Reaction of 2-Butenoic Acid Dianion and Its N-(4-Methoxyphenyl)amide with Methoxy-Substituted Arynes

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Received September 5, 1991

N-(4-Methoxyphenyl)-1-butenamide dianion (**6**), generated by the reaction of *N*-(4-methoxyphenyl)-2-butenamide (**3**) with LDA or LTMP, undergoes exclusive 4-arylation with various methoxy-substituted arynes **2a–e** yielding mixtures consisting of a *N*-(4-methoxyphenyl)-(*E*)-4-aryl-3-butenamide **9** (85–90%) and a *N*-(4-methoxyphenyl)-(*E*)-4-aryl-2-butenamide **9′** (10–15%). Under certain conditions, 4,4-diarylated products **12** are also obtained. 2-Butenoic acid dianion (**14**) also reacts with methoxy-substituted arynes affording predominantly 4-aryl-3-butenoic acids **15** and minor amounts of 4-aryl-2-butenoic acids **15′**. The exclusive low temperature (−30 to −40 °C) 4-addition of arynes to dianion **14** is in contrast to the predominant 2-addition that **14** undergoes with certain aldehydes and ketones at comparable temperatures. The mixtures of 4-arylbutenoic acids **15** and **15′** and 4-arylbutenamides **9** and **9′** were readily hydrogenated (Pd/C) and esterified ($MeOH/H_2SO_4$) to synthetically valuable methyl 4-arylbutanoates **17**.

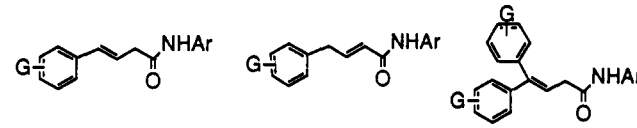
As an extension to our ongoing study of annulations involving arynes,[1] we attempted to prepare *N*-aryl-4-methyl-3,4-dihydro-2-pyridones **5** by treatment with equimolar amounts of *N*-(4-methoxyphenyl)-2-butenamide (**3**) and bromoarenes **1a–e** with LTMP or LDA in THF at −40 °C. We anticipated that the arynes **2a–e** and lithiated 1,2-dipolar nucleophilic derivatives **4** so generated would engage in [4 + 2] nonsynchronous cycloadditions to yield pyridones **5**, after proton quench of the cycloadducts.[2] However, 2-pyridones were not formed in these reactions. Rather, amide **3** under these conditions was converted to its dianion **6**, to which arynes **2a–e** added exclusively to the 4-position providing *N*-(4-methoxyphenyl) derivatives of (*E*)-4-aryl-3-butenamide ((*E*)-4-arylcrotonamide) **9a–e** (39–61%) as major products and (*E*)-4-aryl-2-butenamide **9′a–e** (<10%) and 4,4-diaryl-3-butenamides (4,4-diarylcrotonamides) **12a–e** (<24%) as minor products (Table I). Diarylated products **12a–e** were not detected when aryne generation was carried out quickly in the presence of dianion **6**, which resulted in significantly higher yields of 4-monoarylated products **9a–e**; e.g., the yield of **9b** increased from 46 to 72% upon rapid generation of aryne **2b**.

The 4-aryl-3-butenamides **9a–e** and 4,4-diaryl-3-butenamides **12a,b,d** were readily obtained in pure form by flash chromatography, and their proposed structures are consistent with their ^1H NMR, ^{13}C NMR, IR, and mass spectra. X-ray crystallographic analysis of single crystals of **9a**[3a] and **12a**[3b] is also consistent with the proposed structure of these two compounds. Careful analysis of the ^1H NMR spectra of crude reaction mixtures revealed the absence of characteristic vinyl splitting patterns, indicating that *N*-(4-methoxyphenyl)-2-aryl-3-butenamides, products of 2-arylation of **3**, were not formed.

Scheme I outlines a possible pathway to account for the formation of **9**, **9′**, and **12** from the reaction of amide **3** and haloarenes **1** using LTMP as base. Accordingly, LTMP first converts **3** to its dianion **6**, which then undergoes 4-arylation by aryne **2a–e** to yield 4-arylated dianions **8a–e**, after a lithium exchange from the 2′-position of the aromatic ring to position 4 of the butenamide chain of the initially formed adduct **7a–e**. This dianion **8a–e** then either supplies the 4-arylated products **9** and **9′**, after proton quench, or reacts with another molecule of aryne to yield **11**, which, upon undergoing a similar lithium exchange followed by proton quench, provides the 4,4-diaryl product **12**.

We found subsequently that LTMP and LDA also transform 2-butenoic acid (**13**) to 2-butenoic dianion (**14**), which also reacts with arynes **2a,c–f** to yield, after proton quench, mixtures consisting mainly of a (*E*)-4-aryl-3-butenoic acid (**15a,c–f**) (52–75%) and small amounts (>5%)

Table I. Yields of Monoaryl Amides 9 and 9′ and Diaryl Amides 12 from Bromoarenes 1 and Amide 3

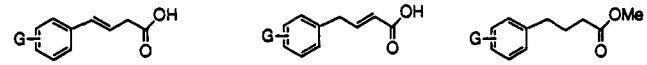


9 **9′** **12**

method[a]	G	yield, %		
A	H	51	6[b]	23
B		69	9	
A	3-MeO	41	>5	16
B		64	8	
A	3,4-$(MeO)_2$	54	5	>5
B		67	6	
A	3,5-$(MeO)_2$	39	tr	10
A	3,6-$(MeO)_2$	61	7	>5

[a] Method A: aryne generated slowly. Method B: aryne generated rapidly. [b] Yields of **9** and **9′** estimated by analyses of ^1H NMR spectra of crude reaction mixtures.

Table II. Yields of 4-Aryl Crotonic Acids 15 and 15′ and Methyl Esters of 4-Arylbutanoic Acids 17



15 **15′** **17**

G	yield, %		
H	47	3[a]	30[b]
3-MeO	31	20	32
3,4-$(MeO)_2$	44	5	28
2,5-$(MeO)_2$	53	tr	34
3,4,5-$(MeO)_3$	63	tr	40
5-(MeO), 2-Me	64	tr	41

[a] Amounts of **15** and **15′** determined by GC analysis of mixtures of methyl esters prepared by treatment of crude reaction mixtures with diazomethane. [b] Yields based on 2-butenoic acid (**13**).

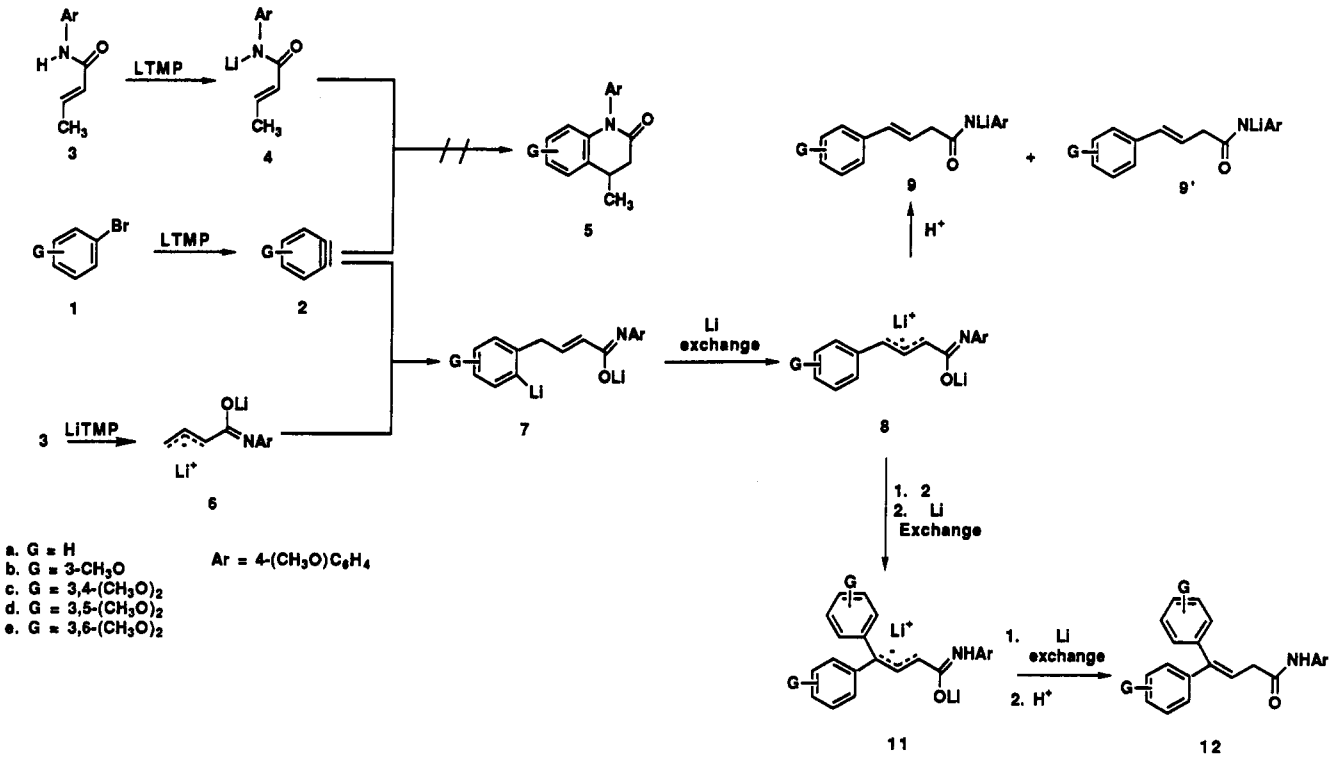
(1) For a review see: Biehl, E. R.; Khanapure, S. P. *Acc. Chem. Res.* **1989**, *22*, 275. See also: Self, J. L.; Khanapure, S. P.; Biehl, E. R. *Heterocycles* **1991**, *32*, 311 and references cited therein.

(2) Gribble, G. W.; Keavy, D. J.; Branz, S. E.; Kelly, W. J.; Pals, M. A. *Tetrahedron Lett.* **1988**, *29*, 6227. Pollart, D. J.; Rickborn, B. *J. Org. Chem.* **1987**, *52*, 792.

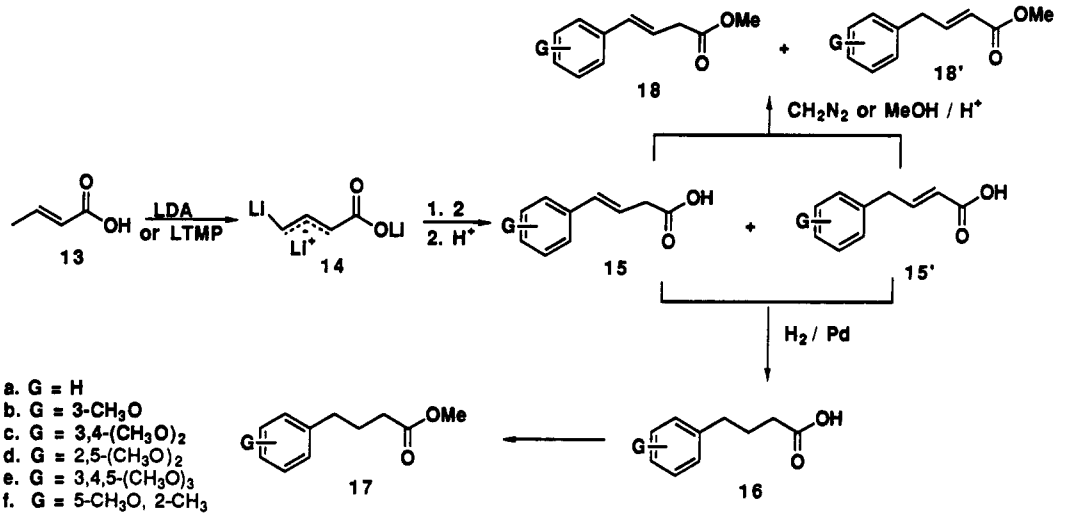
(3) (a) Zhang, H.; Deshmukh, A. R.; Biehl, E. R. *Acta Crystallorg.*, submitted for publication. (b) Zhang, H.; Deshmukh, A. R.; Biehl, E. R. *Acta Crystallogr.*, submitted for publication.

0022-3263/92/1957-0667$03.00/0

Scheme I



Scheme II



of a (*E*)-4-aryl-2-butenoic acid (**15′a,c–f**). The reaction of aryne **2b** with **13** gave both positional isomers (**15b** and **15′b**) in yields of 31 and 20%, respectively (Table II). The acid mixtures were readily purified, characterized, and analyzed as their methyl esters **18**, which were prepared by treatment with either diazomethane or with methyl alcohol/H_2SO_4 (Scheme II).

GC/MS and ^1H NMR spectroscopic analysis of each mixture confirmed the presence of the 4-arylated esters and the absence of 2-arylated esters. The exclusive arylation by arynes to the 4-position of dianion **14** is in contrast to predominant 2-addition that **14** undergoes with certain aldehydes and ketones at comparable low temperatures (−40 °C).[4] The exceptional behavior of aryne addition to **14** may be due to steric effects. However, such effects influencing the course of aryne additions are rare because of the high reactivity of these intermediates, and thus further studies need to be done before a definitive statement can be made concerning the factor(s) attributing to the regiochemistry of 4-aryl additions to butenoic acid dianions. The efficient one-pot arynic synthesis of 4-aryl-3-butenoic acids reported here from readily available starting materials compares well with the previously reported thermal ene reaction of diethyl oxomalonate, which requires heating at 145–180 °C for 1–3 days,[5] the two-step vinyl carboxylation of allylbenzene, which requires refuxing conditions for at least 24 h with CF_2Br_2 followed by treatment of the halogenated alkane so formed at 130 °C for 5 h with KOH,[6] and the hydrolysis (48 h at 50 °C in 95% H_2SO_4) of 3-tris(benzotriazol-1-yl)-1-phenylpropene.[7]

(4) Johnson, P. R.; White, J. D. *J. Org. Chem.* **1984**, *49*, 4424.

(5) Salomon, M. F.; Pardo, S. N.; Salomon, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 2473.

(6) Elsheimer, S.; Slattery, D. K.; Michael, M.; Weeks, J.; Topoleski, K. *J. Org. Chem.* **1989**, *54*, 3992.

The synthetic usefulness of the 4-aryne arylation of 2-butenoic acid dianions was next studied. Thus, the reactions of 2-butenoic dianion **14** with arynes **2** were repeated and the mixtures of 4-arylated butenoic acids **15** and **15′** obtained were first hydrogenated (Pd/C) then esterified (CH_3OH/dil H_2SO_4) to yield synthetically valuable methyl 4-arylbutanoates[8] **16** with well-defined aromatic substitution patterns, and as such should complement the classical Friedel–Crafts reduction methodology.[9] For example, 4-(3-methoxyaryl)butanoic acids, which are not readily accessible by the latter method, can be regioselectively synthesized by the arynic method. The yields of **16** ranged between 35 and 50% (based on 2-butenoic acid). Mixtures of amides **9** and **9′** previously obtained from the 4-arylation of amide dianion **6** could also be converted to the methyl esters **16** by hydrogenation (Pd/C) followed by successive hydrolysis and esterification, which, although less significantly useful (e.g., lower yields and longer reaction times) than the 2-butenoic acid sequence, does provide additional structural proof of the 4-arylated amide products **9**.

Experimental Section

Melting points were determined on an electrothermal apparatus and are uncorrected. ^1H NMR (200 MHz) and ^{13}C NMR (200 MHz) spectra were obtained in $CDCl_3$, and the chemical shifts were related to TMS. E. Merck silica gel 9385 (230–400 mesh) was used for flash chromatography. THF and *i*-Pr_2NH were obtained from Aldrich Chemical Co. and were thoroughly dried and distilled prior to use. Most of the other organic starting materials were also obtained from Aldrich Chemical Co. Bromoarenes **2d** and **2e** were on hand from previous studies.[10] *N*-(4-Methoxyphenyl)-2-butenamide (**3**) was prepared by treating crotonyl chloride with 4-methoxyaniline and potassium carbonate.

General Procedure for the Arylation of *N*-(4-Methoxyphenyl)-2-butenamide (3) with Bromoarenes 1a–e. LTMP (or LDA) (30 mmol) was prepared by adding *n*-BuLi (30 mmol, 2.5 M in hexane) to a stirred solution of 2,2,6,6-tetramethylpiperidine (*i*-Pr_2NH) (30 mmol) in THF (50 mL) at −78 °C (internal temperature) under a N_2 atmosphere. After 10 min, amide **3** (10 mmol) in THF (25 mL) was added over a period of 10 min, and the resulting solution was allowed to warm to −40 °C. The haloarene (10 mmol in 25 mL THF) was then injected as rapidly as possible, and the resulting solution, which immediately developed a dark reddish hue, indicative of aryne reactions, was allowed to warm slowly (ca. 2 h) to rt. The reaction mixture was then quenched with EtOH, and the solvent was removed under reduced pressure. The remaining residue was dissolved in CH_2Cl_2 (100 mL), and the resulting solution was washed (dilute HCl then brine), dried (Na_2SO_4), and concentrated (in vacuo) to yield a crude mixture which upon flash chromatography using hexane/acetone (19:1) as the eluent, yielded the *N*-(4-methoxyphenyl)-4-aryl-3-butenamides **9**, contaminated with a small amount (ca. 5–7%) of the *N*-(4-methoxyphenyl)-4-aryl-2-butenamide **9′**. The usual addition (10 min) of the haloarene to the dianion results in significant amounts of the 4,4-diaryl amide (**12**) which can be easily separated from **9** by flash chromatography. Analytical samples of **9** and **12** were obtained by recrystallization from ethanol.

***N*-(4-Methoxyphenyl)-4-phenyl-3-butenamide (9a)**: mp 135–137 °C (EtOH); ^1H NMR δ 3.29 (d, 2 H, *J* = 7 Hz), 3.76 (s, 3 H), 6.26–6.41 (m, 1 H), 6.61 (d, 1 H, *J* = 16 Hz), 6.82 (d, 2 H, *J* = 9 Hz), 7.22–7.40 (m, 7 H); ^{13}C NMR δ 41.63, 55.46, 114.18, 122.03, 122.24, 126.38, 127.80, 128.6, 130.94, 134.94, 136.61, 156.61, 168.92; IR ($CHCl_3$) 3403, 1678, 1597, 1510, 972 cm^{-1}. Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.37; H, 6.41; N, 5.23. Found: C, 76.34; H, 6.38; N, 5.20.

***N*-(4-Methoxyphenyl)-4-(3-methoxyphenyl)-3-butenamide (9b)**: mp 133–134 °C (EtOH); ^1H NMR δ 3.27 (d, 2 H, *J* = 7 Hz), 3.74 (s, 3 H), 3.78 (s, 3 H), 6.26–6.41 (m, 1 H), 6.53 (d, 1 H, *J* = 16 Hz), 6.77–6.97 (m, 4 H), 7.16–7.26 (m, 2 H), 7.44 (d, 2 H, *J* = 9 Hz), 7.52 (s, 1 H); ^{13}C NMR δ 41.63, 55.26, 55.47, 111.75, 113.62, 114.07, 114.20, 121.95, 122.49, 129.63, 130.87, 134.99, 138.00, 156.64, 154.94, 168.68; IR ($CHCl_3$) 3404, 1679, 1600, 1513, 974 cm^{-1}. Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.49; N, 4.70. Found: C, 72.98; H, 6.49; N, 4.67.

***N*-(4-Methoxyphenyl)-4-(3,4-dimethoxyphenyl)-3-butenamide (9c)**: mp 153–154 °C (EtOH); ^1H NMR δ 3.27 (d, 2 H, *J* = 7 Hz), 3.76 (s, 3 H), 3.82 (s, 3 H), 3.88 (s, 3 H), 6.26–6.41 (m, 1 H), 6.54 (d, 1 H, *J* = 16 Hz), 6.79–6.94 (m, 5 H), 7.38 (d, 2 H, *J* = 9 Hz), 7.52 (s, 1 H); ^{13}C NMR δ 168.92 (C=O); IR ($CHCl_3$) 3400, 1677, 1599, 1513, 971 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.70; H, 6.46; N, 4.25. Found: C, 69.61; H, 6.47; N, 4.21.

***N*-(4-Methoxyphenyl)-4-(3,5-dimethoxyphenyl)-3-butenamide (9d)**: mp 107–109 °C (EtOH); ^1H NMR δ 3.25 (d, 2 H, *J* = 7 Hz), 3.73 (s, 6 H), 3.75 (s, 3 H), 6.34–6.51 (m, 5 H), 6.79 (d, 1 H, *J* = 16 Hz), 7.38 (d, 2 H, *J* = 9 Hz), 7.61 (s, 1 H); ^{13}C NMR δ 41.48, 55.34, 100.47, 104.56, 114.17, 122.00, 122.84, 130.95, 134.75, 138.65, 156.60, 161.03, 168.87; IR ($CHCl_3$) 3400, 1679, 1598, 1513, 971 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.70; H, 6.46; N, 4.25. Found: C, 69.75; H, 6.51; N, 4.31.

***N*-(4-Methoxyphenyl)-4-(3,6-dimethoxyphenyl)-3-butenamide (9e)**: mp 126 °C (EtOH); ^1H NMR δ 3.30 (d, 2 H, *J* = 7 Hz), 3.77 (s, 6 H), 3.80 (s, 3 H), 6.36–6.51 (m, 1 H), 6.79–6.93 (m, 8 H), 7.38 (d, 2 H, *J* = 9 Hz), 7.61 (s, 1 H); IR ($CHCl_3$) 3273, 1654, 1616, 1498, 967 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.70; H, 6.46; N, 4.25. Found: C, 69.75; H, 6.51; N, 4.31.

***N*-(4-Methoxyphenyl)-4,4-diphenyl-3-butenamide (12a)**: mp 133–134 °C (EtOH); ^1H NMR δ 3.17 (d, 2 H, *J* = 7 Hz), 3.75 (s, 3 H), 6.34 (t, 1 H, *J* = 7 Hz), 6.80 (d, 1 H, *J* = 9 Hz), 7.17–7.44 (m, 13 H); ^{13}C NMR δ 33.54, 55.48, 114.21, 102.77, 121.79, 127.40, 127.65, 128.24, 128.50, 129.68, 130.97, 139.17, 141.67, 145.98, 156.57, 168.88; IR ($CHCl_3$) 3400, 1676, 1602, 1514, 928 cm^{-1}. Anal. Calcd for $C_{23}H_{21}NO_2$: C, 80.43; H, 6.16; N, 4.07. Found: C, 80.65; H, 6.20; N, 4.05.

***N*-(4-Methoxyphenyl)-4,4-bis(3-methoxyphenyl)-3-butenamide (12b)**: mp 144–145 °C (EtOH); ^1H NMR δ 3.17 (d, 2 H, *J* = 7 Hz), 3.74 (s, 3 H), 3.76 (s, 6 H), 6.35 (t, 1 H, *J* = 7 Hz), 6.74–6.88 (m, 6 H), 7.05 (s, 1 H), 7.15–7.37 (m, 6 H); IR ($CHCl_3$) 3248, 1681, 974 cm^{-1}. Anal. Calcd for $C_{25}H_{25}NO_4$: C, 74.41; H, 6.24; N, 3.47. Found: C, 74.48; H, 6.22; N, 3.45.

***N*-(4-Methoxyphenyl)-4,4-bis(3,5-dimethoxyphenyl)-3-butenamide (12d)**: thick liquid; ^1H NMR δ 3.15 (d, 2 H, *J* = 7 Hz), 3.70 (s, 12 H), 3.71 (s, 3 H), 6.29–6.47 (m, 7 H), 6.81 (d, 2 H, *J* = 9 Hz), 7.18 (s, 1 H), 7.35 (d, 2 H, *J* = 7 Hz); ^{13}C NMR δ 38.44, 55.35, 99.68, 99.77, 105.80, 107.69, 114.16, 121.18, 121.76, 131.04, 141.03, 132.21, 145.42, 156.49, 160.95, 168.98; IR ($CHCl_3$) 3429, 1676, 1597, 1513, 927 cm^{-1}. Anal. Calcd for $C_{27}H_{29}NO_6$: C, 57.95; H, 5.22; N, 2.50. Found: C, 57.81; H, 5.32; N, 2.61.

General Procedure for the Arylation of 2-Butenoic Acid (13) with Bromoarenes 1a–f and Subsequent Conversion of 4-Aryl-3-butenoic Acids 15 to 18 and Preparation of Methyl 4-Aryl-3-butanoates 17. LDA or LTMP (30 mmol), 2-butenoic acid (**13**) (10 mmol), and bromoarene **1** (10 mmol) were treated identically to that described for the arylation of amide **3** with the exception that the 4-aryl-3-butenoic acids were, without purification, added to CH_3OH (50 mL) containing one drop of concd H_2SO_4 and refluxed for 5 h. The CH_3OH was then removed (in vacuo), and the remaining residue was dissolved in CH_2Cl_2 which was washed (water then brine), dried (Na_2SO_4), and evaporated to yield crude ester **18** which was purified by column chromatography using an acetone–hexane mixture (5:95–1:90, respectively) as eluent.

Methyl 4-phenyl-3-butenoate (18a): thick liquid; ^1H NMR δ 3.23 (d, 2 H, *J* = 7 Hz), 3.70 (s, 3 H), 6.28 (dt, 1 H, *J* = 7, 16 Hz), 6.48 (d, 1 H, *J* = 16 Hz), 7.13–7.37 (m, 5 H); IR ($CHCl_3$) 1736, 1599, 1495, 966 cm^{-1}. Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.83; H, 6.97.

(7) Katritsky, A. R.; Yang, Z.; Lam, J. N. *Synthesis* **1990**, 666.

(8) For example, considerable attention has been focused on the synthesis of 1-tetralone analogues from 4-arylbutanoic acids in connection with the preparation of dihydrodiol and diol epoxide metabolites of carcinogenic polycyclic aromatic hydrocarbons (See: Harvey, R. G. *Acc. Chem. Res.* **1981**, *14*, 218 and references therein).

(9) Overbaugh, S. C.; Allen, C. F. H.; Martin, E. L.; Fieser, L. F. *Org. Synth.* **1935**, *15*, 64.

(10) Khanapure, S. P.; Crenshaw, L.; Reddy, R. T.; Biehl, E. R. *J. Org. Chem.* **1988**, *53*, 491.

Methyl 4-(3-methoxyphenyl)-3-butenoate (18b): thick liquid; ^{1}H NMR δ 3.23 (d, 2 H, J = 7 Hz), 3.69 (s, 3 H), 3.89 (s, 3 H), 6.30 (dt, 1 H, J = 7, 16 Hz), 6.45 (d, 1 H, J = 16 Hz), 6.74–7.20 (m, 4 H); ^{13}C NMR δ 171.89 (C=O). Anal. Calcd for $C_{12}H_{14}O_3$: C, 70.58; H, 5.92. Found: C, 70.72; H, 5.97.

Methyl 4-(3,4-dimethoxyphenyl)-3-butenoate (18c): thick liquid; ^{1}H NMR δ 3.21 (d, 2 H, J = 7 Hz), 3.69 (s, 3 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 6.13 (dt, 1 H, J = 7, 16 Hz), 6.14 (d, 1 H, J = 16 Hz), 6.69–6.90 (m, 3 H); ^{13}C NMR δ 171.93 (C=O); IR ($CHCl_3$) 1737, 1602, 1514, 967 cm^{-1}. Anal. Cancd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.15; H, 6.92.

Methyl 4-(2,5-dimethoxyphenyl)-3-butenoate (18d): thick liquid; ^{1}H NMR δ 3.23 (d, 2 H, J = 7 Hz), 3.68 (s, 3 H), 3.75 (s, 3 H), 3.78 (s, 3 H), 6.27 (dt, 1 H, J = 7, 16 Hz), 6.65–7.11 (m, 4 H); ^{13}C NMR δ 38.43, 51.65, 55.62, 56.08, 112.43, 113.68, 122.43, 128.10, 147.20, 151.01, 153.70, 171.89; IR ($CHCl_3$) 1736, 1609, 973 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.03; H, 6.99.

Methyl 4-(3,4,5-trimethoxyphenyl)-3-butenoate (18e): thick liquid; ^{1}H NMR δ 3.22 (d, 2 H, J = 7 Hz), 3.70 (s, 3 H), 3.81 (s, 3 H), 3.84 (s, 6 H), 6.18 (dt, 1 H, J = 7, 16 Hz), 6.40 (d, 1 H, J = 7 Hz), 6.57 (s, 1 H); IR ($CHCl_3$) 1736, 1582, 967 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.18; H, 6.89.

Methyl 4-(5-methoxy-2-methylphenyl)-3-butenoate (18f): thick liquid; ^{1}H NMR δ 2.24 (s, 3 H), 3.25 (d, 2 H, J = 7 Hz), 3.65 (s, 3 H), 3.75 (s, 3 H), 6.23 (dt, 1 H, J = 7, 16 Hz), 6.71–7.02 (m, 4 H); ^{13}C NMR δ 20.36, 38.55, 51.64, 55.50, 110.87, 121.90, 125.54, 127.31, 128.31, 128.92, 129.05, 154.56, 172.01; IR ($CHCl_3$) 1736, 1608, 972 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.76; H, 7.21.

Preparation of Methyl 4-Arylbutanoates 17. a. From 4-Aryl Amides 9. A mixture containing 4-aryl butenamide **9** (10 mmol), Pd/C (10%, 300 mg), and ethanol (30 mL) was hydrogenated under 40 psi hydrogen pressure at rt for 3 h with shaking. After the catalyst was removed by filtration, the ethanol was removed (rotatory evaporator), the remaining material, without purification, was dissolved in ethanol (25 mL) and 6 N HCl (25 mL), and the resulting solution was refluxed for 8 h. At that time, the solution was concentrated to half of its volume under reduced pressure and the remaining solution extracted with CH_2Cl_2 (2 × 20 mL). The combined extracts were washed (water then brine) and concentrated (in vacuo), and the remaining acid-containing brown oil was esterified by refluxing with methanol (50 mL) containing a few drops of concd H_2SO_4 for 5 h. The resulting mixture was worked up in the usual way, and the oily residue was purified by flash chromatography using acetone–hexane (5–10%) mixture as eluent to give **17**.

b. From 4-Aryl Acids 15. A sample containing a mixture of 4-arylbutenoic acid **15** and **15′** (10 mmol) was hydrogenated and esterified in similar manner as that described previously for the 4-arylbutenamides to give the ester **17**.

Methyl 4-phenylbutanoate (17a): thick liquid; ^{1}H NMR δ 1.96 (m, 2 H), 2.33 (t, 2 H, J = 7 Hz), 2.65 (t, 2 H, J = 7 Hz, 3.66 (s, 3 H), 7.16–7.31 (m, 5 H). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.12; H, 7.91. Found: C, 74.23; H, 7.97.

Methyl 4-(3-methoxyphenyl)butanoate (17b): thick liquid; ^{1}H NMR δ 1.93 (m, 2 H), 2.31 (t, 2 H, J = 7 Hz), 2.61 (t, 2 H, J = 7 Hz), 3.64 (s, 3 H), 3.76 (s, 3 H), 7.16–7.31 (m, 5 H); ^{13}C NMR δ 26.16, 33.11, 34.95, 51.12, 54.83, 111.14, 114.08, 120.66, 129.11, 142.76, 159.59, 173.54; IR ($CHCl_3$) 1737, 1601, 1488, 1225 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.20; H, 7.74. Found: C, 69.09; H, 7.84.

Methyl 4-(3,4-dimethoxyphenyl)butanoate (17c): thick liquid; ^{1}H NMR δ 1.86 (m, 2 H), 2.28 (t, 2 H, J = 7 Hz), 2.55 (t, 2 H, J = 7 Hz), 3.61, (s, 3 H), 3.80 (s, 3 H), 3.82 (s, 3 H), 6.64–6.76 (m, 3 H); ^{13}C NMR δ 173.47; IR ($CHCl_3$) 1735, 1607 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.52; H, 7.61. Found: C, 65.39; H, 7.81.

Methyl 4-(2,5-dimethoxyphenyl)butanoate (17d): thick liquid; ^{1}H NMR δ 1.89 (m, 2 H), 2.31 (t, 2 H, J = 7 Hz), 2.61 (t, 2 H, J = 7 Hz), 3.63 (s, 3 H), 3.73 (s, 3 H), 3.74 (s, 3 H), 6.69–6.72 (m, 3 H). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.52; H, 7.61. Found: C, 65.65; H, 7.52.

Methyl 4-(3,4,5-trimethoxyphenyl)butanoate (17e): thick liquid; ^{1}H NMR δ 1.91 (m, 2 H), 2.31 (t, 2 H, J = 7 Hz), 2.56 (t, 2 H, J = 7 Hz), 3.65 (s, 3 H), 3.80 (s, 6 H), 6.36 (s, 2 H); ^{13}C NMR δ 26.30, 33.17, 35.31, 51.22, 55.93, 105.47, 136.94, 153.04, 173.65; IR ($CHCl_3$) 1735, 1595, 1498, 1347, 1222 cm^{-1}. Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.66; H, 7.51. Found: C, 66.73; H, 7.52.

Methyl 4-(5-methoxy-2-methylphenyl)butanoate (17f): thick liquid; ^{1}H NMR δ 1.90 (m, 2 H), 2.25 (s, 3 H), 2.32 (t, 2H, J = 7 Hz), 2.60 (t, 2 H, J = 7 Hz), 3.04 (s, 3 H), 3.76 (s, 6 H), 6.71–6.92 (m, 3 H); IR ($CHCl_3$) 1738, 1610 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.47; H, 8.23.

Acknowledgment. This work was supported in part by grants from the Welch Foundation of Houston, TX, and the Donors of the Petroleum Research Foundation, administered by the American Chemical Society.

Registry No. **1a**, 108-86-1; **1b**, 2398-37-0; **1c**, 2859-78-1; **1d**, 20469-65-2; **1e**, 25245-34-5; **1f**, 36942-56-0; **3**, 127683-81-2; **9a**, 137744-63-9; **9b**, 137744-65-1; **9c**, 137744-66-2; **9d**, 137744-67-3; **9e**, 137744-68-4; **9′a**, 137744-64-0; **9′b**, 137744-69-5; **9′c**, 137744-70-8; **9′e**, 137744-71-9; **12a**, 53774-24-6; **12b**, 137744-72-0; **12c**, 137744-73-1; **12d**, 137744-74-2; **12e**, 137744-75-3; **13**, 3724-65-0; **15a**, 2243-53-0; **15b**, 137744-81-1; **15c**, 137744-82-2; **15d**, 83655-42-9; **15e**, 137744-83-3; **15f**, 137744-84-4; **15′a**, 2243-52-9; **15′b**, 137744-85-5; **15′c**, 137744-86-6; **17a**, 2046-17-5; **17b**, 57816-04-3; **17c**, 51686-49-8; **17d**, 42604-40-0; **17e**, 79117-98-9; **17f**, 137744-76-4; **18a**, 24891-74-5; **18b**, 130028-20-5; **18c**, 137744-77-5; **18d**, 137744-78-6; **18e**, 137744-79-7; **18f**, 137744-80-0; 1-bromo-3,4,5-trimethoxybenzene, 2675-79-8.