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Extension of β-chloroenals to ethyl 5-chloro-2,4-pentadienoates using Wadsworth–Emmons reactions: subsequent conversions to 5-aryl-5-chloro-2,4-pentadienoic acids and 5-aryl-2-penten-4-ynoic acids

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Abstract—Convenient routes from (*Z*)-3-aryl-3-chloroenals to (2*E*,4*Z*)-5-aryl-5-chloro-2,4-pentadienoates and (2*E*)-5-aryl-2-penten-4-ynoates are described. The stereochemical assignments are based on NMR spectral data.

1. Introduction

Vinamidinium salts, chloropropenium salts, and β-chloroenals have served effectively as three carbon synthons[1] in the synthesis of a wide variety of heterocyclic systems including pyrroles,[2] pyrazoles,[3] pyrimidines,[4] and pyridines.[5] This resulting chemistry has been successfully applied to the synthesis of a number of natural products including Ningalin B[6] and Lukianol A[7] as well as compounds of pharmaceutical interest.[8] This paper explores the extension of the three carbon β-chloroenal synthons to analogous five carbon synthons.

Over the years there has been interest in polyenes and enynes as a consequence of the physiological behavior exhibited by representatives of these systems.[9–15] They have also been shown in many cases to serve as effective synthons in the construction of a wide variety of interesting molecules.[16–19] Welker has recently reported transition metal-mediated Diels–Alder reactions involving the zinc-mediated hydrocobaltation of enynes.[20] As a result, a number of synthetic approaches to the synthesis of conjugated dienes and enynes have been reported. For example, Wiley described the stereochemistry of several of these unsaturated systems including 3-methyl-5-arylpent-2-en-4-ynoic acids.[21] A highly stereoselective method for the synthesis of (*Z*)-2-en-4-ynoic acid derivatives involving cross coupling of propiolic acid derivatives with terminal alkynes in the presence of a palladium (0) catalyst has been describe by Lu, Huang, and Ma.[22]

2. Results and discussion

We report here convenient syntheses of (2*E*,4*Z*)-5-aryl-5-chloro-2,4-pentadienoic acid derivatives and (*E*)-5-aryl-2-penten-4-ynoic acids that were discovered in the course of our exploration of the chemistry of 5-aryl-5-halo-2,4-pentadienoates. We have found that the Wadsworth–Emmons[23] reactions with triethyl phosphonoacetate (TEPA) and (*Z*)-3-aryl-3-chloropropenals (**1a–f**),[24] using procedures patterned after those reported by Villieras and Rambaud,[25] yield alkyl (2*E*,4*Z*)-5-aryl-5-halo-2,4-pentadienoates (**2a–f**) with a high degree of stereoselectivity (Scheme 1) The stereochemistry of the β-chloroenals has been well established as the (*Z*) isomer in all cases,[10] and the stereochemistry is unchanged in the course of the reaction. The stereochemistry of the Wadsworth–Emmons product is shown to be (2*E*,4*Z*) based on the coupling constants observed (see Table 1) and NOESY experiments which indicated the proton at the 2′-position on the aromatic ring and the vinyl hydrogen at C-3 were in close proximity.

Hydrolysis of the esters under basic conditions (room temperature with 1.1 equiv of aqueous sodium hydroxide)

Keywords: Chloroenals; Chlorodienoates; Enynoic acids.
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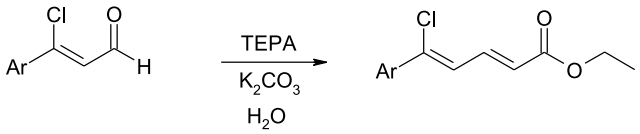


1 a-f **2 a-f**

a Ar = phenyl

b. Ar = p-methylphenyl

c. Ar = p-methoxyphenyl

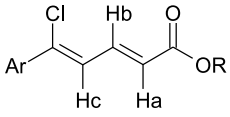
d. Ar = p-chlorophenyl

e. Ar = p-fluorophenyl

f. Ar = 3'4'-methylenedioxyphenyl

Scheme 1.

Table 1. Coupling constants of vinyl hydrogens (Hz)



2 R = ethyl
3 R = H

Compound	Ar	J_{ab} (Hz)	J_{bc} (Hz)	% Yield
2a	Phenyl	15.5	10.9	86
2b	*p*-Methylphenyl	15.5	10.7	87
2c	*p*-Methoxyphenyl	15.3	11.3	83
2d	*p*-Chlorophenyl	15.6	10.8	91
2e	*p*-Fluorophenyl	15.4	10.7	74
2f	3′,4′-Methylenedioxyphenyl	15.5	10.9	96
3a	Phenyl	15.9	10.9	57
3b	*p*-Tolyl	15.5	10.9	60
3c	*p*-Methoxy	15.5	10.9	63
3d	*p*-Chlorophenyl	15.4	10.9	52
3e	*p*-Fluoro	15.2	10.8	76

followed by protonation provides a route to the (2*E*,4*Z*)-5-aryl-5-halo-2,4-pentadienoic acids (**3a**–**e**) with no change in the stereochemistry of the conjugated system (Scheme 2).The stereochemical assignments were clearly indicated by the coupling constants (Table 1) which are very much in accord with coupling constants reported for similar systems[26] and from NOESY experiments.

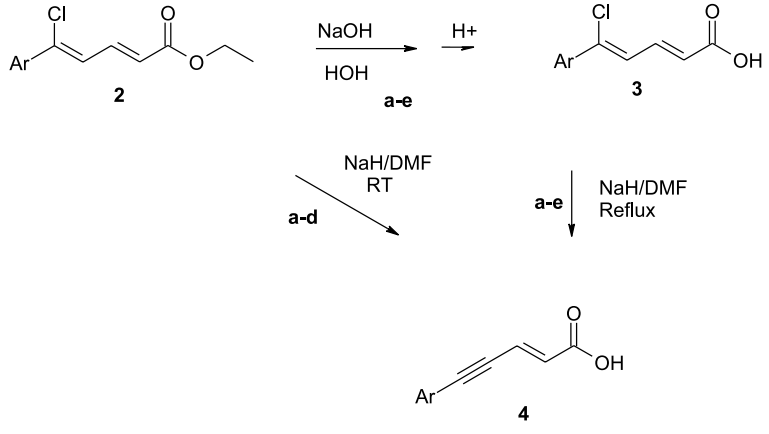
When harsher hydrolysis conditions were employed we observed some dehydrohalogenation occurring resulting in the formation of small amounts of 5-aryl-2-penten-4-ynoic acids. This suggested to us that perhaps use of a stronger base might provide a clean route to these compounds.

Treatment of the halo esters **2a**–**e** with 6 equiv of sodium hydride in DMF at room temperature followed by protonation resulted in a smooth and rapid dehydrohalogenation and dealkylation to (*E*)-5-aryl-2-penten-4-ynoic acid (**4**) in every case explored with the exception of the 5-(*p*-fluorophenyl)-derivative which yielded clean **3e** (Scheme 2). The geometry was again clear from the coupling constants of the vinyl hydrogens (Table 2).

This suggested to us that in aqueous base at room temperature the hydroxide was acting as a nucleophile to saponify the ester but was not a strong enough base to promote the dehydrohalogenation of the resulting carboxylates. Sodium hydride in DMF was a strong enough base such that the dehydrohalogenation reactions of **2a**–**d** proceeded rapidly at room temperature to give the enynoic esters, which then underwent a subsequent dealkylation to form the sodium salt of the carboxylic acid in every case except the *p*-fluorophenyl derivative (**2e**). In this case formation of the carboxylate anion **3e** is apparently faster than dehydrohalogenation. Dehydrohalogenation of the carboxylate anion is more difficult, and thus the enynoic acid is not formed under such reaction conditions. Although the chlorodienoic acids do not dehydrohalogenate when treated with NaH in DMF at room temperature, the enynoic acids (**4a**–**e**) are formed when the chlorodienoic acids (**3a**–**e**) are refluxed with sodium hydride in DMF.

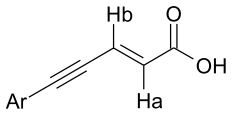
3. Conclusions

We have shown that the versatile β-chloroenals can be converted in high yield using Wadsworth–Emmons chemistry to ethyl 5-aryl-5-chloro-2,4-pentadieoates with a high degree of stereochemical control. These esters can subsequently be converted to the corresponding 5-aryl-5-chlorodienoic acids with aqueous base under mild conditions. Furthermore, they can be dehydrohalogenated and dealkylated under remarkably mild conditions to form



Scheme 2.

Table 2. Coupling constants of vinyl hydrogens (Hz)



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Compound	Ar	J_{ab} (Hz)	% Yield
4a	Phenyl	15.9	87
4b	*p*-Methylphenyl	15.9	87
4c	*p*-Methoxyphenyl	15.8	98
4d	*p*-Chlorophenyl	15.4	82
4e	*p*-Fluorophenyl	16.1	67

5-aryl-2-penten-4-ynoic acids, thus providing convenient new routes to these important classes of compounds.

4. Experimental

4.1. General

The 300 MHz NMR data was collected with a GE Omega 300 MHz instrument. The 500 MHz NMR data was collected on a Bruker 500. The IR data was collected using a Nicolet Avatar fitted with a HATR accessory. The low resolution mass spectral data was obtained using a Shimadzu Model QP 5050 GC–MS equipped with a direct insert sampling device. HRMS data was provided by the Nebraska Center for Mass Spectrometry at the University of Nebraska-Lincoln. The purity of the esters was estimated at better than 95% based on gas chromatographic analysis. The purity of the acids was estimated at better than 95% based on the ^{13}C NMR data. Solvents and reagents were used as received from the manufacturer (Aldrich Chemicals and Fisher Scientific).

4.1.1. Ethyl (2*E*,4*Z*)-5-chloro-5-phenyl-2,4-pentadienoate (2a). A mixture of triethyl phosphonoacetate (5.93 g, 0.027 mol), (*Z*)-3-chloro-3-phenyl-2-propenal **1a** (3.69 g, 0.022 mol), potassium carbonate (8.0 g, 0.058 mol), and 6 mL of water was stirred at room temperature for 46 h. Water (10 mL) was added and the mixture was washed twice with ethyl acetate (25 mL). After drying ($MgSO_4$), the organic solvent was evaporated using a rotary evaporator yielding 4.46 g (86%) of **2a** as an oil. A Kugelrohr distillation provided an analytical sample: bp 140–145 °C at 0.25 mm Hg; mp 22–26 °C; IR (HATR) 2975, 1703, and 1137 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 1.30 (J=7.2 Hz, 3), 4.23 (q, J=7.2 Hz, 2), 6.07 (d, J=15.5 Hz, 1), 6.84 (d, J=10.9 Hz, 1), and 7.83 ppm (dd, J=15.5, 10.9 Hz, 1); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3, 60.4, 123.2, 124.2, 126.7, 128.5, 129.9, 136.8, 139.4, 140.3, and 166.4 ppm; MS *m*/*z* 238 (4), 236 (12), 203 (11), 201 (74), 191 (19), 173 (100), 155 (14), 145 (7), 127 (52), 117 (20), and 102 (15); HRMS (EI, M+) calcd for $C_{13}H_{13}O_2Cl$ 236.0604, found 236.0607.

4.1.2. Ethyl (2*E*,4*Z*)-5-chloro-5-(*p*-methylphenyl)-2,4-pentadienoate (2b). This compound was prepared from **1b** in 87% yield using the procedure described above for the synthesis of **2a**: bp 155–160 °C at 0.25 mm Hg; mp 41–43 °C; IR (HATR) 2974, 1697, 1615, 1130 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (s, J=7.2 Hz, 3), 2.40 (s, 3), 4.27 (q, J=7.2 Hz, 2), 6.09 (d, J=15.5 Hz, 1), 6.85 (d, J=10.7 Hz, 1), 7.22 (d, J=7.2 Hz, 2), 7.60 (d, J=7.2 Hz, 2), and 7.86 ppm (dd, J=15.5, 10.7 Hz, 1); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3, 21.3, 60.5, 122.4, 123.6, 126.7, 129.3, 134.1, 139.7, 140.3, 140.6, and 166.7; MS *m*/*z* 250 (13), 252 (4), 215 (100), 205 (15), 187 (87), 141 (33), 119 (50). HRMS (EI, M+) calcd for $C_{14}H_{15}O_2Cl$ 250.0761, found 250.0764.

4.1.3. Ethyl (2*E*,4*Z*)-5-chloro-5-(*p*-methoxyphenyl)-2,4-pentadienoate (2c). This compound was prepared from **1c** in 84% yield using the procedure described above for the synthesis of **2a**: bp 205 °C at 2.25 mm Hg; mp 52–55 °C; IR (HATR) 2983, 2839, and 1701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (t, J=7.2 Hz, 3), 3.87 (s,3), 4.28 (q, J=7.2 Hz, 2), 6.08 (d, J=15.3 Hz, 1), 6.80 (d, J=11.3 Hz, 1), 6.93 (d, J=8.2 Hz, 2), 7.66 (d, J=8.2 Hz, 2), and 7.85 ppm (dd, J=15.3, 11.3 Hz, 1); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.2, 55.4, 60.5, 113.9, 121.4, 123.1, 128.2, 129.4, 139.9, 140.3, 161.0, and 166.8 ppm; MS *m*/*z* 266 (8), 232 (15), 231 (100), 203 (63), 158 (24), 135 (85), and 115 (31); HRMS (EI, M+) calcd for $C_{14}H_{15}O_3Cl$ 266.0710, found 266.0704.

4.1.4. Ethyl (2*E*,4*Z*)-5-chloro-5-(*p*-chlorophenyl)-2,4-pentadienoate (2d). This compound was prepared from **1d** in 92% yield using the procedure described above for the synthesis of **2a**: bp 160–165 °C at 0.45 mm Hg; mp 65–68 °C; IR (HATR) 3060, 2975, 2897, and 1700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.35 (t, J=7.1 Hz, 3), 4.28 (q, J=7.1 Hz, 2), 6.13 (d, J=15.6 Hz, 1), 6.86 (d, J=10.8 Hz, 1), 7.39 (d, J=7.2 Hz, 2), 7.64 (d, J=7.2 Hz, 2), and 7.82 ppm (dd, J=15.6, 10.8 Hz, 1); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3, 60.6, 123.6, 124.6, 128.0, 128.8, 135.0, 136.0, 139.0, 139.2, and 166.5 ppm; MS *m*/*z* 270 (10), 235 (79), 225 (18), 207 (100), 189 (11), 162 (32), 139 (19), 126 (26), and 115 (11); HRMS (EI, M+) calcd for $C_{13}H_{12}O_2Cl_2$ 270.0214, found 270.0214.

4.1.5. Ethyl (2*E*,4*Z*)-5-chloro-5-(*p*-fluorophenyl)-2,4-pentadienoate (2e). This compound was prepared from **1e** in 74% yield using the procedure described above for the synthesis of **2a**: bp 139 °C at 1.25 mm Hg; IR (HATR) 2981, 1708, 1598 and 1235 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.34 (t, J=7.2 Hz, 3), 4.27 (q, J=7.2 Hz, 2), 6.11 (d, J=15.4 Hz, 1),6.81 (d, J=10.7 Hz, 1), 7.10 (m, 3), 7.68 (m, 2), and 7.82 ppm (dd, J=15.4, 10.7 Hz, 1); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3, 60.6, 115.6 (d, J=22.0 Hz), 123.2 (d, J=0.7 Hz), 124.2, 128.7 (d, J=8.2 Hz), 133.2 (d, J=3.5 Hz), 139.2, 139.4, 163.6 (d, J=251.5 Hz), and 166.6 ppm; MS *m*/*z* 256 (4), 254 (12), 219 (79), 209 (19), 191 (100), 173 (13), 146 (46), 135 (16), 123 (29), 99 (5), 87 (7), and 73 (29); HRMS (EI, M+) calcd for $C_{13}H_{12}O_2ClF$ 254.0510, found 254.0511.

4.1.6. Ethyl (2*E*,4*Z*)-5-chloro-5-(3′,4′-methylenedioxyphenyl)-2,4-pentadienoate (2f). This compound was prepared from **1f** in 96% yield using the procedure described above for the synthesis of **2a**: bp 164 °C at 0.8 mm Hg; IR (HATR) 2899, 1706, 1614, and 1486 cm^{-1}; ^1H NMR

(500 MHz, $CDCl_3$) δ 1.34 (t, $J=7.1$ Hz, 3), 4.26 (q, $J=7.2$ Hz, 2), 6.03 (s, 2), 6.07 (dd, $J=0.8$, 15.5 Hz, 1), 6.75 (dd, $J=0.8$, 10.9 Hz, 1), 6.83 (d, $J=8.3$ Hz, 1), 7.16 (d, $J=1.9$ Hz, 1), 7.25 (dd, $J=1.9$, 8.3 Hz, 1), and 7.82 ppm (dd, $J=15.5$, 10.9 Hz, 1); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 14.3, 60.5, 101.7, 107.0, 108.2, 121.6, 122.1, 123.4, 131.2, 139.7, 1390.0, 148.1, 149.2, and 166.7 ppm; MS *m/z* 282 (6), 280(18), 245 (100), 235 (15), 217 (59), 207 (17), 172 (20), 149 (74), 131 (6), 117 (17), and 85 (14); HRMS (EI, M+) calcd for $C_{14}H_{13}O_4Cl$ 280.0502, found 280.0494.

4.1.7. (2*E*,4*Z*)-5-Chloro-5-phenyl-2,4-pentadienoic acid (3a). A solution of ethyl (2*E*,4*Z*)-5-chloro-5-phenyl-2,4-pentadienoate **2a** (0.5 g, 2.12 mmol) in a 1:1 mixture of H_2O/EtOH (100 mL) was treated with NaOH (0.093 mL, 2.23 mmol) and stirred at room temperature. After 48 h, the reaction mixture was made slightly acidic with 5% HCl (10 mL), extracted into ethyl acetate (2×75 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was recrystallized in chloroform (10 mL) and filtered to give 0.25 g (57%) of **3a** as a yellow powder: mp 161–163 °C; IR (HATR) 3200–2500 (broad), 3390, 2350, 2334, 1678, and 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.29 (d, $J=15.9$ Hz, 1), 7.29 (d, $J=10.9$ Hz, 1), 7.49 (m, 3), and 7.82 ppm (m, 3); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 123.2, 124.4, 126.2, 128.2, 129.5, 136.2, 138.6, 138.7, and 166.1 ppm; MS *m/z* 208 (39), 191 (30), 173 (100), 162 (31), 127 (80), 115 (57), 105 (60), 86 (21), and 77 (64); HRMS (EI, M+) calcd for $C_{11}H_9ClO_2$ 208.0291,, found 208.0288.

4.1.8. (2*E*,4*Z*)-5-Chloro-5-(*p*-methylphenyl)-2,4-pentadienoic acid (3b). This compound was prepared from **2b** in 60% yield using the procedure described above for the synthesis of **3a**: mp 177–180 °C; IR (HATR) 3479, 3390, 3025, 2904, 1619, and 1541 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.414 (s, 3H), (6.110 (d, $J=15.6$ Hz, 1), 6.896 (d, 1H, $J=10.7$ Hz, 1), 7.236 (d, 2H), 7.622 (d, 2H), 7.958 (dd,, $J=15.6$, 10.7 Hz, 1); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 21.2, 123.6, 125.3, 127.5, 130.2, 134.9, 140.2, 140.3, 141.3, and 167.5 ppm; MS *m/z* 222(29), 187 (100), 141 (73), 131 (37), 119 (77), 115 (75), 91 (38) and 10 (50); HRMS (EI, M+) calcd for $C_{12}H_{11}ClO_2$ 222.0448,, found 222.0446.

4.1.9. (2*E*,4*Z*)-5-Chloro-5-(*p*-methoxyphenyl)-2,4-pentadienoic acid (3c). This compound was prepared from **2c** in 63% yield using the procedure described above for the synthesis of **3a**. The crude solid was recrystallized from hexane: mp 163–165 °C; IR (HATR) 2951 (broad), 2838, 2528, 1669, 1588 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 3H), 6.09 (d, $J=15.5$ Hz, 1), 6.755 (d, $J=10.9$ Hz, 1), 6.86 (d, 2H), 7.58 (d, 2H), 7.87 (dd, $J=15.3$, 15.4 Hz, 1H); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 55.9, 115.0, 122.5, 124.7, 129.1, 129.8, 140.1, 140.4, 162.3, and 167.5 ppm; MS *m/z* 238 (16), 203 (100), 158 (27), 135 (67), 115 (30), 89 (14), 77 (11), and 63 (19); HRMS (EI, M+) calcd for $C_{12}H_{11}ClO_3$ 238.0397,, found 238.0404.

4.1.10. (2*E*,4*Z*)-5-Chloro-5-(*p*-chlorophenyl)-2,4-pentandienoic acid (3d). This compound was prepared from **2d** in 52% yield using the procedure described above for the synthesis of **3a**: mp 218–222 °C; IR (HATR) 3321–1947 (broad), 1674, 1600, 1577, and 1491 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.28 (s, 1), 6.11 (d, $J=15.4$ Hz, 1), 6.90 (d, $J=10.9$ Hz, 1), 7.24 (d, $J=8.0$ Hz, 2), 7.62 (d, $J=8.0$ Hz, 2) and 7.96 ppm (dd, $J=15.4$, 10.9 Hz, 1); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 123.9, 125.0, 127.3, 128.4, 133.0, 135.0, 137.3, 138.5, and 166.0 ppm; MS *m/z* 242 (13), 207 (100), 196 (6), 189 (7), 162 (20), 139 (18), and 115 (28); HRMS (EI, M+) calcd for $C_{11}H_8O_2Cl_2$ 241.9901, found 241.9896.

4.1.11. (2*E*,4*Z*)-5-Chloro-5-(*p*-fluorophenyl)-2,4-pentadienoic acid (3e). This compound was prepared from **2e** in 76% yield using the procedure described above for the synthesis of **3a**: mp 223–225°; IR (HATR) 3370–2180 (broad), 1674, 1600, and 1425 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.59 (s, 1), 6.14 (d, $J=15.2$ Hz, 1), 6.86 (d, $J=10.8$ Hz, 1), 7.13 (m, 2), 7.71 (m, 3), and 7.93 ppm (dd, $J=10.8$, 15.2 Hz, 1); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 115.4 (d, $J=23.9$ Hz), 124.5, 130.7, 132.3 (d, $J=8.3$ Hz), 134.1, 134.2, 165.6 (d, $J=165.6$ Hz), and 165.7 ppm; MS *m/z* 226 (18), 191(100), 173 (11), 145 (40), 135 (24), 123 (33), 95 (10), and 73 (23); HRMS (EI, M+) calcd for $C_{11}H_8O_2ClF$ 266.0197, found 266.0194.

4.1.12. (*E*)-5-Phenyl-pent-2-en-4-ynoic acid (4a) from 2a. A slurry of sodium hydride (0.63 g, 0.026 mol) in dry *N*,*N*-dimethylformamide (30 mL) was added to ethyl (2*E*,4*Z*)-5-chloro-5-phenyl-2,4-pentadienoate (1.0 g, 0.00425 mol). The resulting slurry was stirred at room temperature for 72 h. Water (200 mL) was carefully added followed by 50 mL of 18% HCl. The aqueous layer was extracted three times with 30 mL of ethyl acetate. The organic layers were combined and washed twice with water (25 mL), and dried ($MgSO_4$). Removal of solvent using a rotary evaporator afforded 0.64 g (87%) of a crude solid. Recrystallization from hexane yielded an analytical sample of (*E*)-5-phenyl-pent-2-en-4-ynoic acid: mp 129–132°; IR (HATR) 3700–2200 (broad), 2197, 1665, 1614, and 1414 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.34 (d, $J=15.9$ Hz, 1), 7.11 (d, $J=15.9$ Hz, 1), 7.40 (m, 3), and 7.52 ppm (m, 2); ^{13}C NMR (125.8 MHz, acetone-d_6) δ86.7, 98.5, 123.0, 125.5, 129.6, 130.4, 131.5, 132.7, and 166.5 ppm; MS *m/z* 172 (100), 146 (20), 144 (13), 127 (30), 122 (24), 115 (64), 105 (68), 97 (17), and 77 (75); HRMS (EI, M+) calcd for $C_{11}H_8O_2$ 172.0524, found 172.0522.

4.1.13. (*E*)-5-(*p*-Methylphenyl)-2-penten-4-ynoic acid (4b) from 2b. This compound was prepared from **2b** in 87% yield using the procedure described above for the synthesis of **4a**: mp 173–179 °C; IR (HATR) 3700–2200 (broad), 2182, 1680, 1593, and 1424 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.4 (s, 3), 3.72 (s, 1), 6.31 (d, $J=15.9$ Hz, 1), 7.09 (d, $J=15.9$ Hz, 1), 7.19 (d, $J=7.5$ Hz, 2), and 7.41 ppm (d, $J=7.5$ Hz, 2); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 21.5, 86.5, 92.9, 119.9, 125.8, 130.3, 131.0, 132.7, 140.8, and 166.5 ppm; MS *m/z* 187 (15), 186 (100), 171 (80), 157 (9), 139 (25), 129 (34), 115 (61), 90 (8), 75 (5), and 70(18); HRMS (EI, M+) calcd for $C_{12}H_{10}O_2$ 186.0677, found 186.0681.

4.1.14. (*E*)-5-(*p*-Methoxyphenyl)-2-penten-4-ynoic acid (4c) from 2c. This compound was prepared from **2c** in 98% yield using the procedure described above for the synthesis of **4a**: mp 164–165 °C; IR (HATR) 3200–2300 (broad), 2187, 1675, 1588, and 1414 cm^{-1}; ^1H NMR (500 MHz,

$CDCl_3$) δ 3.86 (s, 3), 6.28 (d, $J=15.8$ Hz, 1), 6.90 (d, $J=9.1$ Hz, 2), 7.09 (d, $J=15.8$ Hz, 1), and 7.46 ppm (d, $J=9.1$ Hz, 2); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 55.9, 115.0, 122.5, 124.7, 129.1, 129.8, 140.1, 140.4, 162.3, and 167.6 ppm; MS *m/z* 202 (100), 187 (10), 185 (7), 159 (28), 136 (25), 131 (28), 113 (15), 103 (17), 77 (24), and 45 (89); HRMS (EI, M+) calcd for $C_{12}H_{10}O_3$ 202.0630, found 202.0630.

4.1.15. (*E*)-5-(*p*-Chlorophenyl)-pent-2-en-4-ynoic acid (4d) from 2d. This compound was prepared from **2d** in 82% yield using the procedure described above for the synthesis of **4a**: mp 196–201 °C; IR (HATR) 3400–2200 (broad), 2197, and 1671 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.34 (d, $J=15.4$ Hz, 1), 7.07 (d, $J=15.4$ Hz, 1), 7.36 (d, $J=8.7$ Hz, 2), and 7.45 ppm (d, $J=8.7$ Hz, 2); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 87.9, 97.0, 121.8, 125.2, 129.9, 132.0, 134.3, 136.0, and 166.4 ppm; MS *m/z* 208 (29), 206 (88), 189 (6), 171 (46), 160 (12), 149 (16), 136 (9), 126 (44) 115 (100), 99 (18), and 81 (20); HRMS (EI, M+) calcd for $C_{11}H_7O_2Cl$ 206.0129, found 206.0135.

4.1.16. (*E*)-5-(*p*-Fluorophenyl)-pent-2-en-4-ynoic acid (4e) from 2e. This compound was prepared from **2e** in 67% yield using the procedure described above for the synthesis of **4a**: mp 148–153 °C; IR (HATR) 2912, 2194, 1669, 1615, and 1588 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.36 (d, $J=16.5$ Hz, 1), 6.97 (d, $J=15.8$ Hz, 1), 7.24 (m, 3), and 7.62 ppm (m, 2); ^{13}C NMR (125.8 MHz, acetone-d_6) δ 85.8, 96.4, 115.9 (d, $J=22.4$ Hz), 118.5 (d, $J=3.4$ Hz), 124.4, 130.7, 134.2 (d, $J=8.8$ Hz), 163.1 (d, $J=250.6$ Hz), and 165.6 ppm; MS *m/z* 190 (100), 173 (10), 162 (18), 144 (38), 134 (53), 133 (100), 125 (44), and 99 (19); HRMS (EI, M+) calcd for $C_{11}H_7O_2F$ 190.0403, found 190.0427.

4.1.17. Dehydrohalogenation of 3 to form 4. A mixture resulting from adding a solution of the 5-aryl-5-chloro-2,4-pentadienoic acid (0.22 mmol) in 40 mL DMF to sodium hydride (0.90 mmol) was refluxed for 20 min. The reaction mixture was cooled to room temperature, diluted with water, made acidic with 10% HCl and extracted three times with 50 mL of ethyl acetate. The organic layer was then washed once with water and dried over $MgSO_4$. Removal of the solvent afforded the crude acid which was purified by recrystallization from hexane (**4a**, 88%; **4b**, 95%, **4c**, 54%; **4d**, 92%; **4e**, 93%).

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