6.23 (dd, J=16.1, 5.8 Hz, 1H), 4.12–4.05 (m, 1H), 4.02–3.95 (m, 1H), 3.60–3.52 (m, 1H), 1.94–1.86 (m, 1H), 1.79–1.72 (m, 1H), 1.66–1.48 ppm (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ=137.1, 131.0, 129.8, 128.6, 127.5, 126.5, 78.1, 68.5, 32.4, 26.0, 23.6 ppm; MS: *m/z*: 188 $[M]^+$; NMR data are in accordance with the reported values.[10]

(*E*)-2-Styryl-1,4-dioxane: Table 2, entry 4. Prepared by using procedure A from β-bromostyrene and 1,4-dioxane with Me_2Zn (4 equiv). DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.37 (d, J=7.2 Hz, 2H), 7.30 (t, J=7.4 Hz, 2H), 7.24 (d, J=7.2 Hz, 1H), 6.68 (d, J=16.0 Hz, 1H), 6.08 (dd, J=16.0, 6.2 Hz, 1H), 4.29–4.21 (m, 1H), 3.90–3.60 (m, 5H), 3.46–3.36 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ=136.3, 132.6, 128.5, 127.8, 126.4, 125.0, 76.0, 70.8, 66.5, 66.2 ppm; MS: *m/z*: 190 $[M]^+$. NMR data are in accordance with the reported values.[23]

(*E*)-2-Styryl-1,3-dioxolane: Table 2, entry 5. Prepared by using procedure A, from β-bromostyrene and 1,3-dioxolane with Me_2Zn (4 equiv). The reaction was worked up with 1.0 M NaOH instead of HCl to avoid formation of cinnemaldehyde. DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.43 (d, J=7.0 Hz, 2H), 7.34 (t, J=7.2 Hz, 2H), 7.30–7.25 (m, 1H), 6.79 (d, J=16.0 Hz, 1H), 6.18 (dd, J=16.0, 6.0 Hz, 1H), 5.44 (d, J=6.0 Hz, 1H), 4.10–4.02 (m, 2H), 4.01–3.92 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ=135.9, 135.0, 128.7, 128.5, 127.1, 125.2, 104.0, 65.2 ppm; MS: *m/z*: 176 $[M]^+$; NMR data are in accordance with the reported values.[3d]

(*E*)-4-Styryl-1,3-dioxolane: Table 2, entry 5. Prepared by using procedure A, from β-bromostyrene and 1,3-dioxolane with Me_2Zn and a reaction time of two days. DCVC eluting with heptane containing 2% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.33–7.29 (m, 2H), 7.27–7.22 (m, 2H), 7.21–7.15 (m, 1H), 6.60 (d, J=15.0 Hz, 1H), 6.10 (dd, J=15.0, 7.5 Hz, 1H), 5.05 (s, 1H), 4.92 (s, 1H), 4.53 (q, J=7.5 Hz, 1H), 4.03 (dd, J=8.0, 6.7 Hz, 1H), 3.55 ppm (dd, J=8.0, 6.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ=136.2, 133.5, 128.2, 126.7, 126.3, 95.6, 77.0, 69.9 ppm; MS: *m/z*: 176 $[M]^+$. HRMS: *m/z* calcd for $C_{11}H_{13}O_2$: 177.0910 $[M+H]^+$; found: 177.0909.

(*E*)-2-Methyl-2-styryl-1,3-dioxolane: Table 2, entry 6. Prepared by using procedure A, from β-bromostyrene and 2-methyl-1,3-dioxolane with Me_2Zn (3 equiv). The reaction was worked up with 1.0 M NaOH instead of HCl to avoid formation of 4-phenylbut-3-en-2-one. DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.40–7.35 (m, 2H), 7.34–7.26 (m, 2H), 7.26–7.19 (m, 1H), 6.69 (d, J=16.0 Hz, 1H), 6.14 (d, J=16.0 Hz, 1H), 4.02–3.89 (m, 4H), 1.55 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ=136.3, 129.9, 129.8, 128.7, 128.0, 126.8, 107.7, 64.7, 25.3 ppm; MS:

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m/z: 190 $[M]^+$. NMR data are in accordance with the reported values.[24]

(*E*)-(3-Ethoxybut-1-en-1-yl)benzene: Table 2, entry 7. Prepared by using procedure A, from β-bromostyrene and diethyl ether with Me_2Zn (4 equiv) and a reaction time of two days. DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (d, J = 7.3 Hz, 2H), 7.30 (t, J = 7.5 Hz, 2H), 7.22 (t, J = 7.3 Hz, 1H), 6.51 (d, J = 15.9 Hz, 1H), 6.12 (dd, J = 15.9, 7.5 Hz, 1H), 3.99 (p, J = 6.7 Hz, 1H), 3.63–3.50 (m, 1H), 3.46–3.35 (m, 1H), 1.34 (d, J = 6.4 Hz, 3H), 1.21 ppm (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.8, 132.2, 130.8, 128.6, 127.6, 126.5, 76.4, 63.6, 21.8, 15.5 ppm; MS: *m/z*: 176 $[M]^+$. NMR data are in accordance with the reported values.[25]

(*E*)-(3-Isopropoxy-3-methylbut-1-en-1-yl)benzene: Table 2, entry 8. Prepared by using procedure A, from β-bromostyrene and diisopropyl ether with Me_2Zn (4 equiv) and a reaction time of two days. DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, J = 7.3 Hz, 2H), 7.25 (t, J = 7.6 Hz, 2H), 7.19–7.13 (m, 1H), 6.39 (d, J = 16.4 Hz, 1H), 6.19 (d, J = 16.4 Hz, 1H), 3.65 (hept, J = 6.2 Hz, 1H), 1.30 (s, 6H), 1.05 ppm (d, J = 6.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.2, 136.6, 128.7, 128.4, 127.6, 126.5, 75.4, 65.0, 27.2, 25.2 ppm; MS: *m/z*: 204 $[M]^+$; HRMS: *m/z* calcd for $C_{14}H_{21}O$: 205.1582 $[M+H]^+$; found: 205.1582.

(*E*)-1-Methyl-2-styrylpyrrolidine: Table 2, entry 9. Prepared by using procedure B, from β-bromostyrene and *N*-methylpyrrolidine with Me_2Zn (4 equiv) and a reaction time of two days to afford the product as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.37 (m, 2H), 7.34–7.28 (m, 2H), 7.25–7.19 (m, 1H), 6.51 (d, J = 15.8 Hz, 1H), 6.12 (dd, J = 15.8, 8.4 Hz, 1H), 3.19–3.12 (m, 1H), 2.67 (dd, J = 16.2, 8.3 Hz, 1H), 2.31 (s, 3H), 2.24–2.20 (m, 1H), 2.06–1.99 (m, 1H), 1.95–1.85 (m, 1H), 1.81–1.70 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.0, 132.1, 131.6, 128.5, 127.3, 126.2, 69.6, 56.7, 40.3, 32.2, 22.3 ppm; MS: *m/z*: 187 $[M]^+$. HRMS: *m/z* calcd for $C_{13}H_{18}N$: 188.1434 $[M+H]^+$; found: 188.1436.

(*E*)-2-(4-Chlorostyryl)tetrahydrofuran: Table 3, entry 1. Prepared by using procedure A, from (*E*)-1-(2-bromovinyl)-4-chlorobenzene and THF with Me_2Zn (3 equiv). DCVC eluting with heptane containing 2% increments of ethyl acetate per fraction gave the product as colorless crystals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.24 (m, 4H), 6.54 (d, J = 15.9 Hz, 1H), 6.19 (dd, J = 15.9, 6.5 Hz, 1H), 4.50–4.42 (m, 1H), 4.01–3.92 (m, 1H), 3.89–3.80 (m, 1H), 2.18–2.07 (m, 1H), 2.04–1.88 (m, 2H), 1.76–1.64 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.4, 133.1, 131.3, 129.2, 128.7, 127.7, 79.5, 68.3, 32.4, 26.0 ppm; MS: *m/z*: 208 $[M]^+$. NMR data are in accordance with the reported values.[10]

(*E*)-2-(4-Bromostyryl)tetrahydrofuran: Table 3, entry 2. Prepared by using procedure A, from (*E*)-1-bromo-4-(2-bromovinyl)benzene and THF with Me_2Zn (3 equiv). DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as colorless crystals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.39 (m, 2H), 7.26–7.20 (m, 2H), 6.52 (d, J = 15.8 Hz, 1H), 6.20 (dd, J = 15.8, 6.5 Hz, 1H), 4.49–4.41 (m, 1H), 4.02–3.91 (m, 1H), 3.88–3.79 (m, 1H), 2.18–2.07 (m, 1H), 2.04–1.88 (m, 2H), 1.76–1.64 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.9, 131.7, 131.5, 129.3, 128.1, 121.3, 79.6, 68.3, 32.4, 26.0 ppm; MS: *m/z*: 254, 252 $[M]^+$; NMR data are in accordance with the reported values.[3d]

(*E*)-2-(4-Fluorostyryl)tetrahydrofuran: Table 3, entry 3. Prepared by using procedure A, from (*E*)-1-(2-bromovinyl)-4-fluorobenzene and THF with Me_2Zn (3 equiv). DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (dd, J = 8.7, 5.4 Hz, 2H), 6.98 (t, J = 8.7 Hz, 2H), 6.54 (d, J = 15.8 Hz, 1H), 6.12 (dd, J = 15.8, 6.6 Hz, 1H), 4.45 (q, J = 6.7 Hz, 1H), 3.96 (q, J = 7.5 Hz, 1H), 3.83 (q, J = 7.9 Hz, 1H), 2.17–2.06 (m, 1H), 2.04–1.87 (m, 2H), 1.75–1.64 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.3 (d, J = 246.5 Hz), 133.1 (d, J = 3.3 Hz), 130.4 (d, J = 2.2 Hz), 129.3, 128.0 (d, J = 8.0 Hz), 115.5 (d, J = 21.6 Hz), 79.6, 68.2, 32.5, 26.0 ppm; MS: *m/z*: 192 $[M]^+$. NMR data are in accordance with the reported values.[3d]

(*E*)-2-(2-Chlorostyryl)tetrahydrofuran: Table 3, entry 4. Prepared by using procedure A, from (*E*)-1-(2-bromovinyl)-2-chlorobenzene and THF with Me_2Zn (3 equiv) and a reaction time of three days. DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (dd, J = 7.6, 1.8 Hz, 1H), 7.33 (dd, J = 7.8, 1.5 Hz, 1H), 7.24–7.10 (m, 2H), 6.98 (d, J = 15.8 Hz, 1H), 6.20 (dd, J = 15.8, 6.5 Hz, 1H), 4.51 (q, J = 6.9 Hz, 1H), 3.97 (dd, J = 14.4, 7.5 Hz, 1H), 3.84 (td, J = 7.9, 6.3 Hz, 1H), 2.19–2.08 (m, 1H), 2.04–1.87 (m, 2H), 1.77–1.66 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.0, 133.5, 133.1, 129.7, 128.5, 126.9, 126.8, 126.6, 79.5, 68.2, 32.4, 25.9 ppm; MS: *m/z*: 208 $[M]^+$; HRMS: *m/z* calcd for $C_{12}H_{14}ClO$: 209.0733 $[M+H]^+$; found: 209.0731.

(*E*)-2-(4-Methylstyryl)tetrahydrofuran: Table 3, entry 5. Prepared by using procedure A, from (*E*)-1-(2-bromovinyl)-4-methylbenzene and THF with Me_2Zn (3 equiv). DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.56 (d, J = 15.8 Hz, 1H), 6.17 (dd, J = 15.8, 6.7 Hz, 1H), 4.47 (q, J = 7.0 Hz, 1H), 3.98 (dd, J = 14.3, 7.5 Hz, 1H), 3.84 (td, J = 7.9, 6.2 Hz, 1H), 2.34 (s, 3H), 2.19–2.07 (m, 1H), 2.06–1.88 (m, 2H), 1.78–1.66 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.4, 134.2, 130.5, 129.6, 129.3, 126.5, 79.9, 68.2, 32.5, 26.0, 21.3 ppm; MS: *m/z*: 188 $[M]^+$; NMR data are in accordance with the reported values.[3d]

(*E*)-4-(2-(Tetrahydrofuran-2-yl)vinyl)phenol: Table 3, entry 6. Prepared by using procedure A, from (*E*)-4-(2-bromovinyl)phenol and THF with Me_2Zn (3 equiv) and a reaction time of two days. DCVC eluting with heptane containing 5% increments of ethyl acetate per fraction gave the product as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16 (d, J = 8.5 Hz, 2H), 7.10 (s, 1H), 6.75 (d, J = 8.5 Hz, 2H), 6.48 (d, J = 15.8 Hz, 1H), 5.99 (dd, J = 15.8, 7.2 Hz, 1H), 4.49 (q, J = 6.8 Hz, 1H), 3.99 (dd, J = 14.9, 7.1 Hz, 1H), 3.87 (td, J = 7.9, 6.0 Hz, 1H), 2.19–2.07 (m, 1H), 2.05–1.89 (m, 2H), 1.79–1.65 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.0, 131.2, 129.0, 127.9, 127.2, 115.7, 80.5, 68.1, 32.5, 26.0 ppm; MS: *m/z*: 190 $[M]^+$; HRMS: *m/z* calcd for $C_{12}H_{15}O_2$: 191.1067 $[M+H]^+$; found: 191.1067.

(*E*)-2-(4-Methoxystyryl)tetrahydrofuran: Table 3, entry 7. Prepared by using procedure A, from (*E*)-1-(2-bromovinyl)-4-methoxybenzene and THF with Me_2Zn (3 equiv) and a reaction time of two days. DCVC eluting with heptane containing 2% increments of ethyl acetate per fraction gave the product as a colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 6.53 (d, J = 15.8 Hz, 1H), 6.07 (dd, J = 15.8, 6.8 Hz, 1H), 4.44 (q, J = 7.0 Hz, 1H), 3.96 (dd, J = 14.3, 7.6 Hz, 1H), 3.87–3.79 (m, 1H), 3.78 (s, 3H), 2.17–2.05 (m, 1H), 2.05–1.86 (m, 2H), 1.75–1.64 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.2, 130.1, 129.7, 128.3, 127.7, 114.0, 79.9, 68.1, 55.3, 32.5, 26.0 ppm; MS: *m/z*: 204 $[M]^+$. NMR data are in accordance with the reported values.[3c]

(*E*)-2-(3,4-Methylenedioxystyryl)tetrahydrofuran: Table 3, entry 8. Prepared by using procedure A, from (*E*)-5-(2-bromovinyl)benzo[*d*][1,3]dioxole and THF with Me_2Zn (3 equiv) and a reaction time of three days. DCVC eluting with heptane containing 2% increments of ethyl acetate per fraction gave the product as a colorless oil.

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, J = 1.5 Hz, 1H), 6.79 (dd, J = 8.0, 1.5 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 6.48 (d, J = 15.8 Hz, 1H), 6.02 (dd, J = 15.8, 6.7 Hz, 1H), 5.91 (s, 2H), 4.41 (q, J = 7.0 Hz, 1H), 3.94 (dd, J = 14.4, 7.5 Hz, 1H), 3.81 (td, J = 7.9, 6.3 Hz, 1H), 2.15–2.04 (m, 1H), 2.03–1.84 (m, 2H), 1.73–1.61 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.0, 147.2, 131.4, 130.2, 128.8, 121.1, 108.2, 105.8, 101.1, 79.7, 68.1, 32.5, 26.0 ppm; MS: *m/z*: 218 $[M]^+$; HRMS: *m/z* calcd for $C_{13}H_{15}O_3$: 219.1021 $[M+H]^+$; found: 219.1044.

(*E*)-2-(2-(Naphthalen-2-yl)vinyl)tetrahydrofuran: Table 3, entry 9. Prepared by using procedure A, from (*E*)-2-(2-bromovinyl)naphthalene and THF with initially Me_2Zn (3 equiv). After heating to reflux overnight, additional $MnCl_2$ (10%) and Me_2Zn (3 equiv) were added and the reaction was heated to reflux for another 16 h. DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a pale-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73–7.62 (m, 4H), 7.51 (dd, J = 8.6, 1.6 Hz, 1H), 7.39–7.30 (m, 2H), 6.66 (d, J = 15.8 Hz, 1H), 6.25 (dd, J = 15.8, 6.6 Hz, 1H), 4.44 (q, J = 6.9 Hz, 1H), 3.91 (dd, J = 14.4, 7.5 Hz, 1H), 3.78 (td, J = 7.9, 6.3 Hz, 1H), 2.13–2.01 (m, 1H), 1.97–1.82 (m, 2H), 1.72–1.61 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 134.5, 133.7, 133.1, 131.1, 130.7, 128.2, 128.1, 127.8, 126.5, 126.3, 125.9, 123.8, 79.9, 68.3, 32.6, 26.1 ppm; MS: *m/z*: 224 $[M]^+$; HRMS: *m/z* calcd for $C_{16}H_{17}O$: 225.1274 $[M+H]^+$; found: 225.1275.

2-(1*H*-Inden-2-yl)tetrahydrofuran: Table 3, entry 10. Prepared by using procedure A, from 2-bromoindene and THF with initially Me_2Zn (3 equiv). After heating to reflux for three days, additional $MnCl_2$ (10%) and Me_2Zn (3 equiv) were added and the reaction was heated to reflux for another 16 h. DCVC eluting with heptane containing 1% increments of ethyl acetate per fraction gave the product as a colorless oil. In addition, 2-bromoindene was recovered in 28% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 (dd, J = 7.3, 0.5 Hz, 1H), 7.33 (d, J = 7.4 Hz, 1H), 7.25 (dd, J = 9.3, 5.6 Hz, 1H), 7.15 (td, J = 7.4, 1.2 Hz, 1H), 6.73 (s, 1H), 4.84 (t, J = 7.0 Hz, 1H), 4.06–3.97 (m, 1H), 3.93–3.85 (m, 1H), 3.41 (d, J = 0.7 Hz, 2H), 2.27–2.15 (m, 1H), 2.07–1.96 (m, 2H), 1.91–1.82 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.6, 144.8, 143.4, 126.8, 126.4, 124.4, 123.8, 120.8, 77.9, 68.3, 38.2, 32.3, 26.1 ppm; MS: *m/z*: 186 $[M]^+$; HRMS: *m/z* calcd for $C_{13}H_{15}O$: 187.1117 $[M+H]^+$; found: 187.1119.

(*E*)-1-Methyl-2-(3,4-methylenedioxystyryl)piperidine: Table 4, entry 1. Prepared by using procedure B, from *N*-methylpiperidine and purified by flash chromatography (heptane/Et_3N, 98:2) to give the product as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, J = 1.4 Hz, 1H), 6.78 (dd, J = 8.0, 1.4 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.39 (d, J = 15.8 Hz, 1H), 5.97 (dd, J = 16.0, 8.7 Hz, 1H), 5.94 (s, 2H), 2.91 (d, J = 11.4 Hz, 1H), 2.46–2.38 (m, 1H), 2.23 (s, 3H), 2.02 (dt, J = 11.6, 3.5 Hz, 1H), 1.75 (dd, J = 12.6, 2.9 Hz, 1H), 1.70–1.53 (m, 3H), 1.52–1.40 (m, 1H), 1.35–1.24 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.1, 147.1, 132.1, 131.8, 130.3, 120.8, 108.4, 105.8, 101.1, 68.2, 56.6, 44.8, 33.7, 26.2, 24.1 ppm; MS: *m/z*: 245 $[M]^+$. HRMS: *m/z* calcd for $C_{15}H_{20}NO_2$: 246.1489 $[M+H]^+$; found: 246.1490.

(*E*)-*N*-(3,4-Methylenedioxycinnamyl)piperidine: Table 4, entry 1. Prepared by using procedure B from *N*-methylpiperidine and isolated as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92 (d, J = 1.3 Hz, 1H), 6.83–6.76 (m, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.42 (d, J = 15.8 Hz, 1H), 6.15 (dt, J = 15.7 Hz, 1H), 5.94 (s, 2H), 3.16 (d, J = 6.8 Hz, 2H), 2.50 (br s, 4H), 1.76–1.56 (m, 4H), 1.51–1.41 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.1, 147.3, 143.5, 133.4, 131.4, 121.1, 108.4, 105.9, 101.2, 61.7, 54.4, 25.6, 24.2 ppm; MS: *m/z*: 245 $[M]^+$; HRMS: *m/z* calcd for $C_{15}H_{20}NO_2$: 246.1489 $[M+H]^+$; found: 246.1494.

(*E*)-1-Ethyl-2-(3,4-methylenedioxystyryl)piperidine: Table 4, entry 7. Prepared by using procedure B from *N*-ethylpiperidine and purified by flash chromatography (heptane/Et_2O/Et_3N, 96:3:1→95:4:1) to give the product as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.90 (d, J = 1.5 Hz, 1H), 6.77 (dd, J = 8.0, 1.5 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.38 (d, J = 15.8 Hz, 1H), 6.00 (d, J = 15.8 Hz, 1H), 5.92 (s, 2H), 3.00 (dt, J = 11.3, 3.1 Hz, 1H), 2.85 (dq, J = 14.6, 7.3 Hz, 1H), 2.75–5.65 (m, 1H), 2.24 (dq, J = 13.9, 7.0 Hz, 1H), 2.01 (dt, J = 11.5, 2.9 Hz, 1H), 1.79–1.41 (m, 5H), 1.37–1.19 (m, 1H), 1.00 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.1, 147.1, 131.8, 131.8, 130.1, 120.8, 108.3, 105.7, 101.1, 65.7, 51.5, 49.4, 33.8, 25.9, 24.0, 10.9 ppm; MS: *m/z*: 259 $[M]^+$; HRMS: *m/z* calcd for $C_{16}H_{22}NO_2$: 260.1645 $[M+H]^+$; found: 260.1643.

(*E*)-*N*-[1-(3,4-Methylenedioxystyryl)ethyl]piperidine: Table 4, entry 7. Prepared by using procedure B from *N*-ethylpiperidine and isolated as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92 (d, J = 1.4 Hz, 1H), 6.78 (dd, J = 8.0, 1.5 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.33 (d, J = 15.8 Hz, 1H), 6.06 (dd, J = 15.8, 8.0 Hz, 1H), 5.93 (s, 2H), 3.09–3.02 (m, 1H), 2.57–2.38 (m, 4H), 1.60 (dt, J = 11.0, 5.6 Hz, 4H), 1.45–1.41 (m, 2H), 1.24 ppm (d, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.1, 147.1, 131.8, 130.9, 130.3, 120.9, 108.4, 105.7, 101.1, 63.1, 51.1, 26.3, 24.7, 17.8 ppm; MS: *m/z*: 259 $[M]^+$. HRMS: *m/z* calcd for $C_{16}H_{22}NO_2$: 260.1645 $[M+H]^+$; found: 260.1649.

(*E*)-1-Ethyl-2-(3,4-methylenedioxystyryl)pyrrolidine: Table 4, entry 9. Prepared by using procedure B from *N*-ethylpyrrolidine and purified by flash chromatography (heptane/Et_3N, 98:2) to give the product as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92 (d, J = 1.6 Hz, 1H), 6.76 (dd, J = 8.0, 1.6 Hz, 1H), 6.72 (d, J = 8.0 Hz, 1H), 6.36 (d, J = 15.7 Hz, 1H), 5.92 (dd, J = 15.6, 8.5 Hz, 1H), 5.91 (s, 2H), 3.22 (dt, J = 8.4, 2.4 Hz, 1H), 2.86 (dq, J = 12.0, 7.5 Hz, 1H), 2.75 (dd, J = 16.1, 8.4 Hz, 1H), 2.12–1.62 (m, 6H), 1.08 ppm (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.1, 147.1, 131.7, 131.1, 130.9, 120.9, 108.3, 105.8, 101.1, 68.6, 53.1, 48.2, 32.0, 22.2, 13.9 ppm; MS: *m/z*: 245 $[M]^+$; HRMS: *m/z* calcd for $C_{15}H_{20}NO_2$: 246.1489 $[M+H]^+$; found: 246.1492.

(*E*)-*N*-[1-(3,4-Methylenedioxystyryl)ethyl]pyrrolidine: Table 4, entry 9. Prepared by using procedure B from *N*-ethylpyrrolidine and isolated as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (d, J = 1.4 Hz, 1H), 6.71 (dd, J = 8.0, 1.5 Hz, 1H), 6.67 (d, J = 8.00 Hz, 1H), 6.30 (d, J = 15.8 Hz, 1H), 5.98 (dd, J = 15.8, 8.5 Hz, 1H), 5.86 (s, 2H), 2.79 (dq, J = 13.0, 6.4 Hz, 1H), 2.58–2.40 (m, 4H), 2.00–1.57 (m, 4H), 1.20 ppm (d, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.1, 147.1, 132.5, 131.9, 129.3, 120.9, 108.4, 105.8, 101.1, 63.1, 52.4, 23.5, 21.2 ppm; MS: *m/z*: 245 $[M]^+$; HRMS: *m/z* calcd for $C_{15}H_{20}NO_2$: 246.1489 $[M+H]^+$; found: 246.1486.

(*E*)-*N*,*N*-Diethyl-[1-(3,4-methylenedioxystyryl)ethyl]amine: Table 4, entry 10. Prepared by using procedure B from triethylamine and purified by flash chromatography (heptane/Et_3N, 99:1) to give the product as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92 (d, J = 1.5 Hz, 1H), 6.79 (dd, J = 8.0, 1.5 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.34 (d, J = 15.9 Hz, 1H), 6.05 (dd, J = 15.9, 7.4 Hz, 1H), 5.93 (s, 2H), 3.45–3.39 (m, 1H), 2.66–2.50 (m, 4H), 1.21 (d, J = 6.6 Hz, 3H), 1.04 ppm (t, J = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.1, 147.0, 132.1, 131.7, 129.6, 120.8, 108.4, 105.7, 101.1, 57.5, 43.6, 17.6, 13.2 ppm; MS: *m/z*: 247 $[M]^+$; HRMS: *m/z* calcd for $C_{15}H_{22}NO_2$: 248.1645 $[M+H]^+$; found: 246.1646.

(*E*)-*N*,*N*-Dipropyl-[1-(3,4-methylenedioxystyryl)propyl]amine: Table 4, entry 11. Prepared by using procedure B from tripropylamine and purified by flash chromatography (heptane/Et_2O, 4:1) to give the product as a light-brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.93 (d, J = 1.4 Hz, 1H), 6.79 (dd, J = 8.0, 1.4 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 6.30 (d, J = 15.8 Hz, 1H), 5.96 (dd, J = 16.0, 8.7 Hz, 1H), 5.94 (s, 2H), 2.99 (td, J = 8.3, 6.3 Hz, 1H), 2.48 (ddd, J = 12.9, 8.8, 7.0 Hz, 2H), 2.38–2.28 (m, 2H), 1.65 (m, 1H), 1.54–1.35 (m, 5H), 0.92–0.85 ppm (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.1, 146.9,

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132.2, 131.3, 128.6, 120.8, 108.4, 105.7, 101.1, 65.1, 52.8, 25.9, 22.0, 12.1, 11.6 ppm; MS: *m/z*: 289 $[M]^+$. HRMS: *m/z* calcd for $C_{18}H_{28}NO_2$: 290.2115 $[M+H]^+$; found: 290.2110.

(*E*)-4-Methyl-2-(3,4-methylenedioxystyryl)morpholine: Table 4, entry 13. Prepared by using procedure B from *N*-methylmorpholine and purified by flash chromatography (toluene/Et_2O/Et_3N, 20:79:1) to give the desired product as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.91$ (d, $J = 1.4$ Hz, 1H), 6.80 (dd, $J = 8.0$, 1.4 Hz, 1H), 6.75 (d, $J = 8.0$ Hz, 1H), 6.53 (d, $J = 15.9$ Hz, 1H), 5.95 (s, 2H), 5.83 (dd, $J = 15.9$, 8.7 Hz, 1H), 3.86 (d, $J = 11.4$ Hz, 1H), 3.79–3.67 (m, 2H), 3.42 (t, $J = 10.6$ Hz, 1H), 2.82–2.75 (m, 2H), 2.37 (dt, $J = 11.6$, 3.2 Hz, 1H), 2.30 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 148.2$, 147.6, 134.1, 131.0, 124.9, 121.3, 108.4, 105.8, 101.3, 71.1, 67.0, 66.8, 54.8, 43.7 ppm; MS: *m/z*: 247 $[M]^+$. HRMS: *m/z* calcd for $C_{14}H_{18}NO_3$: 248.1281 $[M+H]^+$; found: 248.1283.

(*E*)-*N*-Methyl-*N*-(3,4-methylenedioxycinnamyl)formamide: Table 4, entry 14. Prepared by using procedure B from *N*,*N*-dimethylformamide and purified by flash chromatography (heptane/EtOAc, 3:7) to give the product as a light-brown oil. Major rotamer: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.14$ (s, 1H), 6.90 (s, 1H), 6.83–6.71 (m, 2H), 6.45 (d, $J = 15.8$ Hz, 1H), 6.00–5.83 (m, 3H), 3.95 (d, $J = 5.8$ Hz, 2H), 2.86 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 162.8$, 148.3, 147.8, 133.5, 130.5, 122.2, 121.5, 108.5, 105.8, 101.3, 51.8, 34.2 ppm; Minor rotamer: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.09$ (s, 1H) 6.90 (s, 1H), 6.83–6.71 (m, 2H), 6.45 (d, $J = 15.8$ Hz, 1H), 6.00–5.83 (m, 3H), 4.07 (d, $J = 6.5$ Hz, 2H), 2.92 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 162.5$, 148.2, 147.6, 133.4, 130.9, 121.6, 121.3, 108.4, 105.8, 101.3, 46.2, 29.6 ppm; MS: *m/z*: 219 $[M]^+$; HRMS: *m/z* calcd for $C_{12}H_{14}NO_3$: 220.0968 $[M+H]^+$; found: 220.0968.

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