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γ-Halo-enones: A Method for their Synthesis from Arylacyl Halides and Their Application to the Preparation of Five-Membered Ring Heterocycles

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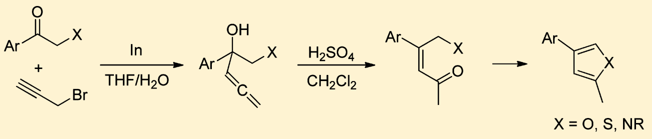
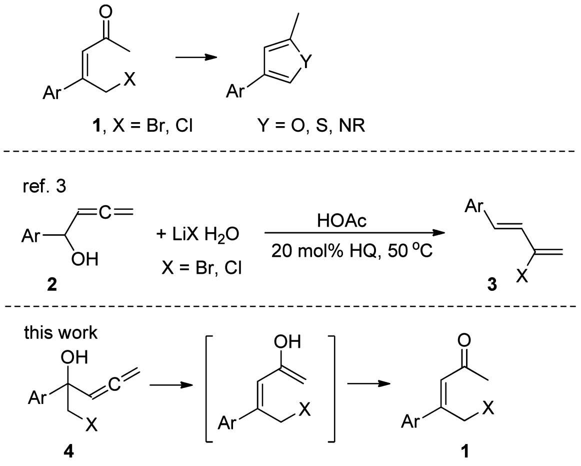
S *Supporting Information*

ABSTRACT: A simple method has been developed for synthesis of γ-halo-enones. The approach employs a sequence involving initial indium-mediated allenylation reactions of phenacyl halides with propargyl bromide. This process is followed by acid-promoted rearrangement reactions of the formed homoallenic halohydrins. The new method can be incorporated into routes for the efficient synthesis of various five-membered heterocyclic compounds.



Recently, gold- and other metal-promoted nucleophilic cyclization reactions of functionalized allenes have become powerful methods to prepare various five-membered heterocyclic substances.[1] Although γ-halo-enones **1**, which have a functionally intriguing skeleton, are useful intermediates in the synthesis of a variety of heterocycles, such as furans, pyrroles, and thiophenes,[2] their preparation and properties have not yet been fully explored. In fact, in this family only (*Z*)-1,3-bis(aryl)-4-bromo-2-buten-1-ones have been studied. Inspiration for the current study came from both a recognition of this deficiency and earlier observations that demonstrated that 1-aryl-3-halo-1,3-dienes **3** can be prepared through S_N2'-type addition–elimination reactions of 1-aryl-2,3-allenols **2** with lithium halides in acetic acid (Scheme 1).[3] In this effort we have successfully explored a new strategy for the preparation of γ-halo-enones **1** that is based on a proposed rearrangement reaction of homoallenic halohydrin **4**.

Scheme 1



The feasibility of the new approach to the preparation of γ-halo-enones **1** is critically dependent on the availability of a method for the efficient synthesis of homoallenic halohydrins **4**. Although an earlier procedure to access these targets, utilizing selective allenylation reactions of allenylboronate pinacol esters with α-bromoacetophenone, has been described,[4,5] the cost and tediousness of the required operations make it nonideal for most applications. We envisaged that a simple approach to the synthesis of homoallenic halohydrin would involve selective allenylation reactions of arylacyl halides **5** with propargyl bromide.

Previously, we reported that homoallylic bromohydrins are generated in indium-mediated allylation reactions of α-bromoketones in water.[6] To explore the applicability of this strategy, indium-mediated allenylation reactions of arylacyl halides with propargyl bromide in aqueous media were investigated. These reactions were found to produce the desired allenic halohydrins in good yields along with small amounts of both the propargyl analogues and corresponding methylketones, formed by direct reduction of the arylacyl halides (Table 1). Importantly, the allenylation versus propargylation product ratios are at least 3:1. Unfortunately, chromatographic purifications of the desired homoallenic halohydrins are difficult in most cases because the allene products and methyl ketones have overlapping chromatographic mobilities. In fact, only homoallenic bromohydrin **4c,h,i** can be isolated as a pure substance by using a meticulous chromatographic procedure. While the analogues **4a,b** and **4d–g** can be isolated in pure form by first treating the crude reaction mixtures with sodium borohydride followed by chromatography, in these cases partial reductive removal of bromine from the homoallenic bromohydrins takes place. As a

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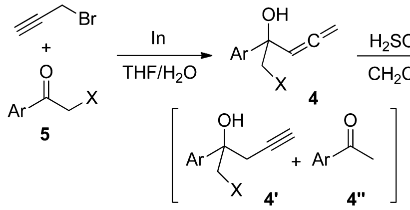
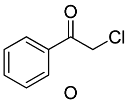
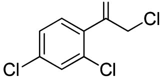
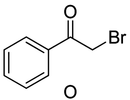
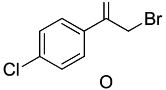
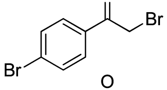
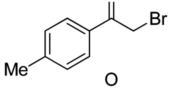
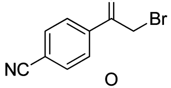
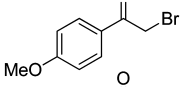
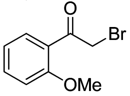
Table 1. Indium-Mediated Allenylation[a] and γ-Halo-enone-Forming Acid-Promoted Rearrangement Reactions[b]



entry	substrate 5	4, yield (%)	4 : 4' : 4''[c]	1, yield (%)[b]
1	 **5a**	--	72 : 23 : 5	45[d]
2	 **5b**	--	76 : 17 : 7	52[d]
3	 **5c**	62	64 : 14 : 22	68
4	 **5d**	--	65 : 20 : 15	50[d]
5	 **5e**	--	80 : 11 : 9	56[d]
6	 **5f**	--	62 : 13 : 25	41[d]
7	 **5g**	--	72 : 17 : 11	50[d]
8	 **5h**	60	61 : 6 : 33	52
9	 **5i**	66	67 : 13 : 20	56

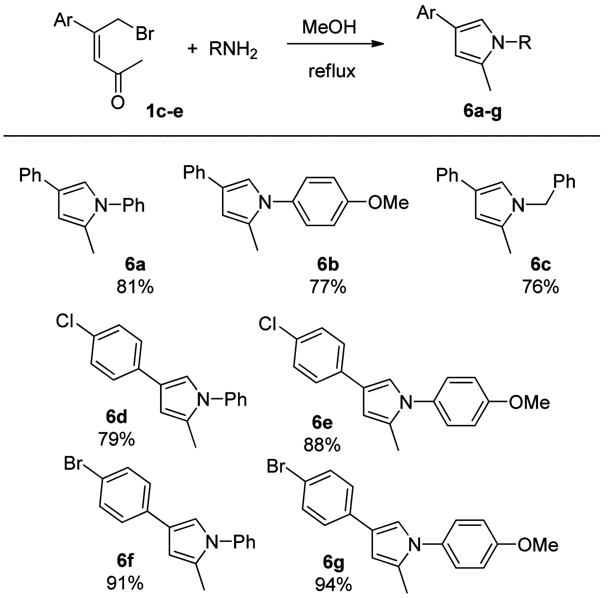
[a] Condition: **5** (1.0 mmol), propargyl bromide (133.8 μL, 1.8 mmol), and indium (99.99%, 325 mesh, 172.2 mg, 1.5 mmol) in THF (1.5 mL)/water (0.5 mL) at rt. [b] Condition: **4** (0.8 mmol) and H_2SO_4 (0.05 mL) in CH_2Cl_2 (5 mL) at rt for 2 h. [c] Ratio was determined by ^{1}H NMR. [d] Overall yield from **5**.

consequence of this issue, crude product mixtures containing the homoallenic halohydrins **4** and methyl ketone **4″** were directly employed in the following γ-halo-enone forming reactions. It is necessary to remove the propargylation product **4′** from the crude product mixture because **4′** and **1** have overlapping chromatographic mobilities.

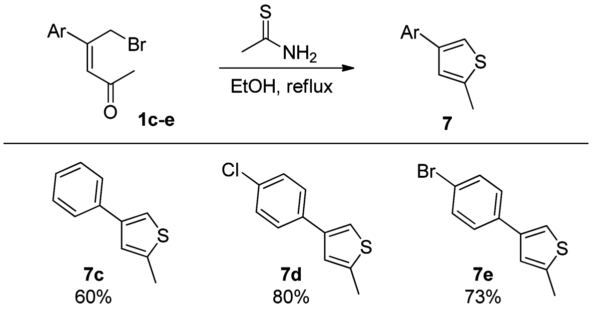
It is known that acid-catalyzed Nazarov-type cyclization reactions of terminally disubstituted tertiary α-allenic alcohols take place to generate benzofulvenes[7] and that these processes occur more slowly when terminally monosubstituted allenes are employed as substrates. This observation suggests that terminally nonsubstituted homoallenic halohydrins **4** might react under acid-promoted conditions by a hydroxyl rearrangement-type pathway to produce the corresponding γ-halo-enones. An exploration using bromohydrin **4e** and a variety of acid catalysts demonstrated the γ-bromo-enone **1e** generating reaction does indeed take place in moderately high efficiency, especially when sulfuric acid is employed as the promoter. It is worth noting that the yield of the process is the same independent of whether a crude mixture containing homoallenic bromohydrin **4c** and acetophenone **4c″** or a meticulously purified sample of **4c** is used as the starting material. Finally, we observed that the γ-halo-enones **1** readily decompose at room temperature and even slowly degrade when stored in a freezer. The stability of these substances is affected by the nature and position of substituents as exemplified by the observation that **1h** is less stable than **1i** and that **1a**−**e** are relatively more stable.

An effort was conducted to explore applications of the γ-bromo-enones **1** as intermediates in the synthesis of a variety of five-membered heterocyclic compounds. As demonstrated by the processes displayed in Schemes 2, 3, and 4, the γ-bromo-

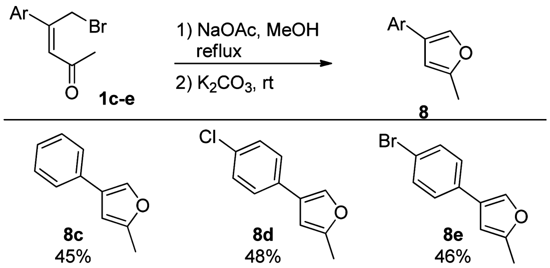
Scheme 2. Formation of 1,2,4-Substituted Pyrroles



Scheme 3. Formation of 2,4-Substituted Thiophenes



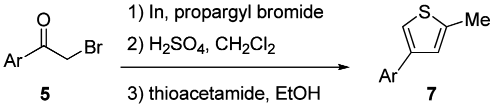
Scheme 4. Formation of 2,4-Substituted Furans

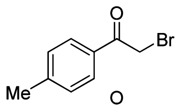
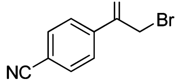
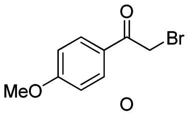
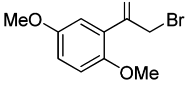
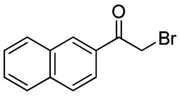
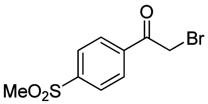
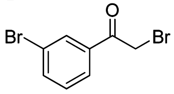


enones **1** can be employed as starting materials for reactions that generate pyrroles, thiophenes, and furans. Interestingly, the furan-forming reactions take place through the intermediacy of γ-hydroxy-enones, which then undergo ready dehydration and tandem cycloaromatization when treated with mild base to form furans.[8] The success of the heterocyclic ring-forming reactions suggests that the acid-promoted rearrangement reactions of homoallenic bromohydrins give (*Z*)-γ-bromo-enones **1**. This stereochemical proposal was confirmed by performing X-ray crystallographic analysis on **1b** and **1g**.[9]

Finally, owing to the intrinsic instability of γ-bromo-enones **1** (see above), a concise procedure was developed for the three-step synthesis of thiophenes from arylacyl bromides, in which only the ultimate heterocyclic products were subjected to purification (Table 2). Using this approach, it was possible to prepare substituted thiophenes from readily available arylacyl bromides in good overall yields even in those cases where the intermediate γ-bromo-enones are highly unstable (**1j**, **1k**) or difficult to purify (**1l**).

Table 2. Preparation of Substituted Thiophenes from Phenacyl Bromides



entry	substrate	**7**, yield (%)
1	 **5f**	32
2	 **5g**	44
3	 **5h**	22
4	 **5j**	30
5	 **5k**	22
6	 **5l**	36
7	 **5m**	46

In conclusion, the studies described above have led to the development of a new and simple method for the preparation of 5-halo-4-aryl-pent-3-en-2-ones **1** from arylacyl halides and applications of these substances to the synthesis of substituted pyrroles, thiophenes, and furans.

■ EXPERIMENTAL SECTION

General Information and Materials. All commercially available chemicals were used without further purification. TLC analyses were run on a TLC glass plate (Silica gel 60 F254) and were visualized using UV and a solution of phosphomolybdic acid in ethanol (5 wt %) or *p*-anisaldehyde stain. Flash chromatography was performed using silica gel (70−230 mesh). ^{1}H NMR spectra were recorded on a 300 MHz spectrometer. ^{13}C NMR spectra were recorded on a 75 MHz spectrometer with complete proton decoupling. Chemical shifts are reported relative to $CHCl_3$ [δ_H 7.24, δ_C (central line) 77.0]. Mass spectra were recorded under electron spray interface (ESI) conditions, and high-resolution mass spectra were recorded by electron impact ionization with magnetic sector or orbitrap analyzer.

General Procedure for Indium-Mediated Allenylation Reactions of Arylacyl Halide 5 with Propargyl Bromide. A mixture of propargyl bromide (133.8 μL, 1.8 mmol), indium powder (325 mesh, 172.2 mg, 1.5 mmol), and arylacyl halide **5** (1.0 mmol) in THF/H_2O (1.5 mL/0.5 mL) was stirred at ambient temperature. The reaction was monitored by TLC until no starting material was observed, and normally the reaction was stirred at rt overnight. Et_2O (10 mL) and water (10 mL) were then added to the reaction, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with Et_2O (5 mL × 2). The combined organic layers were washed with brine (3 mL), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:20) as eluent to give the product **4** and the corresponding methyl ketone **4″**, which were used for the next step directly. Pure compounds **4c**, **4h**, and **4i** were purified by using hexanes to Et_2O/hexanes (1:100) as eluent.

General Procedure for Acid-Promoted Rearrangement Reactions of Homoallenic Bromohydrins 4. To a solution of homoallenic bromohydrin **4** (0.8 mmol) in CH_2Cl_2 (5 mL) was added concentrated sulfuric acid (0.05 mL). The resulting mixture was stirred at ambient temperature. The reaction was monitored by TLC until no starting material was observed, and normally the reaction was stirred at rt for 2 h. Water (10 mL) and CH_2Cl_2 (10 mL) were then added to the reaction, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with CH_2Cl_2 (10 mL × 2). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:100) as eluent to give the product **1**. For compound **1g**, Et_2O/hexanes (1:100) to Et_2O/hexanes (1:15) was used as eluent.

General Procedure for the Formation of Thiophenes 7 from Phenacyl Bromides in the 3-Step Sequence. A mixture of propargyl bromide (1.8 mmol, 133.8 μL), indium powder (325 mesh, 172.2 mg, 1.5 mmol), and arylacyl halide (**5**, 1.0 mmol) in THF/H_2O (1.5 mL/0.5 mL) was stirred at ambient temperature. The reaction was monitored by TLC until no starting material was observed, and normally the reaction was stirred at rt overnight. Et_2O (10 mL) and water (5 mL) were then added to the reaction, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with Et_2O (5 mL × 2). The combined organic layers were washed with brine (3 mL), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was dissolved in CH_2Cl_2 (5 mL), and then concentrated sulfuric acid (0.05 mL) was added. The resulting mixture was stirred at ambient temperature for 2 h. Water (10 mL) and CH_2Cl_2 (10 mL) were then added to the reaction, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with CH_2Cl_2 (10 mL × 2). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was dissolved in EtOH (2 mL), and then thioacetamide (1.0 mmol, 75.1 mg) was added. The resulting mixture was heated to reflux for 1 h, cooled to rt, and concentrated in a rotary evaporator. The mixture was diluted with CH_2Cl_2 (10 mL) and washed with water (5 mL). The aqueous layer was back extracted with CH_2Cl_2 (10 mL × 2). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to EtOAc/hexanes (1:8) as eluent to give the product **7**.

General Procedure for the Formation of 1,2,4-Substituted-pyrroles 6a−g from γ-Bromo-enones 1c−e. A mixture of γ-bromo-enones **1** (0.6 mmol) and aniline (1.2 mmol, 109.6 μL) in methanol (2.0 mL) was heated to reflux overnight. The mixture was cooled to rt and concentrated in a rotary evaporator. CH_2Cl_2 (10 mL) and water (10 mL) were added to the residue, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with CH_2Cl_2 (10 mL × 2). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:100) as eluent to give the product **6**.

General Procedure for the Formation of 2,4-Substituted-thiophenes 7c−e from γ-Bromo-enones 1c−e. A mixture of γ-bromo-enones **1** (0.6 mmol) and thioacetamide (0.6 mmol, 45.1 mg) in ethanol (2.0 mL) was heated to reflux for 1 h. The mixture was cooled to rt and concentrated in a rotary evaporator. CH_2Cl_2 (10 mL) and water (5 mL) were added to the residue, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with CH_2Cl_2 (10 mL × 2). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes as eluent to give the product **7**.

General Procedure for the Formation of 2,4-Substituted-furans 8c−e from γ-Bromo-enones 1c−e. A mixture of γ-bromo-enones **1** (0.6 mmol) and NaOAc (1.2 mmol, 91.9 mg) in methanol (2.0 mL) was heated to reflux for 5 h. The mixture was cooled to rt, and then anhydrous K_2CO_3 (1.2 mmol, 165.8 mg) was added. The resulting mixture was stirred at rt overnight and then filtered. The filtrate was concentrated in a rotary evaporator. CH_2Cl_2 (10 mL) and water (5 mL) were added to the residue, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with CH_2Cl_2 (10 mL × 2). The combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes as eluent to give the product **8**.

(*Z*)-5-Chloro-4-phenylpent-3-en-2-one (1a, Table 1, entry 1). Following the general procedure, the title compound was obtained (88 mg, 45% from **5a**). An oil; TLC (Et_2O/hexanes (1:5)) $R_f = 0.38$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3 H), 4.98 (s, 2 H), 6.55 (s, 1 H), 7.39−7.42 (m, 3 H), 7.51−7.55 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.2 (CH_3), 39.2 (CH_2), 126.5 (CH), 126.7 (CH × 2), 128.7 (CH × 2), 129.7 (CH), 138.2 (C), 150.4 (C), 198.1 (C); IR (neat) 3022, 1669, 1599 cm^{-1}; EI-MS m/z (rel intensity) 196 ($[M + 2]^+$, 22), 194 ($[M]^+$, 74), 158 (37), 115 (100); HRMS $[M]^+$ calcd for $C_{11}H_{11}ClO$ 194.0498, found 194.0493.

(*Z*)-5-Chloro-4-(2,4-dichlorophenyl)pent-3-en-2-one (1b, Table 1, entry 2). Following the general procedure, the title compound was obtained (138 mg, 52% from **5b**). Solid, mp 64−65 °C; TLC (Et_2O/hexanes (1:5)) $R_f = 0.30$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3 H), 4.89 (s, 2 H), 6.23 (s, 1 H), 7.19 (d, $J = 8.1$ Hz, 1 H), 7.27 (d, $J = 8.0$ Hz, 1 H), 7.41 (d, $J = 1.8$ Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.0 (CH_3), 40.9 (CH_2), 127.1 (CH), 129.6 (CH), 130.1 (CH), 131.5 (CH), 132.7 (C), 135.1 (C), 136.5 (C), 149.1 (C), 197.9 (C); IR (KBr) 2956, 1708, 1606 cm^{-1}; EI-MS m/z (rel intensity) 264 ($[M + 2]^+$, 19), 262 ($[M]^+$, 20), 227 (100), 183 (29); HRMS $[M]^+$ calcd for $C_{11}H_9Cl_3O$ 261.9719, found 261.9726.

(*Z*)-5-Bromo-4-phenylpent-3-en-2-one (1c, Table 1, entry 3). Following the general procedure, the title compound was obtained (130 mg, 68%). An oil; TLC (Et_2O/hexanes (1:5)) $R_f = 0.33$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3 H), 4.87 (s, 2 H), 6.51 (s, 1 H), 7.30−7.41 (m, 3 H), 7.50−7.55 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.7 (CH_2), 32.2 (CH_3), 125.6 (CH), 126.5 (CH × 2), 128.6 (CH × 2), 129.6 (CH), 138.3 (C), 150.8 (C), 197.9 (C); IR (neat) 3059, 1682, 1353 cm^{-1}; EI-MS m/z (rel intensity) 240 ($[M + 2]^+$, 26), 238 ($[M]^+$, 27), 223 (11), 159 (100); HRMS $[M]^+$ calcd for $C_{11}H_{11}BrO$ 237.9993, found 237.9983.

(*Z*)-5-Bromo-4-(4-chlorophenyl)pent-3-en-2-one (1d, Table 1, entry 4). Following the general procedure, the title compound was obtained (137 mg, 50% from **5d**). An oil; TLC (Et_2O/hexanes (1:5)) $R_f = 0.30$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3 H), 4.84 (s, 2 H), 6.49 (s, 1 H), 7.36 (d, $J = 8.0$ Hz, 2 H), 7.47 (d, $J = 8.0$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.4 (CH_2), 32.3 (CH_3), 125.8 (CH), 127.9 (CH × 2), 128.8 (CH × 2), 135.7 (C), 136.8 (C), 149.5 (C), 197.8 (C); IR (neat) 3029, 1690, 1611 cm^{-1}; EI-MS m/z (rel intensity) 274 ($[M + 2]^+$, 46), 272 ($[M]^+$, 35), 257 (28), 193 (100); HRMS $[M]^+$ calcd for $C_{11}H_{10}BrClO$ 271.9604, found 271.9614.

(*Z*)-5-Bromo-4-(4-bromophenyl)pent-3-en-2-one (1e, Table 1, entry 5). Following the general procedure, the title compound was obtained (178 mg, 56% from **5e**). An oil; TLC (Et_2O/hexanes (1:5)) $R_f = 0.33$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 4.82 (s, 2 H), 6.49 (s, 1 H), 7.39 (d, $J = 8.0$ Hz, 2 H), 7.51 (d, $J = 8.0$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3 (CH_2), 32.3 (CH_3), 124.1 (C), 125.9 (CH), 128.2 (CH × 2), 131.9 (CH × 2), 137.3 (C), 149.7 (C), 197.8 (C); IR (neat) 3076, 1692, 1595 cm^{-1}; EI-MS m/z (rel intensity) 318 ($[M + 2]^+$, 23), 316 ($[M]^+$, 14), 237 (33), 158 (100); HRMS $[M]^+$ calcd for $C_{11}H_{10}Br_2O$ 315.9098, found 315.9109.

(*Z*)-5-Bromo-4-(p-tolyl)pent-3-en-2-one (1f, Table 1, entry 6). Following the general procedure, the title compound was obtained (104 mg, 41% from **5f**). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.33;); ^1H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 2.37 (s, 3 H), 4.88 (s, 2 H), 6.52 (s, 1 H), 7.20 (d, $J = 8.4$ Hz, 2 H), 7.44 (d, $J = 8.4$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3 (CH_3), 26.7 (CH_2), 32.4 (CH_3), 124.9 (CH), 126.6 (CH × 2), 129.5 (CH × 2), 135.5 (C), 140.2 (C), 151.1 (C), 198.1 (C); IR (neat) 3022, 1687, 1599 cm^{-1}; EI-MS m/z (rel intensity) 254 ($[M + 2]^+$, 9), 252 ($[M]^+$, 10), 237 (16), 173 (100); HRMS $[M]^+$ calcd for $C_{12}H_{13}BrO$ 252.0150, found 252.0146.

(*Z*)-4-(1-Bromo-4-oxopent-2-en-2-yl)benzonitrile (1g, Table 1, entry 7). Following the general procedure, the title compound was obtained (132 mg, 50% from **5g**). Solid, mp 73−74 °C; TLC (Et_2O/hexanes (1:5)) $R_f = 0.33$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3 H), 4.81 (s, 2 H), 6.51 (s, 1 H), 7.61 (d, $J = 8.7$ Hz, 2 H), 7.68 (d, $J = 8.7$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.0 (CH_2), 32.3 (CH_3), 113.3 (C), 118.1 (C), 127.4 (CH × 2), 127.7 (CH), 132.4 (CH × 2), 143.1 (C), 148.8 (C), 197.7 (C); IR (KBr) 2216, 1690, 1597 cm^{-1}; EI-MS m/z (rel intensity) 265 ($[M + 2]^+$, 41), 263 ($[M]^+$, 42), 184 (82), 140 (100); HRMS $[M]^+$ calcd for $C_{12}H_{10}BrNO$ 262.9946, found 262.9949.

(*Z*)-5-Bromo-4-(4-methoxyphenyl)pent-3-en-2-one (1h, Table 1, entry 8). Following the general procedure, the title compound was obtained (112 mg, 52%). An oil; TLC (Et_2O/hexanes (1:5)) $R_f = 0.33$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3 H), 3.82 (s, 3 H), 4.89 (s, 2 H), 6.51 (s, 1 H), 6.92 (d, $J = 9.0$ Hz, 2 H), 7.53 (d, $J = 9.0$ Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.6 (CH_2), 32.4 (CH_3), 55.3 (CH_3), 114.2 (CH × 2), 123.8 (CH), 128.1 (CH × 2), 130.4 (C), 150.5 (C), 161.0 (C), 198.0 (C); IR (KBr) 2947, 1671, 1578 cm^{-1}; EI-MS m/z (rel intensity) 270 ($[M + 2]^+$, 18), 268 ($[M]^+$, 18), 189 (100), 130 (43); HRMS $[M]^+$ calcd for $C_{12}H_{13}BrO_2$ 268.0099, found 268.0092.

(*Z*)-5-Bromo-4-(2-methoxyphenyl)pent-3-en-2-one (1i, Table 1, entry 9). Following the general procedure, the title compound was obtained (121 mg, 56%). An oil; TLC (Et_2O/hexanes (1:5)) $R_f = 0.33$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.28 (s, 3 H), 3.81 (s, 3 H), 4.91 (s, 2 H), 6.25 (s, 1 H), 6.80−6.96 (m, 2 H), 7.18 (d, $J = 8.0$ Hz, 1 H), 7.35 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.0 (CH_2), 32.1 (CH_3), 55.4 (CH_3), 110.7 (CH), 120.6 (CH), 128.2 (CH), 128.5 (C), 130.3 (CH), 130.5 (CH), 152.1 (C), 156.4 (C), 198.2 (C); IR (neat) 3075, 1635, 1355 cm^{-1}; EI-MS m/z (rel intensity) 270 ($[M + 2]^+$, 5), 268 ($[M]^+$, 5), 239 (100), 189 (50); HRMS $[M]^+$ calcd for $C_{12}H_{13}BrO_2$ 268.0099, found 268.0096.

1-Chloro-2-phenylpenta-3,4-dien-2-ol (4a, Table 1, entry 1). Following the general procedure, a mixture of **4a** and its corresponding methyl ketone **4a″** was obtained. To the mixture in MeOH (2 mL) was added $NaBH_4$ (25 mg, 0.65 mmol) at rt, and the resulting mixture was stirred at rt for 2 h. Et_2O (15 mL) and water (3 mL) were added, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with Et_2O (15 mL × 2). The combined organic layers were concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:100) as eluent to give the product **4a** (94 mg, 48%). An oil; TLC (Et_2O/hexanes (1:5)) $R_f = 0.35$; ^1H NMR (300 MHz, $CDCl_3$) δ 2.93 (s, 1 H), 3.81 (d, $J = 11.1$ Hz, 1 H), 3.89 (d, $J = 11.1$ Hz, 1 H), 5.02 (d, J = 6.6 Hz, 2 H), 5.55 (t, J = 6.6 Hz, 1 H), 7.27−7.39 (m, 3 H), 7.50 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.7 (CH_2), 74.5 (C), 79.7 (CH_2), 96.3 (CH), 125.5 (CH × 2), 127.8 (CH), 128.3 (CH × 2), 142.2 (C), 206.7 (C); IR (neat) 3538, 3067, 1967 cm^{-1}; ESI-MS m/z (rel intensity) 219 ([M + Na + 2]$^+$, 21), 217 ([M + Na]$^+$, 58), 197 (37), 55 (100); HRMS [M + Na]$^+$ calcd for $C_{11}H_{11}OClNa$ 217.0391, found 217.0383.

1-Chloro-2-(2,4-dichlorophenyl)penta-3,4-dien-2-ol (4b, Table 1, entry 2). Following the general procedure, a mixture of **4b** and its corresponding methyl ketone **4b″** was obtained. To the mixture in MeOH (2 mL) was added $NaBH_4$ (25 mg, 0.65 mmol) at rt, and the resulting mixture was stirred at rt for 2 h. Et_2O (15 mL) and water (3 mL) were added and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with Et_2O (15 mL × 2). The combined organic layers were concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:100) as eluent to give the product **4b** (158 mg, 60%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.38; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.01 (s, 1 H), 4.14 (d, J = 10.5 Hz, 1 H), 4.16 (d, J = 10.5 Hz, 1 H), 4.98 (d, J = 6.6 Hz, 2 H), 5.81 (t, J = 6.6 Hz, 1 H), 7.24−7.29 (m, 1 H), 7.36 (s, 1 H), 7.81 (d, J = 8.7 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.2 (CH_2), 74.3 (C), 80.2 (CH_2), 94.3 (CH), 127.2 (CH), 129.7 (CH), 130.8 (CH), 131.6 (C), 134.4 (C), 137.6 (C), 207.3 (C); IR (neat) 3552, 1956, 1581 cm^{-1}; ESI-MS m/z (rel intensity) 264 ([M + 2]$^+$, 57), 262 ([M]$^+$, 54), 214 (100), 158 (93); HRMS [M]$^+$ calcd for $C_{11}H_9OCl_3$ 261.9713, found 261.9722.

1-Bromo-2-phenylpenta-3,4-dien-2-ol (4c, Table 1, entry 3). Following the general procedure, the title compound was obtained (148 mg, 62%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.38; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.89 (s, 1 H), 3.72 (d, J = 10.2 Hz, 1 H), 3.81 (d, J = 10.2 Hz, 1 H), 5.03 (d, J = 6.9 Hz, 2 H), 5.55 (t, J = 6.9 Hz, 1 H), 7.26−7.40 (m, 3 H), 7.47−7.51 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.3 (CH_2), 73.4 (C), 79.9 (CH_2), 96.7 (CH), 125.4 (CH × 2), 127.8 (CH), 128.3 (CH × 2), 142.2 (C), 206.6 (C); IR (neat) 3538, 3067, 1949 cm^{-1}. These data are in agreement with those reported in the literature.[4]

1-Bromo-2-(4-chlorophenyl)penta-3,4-dien-2-ol (4d, Table 1, entry 4). Following the general procedure, a mixture of **4d** and its corresponding methyl ketone **4d″** was obtained. To the mixture in MeOH (2 mL) was added $NaBH_4$ (25 mg, 0.65 mmol) at rt, and the resulting mixture was stirred at rt for 2 h. Et_2O (15 mL) and water (3 mL) were added, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with Et_2O (15 mL × 2). The combined organic layers were concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:100) as eluent to give the product **4d** (140 mg, 51%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.30; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.87 (s, 1 H), 3.68 (d, J = 10.5 Hz, 1 H), 3.76 (d, J = 10.5 Hz, 1 H), 5.02 (d, J = 6.6 Hz, 2 H), 5.50 (t, J = 6.6 Hz, 1 H), 7.31 (d, J = 8.7 Hz, 2 H), 7.41 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.9 (CH_2), 73.5 (C), 80.1 (CH_2), 96.4 (CH), 127.0 (CH × 2), 128.4 (CH × 2), 133.7 (C), 140.8 (C), 206.6 (C); IR (neat) 3544, 1956, 1488 cm^{-1}; ESI-MS m/z (rel intensity) 274 ([M + 2]$^+$, 28), 272 ([M]$^+$, 42), 224 (100), 183 (41); HRMS [M]$^+$ calcd for $C_{11}H_{10}OBrCl$ 271.9598, found 271.9600.

1-Bromo-2-(4-bromophenyl)penta-3,4-dien-2-ol (4e, Table 1, entry 5). Following the general procedure, a mixture of **4e** and its corresponding methyl ketone **4e″** was obtained. To the mixture in MeOH (2 mL) was added $NaBH_4$ (25 mg, 0.65 mmol) at rt, and the resulting mixture was stirred at rt for 2 h. Et_2O (15 mL) and water (3 mL) were added, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with Et_2O (15 mL × 2). The combined organic layers were concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:100) as eluent to give the product **4e** (118 mg, 37%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.30; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.85 (s, 1 H), 3.68 (d, J = 10.5 Hz, 1 H), 3.76 (d, J = 10.5 Hz, 1 H), 5.02 (d, J = 6.6 Hz, 2 H), 5.50 (t, J = 6.6 Hz, 1 H), 7.34 (d, J = 9.0 Hz, 2 H), 7.46 (d, J = 9.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.8 (CH_2), 73.6 (C), 80.2 (CH_2), 96.3 (CH), 121.9 (C), 127.3 (CH × 2), 131.4 (CH × 2), 141.3 (C), 206.6 (C); IR (neat) 3548, 1958, 1514 cm^{-1}; ESI-MS m/z (rel intensity) 321 ([M + H + 4]$^+$, 50), 319 ([M + H + 2]$^+$, 100), 317 ([M + H]$^+$, 55) 305 (8); HRMS [M + H]$^+$ calcd for $C_{11}H_{11}OBr_2$ 316.9171, found 316.9187.

1-Bromo-2-(*p*-tolyl)penta-3,4-dien-2-ol (4f, Table 1, entry 6). Following the general procedure, a mixture of **4f** and its corresponding methyl ketone **4f″** was obtained. To the mixture in MeOH (2 mL) was added $NaBH_4$ (25 mg, 0.65 mmol) at rt, and the resulting mixture was stirred at rt for 2 h. Et_2O (15 mL) and water (3 mL) were added, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with Et_2O (15 mL × 2). The combined organic layers were concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:100) as eluent to give the product **4f** (104 mg, 41%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.40; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3 H), 2.84 (s, 1 H), 3.72 (d, J = 10.5 Hz, 1 H), 3.79 (d, J = 10.5 Hz, 1 H), 5.02 (d, J = 6.6 Hz, 2 H), 5.54 (t, J = 6.6 Hz, 1 H), 7.17 (d, J = 8.1 Hz, 2 H), 7.37 (d, J = 8.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0 (CH_3), 44.5 (CH_2), 73.6 (C), 79.9 (CH_2), 96.8 (CH), 125.3 (CH × 2), 128.9 (CH × 2), 137.6 (C), 139.3 (C), 206.5 (C); IR (neat) 3548, 1948, 1477 cm^{-1}; ESI-MS m/z (rel intensity) 255 ([M + H + 2]$^+$, 37), 253 ([M + H]$^+$, 34), 197 (51), 175 (100); HRMS [M + H]$^+$ calcd for $C_{12}H_{14}OBr$ 253.0223, found 253.0213.

4-(1-Bromo-2-hydroxypenta-3,4-dien-2-yl)benzonitrile (4g, Table 1, entry 7). Following the general procedure, a mixture of **4g** and its corresponding methyl ketone **4g″** was obtained. To the mixture in MeOH (2 mL) was added $NaBH_4$ (25 mg, 0.65 mmol) at rt, and the resulting mixture was stirred at rt for 2 h. Et_2O (15 mL) and water (3 mL) were added, and the mixture was transferred to a separatory funnel. The aqueous layer was back extracted with Et_2O (15 mL × 2). The combined organic layers were concentrated in a rotary evaporator. The residue was purified by silica gel chromatography using hexanes to Et_2O/hexanes (1:100) as eluent to give the product **4g** (87 mg, 33%). An oil; TLC (Et_2O/hexanes (1:1)) R_f = 0.28; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.92 (s, 1 H), 3.69 (d, J = 10.5 Hz, 1 H), 3.78 (d, J = 10.5 Hz, 1 H), 5.03 (d, J = 6.6 Hz, 2 H), 5.51 (t, J = 6.6 Hz, 1 H), 7.59 (d, J = 8.7 Hz,, 2 H), 7.65 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.2 (CH_2), 73.7 (C), 80.4 (CH_2), 96.1 (CH), 111.8 (C), 118.5 (C), 126.5 (CH × 2), 132.1 (CH × 2), 147.6 (C), 206.8 (C); IR (neat) 3464, 2235, 1948 cm^{-1}; ESI-MS m/z (rel intensity) 288 ([M + Na + 2]$^+$, 14), 286 ([M + Na]$^+$, 18), 192 (72), 96 (100); HRMS [M + Na]$^+$ calcd for $C_{12}H_{10}ONBrNa$ 285.9838, found 285.9824.

1-Bromo-2-(4-methoxyphenyl)penta-3,4-dien-2-ol (4h, Table 1, entry 8). Following the general procedure, the title compound was obtained (161 mg, 60%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.35; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.87 (s, 1 H), 3.69 (d, J = 10.5 Hz, 1 H), 3.77 (d, J = 10.5 Hz, 1 H), 3.79 (s, 3 H), 5.01 (d, J = 6.6 Hz, 2 H), 5.53 (t, J = 6.6 Hz, 1 H), 6.88 (d, J = 6.9 Hz, 2 H), 7.41 (d, J = 6.9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.5 (CH_2), 55.2 (CH_3), 73.5 (C), 79.8 (CH_2), 96.7 (CH), 113.6 (CH × 2), 126.7 (CH × 2), 134.2 (C), 159.1 (C), 206.5 (C); IR (neat) 3557, 1606, 1523 cm^{-1}; ESI-MS m/z (rel intensity) 293 ([M + Na + 2]$^+$, 35), 291 ([M + Na]$^+$, 36), 251 (68), 171 (100); HRMS [M + Na]$^+$ calcd for $C_{12}H_{13}O_2BrNa$ 290.9991, found 290.9978.

1-Bromo-2-(2-methoxyphenyl)penta-3,4-dien-2-ol (4i, Table 1, entry 9). Following the general procedure, the title compound was obtained (178 mg, 66%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.33; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.57 (s, 1 H), 3.86 (s, 3 H), 3.95 (d, J = 10.2 Hz, 1 H), 4.001 (d, J = 10.2 Hz, 1 H), 4.92−5.04 (m, 2 H), 5.84 (t, J = 6.6 Hz, 1 H), 6.90 (d, J = 7.5 Hz, 1 H), 7.01 (d, J = 7.5 Hz, 1 H), 7.26−7.32 (m, 1 H), 7.60 (d, J = 7.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 42.4 (CH_2), 55.3 (CH_3), 73.4 (C), 79.7 (CH_2), 95.7 (CH), 111.1 (CH), 120.8 (CH), 127.3 (CH), 129.2 (CH), 129.7 (C), 155.9 (C), 206.5 (C); IR (neat) 3538, 2953, 1477 cm^{-1}; ESI-MS m/z (rel intensity) 293 ([M + Na + 2]$^+$, 77), 291 ([M + Na]$^+$, 82), 211 (100), 172 (95); HRMS [M + Na]$^+$ calcd for $C_{12}H_{13}O_2BrNa$ 290.9991, found 290.9981.

2-Methyl-1,4-diphenyl-1*H*-pyrrole (6a). Following the general procedure, the title compound was obtained (113 mg, 81%). Solid, mp 68−70 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.63; ^1H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.36 (s, 1 H), 7.06 (s, 1 H), 7.13 (t, J = 8.7 Hz, 1 H), 7.29−7.38 (m, 5 H), 7.43 (d, J = 8.7 Hz, 2 H), 7.45 (J = 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.9 (CH_3), 106.5 (CH), 117.8 (CH), 124.4 (C), 124.8 (CH × 2), 125.3 (CH), 125.5 (CH × 2), 126.9 (CH), 128.5 (CH × 2), 129.0 (CH × 2), 130.4 (C), 135.5 (C), 140.3 (C); IR (KBr) 3026, 1602, 1504 cm^{-1}. These data are in agreement with those reported in the literature.[10]

1-(4-Methoxyphenyl)-2-methyl-4-phenyl-1*H*-pyrrole (6b). Following the general procedure, the title compound was obtained (122 mg, 77%). Solid, mp 105−106 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.70; ^1H NMR (300 MHz, $CDCl_3$) δ 2.22 (s, 3 H), 3.85 (s, 3 H), 6.37 (s, 1 H), 6.99 (d, J = 8.1 Hz, 2 H), 7.05 (s, 1 H), 7.18 (t, J = 8.1 Hz, 1 H), 7.29 (d, J = 8.1 Hz, 2 H), 7.35 (t, J = 8.1 Hz, 2 H), 7.53 (d, J = 8.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.7 (CH_3), 55.4 (CH_3), 105.8 (CH), 114.1 (CH × 2), 118.1 (CH), 124.0 (C), 124.8 (CH × 2), 125.3 (CH), 126.9 (CH × 2), 128.5 (CH × 2), 130.4 (C), 133.1 (C), 135.6 (C), 158.5 (C); IR (KBr) 2937, 1602, 1504 cm^{-1}; EI-MS m/z (rel intensity) 263 ($[M]^+$, 100), 248 (30), 207 (14), 115 (11); HRMS $[M]^+$ calcd for $C_{18}H_{17}NO$ 263.1310, found 263.1315.

1-Benzyl-2-methyl-4-phenyl-1*H*-pyrrole (6c). Following the general procedure, the title compound was obtained (113 mg, 76%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.58; ^1H NMR (300 MHz, $CDCl_3$) δ 2.16 (s, 3 H), 5.03 (s, 2 H), 6.26 (s, 1 H), 6.93 (s, 1 H), 7.03−7.15 (m, 3 H), 7.22−7.32 (m, 5 H), 7.45 (d, J = 8.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0 (CH_3), 50.4 (CH_3), 105.3 (CH), 117.5 (CH), 123.5 (C), 124.7 (CH × 2), 125.0 (CH), 126.3 (CH × 2), 127.3 (CH), 128.4 (CH × 2), 128.7 (CH × 2), 129.9 (C), 135.8 (C), 138.0 (C); IR (neat) 2921, 1608, 1519 cm^{-1}. These data are in agreement with those reported in the literature.[11]

4-(4-Chlorophenyl)-2-methyl-1-phenyl-1*H*-pyrrole (6d). Following the general procedure, the title compound was obtained (127 mg, 79%). Solid, mp 106−107 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.63; ^1H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.34 (s, 1 H), 7.05 (s, 1 H), 7.28−7.49 (m, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.9 (CH_3), 106.3 (CH), 118.0 (CH), 123.3 (C), 125.6 (CH × 2), 126.0 (CH × 2), 127.1 (CH), 128.6 (CH × 2), 129.1 (CH × 2), 130.4 (C), 130.8 (C), 134.0 (C), 139.9 (C); IR (KBr) 2960, 1523, 1161 cm^{-1}; EI-MS m/z (rel intensity) 269 ($[M + 2]^+$, 33), 267 ($[M]^+$, 100), 228 (5), 191 (20); HRMS $[M]^+$ calcd for $C_{17}H_{14}ClN$ 267.0815, found 267.0818.

4-(4-Chlorophenyl)-1-(4-methoxyphenyl)-2-methyl-1*H*-pyrrole (6e). Following the general procedure, the title compound was obtained (157 mg, 88%). Solid, mp 108−109 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.50; ^1H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3 H), 3.84 (s, 3 H), 6.28 (s, 1 H), 6.93−6.98 (m, 3 H), 7.20−7.28 (m, 4 H), 7.42 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.7 (CH_3), 55.5 (CH_3), 105.7 (CH), 114.2 (CH × 2), 118.2 (CH), 122.9 (C), 126.0 (CH × 2), 126.9 (CH × 2), 128.6 (CH × 2), 130.6 (C), 130.7 (C), 132.9 (C), 134.2 (C), 158.6 (C); IR (KBr) 2919, 1514, 1245 cm^{-1}; EI-MS m/z (rel intensity) 299 ($[M + 2]^+$, 33), 297 ($[M]^+$, 100), 282 (24), 221 (26); HRMS $[M]^+$ calcd for $C_{18}H_{16}ClNO$ 297.0920, found 297.0914.

4-(4-Bromophenyl)-2-methyl-1-phenyl-1*H*-pyrrole (6f). Following the general procedure, the title compound was obtained (170 mg, 91%). Solid, mp 106−107 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.55; ^1H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 6.35 (s, 1 H), 7.06 (s, 1 H), 7.24−7.49 (m, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.9 (CH_3), 106.3 (CH), 118.0 (CH), 118.7 (C), 123.2 (C), 125.5 (CH × 2), 126.4 (CH × 2), 127.1 (CH), 129.1 (CH × 2), 130.4 (C), 131.5 (CH × 2), 134.5 (C), 139.8 (C); IR (KBr) 2960, 1601, 1495 cm^{-1}; EI-MS m/z (rel intensity) 313 ($[M + 2]^+$, 100), 311 ($[M]^+$, 99), 230 (14), 191 (27); HRMS $[M]^+$ calcd for $C_{17}H_{14}BrN$ 311.0310, found 311.0304.

4-(4-Bromophenyl)-1-(4-methoxyphenyl)-2-methyl-1*H*-pyrrole (6g). Following the general procedure, the title compound was obtained (193 mg, 94%). Solid, mp 98−99 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.45; ^1H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3 H), 3.84 (s, 3 H), 6.28 (s, 1 H), 6.92−6.98 (m, 3 H), 7.20−7.25 (m, 2 H), 7.33−7.43 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.7 (CH_3), 55.5 (CH_3), 105.6 (CH), 114.2 (CH × 2), 118.3 (CH), 118.6 (C), 122.9 (C), 126.4 (CH × 2), 127.0 (CH × 2), 130.7 (C), 131.5 (CH × 2), 132.9 (C), 134.6 (C), 158.6 (C); IR (KBr) 2930, 1680, 1518 cm^{-1}; EI-MS m/z (rel intensity) 343 ($[M + 2]^+$, 99), 341 ($[M]^+$, 100), 326 (17), 221 (33); HRMS $[M]^+$ calcd for $C_{18}H_{16}BrNO$ 341.0415, found 341.0421.

2-Methyl-4-phenylthiophene (7c). Following the general procedure, the title compound was obtained (63 mg, 60%). Solid, mp 74−75 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.75; ^1H NMR (300 MHz, $CDCl_3$) δ 2.53 (s, 3 H), 7.05 (s, 1 H), 7.19 (s, 1 H), 7.25 (d, J = 8.1 Hz, 1 H), 7.35 (d, J = 8.1 Hz, 2 H), 7.54 (d, J = 8.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4 (CH_3), 117.9 (CH), 124.5 (CH), 126.1 (CH × 2), 126.8 (CH), 128.6 (CH × 2), 136.0 (C), 140.4 (C), 141.9 (C); IR (KBr) 2917, 1502, 1198 cm^{-1}. These data are in agreement with those reported in the literature.[12]

4-(4-Chlorophenyl)-2-methylthiophene (7d). Following the general procedure, the title compound was obtained (100 mg, 80%). Solid, mp 121−122 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.70; ^1H NMR (300 MHz, $CDCl_3$) δ 2.52 (s, 3 H), 7.00 (s, 1 H), 7.16 (s, 1 H), 7.32 (d, J = 9.0 Hz, 2 H), 7.47 (d, J = 9.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3), 118.2 (CH), 124.3 (CH), 127.3 (CH × 2), 128.8 (CH × 2), 132.6 (C), 134.5 (C), 140.6 (C), 140.8 (C); IR (KBr) 2918, 1496, 1199 cm^{-1}; EI-MS m/z (rel intensity) 210 ($[M + 2]^+$, 36), 208 ($[M]^+$, 100), 171 (13), 128 (8); HRMS $[M]^+$ calcd for $C_{11}H_9SCl$ 208.0113, found 208.0121.

4-(4-Bromophenyl)-2-methylthiophene (7e). Following the general procedure, the title compound was obtained (111 mg, 73%). Solid, mp 134−135 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.70; ^1H NMR (300 MHz, $CDCl_3$) δ 2.51 (s, 3 H), 7.00 (s, 1 H), 7.17 (s, 1 H), 7.39 (d, J = 8.1 Hz, 2 H), 7.48 (d, J = 8.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3), 118.3 (CH), 120.7 (C), 124.2 (CH), 127.6 (CH × 2), 131.7 (CH × 2), 134.9 (C), 140.6 (C), 140.8 (C); IR (KBr) 2923, 1508, 1191 cm^{-1}; EI-MS m/z (rel intensity) 254 ($[M + 2]^+$, 100), 252 ($[M]^+$, 98), 228 (9), 171 (28); HRMS $[M]^+$ calcd for $C_{11}H_9BrS$ 251.9608, found 251.9611.

2-Methyl-4-(*p*-tolyl)thiophene (7f, Table 2, entry 1). Following the general procedure, the title compound was obtained (90 mg, 32%). Solid, mp 107−108 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.73; ^1H NMR (300 MHz, $CDCl_3$) δ 2.35 (s, 3 H), 2.51 (s, 3 H), 7.03 (s, 1 H),7.15 (d, J = 8.1 Hz, 2 H), 7.19 (s, 1 H), 7.45 (d, J = 8.1 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3), 21.0 (CH_3), 117.3 (CH), 124.5 (CH), 126.0 (CH × 2), 129.3 (CH × 2), 133.2 (C), 136.5 (C), 140.2 (C), 141.9 (C). These data are in agreement with those reported in the literature.[13]

4-(5-Methylthiophen-3-yl)benzonitrile (7g, Table 2, entry 2). Following the general procedure, the title compound was obtained (132 mg, 44%). Solid, mp 109−110 °C; TLC (Et_2O/hexanes (1:1)) R_f = 0.65; ^1H NMR (300 MHz, $CDCl_3$) δ 2.51 (s, 3 H), 7.03 (s, 1 H), 7.29 (s, 1 H), 7.57 (d, J = 9.0 Hz, 2 H), 7.62 (d, J = 9.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3), 110.0 (C), 118.9 (C), 120.3 (CH), 123.9 (CH), 126.4 (CH × 2), 132.5 (CH × 2), 139.8 (C), 140.0 (C), 141.4 (C); IR (KBr) 2920, 2232, 1604 cm^{-1}; EI-MS m/z (rel intensity) 199 ($[M]^+$, 100), 198 (77), 166 (8), 154 (9); HRMS $[M]^+$ calcd for $C_{12}H_9NS$ 199.0456, found 199.0454.

4-(4-Methoxyphenyl)-2-methylthiophene (7h, Table 2, entry 3). Following the general procedure, the title compound was obtained (67 mg, 22%). Solid, mp 110−111 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.60; ^1H NMR (300 MHz, $CDCl_3$) δ 2.50 (s, 3 H), 3.81 (s, 3 H), 6.89 (d, J = 9.0 Hz, 2 H), 6.99 (s, 1 H), 7.06 (s, 1 H), 7.46 (d, J = 9.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3), 55.3 (CH_3), 114.1 (CH × 2), 116.6 (CH), 124.5 (CH), 127.3 (CH × 2), 129.0 (C), 140.3 (C), 141.7 (C), 158.7 (C); IR (KBr) 2919, 1532, 1255 cm^{-1}; EI-MS m/z (rel intensity) 204 ($[M]^+$, 100), 189 (74), 161 (25), 115 (6); HRMS $[M]^+$ calcd for $C_{12}H_{12}OS$ 204.0609, found 204.0600.

4-(2,5-Dimethoxyphenyl)-2-methylthiophene (7j, Table 2, entry 4). Following the general procedure, the title compound was obtained (105 mg, 30%). An oil; TLC (Et_2O/hexanes (1:5)) R_f = 0.50; ^1H NMR (300 MHz, $CDCl_3$) δ 2.51 (s, 3 H), 3.79 (s, 3 H), 3.80 (s, 3

H), 6.78 (dd, *J* = 9.0, 3.0 Hz, 1 H), 6.88 (d, *J* = 9.0 Hz, 1 H), 7.02 (d, *J* = 3.0 Hz, 1 H), 7.08 (s, 1 H), 7.34 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3), 55.7 (CH_3), 56.1 (CH_3), 112.4 (CH), 112.5 (CH), 115.4 (CH), 121.2 (CH), 126.2 (C), 126.6 (CH), 137.8 (C), 138.7 (C), 150.7 (C), 153.5 (C); IR (neat) 2956, 1690, 1496 cm^{-1}; EI-MS *m*/*z* (rel intensity) 234 ([M]$^+$, 100), 219 (59), 204 (12), 191 (17); HRMS [M]$^+$ calcd for $C_{13}H_{14}SO_2$ 234.0715, found 234.0713.

2-Methyl-4-(naphthalen-2-yl)thiophene (7k, Table 2, entry 5). Following the general procedure, the title compound was obtained (74 mg, 22%). Solid, mp 114−116 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.63; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.55 (s, 3 H), 7.18−7.20 (m, 1 H), 7.30 (d, *J* = 1.8 Hz, 1 H), 7.40−7.49 (m, 2 H), 7.70 (dd, *J* = 8.4, 1.8 Hz, 1 H), 7.79−7.85 (m, 3 H), 7.95 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4 (CH_3), 118.4 (CH), 124.4 (CH), 124.7 (CH), 124.8 (CH), 125.6 (CH), 126.2 (CH), 127.6 (CH), 127.9 (CH), 128.3 (CH), 132.5 (C), 133.4 (C), 133.7 (C), 140.6 (C), 141.9 (C); IR (KBr) 3048, 1600, 1217 cm^{-1}; EI-MS *m*/*z* (rel intensity) 224 ([M]$^+$, 100), 223 (25), 178 (8), 112 (7); HRMS [M]$^+$ calcd for $C_{15}H_{12}S$ 224.0660, found 224.0654.

2-Methyl-4-(4-(methylsulfonyl)phenyl)thiophene (7l, Table 2, entry 6). Following the general procedure, the title compound was obtained (136 mg, 36%). Solid, mp 140−141 °C; TLC (EtOAc/hexanes (1:1)) R_f = 0.70; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.52 (s, 3 H), 3.05 (s, 3 H), 7.06 (s, 1 H), 7.33 (s, 1 H), 7.70 (d, *J* = 8.7 Hz, 2 H), 7.91 (d, *J* = 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2 (CH_3), 44.4 (CH_3), 120.5 (CH), 124.0 (CH), 126.6 (CH × 2), 127.8 (CH × 2), 138.1 (C), 139.6 (C), 141.0 (C), 141.3 (C); IR (KBr) 3011, 2928, 1599 cm^{-1}; EI-MS *m*/*z* (rel intensity) 252 ([M]$^+$, 28), 201 (11), 173 (15), 130 (100); HRMS [M]$^+$ calcd for $C_{12}H_{12}O_2S_2$ 252.0279, found 252.0275.

4-(3-Bromophenyl)-2-methylthiophene (7m, Table 2, entry 7). Following the general procedure, the title compound was obtained (175 mg, 46%). Solid, mp 45−47 °C; TLC (Et_2O/hexanes (1:5)) R_f = 0.75; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.51 (s, 3 H), 7.00 (s, 1 H), 7.18−7.24 (m, 2 H), 7.39 (d, *J* = 8.7 Hz, 1 H), 7.45 (d, *J* = 8.7 Hz, 1 H), 7.69 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3 (CH_3), 118.8 (CH), 122.8 (C), 124.3 (CH), 124.7 (CH), 129.2 (CH), 129.7 (CH), 130.1 (CH), 138.1 (C), 140.4 (C), 140.8 (C); IR (KBr) 3113, 1570, 1070 cm^{-1}; EI-MS *m*/*z* (rel intensity) 254 ([M + 2]$^+$, 100), 252 ([M]$^+$, 97), 171 (24), 129 (18); HRMS [M]$^+$ calcd for $C_{11}H_9BrS$ 251.9608, found 251.9605.

2-Methyl-4-phenylfuran (8c). Following the general procedure, the title compound was obtained (43 mg, 45%). Solid, mp 67−68 °C; TLC (EtOAc/hexanes (1:4)) R_f = 0.70; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.37 (s, 3 H), 6.35 (s, 1 H), 7.25−7.31 (m, 1 H), 7.41 (t, *J* = 8.1 Hz, 2 H), 7.50 (d, *J* = 8.1 Hz, 2 H), 7.63 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5 (CH_3), 104.8 (CH), 125.6 (CH × 2), 126.6 (CH), 127.1 (C), 128.6 (CH × 2), 132.7 (C), 136.5 (CH), 153.1 (C); IR (KBr) 2929, 1558, 1122 cm^{-1}. These data are in agreement with those reported in the literature.[14]

4-(4-Chlorophenyl)-2-methylfuran (8d). Following the general procedure, the title compound was obtained (55 mg, 48%). Solid, mp 91−92 °C; TLC (EtOAc/hexanes (1:4)) R_f = 0.70; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3 H), 6.24 (s, 1 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 7.34 (d, *J* = 8.0 Hz, 2 H), 7.54 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5 (CH_3), 104.6 (CH), 126.1 (C), 126.8 (CH × 2), 128.8 (CH × 2), 131.3 (C), 132.2 (C), 136.7 (CH), 153.4 (C); IR (KBr) 2919, 1553, 1137 cm^{-1}; EI-MS *m*/*z* (rel intensity) 194 ([M + 2]$^+$, 33), 192 ([M]$^+$, 100), 163 (24), 128 (53); HRMS [M]$^+$ calcd for $C_{11}H_9ClO$ 192.0342, found 192.0346.

4-(4-Bromophenyl)-2-methylfuran (8e). Following the general procedure, the title compound was obtained (65 mg, 46%). Solid, mp 109−110 °C; TLC (EtOAc/hexanes (1:4)) R_f = 0.68; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 6.24 (s, 1 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 7.45 (d, *J* = 8.0 Hz, 2 H), 7.56 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5 (CH_3), 104.5 (CH), 120.3 (C), 126.1 (C), 127.1 (CH × 2), 131.7 (CH × 2), 131.7 (C), 136.7 (CH), 153.5 (C); ^{13}C NMR (75 MHz, acetone-d_6) δ 13.4 (CH_3), 105.2 (CH), 120.5 (C), 126.8 (C), 128.1 (CH × 2), 132.5 (CH × 2), 132.9 (C), 138.3 (CH), 154.2 (C); IR (KBr) 2922, 1553, 1410 cm^{-1}; EI-MS *m*/*z* (rel intensity) 238 ([M + 2]$^+$, 100), 236 ([M]$^+$, 99), 207 (17), 128 (85); HRMS [M]$^+$ calcd for $C_{11}H_9BrO$ 235.9837, found 235.9841.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

X-ray crystallographic data (**1b**, **1g**) and complete characterization data (^{1}H and ^{13}C{^{1}H} NMR data) for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Krause, N.; Winter, C. *Chem. Rev.* **2011**, *111*, 1994. (b) Álvarez-Corral, M.; Muñoz-Dorado, M.; Rodríguez-García, I. *Chem. Rev.* **2008**, *108*, 3174. (c) Peng, L.; Zhang, X.; Ma, M.; Wang, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 1905. (d) Kim, S.; Lee, P. H. *J. Org. Chem.* **2012**, *77*, 215.

(2) (a) Rodebaugh, R. M.; Cromwell, N. H. *Tetrahedron Lett.* **1967**, *8*, 2859. (b) Wang, D.-L.; Imafuku, K. *Heterocycles* **2001**, *54*, 647. (c) Potikha, L. M.; Turelik, A. R.; Kovtunenko, V. A. *Chem. Heterocycl. Compd.* **2009**, *45*, 1184. (d) Potikha, L. M.; Kovtunenko, V. A. *Chem. Heterocycl. Compd.* **2007**, *43*, 521. (e) Potikha, L. M.; Kovtunenko, V. A. *Chem. Heterocycl. Compd.* **2007**, *43*, 523. (f) Potikha, L. M.; Kovtunenko, V. A. *Chem. Heterocycl. Compd.* **2009**, *45*, 1396. (g) Potikha, L. M.; Kovtunenko, V. A.; Turov, A. V. *Chem. Heterocycl. Compd.* **2009**, *45*, 815. (h) Potikha, L. M.; Kovtunenko, V. A.; Turov, A. V.; Palamarchuk, G. V.; Zubatyuk, R. I.; Shishkin, O. V. *Chem. Heterocycl. Compd.* **2009**, *45*, 327. (i) Potikha, L. M.; Kovtunenko, V. A. *Chem. Heterocycl. Compd.* **2006**, *42*, 741.

(3) Ma, S.; Wang, G. *Tetrahedron Lett.* **2002**, *43*, 5723.

(4) Fandrick, D. R.; Saha, J.; Fandrick, K. R.; Sanyal, S.; Ogikubo, J.; Lee, H.; Roschangar, F.; Song, J. J.; Senanayake, C. H. *Org. Lett.* **2011**, *13*, 5616.

(5) Tonogaki, K.; Itami, K.; Yoshida, J.-I. *J. Am. Chem. Soc.* **2006**, *128*, 1464.

(6) Lin, M.-H.; Kuo, C.-K.; Lin, W.-C.; Huang, Y.-C.; Tsai, Y.-T.; Liang, K.-Y.; Li, Y.-S.; Chuang, T.-H. *Tetrahedron* **2013**, *69*, 8263.

(7) Cordier, P.; Aubert, C.; Malacria, M.; Lacôte, E.; Gandon, V. *Angew. Chem., Int. Ed.* **2009**, *48*, 8757.

(8) Greatrex, B. W.; Kimber, M. C.; Taylor, D. K.; Tiekink, E. R. T. *J. Org. Chem.* **2003**, *68*, 4239.

(9) The structures have been deposited with the Cambridge Crystallographic Data Centre (**1b**: CCDC 978053, **1g**: CCDC 978502). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(10) Kim, S. H.; Lim, J. W.; Lim, C. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2012**, *33*, 620.

(11) Kiren, S.; Hong, X.; Leverett, C. A.; Padwa, A. *Org. Lett.* **2009**, *11*, 1233.

(12) Kashulin, I. A.; Nifant'ev, I. E. *J. Org. Chem.* **2004**, *69*, 5479.

(13) Funaki, K.; Sato, T.; Qi, S. *Org. Lett.* **2012**, *14*, 6186.

(14) Okazaki, R.; Negishi, Y.; Inamoto, N. *J. Org. Chem.* **1984**, *49*, 3819.